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Editorial

How to Deal with Insulin Resistance

Prof. Dr. Azhar Masud Bhatti
Editor-in-Chief

Introduction: Insulin resistance is a physiological condition in which cells in the body become less responsive to the effects of insulin, a hormone produced by the pancreas. Insulin plays a crucial role in regulating blood sugar (glucose) levels by facilitating the uptake of glucose from the bloodstream into cells, where it can be used for energy or stored for future use. In a healthy individual, when blood sugar levels rise after eating, the pancreas releases insulin to signal cells to absorb glucose from the bloodstream. This helps lower blood sugar levels back to a normal range.

All tissues with insulin receptors can become insulin resistant, but the tissues that primarily drive insulin resistance are the liver, skeletal muscle, and adipose tissue. Insulin resistance impairs glucose disposal, resulting in a compensatory increase in beta-cell insulin production and hyperinsulinemia. Recent studies have debated whether hyperinsulinemia precedes insulin resistance, as hyperinsulinemia itself is a driver of insulin resistance. This concept may be clinically valuable, suggesting that hyperinsulinemia associated with excess caloric intake may drive the metabolic dysfunction associated with insulin resistance. The metabolic consequences of insulin resistance include hyperglycemia, hypertension, dyslipidemia, hyperuricemia, elevated inflammatory markers, endothelial dysfunction, and a prothrombotic state. Progression of insulin resistance can lead to metabolic syndrome, nonalcoholic fatty liver disease, and type 2 diabetes.[1-5]

Insulin resistance is primarily an acquired condition related to excess body fat, though genetic causes are also identified. The clinical definition of insulin resistance remains elusive, as there is no generally accepted test for insulin resistance. Clinically, insulin resistance is recognized via the metabolic consequences associated with insulin resistance as described in metabolic syndrome and insulin resistance syndrome.[6-7]

Etiology: Insulin resistance may be acquired, hereditary, or mixed. Majority of people with insulin resistance fall have an acquired etiology.[8]

Acquired Etiology[9]: Fat deposition and overflow from subcutaneous fat stores, Aging process, Physical inactivity, Nutritional imbalance, Medications, High-sodium diets, Glucose toxicity and Lipotoxicity from excess circulating free fatty acids.

Genetic Etiology: Myotonic dystrophy, Ataxia-telangiectasia, Alstom syndrome, Rabson-Mendenhall syndrome, Werner syndrome, Lipodystrophy and Polycystic ovarian syndrome.

Epidemiology: Epidemiologic assessment of insulin resistance is typically measured in relation to the prevalence of metabolic syndrome or insulin resistance syndrome.

There has been a rapid rise in pediatric obesity and type 2 diabetes, no consensus has been reached on the pediatric population's diagnostic criteria for insulin resistance. From a demographic standpoint, insulin resistance affects all races and ethnicities.

Pathophysiology: Three primary sites of insulin resistance are the skeletal muscle, liver, and adipose tissue.

Skeletal Muscle Tissue: After intake of a caloric load and conversion to glucose, muscle is the primary site for glucose disposal, accounting for up to 70% of tissue glucose uptake.

Hepatic Tissue: The liver is responsible for processing energy substrates. It packages, recirculates, and creates fatty acids and processes, stores, and creates glucose. If the liver becomes insulin-resistant, these processes are severely affected, resulting in significant metabolic consequences.

Adipose Tissue: The researchers determined that lipolysis is sensitive to insulin. The failure of insulin to suppress lipolysis in insulin-resistant adipose tissue, especially visceral adipose tissue, increases circulating free fatty acids FFAs. Higher levels of circulating FFAs directly affect both liver and muscle metabolism,[10]

Associated Diseases: Non-alcoholic fatty liver disease (NAFLD), Metabolic syndrome, Prediabetes or type 2 diabetes, Polycystic ovarian syndrome (PCOS), Obesity, Microvascular disease (retinopathy, neuropathy, or nephropathy) and Macrovascular disease (stroke, PAD, and CAD).

Associated Symptoms: Hypertension, Hyperlipidemia, Gender and ethnicity-specific increased waist circumference, The stigmata of PCOS (menstrual irregularities, hirsutism, acne, and alopecia), Acanthosis nigricans (see Image. Acanthosis Nigricans), The stigmata of one of several genetic syndromes that include insulin resistance syndromes and Type A or type B insulin resistance syndrome.

Treatment / Management

Lifestyle Intervention: Lifestyle intervention represents the cornerstone of treatment for insulin resistance. Dietary intervention should include a combination of calorie restriction and high glycemic index carbohydrate reduction. Physical activity improves both calorie expenditure and insulin sensitivity in muscle tissue.[11]

These interventions include, Dietary therapy with sodium reduction, fat reduction, calorie restriction, and attention to the glycemic index of foods, Education, support, and personalized programs, A 7% weight loss

reduced the onset of T2D by 58% and DPP included a metformin arm which reduced the onset of T2D by 31%

In dietary therapy, the following foods may help to Improve Insulin Resistance:

Leafy Greens: Vegetables like spinach, kale, Swiss chard, and collard greens are rich in fiber, vitamins, and minerals. They have a low glycemic index and can help stabilize blood sugar levels.

Berries: Berries such as blueberries, strawberries, and raspberries are loaded with antioxidants, fiber, and vitamins. They have a relatively low sugar content compared to other fruits and can help prevent rapid spikes in blood sugar.

Whole Grains: Choose whole grains like quinoa, brown rice, whole wheat, and oats over refined grains. Whole grains contain more fiber, which slows down the digestion and absorption of carbohydrates, leading to better blood sugar control.

Lean Proteins: Incorporate lean sources of protein like chicken, turkey, fish, tofu, and legumes into your diet. Protein can help regulate blood sugar levels and promote satiety, reducing the likelihood of overeating.

Healthy Fats: Include sources of healthy fats like avocados, nuts, seeds, and olive oil. These fats can improve insulin sensitivity and help maintain stable blood sugar levels.

Pharmacological Interventions: Metformin is a common first-line therapy for medication treatment of T2D and is approved for use in PCOS. The DPP & DPPOS study showed that the combination of metformin and lifestyle interventions was medically useful and cost-effective.

Surgery: Surgical intervention in the form of gastric sleeves, banding, and bypass is available for qualified individuals with obesity.

Prognosis: The prognosis of insulin resistance depends on the subset of the disease, the severity of the disease, underlying pancreatic beta-cell function.

Complications: The microvascular disease manifests as retinopathy, nephropathy, and peripheral neuropathy. In the central nervous system, dementia, stroke, mood disturbance, and gait instability may occur. Cardiac microvascular disease can manifest as angina, coronary artery spasm, and cardiomyopathy. Renal microvascular disease is a significant cause of chronic kidney disease, renal failure, and dialysis. Ophthalmological small vessel disease is a leading cause of retinopathy and visual impairment. Macrovascular disease, secondary to insulin resistance, causes PAD, CAD, and CVA.

REFERENCES

1. Seong J, Kang JY, Sun JS, Kim KW. Hypothalamic inflammation and obesity: a mechanistic review. Arch Pharm Res 2019;42(5): 383-392.
2. Brown JC, Harhay MO, Harhay MN. The Value of Anthropometric Measures in Nutrition and Metabolism: Comment on Anthropometrically Predicted Visceral Adipose Tissue and Blood-Based Biomarkers: A Cross-Sectional Analysis. Nutr Metab Insights 2019;12: 1178638819831712.
3. Nolan CJ, Prentki M. Insulin resistance and insulin hypersecretion in the metabolic syndrome and type 2 diabetes: Time for a conceptual framework shift. Diab Vasc Dis Res 2019;16(2):118-127.
4. Deacon CF. Physiology and Pharmacology of DPP-4 in Glucose Homeostasis and the Treatment of Type 2 Diabetes. Front Endocrinol (Lausanne) 2019;10:80.
5. Thomas DD, Corkey BE, Istfan NW, Apovian CM. Hyperinsulinemia: An Early Indicator of Metabolic Dysfunction. J Endocr Soc 2019 Sep 01;3(9):1727-1747.
6. Hossan T, Kundu S, Alam SS, Nagarajan S. Epigenetic Modifications Associated with the Pathogenesis of Type 2 Diabetes Mellitus. Endocr Metab Immune Disord Drug Targets 2019; 19(6):775-786.
7. Bothou C, Beuschlein F, Spyroglou A. Links between aldosterone excess and metabolic complications: A comprehensive review. Diabetes Metab 2020 Feb;46(1):1-7.
8. Samuel VT, Shulman GI. The pathogenesis of insulin resistance: integrating signaling pathways and substrate flux. J Clin Invest 2016;126(1): 12-22.
9. Ogawa W, Araki E, Ishigaki Y, Hirota Y, Maegawa H, Yamauchi T, et al. New classification and diagnostic criteria for insulin resistance syndrome. Endocr J 2022;69(2):107-113.
10. Petersen MC, Shulman GI. Mechanisms of Insulin Action and Insulin Resistance. Physiol Rev 2018; 98(4):2133-2223.
11. Yaribeygi H, Atkin SL, Simental-Mendía LE, Sahebkar A. Molecular mechanisms by which aerobic exercise induces insulin sensitivity. J Cell Physiol 2019;234(8):12385-12392.

Original Article

Safety of Propofol in Patients Undergoing Endoscopy and Colonoscopy

Arslan Shahzad[1], Faria Mumtaz[1], Javaria Isram[1] and Muhammad Tahir[2]

ABSTRACT

Objective: To evaluate the safety profile of propofol sedation in patients undergoing endoscopy and colonoscopy.

Study Design: A retrospective observational study

Place and Duration of Study: This study was conducted at the department of Medicine and Gastroenterology, PAF Hospital, Islamabad, from January 2019 and September 2024.

Methods: Inclusion criteria encompassed all adult patients (≥18 years) who received propofol for sedation during endoscopy or colonoscopy. Patients with incomplete medical records, those who received sedation other than propofol, or those with contraindications to sedation were excluded. Data collection included demographic information, comorbidities, procedure details, sedation-related parameters, safety parameters evalauation, and procedural outcomes.

Results: In a total of 6220 patients, 4806 (77.3%) underwent upper endoscopy whereas 1414 (22.7%) had colonoscopy performed. There were 3492 (56.1%) male patients. The mean age was 53.28±15.70 years. The mean propofol induction dose was 0.6±0.1 mg/kg in patients undergoing upper endoscopy, and 0.7±0.2 mg/kg in those undergoing colonoscopy ($p<0.001$). The mean procedure duration in patients undergoing upper endoscopy, and colonoscopy were 18.25±4.77 minutes, and 21.59±5.24 minutes ($p<0.001$), respectively. Procedural complications were reported in 108 (1.7%) patients, and the most common complications were respiratory depression, and hypotension, noted in 37 (0.6%), and 30 (0.5%), patients, respectively. Procedural success was reported in 6189 (99.5%) patients. The mean recovery time was significantly higher in patients undergoing colonoscopy (32.1±6.1 minutes vs. 30.5±5.2 minutes, $p<0.001$).

Conclusion: This study reaffirms the safety and efficacy of propofol sedation in gastrointestinal endoscopy. With high procedural success rates, minimal adverse events, and rapid recovery times, propofol remains the sedative of choice for endoscopic procedures.

Key Words: Colonoscopy, endoscopy, hypotension, propofol, respiratory depression, sedation.

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INTRODUCTION

Endoscopy and colonoscopy are essential diagnostic and therapeutic procedures commonly performed in gastroenterology and medicine clinics globally. The estimates show that around 18 million endoscopic proedures are performed annually in the US.[1] The increasing utilization of endoscopy and colonoscopy for gastrointestinal evaluations necessitates effective sedation protocols to ensure patient's comfort, reduce anxiety, and improve procedural outcomes.[2]

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While endoscopy, and colonoscopy procedures are generally safe when performed by trained professionals, but these are not without risks.[3] Safety concerns arise due to the invasiveness of the procedures, the use of sedatives or anesthetics, and patient-specific factors such as comorbidities.[4] Identifying and addressing these safety issues is critical to ensuring patient safety, optimizing procedural outcomes, and reducing complications.[5]

Propofol, a short-acting sedative-hypnotic agent, has become a preferred choice due to its rapid onset, predictable recovery profile, and patient tolerability.[6,7] Propofol is a popular form sedation for endoscopic procedures worldwide due to its rapid action and favorable recovery profile.[8] Propofol, administered by trained professionals, provides deep sedation with minimal residual effects. While its efficacy is well-documented, concerns remain about potential adverse events such as respiratory depression, hypotension, and rare cardiac complications.[9]

Understanding the safety and outcomes of propofol sedation, especially in large-scale settings, is essential to inform clinical guidelines and improve patient outcomes.

This study aims to provide real-world evidence of propofol's safety profile, focusing on complications, and patient outcomes. By analyzing data from a large sample size, this study seeks to identify factors that may predispose patients to adverse events, thereby guiding future clinical practice. The objective of this study was to evaluate the safety profile of propofol sedation in patients undergoing endoscopy and colonoscopy, with a focus on identifying the incidence of adverse events, procedural success rates, and patient outcomes.

METHODS

This retrospective observational study was conducted at the department of Medicine and Gastroenterology, PAF Hospital, Islamabad, Pakistan. The study included all patients who underwent endoscopic procedures between January 2019 and September 2024. A total of 6220 patients undergoing endoscopic evaluation were included in the analysis. The data were retrieved from the hospital's electronic medical records, ensuring strict confidentiality and adherence to ethical guidelines. Inclusion criteria encompassed all adult patients (≥18 years) who received propofol for sedation during endoscopy or colonoscopy. Patients with incomplete medical records, those who received sedation other than propofol, or those with contraindications to sedation were excluded. Ethical approval was obtained from the institutional review board (letter number: 241211-B). Given the retrospective design, the need for informed consent was waived, as no interventions or direct patient contact were involved.

Data collection included demographic information (age, gender, and body mass index), comorbidities (e.g., cardiovascular or pulmonary diseases), procedure details (type of procedure, duration, and therapeutic interventions), and sedation-related parameters (total dose of propofol, complications, and recovery time). The sedation protocol was standardized for all procedures. Propofol was administered by an anesthesiologist. Propofol dosage was tailored to patient needs and procedural requirements. The induction dose ranged from 0.5–1.0 mg/kg, administered over 1–2 minutes, with lower doses (0.25–0.5 mg/kg) used for elderly or debilitated patients to minimize complications. For maintenance of sedation, intermittent boluses (10–20 mg) or a continuous infusion (25–75 mcg/kg/min) was used, adjusted based on the desired sedation level and patient response. Propofol was delivered via IV with slow administration to avoid oversedation or cardiorespiratory depression. Supplemental oxygen was provided to all patients, and vital signs, including oxygen saturation, blood pressure, heart rate, and respiratory rate, were continuously monitored. Emergency airway management equipment was available throughout the procedures. Pre-procedural fasting was ensured in all patients in accordance with established guidelines to minimize the risk of aspiration. Safety parameters included the incidence of adverse events. Respiratory depression was labeled as oxygen saturation <90% for >30 seconds, apnea ≥20 seconds, or requiring assisted ventilation. Hypotension was defined as systolic BP <90 mmHg or >20% drop from baseline, requiring intervention. Bradycardia was deemed as heart rate <50 bpm or >20% drop from baseline, persisting ≥30 seconds, requiring treatment. Arrhythmia was named if there was any abnormal rhythm (e.g., AF, VT) requiring clinical intervention. Bleeding was labeled as blood loss during/after the procedure needing hemostatic intervention or transfusion. Perforation was defined as the full-thickness GI tract tear confirmed by imaging or clinical signs, requiring repair. Aspiration was termed as inhalation of contents causing respiratory distress, oxygen desaturation, or confirmed on imaging. Adverse events were categorized as minor (e.g., transient hypoxemia or mild hypotension) or major (e.g., severe hypoxemia requiring intervention, prolonged hypotension, or cardiac arrest). The severity and management of complications were documented. Outcome measures included the incidence of adverse events, successful procedure completion rates, and recovery time. Secondary outcomes included the identification of patient- and procedure-related factors associated with adverse events. Statistical analysis was performed using IBM-SPSS Statistics, version 26.0. Continuous variables were expressed as means and standard deviations, while categorical variables were presented as frequencies and percentages. Comparisons between groups were made using the chi-square test for categorical data and t-tests for continuous data. A p-value of <0.05 was considered statistically significant.

RESULTS

In a total of 6220 patients, 4806 (77.3%) underwent upper endoscopy whereas 1414 (22.7%) had colonoscopy performed. There were 3492 (56.1%) male, and 2728 (43.9%) female patients. The mean age was 53.28±15.70 years. It was found that there were significantly more male patients who underwent colonoscopy (60.0% vs. 55.0%, p<0.001). Age of patients undergoing colonoscopy was significantly higher (54.92±16.81 years vs. 52.14±15.37 years, p<0.001). The mean BMI was 24.8±4.5 kg/m2 in patients undergoing upper endoscopy, while it was 26.2±5.0 in patients who had colonoscopy performed (p<0.001). Comorbodities were reported in 1574 (25.3%) patients and distinct patterns were identified in patients undergoing upper endoscopy, and colonoscopy. Table-1 is showing comaprison of characteristics of patients undergoing upper endoscopy, and colonoscopy.

Table No. 1: Characteristics of patients (N=6220)

Characteristics		Total (N=6220)	Upper Endoscopy (n=4806)	Colonoscopy (n=1414)	P-value
Gender	Male	3492 (56.1%)	2644 (55.0%)	848 (60.0%)	<0.001
	Female	2728 (43.9%)	2162 (45.0%)	566 (40.0%)	
Age (years)		53.28±15.70	52.14±15.37	54.92±16.81	<0.001
Body mass index (kg/m^2)	Underweight (<18.5)	593 (9.5%)	480 (10.0%)	113 (8.0%)	<0.001
	Normal (18.5-24.9)	2941 (47.3%)	2403 (50.0%)	538 (38.0%)	
	Overweight (25-29.9)	1949 (31.3%)	1442 (30.0%)	507 (35.9%)	
	Obese (≥30)	737 (11.9%)	481 (10.0%)	256 (18.1%)	
Comorbidities	Cardiovascular diseases	634 (10.2%)	424 (8.8%)	210 (14.9%)	<0.001
	Diabetes mellitus	476 (7.7%)	302 (6.3%)	174 (12.3%)	<0.001
	Pulmonary diseases	297 (4.8%)	184 (3.8%)	113 (8.0%)	<0.001
	Others	167 (2.7%)	104 (2.2%)	63 (4.5%)	<0.001

The mean propofol induction dose was 0.6±0.1 mg/kg in patients undergoing upper endoscopy, and 0.7±0.2 mg/kg in those undergoing colonoscopy (p<0.001). The mean maintenance dose was 35.1±5.5 mcb/kg/min in upper endoscopy patients while it was 38.4±6.8 mcg/kg/min in patients undergoing colonoscopy (p<0.001). The mean procedure duration in patients undergoing upper endoscopy, and colonoscopy were 18.25±4.77 minutes, and 21.59±5.24 minutes (p<0.001), respectively. Procedural complications were reported in 108 (1.7%) patients, and the most common complications were respiratory depression, hypotension, bradycardia, arrhthmias, and bleeding, noted in 37 (0.6%), 30 (0.5%), 18 (0.3%), 15 (0.2%), and 8 (0.1%) patients, respectively. None of the patients reported perforation, or aspiration. Table-2 is showing details of safety parameters in patients undergoing endoscopic evaluation.

Table No. 2: Safety parameters evaluation

Safety parameters	Total (N=6220)	Upper Endoscopy (n=4806)	Colonoscopy (n=1414)	P-value
Respiratory depression	37 (0.6%)	26 (0.5%)	11 (0.8%)	0.308
Hypotension	30 (0.5%)	22 (0.5%)	8 (0.6%)	0.606
Bradycardia	18 (0.3%)	12 (0.2%)	6 (0.4%)	0.283
Arrhythmias	15 (0.2%)	11 (0.2%)	4 (0.3%)	0.716
Bleeding	8 (0.1%)	6 (0.1%)	2 (0.1%)	0.878

Procedural success was reported in 6189 (99.5%) patients. Procedural failure was reported in 20 (0.4%) upper endoscopies and 11 (0.8%) colonoscopies. In upper endoscopy, the most common reasons were patient intolerance or inability to cooperate (n=10), followed by obstructive lesions or anatomical challenges (n=5), equipment malfunction (n=3), and complications such as bleeding (n=2). For colonoscopy, the primary reason was inadequate bowel preparation (n=6), with additional failures due to patient discomfort or refusal to continue (n=3) and anatomical variations or obstructive pathology (n=2). The mean recovery time was significantly higher in patients undergoing colonoscopy (32.1±6.1 minutes vs. 30.5±5.2 minutes, p<0.001), as shown in table-3.

Table No. 3: Comparison of Outcomes

Outcomes		Total (N=6220)	Upper Endoscopy (n=4806)	Colonoscopy (n=1414)	P-value
Procedural success	Yes	6189 (99.5%)	4786 (99.6%)	1403 (99.2%)	0.089
	No	31 (0.5%)	20 (0.4%)	11 (0.8%)	
Recovery time (minutes)		31.4±5.5	30.5±5.2	32.1±6.1	<0.001

DISCUSSION

This study demonstrated that propofol sedation is safe and effective, with high procedural success rates and minimal complications. Our study reported a procedural success rate of 99.5%, with 99.6% success in upper endoscopy and 99.2% in colonoscopy. These rates align closely with those reported by Horiuchi et al., who

observed a 100% procedural success rate in their analysis of 2,101 outpatient colonoscopies under propofol sedation.[10] Sato et al., reported success rates exceeding 99% in their cohort of 32,550 colonoscopies and 117,661 esophagogastroduodenoscopies.[11] A recently study by Lu et al reported the sedation success rates of propofol as 98.3% in elderly oupateints udnergoing GI endoscopy exhibiting its effectiveness.[12] The consistency across studies underscores propofol's efficacy in facilitating successful endoscopic procedures.

The low incidence of adverse events in our study corroborates findings from previous research. Respiratory depression, hypotension, bradycardia, arrhythmias, and bleeding were observed in 0.6%, 0.5%, 0.3%, 0.2%, and 0.1% of patients, respectively. In comparison, Heuss et al. reported transient oxygen desaturation (<90%) in 1.7% of low-risk patients (ASA I and II) and 3.6% of high-risk patients (ASA III and IV).[13] Sato et al. observed a 1.3% incidence of transient oxygen desaturation in their large-scale study.[11] These minor discrepancies may be attributed to differences in patient populations, sedation protocols, and monitoring techniques. The present study involved anesthesiologist-administered sedation, whereas many previous studies utilized nurse-administered protocols.[14,15]

The mean recovery time in our study was 31.4±5.5 minutes, with shorter times for upper endoscopy (30.5±5.2 minutes) compared to colonoscopy (32.1±6.1 minutes; p<0.001). Sipe et al. reported similar recovery times, with most patients standing unassisted within 10 minutes and being discharged within 37 minutes.[16] The rapid recovery associated with propofol reflects its favorable pharmacokinetic profile, characterized by a short half-life and rapid clearance.

The clinical implications of our findings are significant. Propofol sedation facilitates high procedural success rates, shortens recovery times, and maintains an excellent safety profile, even in resource-limited settings.[17,18] These advantages make propofol an ideal sedative for gastrointestinal endoscopy. The findings of this study support the continued use of propofol by trained anesthesiologists, particularly in settings where patient safety is paramount.[19] Notably, our study highlights the importance of individualized dosing with propofol.[20] The mean propofol induction dose was 0.6±0.1 mg/kg for upper endoscopy and 0.7±0.2 mg/kg for colonoscopy (p<0.001), reflecting procedural differences in sedation requirements. Maintenance doses were similarly tailored, with colonoscopy patients requiring higher doses (38.4±6.8 mcg/kg/min) compared to upper endoscopy patients (35.1±5.5 mcg/kg/min; p<0.001). These findings underscore the need for dose adjustments based on procedural complexity, patient factors, and desired sedation depth.[21] This study also highlights the role of robust monitoring and preparation in minimizing adverse events. Pre-procedural fasting, continuous monitoring of vital signs, and the availability of emergency airway management equipment contributed to the low incidence of complications.[22] These measures should remain standard practice in endoscopic sedation protocols.

This study has several limitations. The retrospective design limits our ability to establish causality or control for unmeasured confounders. The single-center setting may limit the generalizability of our findings to other populations or healthcare systems. While we documented adverse events during the procedures, post-discharge complications were not assessed, potentially underestimating the true incidence of adverse events. Finally, our reliance on electronic medical records may have introduced reporting bias, as minor events might not have been consistently documented.

CONCLUSION

This study reaffirms the safety and efficacy of propofol sedation in gastrointestinal endoscopy. With high procedural success rates, minimal adverse events, and rapid recovery times, propofol remains the sedative of choice for endoscopic procedures. The findings emphasize the importance of individualized dosing, robust monitoring, and adherence to sedation protocols to optimize patient outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Arslan Shahzad, Faria Mumtaz
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Peery AF, Crockett SD, Murphy CC, Lund JL, Dellon ES, Williams JL, et al. Burden and Cost of Gastrointestinal, Liver, and Pancreatic Diseases in the United States: Update 2018. Gastroenterol 2019;156(1):254-272.e11. Epub 2018 Oct 10. Erratum in: Gastroenterol 2019;156(6):1936.
2. Viazis N, Vlachogiannakos J, Apostolopoulos P, Mimidis K, Tzouvala M, Tsionis T, et al. Sedation during endoscopic procedures: a Hellenic Society of Gastroenterology Position Statement. Ann Gastroenterol 2023;36(3):231-243.

3. Correa CSM, Bagatini A, Prates CG, Sander GB. Patient safety in an endoscopy unit: an observational retrospective analysis of reported incidents. Braz J Anesthesiol 2021;71(2):137-141.
4. Artunduaga M, Liu CA, Morin CE, Serai SD, Udayasankar U, Greer MC, et al. Safety challenges related to the use of sedation and general anesthesia in pediatric patients undergoing magnetic resonance imaging examinations. Pediatr Radiol 2021;51(5):724-735.
5. Matharoo M, Haycock A, Sevdalis N, Thomas-Gibson S. A prospective study of patient safety incidents in gastrointestinal endoscopy. Endosc Int Open 2017;5(1):E83-E89.
6. Currò JM, Santonocito C, Merola F, Messina S, Sanfilippo M, Brancati S, et al. Ciprofol as compared to propofol for sedation and general anesthesia: a systematic review of randomized controlled trials. J Anesth Analg Crit Care 2024;4(1):24.
7. Paramsothy J, Gutlapalli SD, Ganipineni VDP, Mulango I, Okorie IJ, Arrey ADB, et al. Propofol in ICU Settings: Understanding and Managing Anti-Arrhythmic, Pro-Arrhythmic Effects, and Propofol Infusion Syndrome. Cureus 2023;15(6): e40456.
8. Benson AA, Cohen LB, Waye JD, Akhavan A, Aisenberg J. Endoscopic sedation in developing and developed countries. Gut Liver 2008;2(2): 105-12.
9. Lv LL, Zhang MM. Up-to-date literature review and issues of sedation during digestive endoscopy. Wideochir Inne Tech Maloinwazyjne 2023;18(3): 418-435.
10. Horiuchi A, Nakayama Y, Kajiyama M, Kato N, Kamijima T, Ichise Y, et al. Safety and effectiveness of propofol sedation during and after outpatient colonoscopy. World J Gastroenterol 2012;18(26):3420-5.
11. Sato M, Horiuchi A, Tamaki M, Ichise Y, Kajiyama M, Yamamoto Y, et al. Safety and Effectiveness of Nurse-Administered Propofol Sedation in Outpatients Undergoing Gastrointestinal Endoscopy. Clin Gastroenterol Hepatol 2019;17(6):1098-1104.e1.
12. Lu L, Chen B, Zhao X, Zhai J, Zhang P, Hua Z. Comparison of Remimazolam and Propofol in Recovery of Elderly Outpatients Undergoing Gastrointestinal Endoscopy: A Randomized, Non-Inferiority Trial. Drug Des Devel Ther 2024; 18:4307-4318.
13. Heuss LT, Schnieper P, Drewe J, Pflimlin E, Beglinger C. Safety of propofol for conscious sedation during endoscopic procedures in high-risk patients-a prospective, controlled study. Am J Gastroenterol 2003;98(8):1751-7.
14. Chen SC, Rex DK. Review article: registered nurse-administered propofol sedation for endoscopy. Aliment Pharmacol Ther 2004; 19(2):147-55.
15. Lee HS, Nagra N, La Selva D, Kozarek RA, Ross A, Weigel W, et al. Nurse-Administered Propofol Continuous Infusion Sedation for Gastrointestinal Endoscopy in Patients Who Are Difficult to Sedate. Clin Gastroenterol Hepatol 2021;19(1): 180-188.
16. Sipe BW, Scheidler M, Baluyut A, Wright B. A prospective safety study of a low-dose propofol sedation protocol for colonoscopy. Clin Gastroenterol Hepatol 2007;5(5):563-6.
17. Godoroja-Diarto D, Constantin A, Moldovan C, Rusu E, Sorbello M. Efficacy and Safety of Deep Sedation and Anaesthesia for Complex Endoscopic Procedures-A Narrative Review. Diagnostics (Basel) 2022;12(7):1523.
18. Gao F, Wu Y. Procedural sedation in pediatric dentistry: a narrative review. Front Med (Lausanne) 2023;10:1186823.
19. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Propofol [Updated 2020 Jul 10]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547909/
20. Schonberger RB, Bardia A, Dai F, Michel G, Yanez D, Curtis JP, et al. Variation in propofol induction doses administered to surgical patients over age 65. J Am Geriatr Soc 2021;69(8): 2195-2209.
21. Sidhu R, Turnbull D, Newton M, Thomas-Gibson S, Sanders DS, Hebbar S, et al. Deep sedation and anaesthesia in complex gastrointestinal endoscopy: a joint position statement endorsed by the British Society of Gastroenterology (BSG), Joint Advisory Group (JAG) and Royal College of Anaesthetists (RCoA). Frontline Gastroenterol 2019;10(2):141-147.
22. Raffay V, Fišer Z, Samara E, Magounaki K, Chatzis D, Mavrovounis G, et al. Challenges in procedural sedation and analgesia in the emergency department. J Emerg Crit Care Med 2020;4:27.

Original Article

Decreased CD4 and CD8 Count are Responsible for Severity of COVID-19 Infection

Muhammad Omar Malik, Yasir Ishaq, Yasar Mehmood Yousafzai and Awal Mir

ABSTRACT

Objective: The goal of this research was to measure and compare CD4:CD8 ratio in critically ill vs. non-critically ill COVID-19 patients.

Study Design: Prospective, and one Pool Cross-sectional Observational study.

Place and Duration of Study: This study was conducted at the Pathology department of Rehman Medical Institute (RMI), Peshawar from March 2021 to August 2021.

Methods: Peripheral blood samples were taken from 26 critically sick and 26 non-critically sick COVID-19 individuals of comparable age and sex. Absolute WBC count, absolute lymphocyte count, and platelet count were checked and flow cytometry was performed to calculate the absolute CD4 and CD8 T cells counts.

Results: The critically ill COVID-19 patients were older ($p<0.001$) than non-critically sick COVID-19 individuals. In patients who got critically ill, absolute lymphocyte count ($p=0.004$), absolute CD4 count ($p=0.002$) and absolute CD8 counts ($p=0.014$) were low. However, the CD4:CD8 ratio did not differ substantially across the groups ($p=0.538$). The two groups did not differ in terms of gender.

Conclusion: When compared to COVID-19 patients who weren't in critical condition, the absolute lymphocyte count, CD4 count, and CD8 count of critically sick COVID-19 patients were significantly lower. This revealed that the lack of adequate cellular immune responses in critically sick COVID-19 patients may be the cause of the disease severity.

Key Words: Coronavirus, COVID-19, CD4 lymphocyte, CD8 lymphocyte.

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INTRODUCTION

Coronavirus was isolated for the first time from a group of atypical lung infection patients in city of Wuhan, China in December 2019[1]. Because of its precipitous global spread like wildfire, WHO classified it as a pandemic on March 2020[2].

Seven infectious coronaviruses have been identified so far. Some particularly virulent human CoVs include SARS-CoV, SARS-CoV-2, and MERS-CoV. These lead to epidemics with a variety of clinical severity levels, including symptoms of the respiratory and extra-respiratory systems. Common human coronaviruses include HCoV-OC43, HCoV-HKU1, HCoV-229E, and HCoVNL-63. They have the ability to cause upper respiratory tract infections and colds in immunocompetent individuals[3].

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COVID-19 is confirmed in an individual if the PCR turns out to be positive for viral RNA. Most of the time, nasopharyngeal or throat swabs are used to obtain the sample but in certain conditions, sputum and bronchoalveolar lavage can be used for sample collection[4].

The immune mechanisms of our body protect us from the invasion of microorganisms, tumour cells, and various toxins. The innate and adaptive immunity works hand in hand to recognize and abort the obnoxious material[5].

For the host to react to any virus that enters the body, innate and acquired immunity must work together. Due to the body's immunological response to viral infections, the number of T lymphocytes, particularly CD4 T cells and CD8 T lymphocytes, varies[6]. For instance, acute HIV-1 infection, cytomegalovirus infection, and glandular fever are known to cause the reversal of the CD4:CD8 ratio. This behaviour, on the other hand, does not occur in those who have HIV non-convertase[6]. Numerous investigations have demonstrated that the immune response brought on by these infections reduces the CD4:CD8 ratio. As a result, Immunosenescence occurs and the patient's immunity gradually deteriorates[7].

In the perspective of COVID-19, recent observation and research has shown that there is a decline in lymphocyte count in patients with COVID-19 (6). Due to this, all of the individuals who had this viral infection showed changes in the usual CD4:CD8 ratio (8,9). In previous studies, it was noted that viral infections lead to the initiation of T-cell responses, which results in changes in the immune response in affected individuals[6].

As a result, in this investigation, we measured the T-cell CD4 and CD8 counts by flow cytometry and assessed the CD4:CD8 ratio in COVID-19 infected patients, and also checked if was related to disease severity. This research will advance our knowledge of the immune reactions to COVID-19 infection, with potential implications for treatment and diagnosis.

METHODS

Study population: From March 19th to August 6th, 2021, a prospective and one-pool cross-sectional observational study was undertaken in two major hospitals in Peshawar, Rehman Medical Institute (RMI) and Hayatabad Medical Complex (HMC). In total, 52 patients infected with COVID-19 were recruited; 26 critically ill patients and 26 non-critically sick patients, all of whom had COVID-19 and were of comparable age (range 20 - 75 years) and gender (M=27,F=25). Patients who were severely ill were admitted to isolation wards or the intensive care unit (ICU), while those who were not critically ill were managed through the pulmonology outpatient clinic for diagnosis and treatment. Patients with ongoing viral, autoimmune, or oncological disorders as well as those with a history of pre-existing chronic diseases particularly those who had been treated with immunosuppressive drugs before contracting COVID-19 infection were excluded from the study. Patients who had taken steroids before the blood sample were also excluded from the study. After taking informed written consent, information like demographics and clinical information was recorded on the purposefully designed questionnaire. The Institutional Research Ethical Board of IBMS KMU Peshawar gave its approval under the Ref. No. KMU/IBMS/IRBE/10th meeting/2024/1753-H. After that the samples were all collected in compliance with the WHO criteria for coronavirus sample collection from human beings (10).

Complete Blood Count: Three milliliters of venous blood were tested for absolute WBC count, absolute lymphocyte count, absolute RBC count, HCT%, HGB, MCH, MCHC, MCV, MPV, and platelet count using a fully automated haematology analyzer (XN-1000, Sysmex, Japan).

Flow Cytometry Analysis: Flow cytometry was performed using anti-human directly conjugated antibodies on Beckman-Coulter Cytoflex (Beckman-Coulter, MA, USA). 50 µl of blood sample of each individual was shifted to a round-bottom tube to count CD4+ and CD8+ T cells. After the addition of 3µl cell surface antibodies anti-CD4-FITC, anti-CD8-PE, CD45-ECD and anti-human CD3-PC7 each, the sample was incubated for 15 minutes in a dark place. Then after the addition of 1ml of lysing solution, it was incubated again in a dark place. After centrifuging the sample for 5 minutes at 2000 rpm, the supernatant was thrown away. Thereafter 2ml of PBS was added to the sediment and it was then re-centrifuged and the supernatant was discarded. Later, after addition of 500 µl PBS, the sample was analyzed by using Beckman Coulter Navios software (Figure 2). The resultant CD4 & CD8 percentages and the absolute lymphocyte count were used to calculate the absolute CD4 & CD8 counts.

Statistical Analysis: SPSS Version 23 was used to record and analyze the data. For all numerical variables, descriptive statistics were employed to derive the Mean and Standard Deviation (SD). The differences between the two groups in terms of CD4, CD8, and CD4/CD8 were compared using an independent sample t-test. The means of the two groups were compared using Fisher's exact test for categorical variables (gender). P-values under 0.05 were considered significant.

RESULTS

In total, absolute WBC count, absolute RBC count, HCT%, HGB, MCH, MCHC, MCV, MPV, and platelets count was not reduced significantly ($p>0.05$) in critically sick COVID-19 infected patients compared with non-critically sick COVID 19 patients (Table 1). Critically ill patients were mostly older ($p=0.001$) (Table 1). Patients who were critically ill had lower absolute lymphocyte count ($p=0.004$), absolute CD4 count ($p=0.002$), and absolute CD8 counts ($p=0.014$), as compared to non-critically ill patients (Fig.1). However, the CD4/CD8 ratio did not change significantly across the groups ($p>0.05$), (Fig. 1). Moreover, no discernible difference was seen between critically sick and non-critically sick across genders.

Table No. 1: Comparison of Immunological/ Haematological markers between critically sick and non-critically sick COVID 19 patients

Factors	Non-Critically ill	Critically ill	P Value
Age	44.15 ± 14.74	57.85 ± 11.66	0.001
Gender (male/female)	14/12	13/13	
Absolute Lymphocyte Count	1.85 ± 0.97	1.12 ± 0.74	0.004
CD4%	52.26 ± 11.67	45.70 ± 18.53	0.134

Absolute CD4 Count	0.98 ± 0.48	0.52 ± 0.52	0.002
CD8%	45.25 ± 11.63	49.92 ± 16.51	0.244
Absolute CD8 Count	0.85 ± 0.52	0.54 ± 0.32	0.014
Absolute WBC Count(10^3/µl)	8.54 ± 3.83	9.72 ± 4.57	0.315
Absolute RBC Count(10^6/µl)	4.90±0.86	4.99±0.66	0.681
HCT%	42.27±8.68	44.09±8.03	0.436
HGB (g/dl)	13.10±2.12	13.32±1.83	0.686
MCH (pg)	26.96±3.33	26.97±2.54	0.996
MCHC (g/dl)	31.55±5.08	30.15±3.07	0.233
MCV (fL)	86.07±8.16	89.70±7.79	0.107
MPV (fL)	11.87±1.06	11.72±0.87	0.579
Platelets count (10^3/µl)	268.73± 88.83	243.15±100.79	0.336

Mean ± SD values of immunological/haematological markers. P for independent T test comparison of critically ill versus non-critically sick individuals. Indices with significant P values (≤0.05) is shown in bold. HCT: Haematocrit. HGB: Haemoglobin. MCHC: Mean Corpuscular Haemoglobin concentration. MCHC: Mean Corpuscular Haemoglobin Concentration. MCV : Mean Corpuscular Volume. MPV: Mean Platelet Volume

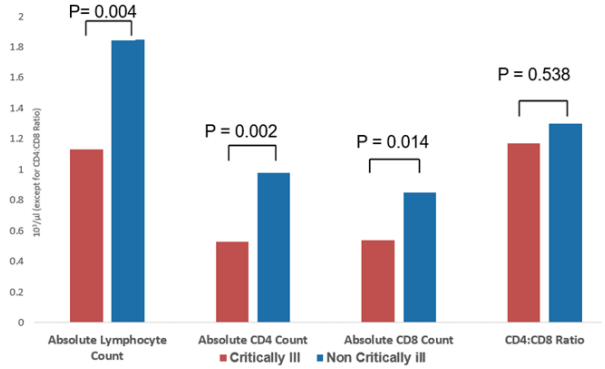

Figure No. 1. Comparison of absolute lymphocyte, CD4, CD8 counts and CD4:CD8 ratio in critically sick vs non-critically sick COVID-19 patients.

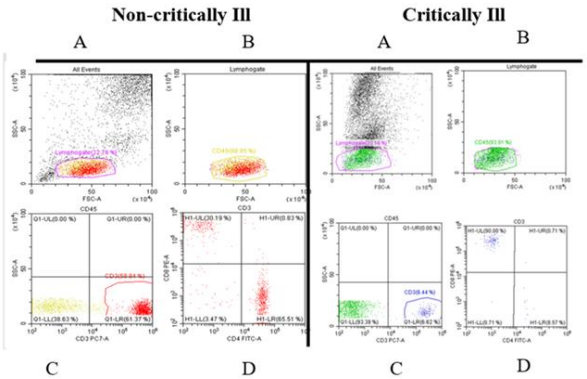

Fig. 2. Flow cytometry analysis graphs of critically sick vs non-critically sick COVID-19 patients

(A) Forward and side scatter plot of red cell lysed whole blood. Lymphocytes are identified by forward and side scatter profile. (B) Precise identification of leukocyte/lymphocytes by staining with CD45 marker. (C) T cell percentages were determined by staining with CD3 marker. (D) The expression of CD4 and CD8 markers on the two-parameter density plot was used to identify and gate the CD3 positive T cells.

P for independent T test comparison of two groups.
Absolute Lymphocyte Count in Critically Ill Patients = 1.12 ± 0.74 10^3/µl; in Non-Critically Ill Patients = 1.85 ± 0.97 10^3/µl; Absolute CD4 Count in Critically Ill Patients = 0.52 ± 0.52 10^3/µl; in Non-Critically Ill Patients = 0.98 ± 0.48 10^3/ µl; Absolute CD8 Count in Critically Ill Patients = 0.54 ± 0.32 10^3/ µl; in Non-Critically Ill Patients = 0.85 ± 0.52 10^3/ µl; CD4:CD8 Ratio in Critically Ill Patients = 1.17 ± 0.89; in Non-Critically Ill Patients = 1.30 ± 0.66

DISCUSSION

In response to viral infections, both the innate and acquired immune systems are triggered. Modulation of T cell associated immune responses occurs in majority of the infections with viruses[11]. Perforin, granzyme, and interferons are just a few of the molecules that CD8 + cytotoxic T lymphocytes (CTLs) might secrete in order to get rid of viruses from the host body[12]. CD4 helper T cells support cytotoxic T cells and B cells in the elimination of viral infection[13].
In a robust immune system, the CD4:CD8 ratio is about 2:1. According to research on the immunological reaction in human beings, the CD4:CD8 ratio is reversed in some viral infections[14]. According to Sainz et al research, this ratio could be utilized to diagnose various viral diseases[15].
In this investigation, flow cytometry was used to calculate the absolute CD4 and CD8 T cell counts in blood specimens of critically and non-critically ill COVID-19 individuals. Then CD4:CD8 ratio was calculated in these two patient groups. Critically sick COVID-19 patients had a considerably lower absolute lymphocyte count in their peripheral blood than non-critically sick COVID-19 individuals. This is consistent with findings from other studies[6,16,17].
In critically ill COVID-19 individuals, absolute CD4 and CD8 counts were also considerably lower than in non-critically ill COVID-19 individuals. These findings

are in harmony with C Pallotto et al. study[8]. This indicates that T cells are important in COVID-19 defence and reduced CD4 and CD8 counts make an individual more prone to severe infection.

The typical value of 2:1 was observed for the CD4:CD8 ratio in COVID-19 individuals, demonstrating that the two groups of COVID-19 individuals who were critically sick and those who were not did not significantly vary from one another. According to the results of research by Ganji A et al., the CD4:CD8 ratio in COVID-19 individuals is within the normal range[6]. The same CD4:CD8 ratio in both groups may be due to the fact that in critically ill patients both CD4 and CD8 counts were reduced, therefore the ratio remained the same as in non-critically ill patients. If only one count was reduced then the ratio must have changed. So overall CD4 and CD8 ratio is not changed but both counts are reduced in critically sick individuals.

In critically sick COVID-19 individuals, decreased absolute lymphocyte count, absolute CD4 count, and absolute CD8 count were seen, indicating reduced protection in these patients. There is a possibility that the counts may have been less due to overconsumption in critically ill patients, resulting in the depletion of these counts. Another possible explanation is that the patients got critical illness due to reduced CD4, CD8, and lymphocyte counts in first place. LI et. al. showed that the number of peripheral T cell subsets was lower in patients with the severe acute respiratory syndrome (SARS). In recovered patients, peripheral T cell subsets were quickly restored; as a result, peripheral T cell amount can be employed as a reliable COVID-19 diagnostic tool[18].

Furthermore, when compared to non-critically sick COVID-19 individuals, the absolute eosinophil count and absolute monocyte count in critically ill patients were significantly lower, which is in line with prior research findings[20]. This suggests that continuous monitoring of the peripheral blood system, particularly eosinophils and monocytes can help forecast severe COVID-19 cases.

In this study, it was also discovered that the critically sick COVID-19 patients were older than the COVID-19 patients who weren't critically ill. This shows that being older could be a risk factor for a poor outcome. However, the ratio of males and females among COVID-19 patients who were severely ill and those who were not; did not differ. These findings contradict a recent study that found males are more susceptible to COVID-19 infection[17]. COVID-19 infection was previously related to Wuhan seafood wholesale market exposure, and the bulk of the patients were male workers, therefore this could be the possible explanation.

CONCLUSION

The changes in the CD4:CD8 ratio in critically ill COVID-19-infected individuals were not significant when compared to the non-critically ill COVID-19 group. However, absolute lymphocyte counts, absolute CD4 counts, and absolute CD8 counts were all significantly lower in critically ill patients. This suggested that the cellular immune responses were low in critically ill COVID-19 patients and may be the reason for disease severity.

Declaration of competing interest: The authors state that they have no competing interests.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Omar Malik, Yasir Ishaq
Drafting or Revising Critically:	Yasar Mehmood Yousafzai, Awal Mir
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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REFERENCES

1. Guarner J. Three Emerging Coronaviruses in Two Decades: The Story of SARS, MERS, and Now COVID-19. Am J Clin Pathol 2020;153(4):420–1.
2. World Health Organization. Coronavirus disease 2019 (COVID-19): situation report, 51 [Internet]. World Health Organization; 2020 Mar [cited 2021 Aug 9]. Available from: https://apps.who.int/iris/handle/10665/331475
3. Ye ZW, Yuan S, Yuen KS, Fung SY, Chan CP, Jin DY. Zoonotic origins of human coronaviruses. Int J Biol Sci 2020;16(10):1686–97.
4. Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, Evaluation, and Treatment of Coronavirus (COVID-19). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 [cited 2021 Aug 7]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK554776/
5. Spiering MJ. Primer on the Immune System. Alcohol Res 2015;37(2):171–5.
6. Ganji A, Farahani I, Khansarinejad B, Ghazavi A, Mosayebi G. Increased expression of CD8 marker

on T-cells in COVID-19 patients. Blood Cells Mol Dis 2020;83:102437.
7. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther 2020;5(1):33.
8. Pallotto C, Suardi LR, Esperti S, Tarquini R, Grifoni E, Meini S, et al. Increased CD4/CD8 ratio as a risk factor for critical illness in coronavirus disease 2019 (COVID-19): a retrospective multicentre study. Infect Dis (Lond) 2020;52(9): 675–7.
9. Calvet J, Gratacós J, Amengual MJ, Llop M, Navarro M, Moreno A, et al. CD4 and CD8 Lymphocyte Counts as Surrogate Early Markers for Progression in SARS-CoV-2 Pneumonia: A Prospective Study. Viruses 2020;12(11):1277.
10. World Health Organization. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases: interim guidance, 19 March 2020 [Internet]. World Health Organization; 2020 [cited 2021 Aug 9]. Report No.: WHO/COVID-19/laboratory/2020.5. Available from: https://apps.who.int/iris/handle/10665/331501
11. Jung MC, Pape GR. Immunology of hepatitis B infection. Lancet Infect Dis. 2002 Jan;2(1):43–50.
12. Mescher MF, Curtsinger JM, Agarwal P, Casey KA, Gerner M, Hammerbeck CD, et al. Signals required for programming effector and memory development by CD8+ T cells. Immunological Reviews 2006;211(1):81–92.
13. Zhu J, Yamane H, Paul WE. Differentiation of Effector CD4 T Cell Populations. Annu Rev Immunol 2010;28:445–89.
14. McBride JA, Striker R. Imbalance in the game of T cells: What can the CD4/CD8 T-cell ratio tell us about HIV and health? PLOS Pathogens 2017;13(11):e1006624.
15. Sainz: CMV and HIV: a double hit on the CD4/CD8 ratio - Google Scholar [Internet]. [cited 2021 Sep 23]. Available from: https://scholar.google.com/scholar_lookup?title=CMV%20and%20HIV%3A%20a%20double%20hit%20on%20the%20CD4%2FCD8%20ratio&author=T.%20Sainz&publication_year=2014
16. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet 2020;395(10223):497–506.
17. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020; 323(11):1061–9.
18. Yang L, Liu S, Liu J, Zhang Z, Wan X, Huang B, et al. COVID-19: immunopathogenesis and Immunotherapeutics. Sig Transduct Target Ther 2020;5(1):1–8.

Original Article

Clinical Outcomes of Managing Congenital Knee Dislocation: An Observational Study

Mohammad Aslam Mengal[1], Saddam Mazar[2], Khawand Bakhsh Umrani[2], Eamaan Abid[3], Nargis Taj[2] and Fahmida Rehman[2]

ABSTRACT

Objective: This study aims to assess the effectiveness, complications, and recurrence rates of various treatment approaches for congenital knee dislocation (CDK) in paediatric patients in our experience.

Study Design: An observational study

Place and Duration of Study: This study was conducted at the Sheikh Khalifa Bin Zayyad Al Nahyan Medical Complex Quetta from January 2022 to January 2024.

Methods: These cases were graded using Tarek CDK Grading System from grade I – III. Treatment modalities included conservative management, minimally invasive techniques, and surgical interventions, depending on CDK severity. The clinical findings included assessment of range of motion (ROM), knee flexion and the occurrence of complications.

Results: Conservative management turned out to be most practical and effective approach with a success rate approaching nearly 95% in paediatric patients of grade I and 85% grade II. The minimally invasive techniques in grade III CDK showed a success rate of 70% in less than three months of age. Meanwhile, older age and patients unresponsive to conservative management had to complete surgical interventions including V-Y Quadricepsplasty with 63% success rate towards CDK grade III. ROM and knee flexion both significantly improved with averages of 76% and 80% respectively adding to the improvement in functional outcomes.

Conclusion: Early diagnosis and severity-based treatment improve CDK outcomes. Non-invasive methods work for early cases, while surgery is crucial for severe cases. Further research is needed to refine surgical techniques and develop innovative treatments.

Key Words: Joint, Tibiofemoral, Congenital Abnormality, Orthopedic Surgical Procedure, Congenital dislocation of knee

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INTRODUCTION

Congenital dislocation of the knee (Genu Recurvatum Congenitum) is rare, occurring in 1 out of 100,000 births[1]. It involves knee hyperextension beyond 0° with limited or no flexion and may occur alone or with conditions like Ehlers-Danlos, Arthrogryposis, and Marfan's Syndrome [1,2].

CDK is commonly diagnosed at birth but can be detected earlier through antenatal ultrasonography, which provides a clear and safe view of the lesion.

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Ultrasonographic diagnosis is faster and cheaper than other radiological methods, both perinatally and post-correction[3]. It can be unilateral or bilateral, with a higher prevalence in females, and its causes may be extrinsic (e.g., maternal trauma) or intrinsic (e.g., genetic abnormalities and developmental deficiencies)[4,5].

The Tarek CDK Grading System, introduced by Tarek Abdelaziz and Samir in 2011, modified the classification by Leveuf and Pais from 1946[6]. It assesses disease severity based on passive knee flexion, analyzed radiographically. The system classifies cases into three stages: GI (recurvatum with >90° passive flexion), GII (subluxation/dislocation with 30–90° passive flexion), and GIII (dislocation with <30° passive flexion). While GIII requires invasive surgery, GI and GII can be managed conservatively or with minimally invasive techniques[3,6].

Newborns and infants up to 3 months are managed conservatively with serial manipulation, casting, and a Pavlik harness once 90° flexion is achieved for proper alignment[6]. Early intervention leads to better functional outcomes[3]. Children over 6 months or those

failing conservative treatment require surgery[2]. Minimally invasive techniques like Percutaneous Quadriceps Recession (PQR), Percutaneous Quadriceps Needle Tenotomy (PCQNT), and Mini Open Quadriceps Tenotomy (MOQT) have shown satisfactory results in infants under 3 months[7].

V-Y Quadricepsplasty (VYQ), introduced by Curtis and Fisher in 1969, is widely used for GIII CDK and failed GI and GII cases[6]. It involves an anterolateral approach with V-Y advancement to address quadriceps extensor pathology, the primary issue in most CDK cases[6]. Femoral shortening, preferred in CDK with CDH, minimizes quadriceps damage, and both techniques show similar satisfactory outcomes[6,8,9].

The pathology should be corrected before the child starts walking to prevent femoral condyle curvature loss and poor surgical outcomes[10]. Treatment can begin at birth or within the first few days[11], though some authors suggest waiting a month for potential spontaneous reduction in isolated CDK cases[7].

METHODS

This observational study was conducted at Sheikh Khalifa bin Zayyad Al Nahyan Medical Complex, Quetta from January 2022 up to January 2024. The purpose was to assess the clinical outcomes of management modalities followed for congenital knee dislocation (CDK) at our institute. Retrospective data collection methods such as medical records review and prospective data collection methods such as follow up of children diagnosed with CDK were utilized.

The study included 46 pediatric patients diagnosed with CDK at birth or early infancy using ultrasonography or clinical examination. The Tarek CDK Grading System assessed disease severity.

Patients with unilateral or bilateral CDK diagnosed at birth or early infancy, who followed conservative management, minimally invasive techniques, or surgical management based on the severity according to Tarek CDK Grading System, were included in the study. Patients with incomplete medical records and additional congenital lower-limb deformities that could influence treatment outcomes, were excluded from the study.

CDK severity was classified according to Tarek CDK Grading System: Grade I (simple recurvatum with >90° passive knee flexion), Grade II (subluxated or dislocated with 30° to 90° of passive knee flexion), and Grade III (dislocated with <30° passive knee flexion). Grades I and II were managed mainly conservatively, while Grade III cases were surgically managed if conservative treatment failed.

Treatment approaches included conservative management through manipulation and casting, followed by a Pavlik harness for infants once 90° of knee flexion was achieved. For minimally invasive techniques, Percutaneous Quadriceps Recession (PQR), Percutaneous Quadriceps Needle Tenotomy (PCQNT), and Mini Open Quadriceps Tenotomy (MOQT) were used for patients with Grade I, II, or early Grade III CDK. Surgical interventions such as V-Y Quadricepsplasty (VYQ) and femoral shortening were reserved for Grade III cases or those unresponsive to conservative treatment.

Outcome measures included ROM, functional scores, complications, recurrence rates, and patient satisfaction via caregiver surveys. Data were analyzed using medical records, chi-square tests for categorical data, and t-tests for continuous data, with significance set at $p < 0.05$.

RESULTS

The study analysed 46 patients with congenital knee dislocation (CDK), with a gender distribution of 59% male and 41% female. The mean age at diagnosis was 18 months, ranging from 1 to 36 months. Clinical severity was classified into three grades, with 41% of cases being Grade I, 28% Grade II, and 31% Grade III.

Table No. 1: Baseline Characteristics of Patients with Congenital Knee Dislocation (CDK)

Characteristic		Details
Total Sample Size		46
Gender Distribution	Male	27 (59%)
	Female	19 (41%)
Mean Age at Diagnosis		18 months (range: 1–36 months)
Unilateral Cases		29 (63%)
Bilateral Cases		17 (37%)
Family History of CDK		1 (24%)

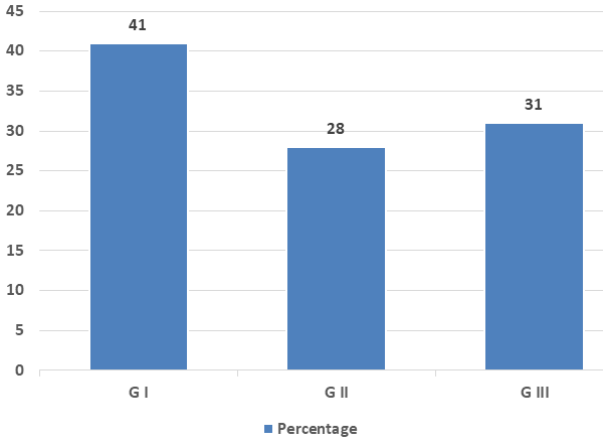

Figure No. 1: Tarek CDK Grading System and Distribution of Cases

Grade	Description	Patients	%
GI	Simple recurvatum with >90° passive flexion	19	41%
GII	Subluxation or dislocation with passive flexion 30°-90°	13	28%
GIII	Dislocation with <30° passive flexion	14	31%

Table No. 2: Treatment Approaches and Outcomes by Age Group and Severity

Age Group	Grade	Treatment	Techniques	Success Rate
New born to 3 months	GI	Conservative	Serial manipulation, casting	95%
	GII	Conservative	Pavlik harness	85%
	GIII	Minimally invasive	PQR, PCQNT, MOQT	70%
3-6 months	GI	Conservative or minimally invasive	Casting, Pavlik harness	90%
	GII	Minimally invasive	PQR, PCQNT, MOQT	75%
	GIII	Surgical	V-Y Quadricepsplasty	63%
Over 6 months	GIII	Surgical	V-Y Quadricepsplasty, femoral shortening	57%

PQR: Percutaneous Quadriceps Recession
PCQNT: Percutaneous Quadriceps Needle Tenotomy
MOQT: Mini Open Quadriceps Tenotomy

Table No. 3: Functional Outcomes and Follow-Up Results

Outcome Measure	Baseline Score	Follow-Up Score	Improvement (%)
Range of Motion (ROM)	22–38 deg	92–120 deg	76%
Knee Flexion	29 deg	109deg	80%
Pain Score (VAS)	6/10	1/10	86%

DISCUSSION

The study emphasizes early diagnosis and stratified management for CDK, confirming previous research. Grade I and II cases had success rates of 95% and 85% with conservative treatment, aligning with Abdelaziz et al.[3], who highlighted the benefits of early serial casting and Pavlik harness use. Evidence also shows that early intervention achieves over 80% success, while delayed treatment lowers efficacy and increases complications[3,13].

In severe Grade III cases, minimally invasive techniques such as percutaneous quadriceps recession (PQR) and mini-open quadriceps tenotomy (MOQT) reached a 70% success rate in patients under three months. These data are consistent with Shah et al.[12], which concluded that less invasive techniques can decrease surgical morbidity with satisfactory correction of severe cases of CDK. However, Grade III cases more than six months old had poorer results with surgical procedures, including V-Y quadricepsplasty and femoral shortening, being successful at a rate of 57%. Recent studies have highlighted the need to combine femoral shortening with capsulorrhaphy in an effort to produce better outcomes and reduce complications, including quadriceps weakness and postoperative stiffness[3,14].

Functional improvement is impressive, with an 80% improvement in knee flexion and a 76% improvement in range of motion (ROM) following treatment. Studies show early conservative or minimally invasive interventions have also been associated with functional mobility gains[3,6,13,14]. In addition, pain scores dropped significantly, supporting evidence that early correction improves long-term comfort and reduces osteoarthritis risk.

The study further emphasizes the importance of ultrasonography in the identification of early CDK. During the perinatal period, CDK can be diagnosed non-invasively and in an economical manner using ultrasonography, providing an early possibility for intervention [15]. Recent literature evidences its help to differentiate CDK from other limb deformities, guiding treatment[15,16].

The study's treatment protocols had minor complications like mild misalignment and skin irritation. However, these were fewer than those seen in cases of delayed or insufficient CDK treatment. B K AR et al.[2] reported higher complication rates, including joint instability and recurrent dislocation, when treatment began after six months.

The study's low recurrence rates confirm the effectiveness of the stratified treatment approach. Abdelaziz et al.[3] similarly reported recurrence rates below 10% for conservative and minimally invasive treatments. Research by Lin et al. (2023) emphasizes individualized treatment based on severity and age to further reduce recurrence and morbidity.

Another classification categorizes CDK based on the anatomical relationship of the distal femur and proximal tibia[17]. Another system defines three types by reducibility and stability: Type I (easily reducible, flexion stable), Type II (unstable but reducible), and Type III (irreducible)[18]. This classification was used in a follow-up study comparing treatment outcomes[19].

CDK not only affects the distal femur and proximal tibia, but it also has proneness to additional malformations affecting the upper extremities, face, digestive tract and reproductive system[17]. CDK might also be an indicator for congenital hip dislocation, which can be detected with associated congenital neuromuscular disabilities[20]. Congenital hip dislocation and other musculoskeletal abnormalities are reported in 82-88% of CDK cases[21].

Early diagnosis and treatment of CDK at birth are crucial to prevent lifelong disability. A 2-year-old girl with neglected bilateral CDK had failed serial casting at birth and presented with -90° knee hyperextension, requiring VYQ surgery with tendon transfers, showing satisfactory results at six months[22]. Another case involved a 12-year-old boy untreated for 5–6 years, initially undergoing bilateral supracondylar femoral osteotomy but remaining unable to walk until a three-stage treatment at age 12, leading to stable knees at a 2.5-year follow-up[23]. These cases highlight the importance of timely intervention for better long-term outcomes.

Such cases highlight the importance of early diagnosis and treatment. Conservative treatments should begin immediately upon recognition of pathology in the initial stage of life[21], followed up with surgeries to be performed when needed, and ideally must be performed within 15 months of life and not later than 2 years[12,24].

The study highlights that early diagnosis and stratified interventions significantly improve CDK outcomes with low complication rates. It emphasizes the need for advancements in diagnostic imaging and minimally invasive techniques to enhance patient care.

CONCLUSION

This study demonstrates the effectiveness of age-appropriate and severity-based management strategies for CDK. Early diagnosis and intervention remain critical for achieving optimal functional outcomes and minimizing complications. Further research is needed to refine surgical techniques and explore innovative approaches for managing severe cases.

Implications: Early diagnosis allows effective conservative treatment for Grades I and II, while severe Grade III cases should attempt conservative management before surgery to optimize outcomes.

Limitations: The study's limitations include a single-center sample and lack of long-term follow-up, highlighting the need for multi-center research with extended follow-up to assess long-term treatment outcomes.

Ethical Considerations: The study adhered to ethical requirements and was approved by the institutional review board of Sheikh Khalifa bin Zayyad Al Nahyan Medical Complex. Parents or guardians of all the children who participated provided informed consent before the study

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Mohammad Aslam Mengal, Saddam Mazar
Drafting or Revising Critically:	Khawand Bakhsh Umrani, Eamaan Abid, Nargis Taj, Fahmida Rehman
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Palco M, Rizzo P, Sanzarello I, Nanni M, Leonetti D. Congenital and Bilateral Dislocation of the Knee: Case Report and Review of Literature. Orthop Rev (Pavia) 2022;14(3):33926.
2. B K AR, Singh KA, Shah H. Surgical management of the congenital dislocation of the knee and hip in children presented after six months of age. Int Orthop 2020;44(12):2635-2644.
3. Abdelaziz TH, Samir S. Congenital dislocation of the knee: a protocol for management based on degree of knee flexion. J Children's Orthopaed 2011;5(2):143-9.
4. Madadi F, Tahririan MA, Karami M, Madadi F. Complicated Congenital Dislocation of the Knee: A Case Report. Arch Bone Jt Surg 2016;4(4):396-398.
5. Yeoh M, Athalye-Jape G. Congenital knee dislocation: a rare and unexpected finding. BMJ Case Rep 2021;14(1):e234881.
6. Bridget K. Ellsworth, Brody J. Dawkins, Sofia Hidalgo Perea, Daniel W. Green, Management of Congenital Dislocation of the Knee. J Pediatr Orthopaed Society North Am 2021;3(3):272.
7. The Earliest Age Limit for Manipulation and Casting to Avoid Surgical Intervention in Idiopathic Congenital Knee Dislocation. J Pak Orthopaed Assoc 2018;30(02):75-81.
8. Johnston, Charles E. II, MD. Simultaneous Open Reduction of Ipsilateral Congenital Dislocation of the Hip and Knee Assisted by Femoral Diaphyseal Shortening. J Pediatr Orthopaed 2011;31(7):732-740.
9. Oetgen Matthew E, Walick Kristina S, Kirsten T, Karol Lori A, Johnston Charles E. Functional Results after Surgical Treatment for Congenital Knee Dislocation. J Pediatr Orthopaed 2010; 30(3):216-223.
10. Functional Outcome of Open Relocation of the Congenital Dislocated Knee with and without Distal Arthrogryposis. J Pak Orthopaed Assoc 2015;27(2):58-62.
11. Abuomira, Ibrahim Elsayed A. Managment of congenital knee dislocation by gradual reduction with serial casting. The Egypt Orthopaed J 2023;58(1):48-52.

12. Shah NR, Limpaphayom N, Dobbs MB. A minimally invasive treatment protocol for the congenital dislocation of the knee. J Pediatr Orthopaed 2009;29(7):720-5.
13. Abdushukurovich SS, Agzamovich FM, Abdunabievich SS. Congenital dislocation of shin bones: treatment tactics. Texas J Med Sci 2024; 29:4-7.
14. Honcharuk EM, Jeans KA, Polk JL, Johnston CE. Long-term Outcomes of Surgically Treated Congenital Dislocation of the Knee. J Pediatric Orthopaedics. 2024 Apr 26:10-97.
15. Cavoretto PI, Castoldi M, Corbella G, Forte A, Moharamzadeh D, Emedoli D, et al. Prenatal diagnosis and postnatal outcome of fetal congenital knee dislocation: systematic review of literature. Ultrasound Obstet Gynecol 2023;62(6):778-87.
16. Yan Z, Yao Y, Yang Q, Ma B, Li T, Wang Y. Application of ultrasound in the early diagnosis of congenital patellar dislocation: a case description. Quantitative Imaging in Medicine and Surgery. 2023 Oct 10;13(10):7362.
17. Qi, B., Jie, Q., Wang, X. et al. Congenital dislocation of the knee complicated with bilateral hip dislocation: a case report and literature review. BMC Musculoskelet Disord 25, 327 (2024). https://doi.org/10.1186/s12891-024-07316-1
18. Mehrafshan M, Wicart P, Ramanoudjame M, Seringe R, Glorion C, Rampal V. Congenital dislocation of the knee at birth – Part I. Clin signs and classification, Orthopaed Traumatol : Surg Res 2016;102(5): 631-633.
19. Rampal V, Mehrafshan M, Ramanoudjame M, Seringe R, Glorion C, Wicart P. Congenital dislocation of the knee at birth – Part 2: Impact of a new classification on treatment strategies, results and prognostic factors, Orthopaedics & Traumatology: Surg Res 2016;102(5):635-638.
20. Wilebski BJ, Alam A, Lambert RR, Douvoyiannis M. Congenital Dislocation of the Knee in the Delivery Room. Am J Case Rep. 2024 May 14;25:e943725. doi: 10.12659/AJCR.943725. PMID: 38741359; PMCID: PMC11106790.
21. Çıraklı S, Çıraklı A. Neglected intrauterine bilateral congenital knee dislocation. Jt Dis Relat Surg 2021;32(2):542-545.
22. Qasim OM, Abdulaziz AA, Aljabri NK, Albaqami KS, Suqaty RM. Neglected congenital bilateral knee dislocation treated by quadricepsplasty with semitendinosus and sartorius transfer: A case report. World J Orthop. 2024 Aug 18;15(8):807-812. doi: 10.5312/wjo.v15.i8.807. PMID: 39165876; PMCID: PMC11331331.
23. Kumar J, Dhammi IK, Jain AK. Neglected surgically intervened bilateral congenital dislocation of knee in an adolescent. Ind J Orthop 2014;48(1):96-9.
24. Morales-Roselló J, Loscalzo G, Hueso-Villanueva M, Buongiorno S, Jakaitė V, Perales-Marín A. Congenital knee dislocation, case report and review of the literature. The Journal of Maternal-Fetal & Neonatal Med 2020;35(4):809–811.

Original Article

Comparison of Efficacy of Buccal Infiltration Versus Buccal and Palatal Infiltration for Maxillary First Molar Extraction

Haseeb Khalid Khan[1], Muhammad Asif Shahzad[1], Shahzada Faiz Ahmad Khan[1], Wedad Sohail[2], Syeda Azka Aamer[3] and Rushda Khalid[4]

ABSTRACT

Objective: To evaluate the effectiveness of palatal and buccal infiltration against buccal infiltration only while extracting the maxillary first molar.

Study Design: quasi experimental study

Place and Duration of Study: This study was conducted at the Oral and Maxillofacial Surgery Department, Azra Naheed Dental College/Chaudhry Muhammad Akram Dental Hospital, Lahore from August 2022 to May 2023.

Methods: After meeting inclusion and exclusion criteria, a total of 100 patients (50 in each of the group) were enrolled for the study. In Group A (experimental) only buccal infiltration was given for extraction of maxillary first molar while in Group B (control) buccal plus palatal infiltration was used for the extraction of maxillary first molar. Efficacy was noted in both groups. The data was entered and analyzed using SPSS version 25.

Results: In our study from only buccal infiltration group the mean visual analogue score (VAS) of the patients was 2.90±1.61 and in buccal and palatal infiltration group the mean VAS of the patients was 2.64±1.67 (p-value=0.432). In only buccal infiltration group efficacy was achieved in 27(54%) patients and in buccal and palatal infiltration group it was achieved in 28(56%) patients (p-value=0.841)

Conclusion: Both buccal infiltrations versus buccal and palatal infiltration are equally efficacious during extraction of maxillary first molar

Key Words: Buccal Infiltrations, Palatal Infiltration, Extraction of Maxillary First Molar

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INTRODUCTION

Anxiety has played a key role in acting as a barrier to dental treatment. The main factor why some patients feel reluctant to undergo dental treatment is fear of pain. There are number of factors which play a crucial role why a patient experiences pain during administration of local anesthetic[1,2]. The most important one is the site in the oral cavity where injection is being given, among these sites palatal infiltration/ anesthesia is the most painful[3,4].

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Palatal injections is not well tolerated because of the rich nerve supply of palatal tissues. Secondly palatal mucosa is more keratinized as compared to buccal mucosa which means it is more resistant to local anesthetic. Due to the firm attachment of the palatal mucosa with the underlying periosteum, diffusion under pressure of local anesthetic can cause extreme discomfort. The pain associated with the palatal injection can be lessened using a variety of techniques, such as topical or pressure surface anesthesia, freezing treatments, injection pressure management, computer-controlled anesthesia delivery systems, transcutaneous electric nerve stimulation (TENS) and eutectic mixtures of local anesthetic. The local anesthetics currently in use can diffuse across the buccal-palatal cortical bone distance and this distance tend to increase when we are moving from anterior to posterior direction is case of maxilla[5-7].

Allergic reactions to local anesthesia can occur. Immediate reaction includes urticaria and anaphylaxis. Mild toxicity to LA can present as slurred speech and confusion, moderate toxicity will be present as headache and blurred vision and severe toxicity will present as cardiac dysrhythmia and cardiac arrest. Patients may have maxillary teeth extracted without

palatal invasion. Badcock et al. used 2% lignocaine and 1:80,000 epinephrine to remove maxillary third molars without palatal injection. A comparative study at a private dental college in Lahore found 51 adult patients, 25 in each group, with 18 (72%) success rates in the control group (buccal and palatal infiltration) and 7 (28%) in the experimental group (single buccal infiltration only). The experimental group had a 40% success rate. Successful cases were defined as extraction without LA repetition. Palatal anesthesia denial is rising among researchers. Due to the maxilla's thin and porous nature, problems are rare and anesthesia is excellent[4,7-9].

In a comprehensive analysis of maxillary extraction pain with buccal infiltration alone, Band Enoch Jones E and colleagues emphasized additional clinic trials with higher sample sizes and identical techniques[10,11]. Aim of this study was that to date most of the dental practitioners rely on buccal as well as palatal infiltration for extraction of maxillary first molar, the local data only shows 28% success rate with buccal infiltration, indicating further studies required in this regard. Therefore, the aim of this was evaluate the effectiveness of palatal and buccal infiltration against buccal infiltration while extracting the maxillary first molar, so as to provide benefit to the population by evaluation pain control without palatal injection and to compare adequate anesthesia in the posterior maxillary region.

METHODS

The study was presented to the ethical review board of Azra Naheed Dental College, Lahore and commenced after approval vide letter no. (ANDC/RAC/2022/34). This study was carried out at Department of Oral and Maxillofacial surgery, Azra Naheed Dental College/Chaudhry Muhammad Akram Dental Hospital, Lahore from August 2022 to May 2023. A sample size of 100 (50 in each group) individuals using the Non-Probability consecutive sampling technique were selected using 5% level of significance efficacy of 72% in palatal group and 28% in buccal alone group.[7]

Inclusion Criteria: Patients ages between 20 to 40 years, both genders, visiting the OPD for extraction of maxillary first molar were enrolled in the study,

Exclusion Criteria: Immunocompromised individuals, having active infection e.g. abscess, coagulopathies, pregnant or lactating females, allergic to local anesthetics and ASA III or IV were not considered for this study.

Data Collection: 100 patients fulfilling the inclusion criteria were included in this study from OPD. Demographic data was collected regarding age, sex. Patients were explained regarding the protocol of study and an informed written consent was obtained in accordance with the guidelines of Helsinki declaration. Patients were allocated into groups A and B using a random balloting technique. In Group A (experimental) only buccal infiltration was given for extraction of upper maxillary first molar while in Group B (control) buccal with palatal infiltration was used for maxillary first molar extraction. The participants were not informed in which group they were allocated to overcome bias. In all patients, extractions were done by the same surgeon with a standard technique. Local anesthesia (2%) Lidocaine hydrochloride with epinephrine 1: 100000 for buccal infiltration alone and for buccal and palatal infiltration technique were used. Dose of LA which was used for experimental group was (0.9ml for buccal infiltration alone) and for control group (0.6ml for buccal infiltration and 0.3ml for palatal infiltration). Effectiveness of local anesthesia perceived by patient as pain during extraction by applying forcep on maxillary first molar after 5 minutes of giving infiltration. This was recorded as degree of pain felt by patient using visual analog scale (VAS) <3 was considered effective after 5 minutes, VAS ≥3 was considered ineffective after 5 minutes. Patients were asked about effectiveness of local anesthesia after five minutes of infiltration when the upper molar forcep was applied and patients was asked to rate the pain, and appropriate entries were made in the predesigned proforma. Other variables i.e. palatal infiltration needed in group A was also recorded.

Data Analysis: The data was entered and analyzed using SPSS version 25. The qualitative data like efficacy and gender was presented as frequency and percentage. The quantitative variables like VAS and age were shown as means and standard deviations. The chi square test was applied to see significant difference, statistically if any, between efficacy of two groups. A p value of ≤0.05 was considered as statistically significant.

RESULTS

After meeting inclusion and exclusion criteria, a total of 100 patients (50 in each of the group) were included in current study. Table 1 shows that in group A, the average age of patients was 30.26±7.73 years, while it was 30.70±6.13 years in group B. The observed change was not statistically significant. The p-value was equal to 0.753. Among the patients in group A, 21 individuals, accounting for 42% of the total, were male. Similarly, in group B, 18 patients, making up 36% of the total, were male. A ratio of 0.6:1 (male to female) was observed. The observed change was not significant as the p-value was equal to 0.539. The average Visual Analogue Scale (VAS) score was 2.90±1.61 for patients in group A, whereas it was 2.64±1.67 in group B. The observed change was not statistically significant. The p-value was equal to 0.432.

Table No. 1: Demographical Data of Patients in Both Groups (n = 100)

	Study Groups		p-value
	Group A	Group B	
n	50	50	0.753
Age (Years)	30.26 ± 7.73	30.70 ± 6.13	
Gender			
Male	21 (42.0%)	18 (36.0%)	0.539
Female	29 (58.0%)	32 (64.0%)	
Pain score using VAS	2.90 ± 1.61	2.64 ± 1.67	0.432

Table 2 showed that in group A, efficacy was attained in 27 patients, accounting for 54% of the total, whereas in group B, efficacy was reached in 28 patients, accounting for 56% of the total. The observed change was not statistically significant. The p-value is equal to 0.841.

Table No. 2: Comparison of Efficacy in Both Groups (n=100)

		Study Groups		Total	p-value
		Group A (n = 50)	Group B (n = 50)		
Efficacy	Yes	27	28	55	0.841
		54.0%	56.0%	55.0%	
	No	23	22	45	
		46.0%	44.0%	45.0%	

While Table 3 demonstrated that 0ut of total 50 patients of group A, the additional palatal infiltration needed in 23(46%) patients.

Table No. 3: Frequency Distribution of Palatal Infiltration Needed in Group A (n = 50)

		Frequency (%)
Palatal infiltration needed in group A	Yes	23 (46%)
	No	27 (54%)
	Total	50 (100%)

DISCUSSION

Fear and anxiety are prevalent and acknowledged as obstacles to seeing the dentist. A patient's reluctance to attend the dentist may stem from a bad experience in the past or a generalized belief that dental care is harmful. Local anesthetic administration is a necessary component of any painful dental operation. The use of needles and injections may cause discomfort and may trigger anxiety. For every dental procedure, perioperative pain and discomfort reduction is essential. In recent years, there have been several changes made to the agents and procedures used in dentistry research[12-13].

The mean VAS of the patients in the present research was 2.90±1.61 in the buccal infiltration group and 2.64±1.67 in buccal with palatal infiltration group (p-value=0.432). Efficiency was attained in 27 (54%) patients in buccal infiltration group alone, while in 28(56%) patients in buccal plus palatal infiltration group (p-value=0.841). According to the results of the present investigation, Vikas Sandilya et al.[15] showed that, for all three measures, there was no statistically significant difference between the two groups (P >0.05). This demonstrates that, in the majority of instances, a single buccal infiltration of articaine may be utilized in place of lignocaine for the extraction of maxillary premolar teeth. This demonstrates that, in the majority of instances, a single buccal infiltration of articaine may be utilized in place of lignocaine for maxillary premolar teeth extractions[14].

According to some research, the longer time it takes for articaine to start working is because it takes longer for a single buccal infusion to produce sufficient palatal anesthesia[15,16]. Fan et al, conducted a review and found that the therapeutic effectiveness of articaine formulations containing 4% vs 2% concentrations with concentrations of 1:100,000 or 1:200,000 adrenaline was comparable.[17]

Abhirup Chatterjee et al. found that, in most situations, a prolonged waiting time was sufficient for extracting the posterior maxillary teeth with a single buccal infiltration without any palatal injection. Dentists may successfully try extractions without using palatal injections. However, if rescue palatal anesthesia is required, the alternative method may be used[18]. According to Majid and Ahmed,[3] the anesthetic effects of lidocaine (2%) and articaine (4%) buccal injections were similar. However, lignocaine's anesthetic effectiveness was noticeably insufficient compared to the 4% articaine anesthesia provided by the conventional method[3].

According to the results of the present research, A.N. Iyengar et al. observed that, in comparison to pain experienced just during the administration of buccal injection, pain experienced during both buccal and palatal injection was clearly on the higher side. None of the patients seemed to be in excruciating agony[19]. The identical results as our research were also reported in another study by D Prasanna Kumar. The effectiveness of a single injection of articaine buccally, according to the author, is equivalent to that of a buccal plus palatal injection of lignocaine[20].

Sekhar et al. performed a study concluding that there was no significant difference in terms of pain experienced during palatal instrumentation when using either 2 ml of 2% buccal injection of lignocaine with 1:80,000 or 1.7 ml buccal plus 0.25 ml palatally, with a latency duration of 8 minutes[22]. In a prior investigation conducted by Fan et al.[17], the process of removing upper teeth was described, both with and without the

administration of a local anesthetic called 4% articaine and 1:100,000 epinephrine, which was injected into the roof of the mouth. The pain evaluation conducted using a Visual Analogue Scale (VAS) did not reveal any notable difference between the injection techniques used, without the need for an additional palatal injection. Hence, the use of articaine as a local anesthetic agent helps prevent the pain and suffering associated with receiving a palatal injection[17].

However, a research done by Somuri et al. showed that using just articaine as a single infiltration buccally is more effective in providing anesthesia for extracting the maxillary premolars compared to using both buccal and palatal injections of lidocaine[22].

From the findings of this study, it was suggested and recommended that

- The choice between buccal infiltration alone and buccal and palatal infiltration should be based on individual patient factors. Consider the patient's anatomy, pain threshold, anxiety level, and any specific considerations that may affect anesthesia efficacy.
- The complexity of the maxillary upper first molar extraction should be considered. For straightforward extractions with minimal anatomical variations, buccal infiltration alone may be sufficient. However, for more challenging cases, such as impacted or multi-rooted molars, the addition of palatal infiltration may enhance anesthesia efficacy.
- The operator's level of experience and skill with each infiltration technique can influence efficacy. Familiarity with both buccal infiltrations alone and buccal and palatal infiltration techniques is essential for accurate administration and optimal results.
- Dental professionals should rely on their clinical judgment and experience when making decisions regarding the choice of infiltration technique.

Considering the above mentioned limitations, suggestions and the variations between the results of this study along with few others, it is recommended that additional research be conducted with a bigger sample size and improved methodology. It is also recommended that in order to reduce bias, data be collected in a multicenter context. In the end, a trained dental practitioner should decide which kind of infiltration to use based on their clinical judgement and assessment of the particular situation. To choose the best anesthetic method, they will take into account the patient's comfort level, the intricacy of the extraction, and the anatomy of the patient.

CONCLUSION

The results of this investigation allow us to draw the conclusion that, when it comes to the extraction of the maxillary first molar, both buccal alone and buccal plus palatal infiltrations are equally effective.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Haseeb Khalid Khan, Muhammad Asif Shahzad
Drafting or Revising Critically:	Shahzada Faiz Ahmad Khan, Wedad Sohail, Syeda Azka Aamer, Rushda Khalid
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Bataineh AB, Nusair YM, Al-Rahahleh RQ. Comparative study of articaine and lidocaine without palatal injection for maxillary teeth extraction. Clinical Oral Investigations 2019;23:3239-48.
2. Gholami M, Banihashemrad A, Mohammadzadeh A, Ahrari F. The efficacy of 4% articaine versus 2% lidocaine in inducing palatal anesthesia for tooth extraction in different maxillary regions. J Oral Maxillofacial Surg 2021;79(8):1643-9.
3. Majid OW, Ahmed AM. The anesthetic efficacy of articaine and lidocaine in equivalent doses as buccal and non-palatal infiltration for maxillary molar extraction: a randomized, double-blinded, placebo-controlled clinical trial. J Oral Maxillofacial Surg 2018;76(4):737-43.
4. Majid OW, Muhammad ZA. Effectiveness of Articaine Buccal infiltration anesthesia for mandibular premolar extraction: a randomized, double-blind, placebo-controlled clinical trial. J Oral Maxillofacial Surg 2019;77(9):1784-9.
5. Durrani F, Vishnu J, Taslim A, Imran F, Kumari E, Pandey A. Palatal bone block: A predictable bone augmentation technique for restricted maxillary defect. J Ind Society Periodontol 2023;27(5):530-5.
6. Cui L, Zhang Z, Huang J, Yin D, Xu L. Extraction of permanent maxillary teeth without palatal injection: a meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol 2018;126(4):e187-e95.
7. Khan S, Qazi S. Extraction of maxillary teeth by dental students without palatal infiltration of local anesthesia: a randomised controlled trial. Eur J Dental Educ 2017;21(4):e39-e42.
8. Ali W, Kazmi S, Mirza K, Chaudhry R, Yaseen S. Use Of Only Buccal Infiltration Of 2% Lidocaine

With Epinephrine For The Removal Of Maxillary Teeth. Biomed 2018;34(1):45.
9. Bataineh AB, Al-Sabri GA. Extraction of maxillary teeth using articaine without a palatal injection: a comparison between the anterior and posterior regions of the maxilla. J Oral Maxillofacial Surg 2017;75(1):87-91.
10. Liu Y, Shi L, Su L, van der Mei HC, Jutte PC, Ren Y, et al. Nanotechnology-based antimicrobials and delivery systems for biofilm-infection control. Chemical Society Reviews 2019;48(2):428-46.
11. Mörch C, Atsu S, Cai W, Li X, Madathil S, Liu X, et al. Artificial intelligence and ethics in dentistry: a scoping review. J Dent Res 2021;100(13):1452-60.
12. Zafar S, Siddiqi A, Yasir M, Zachar J. Pedagogical development in local anaesthetic training in paediatric dentistry using virtual reality simulator. Eur Archives Paediatr Dent 2021;22:667-74.
13. Wang YH, Wang DR, Liu JY, Pan J. Local anesthesia in oral and maxillofacial surgery: a review of current opinion. J Dent Sci 2021;16(4):1055-65.
14. Sandilya V, Andrade NN, Mathai PC, Aggarwal N, Sahu V, Nerurkar S. A randomized control trial comparing buccal infiltration of 4% articaine with buccal and palatal infiltration of 2% lignocaine for the extraction of maxillary premolar teeth. Contemporary Clin Dent 2019;10(2):284.
15. Alzahrani F, Duggal MS, Munyombwe T, Tahmassebi JF. Anaesthetic efficacy of 4% articaine and 2% lidocaine for extraction and pulpotomy of mandibular primary molars: an equivalence parallel prospective randomized controlled trial. Int J Paediatr Dent 2018;28(3): 335-44.
16. Martin E, Nimmo A, Lee A, Jennings E. Articaine in dentistry: an overview of the evidence and meta-analysis of the latest randomised controlled trials on articaine safety and efficacy compared to lidocaine for routine dental treatment. BDJ Open 2021;7(1):27.
17. Fan S, Chen Wl, Yang ZH, Huang ZQ. Comparison of the efficiencies of permanent maxillary tooth removal performed with single buccal infiltration versus routine buccal and palatal injection. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiol Endodontol 2009;107(3):359-63.
18. Chatterjee A, Gadicherla S, Roy S, Pentapati KC. Efficacy of Buccal Infiltration with or without Palatal Injection for Posterior Maxillary Teeth Extraction–A Split-Mouth Randomized Trial. Pesquisa Brasileira em Odontopediatria e Clínica Integrada 2023;23:e210215-e.
19. Iyengar A, Dugal A, Ramanojam S, Patil V, Limbhore M, Narla B, et al. Comparison of the buccal injection versus buccal and palatal injection for extraction of permanent maxillary posterior teeth using 4% articaine: a split mouth study. Br J Oral Maxillofac Surg 2021;59(3):281-5.
20. Kumar DP, Sharma M, Patil V, Subedar RS, Lakshmi GV, Manjunath NV. Anesthetic Efficacy of Single Buccal Infiltration of 4% Articaine and 2% Lignocaine in Extraction of Maxillary 1(st) Molar. Ann Maxillofac Surg 2019;9(2):239-46.
21. Sekhar GR, Nagaraju T, Nandagopal V, Sudheer R. Is palatal injection mandatory prior to extraction of permanent maxillary tooth: A preliminary study. Ind J Dent Res 2011;22(1):100.
22. Somuri AV, Rai AB, Pillai M. Extraction of permanent maxillary teeth by only buccal infiltration of articaine. J Maxillofac Oral Surg 2013;12:130-2..

Original Article

Association of PD-1 and PDL-1 Gene Polymorphisms in Type 2 Diabetes with Toxoplasmosis

Farah E. Mohammed[1], Ali N. Yaseen[2] and Muhammed A. H. Aldabagh[3]

ABSTRACT

Objective: To investigate the relationship between PD1 and PDL-1 gen polymorphisms with incidence toxoplasmosis in type 2 diabetes disease (T2DM).

Study Design: Case control study

Place and Duration of Study: This study was conducted at the Al-Iamamain Al-Kadhumain Teaching Hospital, Baghdad Iraq from 1st December 2018 to 30th April 2019.

Methods: One hundred and eighty patients with Type 2 diabetes mellitus (T2DM) aged 31-79 years, attending the diabetes were enrolled. A control group of 163 healthy subjects was also included. The PCR products of the SNPs were sequenced using the Big Dye Terminator method and compared to sequences in GenBank.

Results: Extracted DNA were used for molecular study for determination of the (PD-1.5 C/T rs 2227981) and the (PDL-1 G\C\A rs1970000) gene polymorphisms by conventional PCR method using specific primer. Sequencing of PCR products revealed three genotypes for the PD-1.5 C/T(CC, CT, TT). Regarding PD-1 showed no significant difference in each CT and CC genotypes between case and control groups while TT genotype showed significant difference between them. As well as related to PDL-1 showed significant difference between case and control while, CC showed non-significant between case and control groups. A allele significantly higher frequency in controls than cases. In contrast, C allele non-significantly higher frequency in cases than controls

Conclusion: There is a significant association between the phenotypic polymorphism of the (PD-1.5 C/T gene rs2227981) Toxoplasmosis and type 2 diabetes for the groups in the current study, as it was found that people who carry the genotype TT are more likely to develop type 2 diabetes than people who carry the genotype CC.

Key Words: PD-1, PDL-1, Polymorphisms, Toxoplasmosis, Type 2 Diabetes

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INTRODUCTION

Diabetes mellitus is a significant global health issue affecting 9% of adults, while Toxoplasma gondii, a protozoan parasite, infects about one-third of the population and is among the most effective human parasites. T. gondii is recognized by the CDC as a significant neglected parasitic infection due to its severity and prevalence, primarily transmitted through contaminated food, water, or soil, with cats being the only definitive hosts.[1-3]

Diabetic patients may be more vulnerable to T. gondii infection due to their weakened immune systems, and chronic toxoplasmosis could be a potential risk factor for type 2 diabetes.[4-6] The text discusses the relationship between (T2DM) and immune dysfunction, suggesting that T2DM may resemble a chronic infection and highlighting the need for further research on its impact on infections like toxoplasmosis, particularly in regions like Iraq and the Middle East.[7-9]

Programmed death-1 (PD-1) is a co-inhibitory receptor that plays a crucial role in regulating T lymphocyte activity and promoting immune tolerance, which can allow tumor cells to evade the immune system. This study focuses on the relationship between PD-1 and PD-L1 polymorphisms and their potential impact on susceptibility to type 2 diabetes (T2DM) and toxoplasmosis. Specifically, it examines two single nucleotide polymorphisms (SNPs): PD-1 rs2227981 C > T and PD-L1 rs1970000 G/C/A, as no prior research has explored this correlation in the context of these conditions.

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METHODS

180 patients (ages 31 to 79) with Type 2 diabetes mellitus (T2DM) who visited the diabetes division at the Al-Iamamain Al-Kadhumain Teaching Hospital in Baghdad, Iraq, between December 2018 and April 2019 were included in this study. Venous blood samples of five ml were collected from patients and healthy individuals at a time of clinical diagnosis and (ELISA and molecular diagnosis) were performed as described in the following sections; all samples divided in two tubes 3 ml of the blood used for immunological diagnosis (ELISA)and 2 ml blood which placed in sterilized EDTA tube for molecular diagnosis.

ELISA T. gondi–IgG: Using ELISA kits supported by the Bioactiva Company in Germany, the sera of all samples (control and patient) were tested for the presence of specific IgG antibodies of Toxoplasma gondii and the test was connected in accordance with the manufacturer's instructions.

Genomic DNA isolation from whole blood: Using a commercial blood DNA purification system (AccuPrep® Genomic DNA Extraction Kit, Bioneer, Korea), genomic DNA was extracted from whole blood samples of the study groups in accordance with the manufacturer's instructions. This was done in order to magnify the (PD-1. Gene polymorphisms: 5 C/T (rs 2227981) and (PDL 1G\C\A) (rs1970000) using a conventional PCR method using a specific primer (Table 1) and green master mix (Promega). The PCR conditions used (Table 2).

The Big Dye Terminator method [Macrogen, Korea] was used to directly sequence all of the PCR products of the SNPs under study. The obtained sequences were compared to the standard Gen Bank sequences.

All statistical analyses were conducted utilizing SPSS-24. P value ≤0.05 was accepted as significant. Diverse genotypes from Hardy-Weinberg Equilibrium (HWE) were employed, and the association between the diverse genotypes and alleles of polymorphisms with the risk of PD-1.5 and PDL-1 was surveyed by calculating the odds ratio (OR) and comparing 95% CI using binary logistic regression.

RESULTS

Table No. 1: SNPs with specific primers

Genes	SNP	Location	Primers (5`- 3`)	PCR Products
PD-1	C/T (rs 2227981)	Exon 5	AGACGGAGTATGCCACCATT CACTGTGGGCATTGAGACAT	333bp
PDL-1	G\C\A (rs1970000)	Intron 4	AATGGCTTGTTGTCCAGAGATG GTACCACATGGAGTGGCTGC	553bp

Table NO. 2: PCR Condition of PD1 and PDL-1

Step	Temperature (c°)		Time		No. of cycles	
	PD1	PDL-1	PD1	PDL-1	PD1	PDL-1
Initial Denaturation	95	95	3 min	10 min	1	1
Denaturation	95	60	15 sec	30 sec	35	37
Annealing	64	72	30 sec	3 min	-	-
Extension	72	95	15 sec	30 sec	-	-
Final extension	72	72	10 min	10 min	1	1

There were 117 (34%) specimens of sera participants have been founded Type 2 diabetes mellitus with toxoplasmosis (T2DMT), 63 (18%) samples have Type 2 diabetes mellitus (T2DM), 55(16%) cases have positive control group (PC) and 108 samples (32 %) were regarded as negative control group (NC) without any infections (Table 3). Gel electrophoresis of PD-1.5 C/T and PDL-1 G\C\A polymorphism PCR product is shown in (Figs 1-2). The fragment length was 333 bp and 553pb sequencing of PCR product revealed three genotypes for the PD-1.5 C/T and PDL-1 G\C\A polymorphism in individuals and healthy subjects (Figs.3-4). The distribution of different genotypes of PD1.5 C/T polymorphism in participants and controls was in a good agreement with HWE.

the table 4 displays an analysis of genotyping and allele frequency between non-diabetic individuals (NC) and Type 2 Diabetic Mellitus (T2DM) patients. The CT genotype was more prevalent in the NC group, while the TT genotype was significantly less frequent. There was no discernible difference in the CC genotype between the two groups. At the allelic level, the T allele was more common among T2DM patients, indicating a significant difference, while the C allele was more frequent in the NC group, though this difference was not significant. In the T2DMT andT2DM groups, The CT genotype was more common in T2DMT patients, while the TT genotype was significantly less common. The CC genotype showed no significant difference between the two groups. Notably, the T allele was more prevalent in diabetic patients than in those with both diabetes and T2DMT, indicating a substantial genetic disparity. However, the C allele frequency did not show a significant difference, suggesting complex interactions between diabetes and T2DMT. In the T2DMT and PC group, In the PC group, the CT

genotype was marginally more common., while the T allele was more common in T2DMT patients. However, none of the observed differences were statistically significant. The study concluded that both groups exhibit similar genetic characteristics, as indicated by various markers, with p-values suggesting no substantial differences in allele frequencies. The CT, TT, and CC genes had the same frequency in both the PC and NC groups (67%, 8%, and 25%) and there was no significant difference between them (P=0.748, 0849, and 0679).The T allele was found at the same frequency in PC and NC, with no significant difference. Also, the frequency of the C allele was equal in the PC and NC groups at 58%, with no significant difference.

The analysis focuses on the frequency of genetic types in non-diabetic controls (NC) and type 2 diabetes mellitus (T2DM) patients(Table 5). The AA genotype is significantly more prevalent in the NC group, while the AC genotype is more common in T2DM patients. The study also shows that the A allele occurs more frequently in NC individuals compared to T2DM patients, indicating a potential association with diabetes risk. Conversely, the C allele is more prevalent among T2DM patients, although the difference is not statistically significant. Overall, the findings highlight important genetic variations linked to diabetes. The AC genotype was more prevalent in T2DMT patients (66%) compared to T2DM patients (33%), However, there was no statistically significant change. The CC genotype was less common in T2DMT (17%) compared to T2DM (50%), also lacking significance. The AA genotype was equally present in both groups (17%). At the allelic level, the A allele was more frequent in T2DMT (50% vs. 33%), while the C allele was more common in T2DM (67% vs. 50%), with the latter showing a statistically significant difference. This research explores the distribution of genotypes AC, CC, and AA among patients with T2DMT compared to a control group. The findings indicate that while the AC genotype was more frequent in T2DMT patients (66%) than in controls (50%), The CC genotype did not significantly differ between the two groups. Similarly, the CC genotype was slightly more prevalent in T2DMT patients (17%) than controls (12%), but again, not significantly. The AA genotype was more common in the control group (38%) compared to T2DMT patients (17%), nearing significance. Overall, no significant allelic differences were found. In PC and NC groups no significant no significant variations in genotype and allele frequencies between the regarding recurrence rates.in genotype and allele frequencies between the regarding recurrence rates.

Table No. 3: Levels of IgG antibodies (IU/ml) for all study groups

Groups	(No. of Samples)	(%)	(Mean ± SD)	(Confidence Interval for Mean)	
				Lower Bound	Upper Bound
Type 2 diabetes mellitus with Toxoplasmosis (T2DMT)	117/180	65.0	22.9±6.42	21.71	24.06
Type 2 diabetes mellitus (T2DM)	63/180	35.0	5.5±1.51	5.17	5.93
Positive control (PC)	55/163	16.0	14.3±8.73	11.90	16.62
Negative control (NC)	108/163	32.	3.0±1.98	2.64	3.39

Table No. 4: Genotypes and alleles of PD-1.5 rs2227981 C/T single nucleotide polymorphism in patients with Type 2 diabetes mellitus and Toxoplasmosis and controls

	T2DM	NC	P value	OR	CI
CC	6 (25%)	6 (25%)	0.083	1.0	Reference
CT	9 (37.5%)	16 (67%)	0.59	6.0	0.932-38.629
TT	9 (37.5%)	2 (8%)	0.029	7.0	1.221-40.124
Allele					
T	27 (57%)	20 (43%)	0.002	0.125	0.032-0.485
C	21 (43%)	28 (57%)	0.322	0.563	0.179-1.765
	T2DMT	T2DM	P value	OR	CI
CC	3 (25%)	3 (25%)	0.087	1.0	Reference
CT	7 (58%)	2 (17%)	0.274	0.286	0.030-2.692
TT	2 (17%)	7 (58%)	0.027	0.082	0.009-0.753
Allele					
T	11 (46%)	16 (67%)	0.006	12.250	1.788-83.946
C	13 (54%)	8 (33%)	0.195	3.50	0.505-24.270
	T2DMT	PC	P value	OR	CI
CC	3 (25%)	3 (25%)	0.642	1.0	Reference
CT	9 (58%)	8 (67%)	0.398	3.333	0.204-54.532

TT	2 (17%)	1 (8%)	0.689	1.714	0.123-54.532
Allele					
T	11 (52%)	10 (48%)	0.407	0.438	0.061-3.160
C	13 (48%)	14 (52%)	0.863	0.875	0.191-3.999
	PC	NC	P value	OR	CI
CC	3 (25%)	3 (25%)	0.679	1.0	Reference
CT	8 (67%)	8 (67%)	0.748	0.60	0.027-13.582
TT	1 (8%)	1 (8%)	0.848	1.333	0.069-25.912
Allele					
T	10 (42%)	10 (42%)	1.0	1.0	0.112-8.947
C	14 (58%)	14 (58%)	1.0	1.0	0.224-4.468

Table 5: Genotypes and alleles of PDL-1 rs1970000 G\C\A single nucleotide polymorphism in patients with Type 2 diabetes mellitus and Toxoplasmosis and controls

	T2DM	**NC**	**P value**	**OR**	**CI**
AA	4 (17%)	9 (56%)	0.040	1.0	Reference
AC	12 (50%)	5 (31%)	0.027	9.0	1.285-63.025
CC	8 (33%)	2 (13%)	0.592	1.667	0.257-10.792
Allele					
A	20 (42%)	23 (72%)	0.010	5.40	1.421-20.518
C	28 (56%)	9 (28%)	0.506	0.60	0.132-2.724
	T2DMT	T2DM	P value	OR	CI
AA	2 (17%)	2 (17%)	0.214	1.0	Reference
AC	8 (66%)	4 (33%)	0.395	0.333	0.027-4.186
CC	2 (17%)	6 (50%)	0.079	0.167	1.153-31.228
Allele					
A	12 (50%)	8 (33%)	0.456	2.0	0.320-12.510
C	12 (50%)	15 (67%)	0.027	6.0	1.153-31.228
	T2DMT	PC	P value	OR	CI
AA	2 (17%)	3 (38%)	0.054	1.0	Reference
AC	8 (66%)	4 (50%)	0.224	6.0	0.335-107.420
CC	2 (17%)	1 (12%)	0.392	0.250	0.010-5.985
Allele					
A	12 (50%)	10 (62.5%)	0.211	3.0	0.525-15.159
C	12 (50%)	6 (37.5%)	1.0	1.0	0.125-7.995
	PC	NC	P value	OR	CI
AA	3 (38%)	6 (76%)	0.290	1.0	Reference
AC	4 (50%)	1 (12%)	0.661	2.0	0.090-44.350
CC	1 (12%)	1 (12%)	0.442	0.250	0.007-8.560
Allele					
A	10 (52.5%)	13 (81%)	0.063	8.0	0.725-88.23
C	6 (37.5%)	3 (19%)	0.343	4.0	0.211-75.66

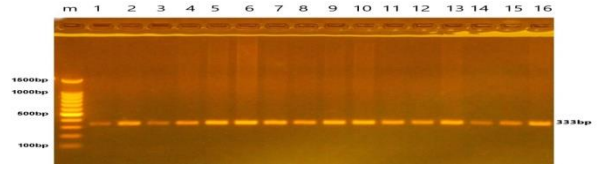

Figure No. 1: Electrophoresis of acarose gel (2%), 75 volts for two hours, which shows the results of a reaction test. Conventional polymerase chain reaction enzyme (PD-1) (333 bp) for all study groups for a specific fraction and size

M: L(100-2000bp). *4-1 Group of patients with type 2 diabetes and toxoplasmosis gondii (T2DMT). *8-5 Group of patients with type 2 diabetes only (T2DM). *12-9 Positive control group (PC). *13-16 negative control group (NC).

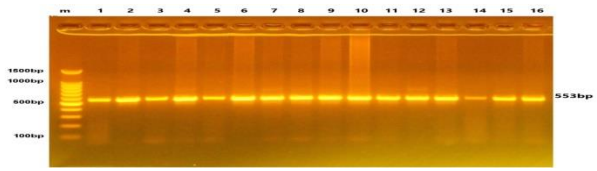

Figure No. 2: Electrophoresis of acarose gel (2%), 75 volts for two hours, which shows the results of a reaction test. Conventional polymerase chain reaction enzyme (PDL-1) (553 bp) for all study groups for a specific fraction and size

M: L(100-2000bp) . *4-1 Group of patients with type 2 diabetes and toxoplasmosis gondii (T2DMT). *8-5 Group of patients with type 2 diabetes only (T2DM). *12-9 Positive control group(PC). *13-16 negative control group(NC).

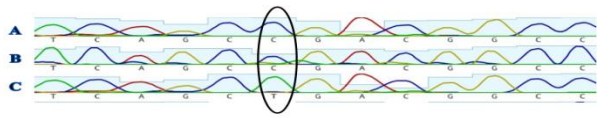

Figure No. 3: Chromatograph of DNA sequencing for PD-1.5 C/T polymorphism. A: wild-type homozygous genotype (CC), B: Heterozygous genotype (CT), C: mutant homozygous genotype (TT)

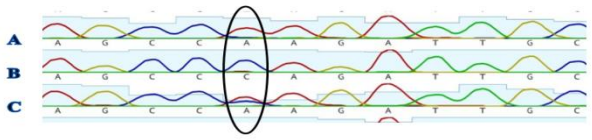

Figure No. 4: Chromatograph of DNA sequencing for PDL-1 G\C\A polymorphism. A: wild-type homozygous genotype (AA), B: mutant homozygous genotype (CC), C: Heterozygous genotype (AC)

DISCUSSION

Studies investigating the connection between toxoplasmosis and type 2 diabetes and the PD1.5 gene variation at rs2227981 are not yet accessible, therefore, the results of the current study were compared with similar studies on the same gene and mutation. The current study's findings were discovered to be nearly identical to those of a study carried out by Hashim[10]. where the frequency of the T allele (41.25%) in patients with cutaneous leishmaniasis was higher than its frequency (26.5%) in healthy individuals. In the current investigation, there was a noteworthy correlation between TT genotypes and allele T were both higher significantly in type 2 diabetes patient and control of PD-1.5 SNP.

Almost similar results were obtained by Hou[11], who found that there is a significant association of PD-1.5 with chronic HBV where the frequency of PD-1.5 TT genotype and allele T were both significantly higher in spontaneously recovered group than chronic HBV infection group.

In another study conducted by Sarvari et al[12], significant differences were found in the genetic patterns and alleles between a group of patients suffering from chronic Hepatitis C virus (HCV) compared to a matched group of recovered individuals and a healthy control group. Mojtahedi et al[13] demonstrated an association between the C/T PD-1.5 polymorphism and the development of colon cancer among the Iranian population. Conversely, The PD-1.5 polymorphism was not linked to breast cancer, according to a study by Haghshenas et al[14].

On the other hand, the present study was designed to assess the possible association of PDL-1SNPs with T2DM and toxoplasmosis. According to the result of sequencing revealed there was significant association between AC genotypes and allele A were both higher significantly in T2DM patient and control of PDL-1, revealed there was significant association between CC genotypes and allele C were both higher significantly in T2DMT and T2DM. There are no available studies on the role of the PDL-1 gene variant rs1970000 in Behcet's disease on one hand and Type 2 diabetes on the other hand. A single study conducted by Meng et al[15] investigated this variant in a chronic autoimmune disease, Behcet's Disease, and the results of this study showed no association between the PDL-1 gene variant and Behcet's Disease among the Han Chinese population..

CONCLUSION

There is a significant association between the phenotypic polymorphism of the (PD-1.5 C/T gene rs2227981) Toxoplasmosis and type 2 diabetes for the groups in the current study, as it was found that people who carry the genotype TT they are more likely to develop type 2 diabetes than people who carry the genotype CC.

Author's Contribution:

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Drafting or Revising Critically:	Ali N. Yaseen, Muhammed A. H. Aldabagh
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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REFERENCES

1. Halonen SK, Weiss LM. Toxoplasmosis. In: Garcia HH, Tanowitz HB, Del Brutto OH, editors. Handbook of clinical neurology. 3rd ed. Amsterda: Elsevier; 2013.p.125-45.
2. Molan A, Nosaka K, Hunter M, Wang W. The association between Toxoplasma gondii and type 2 diabetes mellitus: a systematic review and meta-analysis of human case-control studies. Bull Nat Res Centre 2020;44(1):7.

3. Dupey JP. The history of Toxoplasma gondii – the first 100 years. J Eukaryot Microbiol 2008;55: 467-75.
4. Molan A, Nosaka K, Hunter M, Wang W. The role of Toxoplasma gondii as a possible inflammatory agent in the pathogenesis of type 2 diabetes mellitus in humans. Fam Med Community Health 2016;4(4):44 62.
5. Majidiani H, Dalvand S, Daryani A, Galvan-Ramirez ML, Foroutan-Rad M. Is chronic toxoplasmosis a risk factor for diabetes mellitus? A systematic review and meta-analysis of case-control studies. Brazilian J Infec Dis 2016;20(6):605-9.
6. Li YX, Xin H, Zhang XY, Wei CY, Duan YH, Wang HF, Niu HT. Toxoplasma gondii Infection in Diabetes Mellitus Patients in China: Seroprevalence, Risk Factors, and Case-Control Studies. Bio Med Res Int 2018; 2018:4723739.
7. Shu CJ, Benoist C, Mathis D. The immune system's involvement in obesity-driven type 2 diabetes. Seminars Immunol 2012;24(6): 436-42.
8. Molan AL, Ismail MH. Study the possible association between toxoplasmosis and diabetes mellitus in IRAQ. World J Pharma Pharmaceutical Scien 2016; 6(3): 85-96.
9. Li Y, Xiao Y, Su M, Zhang R, Ding J, Hao X, Ma Y. Role of soluble programmed death-1 (sPD-1) and sPD-ligand 1 in patients with cystic echinococcosis. Experimental Therapeutic Med 2016;11(1):251-6.
10. Hashim SM. The association of programmed celldeath -1 (PD-1) gene polymorphism with serum soluble PD-1protein and Interleukin-2 (IL-2) in patients with cutaneous leishmaniasis: [Thesis] College of Medicin-Al-Nahrain Univ 2019;11-49.
11. Hou Z, Zhou Q, Lu M, Tan D, Xu X. A Programmed Cell Death-1 Haplotype is Associated with Clearance of Hepatitis B Virus. Ann Clin Lab Sci 2017;47(3): 334-43.
12. Sarvari J, Dowran R, Hosseini SY, Fattahi MR, Erfani N. Association of PD-1 gene with outcome of hepatitis C virus infection. EXCLI J 2018;17:935-44.
13. Mojtahedi Z, Mohmedi M, Rahimifar S, Erfani N, Hosseini SV, Ghaderi A. Programmed death-1 gene polymorphism (PD-1.5 C/T) is associated with colon cancer. Gene 2012;508(2): 229-32.
14. Haghshenas MR, Naeimi S, Talei A, Ghaderi A, Erfani N. Program death 1 (PD1) haplotyping in patients with breast carcinoma. Molecular Biol Reports 2011;38(6), 4205-10.
15. Meng Q, Guo H, Hou S, Jiang Z, Kijlstra A, Yang P. Lack of an association of PD-1 and its ligand genes with Behcet's disease in a Chinese Han population. PloS One 2011; 6(10): e25345.

Original Article

Frequency of Postnatal Depression among Patients in the Obstetrics and Gynaecology Department at a Tertiary Care Hospital

Postnatal Depression and Risk Factors Among Female Patients

Simone Rehan, Shadia Shah, Waleed Ahmad, Ayesha Saif, Nabiha Iqbal and Nabeela Shami

ABSTRACT

Objective: To identify the percentage of postnatal depression and risk factors related to the condition among female patients.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynaecology at Lahore Medical Dental College/Ghurki Trust & Teaching Hospital, Lahore from 28th July 2021 to 27th January 2022.

Methods: Three hundred and sixty-nine postpartum women within six weeks of delivery, using the Edinburgh Postnatal Depression Scale to identify depressive symptoms were enrolled. An Edinburgh Postnatal Depression Scale score of 10 or higher indicated postnatal depression.

Results: Mean age of patients was 30.60±4.34 years. Postnatal depression prevalence of 3.25% and mean Edinburgh Postnatal Depression Scale score was 6.78±4.33. Notably, 5.88% of mothers with male infants experienced postnatal depression compared to 1.39% with female infants (p = 0.017). Additionally, postnatal depression was frequent in cesarean section patients (5.88% vs. 1.01%, p = 0.009) and among those without social (6.67% vs 0.91%, p = 0.002) and partner support (4.40% without vs. 0% with, p=0.037). Unintended pregnancies had a higher association with postnatal depression (8.33% vs. 1.15%, p=0.0004), and those earning above 40,000 had increased depression rates (9.41%, p=0.001).

Conclusion: There is a need for mental health screening and support services to mitigate the adverse effects on maternal and child well-being.

Key Words: Postnatal depression, Obstetrics, Tertiary care, Edinburgh Postnatal Depression Scale (EPDS), Mental health

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INTRODUCTION

Post-natal depression (PND) is the prevalent pathological condition associated with early motherhood. It has become a significant concern from both psychological and public health perspectives for the mother, her baby and the entire family.[1] In the postnatal period, there are physical and psychological stresses which may lead to debility due to PND, which may affect the ability of the woman to be a mother, for instance, being able to care for the newborn baby. Sometimes, the woman's response may be limited or negative towards the child.[2] If a woman receives no diagnosis and treatment for PND, then she will possibly find it hard to engage in appropriate interaction, which can impair her family and other social relations[3].These problems may interfere with maternal-infant relations, and there is a likelihood that they may result in poor child cognitive, behavioural, and social development. It has also been established that the spouses of women with PND are more likely to experience issues with their mental health.[4]

This is because methods used to determine the prevalence rates of PND vary or because cultural beliefs influence women's disclosure of their symptoms.[5] The percentage of post-natal depression ranged between 8-50% in a local study, and post-natal depression was 17.3%.[6]In another study, the estimates of worldwide postpartum depression rate were 15.6%.[7]

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The screening tool, study design, and sample size used in these investigations may be responsible for the greater number of cases reported in these investigations. The same review has indicated that the level of maternal PND was found to be ranging between 4.0% and 63.9%.[8]

According to Karachi-based research, the frequency of depression among working mothers was 64.4%, while among stay-at-home mothers was 19.2%.[9] Common contributing factors in Pakistani women are economic deprivation, poor relationship with the husband, female infant gender, increased number of children, and illiteracy.

Researcher reported that treatment update on reproductive Psychiatry, "During pregnancy, depressive symptoms like changes in sleep and appetite are rarely easy to differentiate from those occasions that are normal during pregnancy". Depression is not constant during pregnancy; most of the studies indicate that women experience the highest level of symptoms during the first trimester, reduced in the second trimester, and then exacerbated in the third trimester.[10]

The screening and intervention programmes for these susceptible categories of women should be carried out during the antenatal and early postpartum period to address the issue.[11] The purpose of this study was to analyse the frequency of postnatal depression in patients attending the Obstetrics and Gynaecology facility of a tertiary health care centre to develop a local database. Pakistani population is different socially, economically, and culturally from the Western population, so different results are expected for these contributing factors for postpartum depression.

METHODS

This descriptive, cross-sectional study was conducted in the Department of Obstetrics &Gynaecology at LMDC/GTTH from 28th July 2021 to 27th January 2022 following the ethical review board's clearance. A total of 369 women were enrolled. Sample size was estimated using the WHO sample size calculator for a population of women of childbearing age, with a 95% confidence interval and a 2% margin of error from anticipated estimate of a 4% prevalence rate of postnatal depression.[12] The postpartum women attending routine checkups in the obstetrics unit, aged 18 to 40 years and both primiparous and multiparous women were included. The history of depression after previous pregnancies or otherwise, current psychotherapy for depression, a history of mood or psychotic disorders or anxiety prior to pregnancy, use of anti-psychotic medication, and any history of drug or substance addiction were excluded. Each participant was assessed for postnatal depression as a form of depression occurring within six weeks after childbirth, identified by an Edinburgh Postnatal Depression Scale (EPDS) score above 9, where the total score ranges from 0 to 30. Statistical analysis was done utilising SPSS-25.0. To control effect modifiers like age, parity, and other demographic factors, stratification was applied. The Chi-square test was used to examine the effect on frequency of postnatal depression, with a significance level set at $p \leq 0.05$.

RESULTS

The mean age of patients was 30.60±4.34 years. Regarding parity, 81.84% were multiparous while 18.16% were primiparous. The gender of babies born was slightly skewed, with 58.54% female and 41.46% male. Vaginal deliveries 53.93% were slightly more common than cesarean sections 46.07%. A considerable proportion of participants 68.29% were homemakers and 31.71% were employed. Monthly income levels varied, with 17.07% earning less than 20,000, 59.89% earning between 20,000 and 40,000, and 23.04% earning above 40,000. Educational levels among the participants showed that over half (52.30%) were graduates, while 28.18% had completed secondary education, 11.92% had primary-level education, and 7.59% were illiterate. Social support was available for 59.35% of participants, while 40.65% reported having no social support. Notably, 73.77% did not have partner support, whereas only 26.23% reported receiving support from their partners. Regarding pregnancy intention, 29.27% of the pregnancies were unintended, while 70.73% were planned. The mean EPDS (Edinburgh Postnatal Depression Scale) score was 6.78±4.33, and postnatal depression was observed in 3.25% (12) of the women (Fig. 1).

The postnatal depression was observed in 1.88% of women aged 18-30 and 4.31% of those aged 31-40. However, they had no statistically significant difference (p=0.192). Parity did not significantly impact postnatal depression with rates of 1.49% in primiparous and 3.64% in multiparous women (p=0.369). The gender of the baby showed an important association with postnatal depression: 5.88% of mothers with male babies experienced postnatal depression compared to 1.39% of those with female babies (p=0.017). Mode of delivery also showed a significant association, as 5.88% of those with caesarean sections reported depression, compared to only 1.01% of those with spontaneous vaginal delivery (p=0.009). Social support was strongly associated with postnatal depression, as only 0.91% of those with social support experienced depression, compared to 6.67% of those without social support (p=0.002). Partner support was similarly significant, with no cases of depression among those with partner support, while 4.40% of those without it experienced depression (p=0.037). Unintended pregnancy was a notable factor, with an 8.33% depression rate among those with unintended pregnancies, compared to only 1.15% for

those with intended pregnancies (p=0.0004). Occupation was also significant; housewives had a depression rate of 1.19%, whereas 7.69% of working women reported depression (p=0.001). Monthly income showed a clear association, as postnatal depression was reported in 1.59% of those earning less than 20,000, 1.36% of those in the 20,000-40,000 range, and a higher rate of 9.41% among those earning above 40,000 (p=0.001). Education level, however, did not have a statistically significant association with postnatal depression, with rates between 2.27% and 3.63% across various education levels (p=0.965) [Table 1].

Table No. 1: Stratification of postnatal depression with respect to demographic and clinical profile of patients

Variable		Postnatal Depression		P value
		Yes	No	
Age (years)	18-30	03 (1.88%)	157 (98.12%)	0192
	31-40	09 (4.31%)	200 (95.69%)	
Parity	Primiparous	1 (1.49%)	66 (98.51%)	0.369
	Multiparous	11 (3.64%)	291 (96.36%)	
Gender of baby	Male	9 (5.88%)	144 (94.12%)	0.017
	Female	3 (1.39%)	213 (98.61%)	
Mode of delivery	SVD	2 (1.01%)	197 (98.99%)	0.009
	CS	10 (5.88%)	160 (94.12%)	
Social support	Yes	2 (0.91%)	217 (99.09%)	0.002
	No	10 (6.67%)	140 (93.33%)	
Partner support	Yes	-	96 (100.0%)	0.37
	No	12 (4.40%)	261 (95.60%)	
Unintended pregnancy	Yes	9 (8.33%)	99 (91.67%)	0.0004
	No	3 (1.15%)	258 (98.85%)	
Occupation	Housewife	3 (1.19%)	249 (98.81%)	0.001
	Working	9 (7.69%)	108 (92.31%)	
Monthly income	<20000	1 (1.59%)	62 (98.41%)	0.001
	20k-40k	3 (1.36%)	218 (98.64%)	
	>40000	8 (9.41%)	77 (90.59%)	
Education	Illiterate	1 (3.57%)	27 (96.43%)	0.965
	Primary	1 (2.27%)	43 (97.73%)	
	Secondary	3 (2.88%)	101 (97.12%)	
	Graduate	7 (3.63%)	186 (96.37%)	

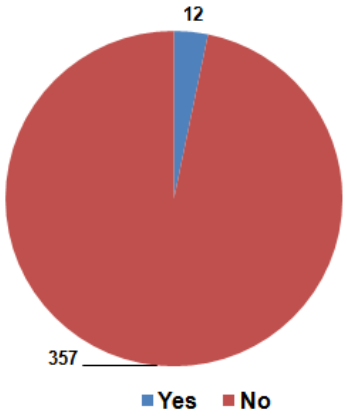

Figure No. 1: Frequency of postnatal depression in patients

DISCUSSION

Postpartum depression (PPD) is an affective disorder affecting 10–15% of women annually during early motherhood. In 25–50% of cases, depressive symptoms persist for more than six months. Postpartum depression is usually experienced within several months up to a year after the birth of the child. Possible causes of PPD include physiological factors, situational factors, or both.[10]

Predisposing factors of PPD are primarily social, in most cases, it is associated with stressful life events, childcare stress, and prenatal anxiety that may predict PPD. However, other factors can also contribute to the prediction, which includes the background of the prior episode of PPD, marital conflict, and single parenthood.[13] The misconception that PPD affected only women from Western societies and that postnatal mood disorders were culture-bound prevailed for a long time.[11] Women in Asia and South Africa are pointed out as being vulnerable to experiencing such issues. The symptoms are also usually like the symptoms of depression at other stages of life. However, alongside perinatal depression, women with PPD include guilt for not being able to care for a new baby among the symptoms they experience, and they demonstrate low mood, sleep disturbance, change in appetite, variation

in mood during the day, poor concentration, and irritability.[14] Around 80% of women experience mild, short-lived mood changes (postpartum blues) after childbirth, while 10–15% face a more severe and prolonged mood disturbance.[12]

The treatment and discovery of PPD have been a challenge due to the different criteria used regarding the time of onset in the DSM-IV and other standardised studies[15]. Mothers often hide their depression due to fear of discrimination and being labelled as bad mothers.[16]

In the present study, number of cases of PND was determined to be 3.25%. The frequency of postpartum depression in a local study conducted was 17.3%.[7] In another study, the overall frequency of postpartum depression was found to be 15.6%.[8] The review has revealed that the global incidence rate of maternal PND was from 4-63.9%.[12] Among the women in Andhra Pradesh resulted in a prevalence of 31.4, that the majority of women fall between the age of 21-25 years.[17] Other research carried out in Goa, Mangalore, and Delhi revealed that the prevalence rate was at 22%,31.44% and 24%, respectively.[13-15]

Some other local research work done in Pakistan pointed high prevalence of postnatal depression (30-40%).[16,17] Recent studies from Turkey suggest that psychosocial adversity increases the risk of first postpartum mood disorders. Over 30% of the women in the study had postpartum depression.[18]

Villegas et al[18] discovered that among rural women in developing nations, the prevalence of postpartum depression is 31%. Yet meta-synthesis provides figures which show that in Asian countries, the rate of PPD was between 3.5% (Malaysia) and 63.3% (Pakistan).[20] There was a cross-sectional study in a group of women from rural South India, where the prevalence of PPD was estimated to be 11%.

Several modifiable and non-modifiable factors have been identified, as reported in the study by Gross et al[19], and they include partner-related stress, physical violence during pregnancy, and failure to breastfeed. In a study carried out in Lebanon, the authors described the overall prevalence of PPD to be 21%. The results also suggested that perceived social support and prenatal depression were independently predictive of PPD. The independent variables concerning postnatal depression highlighted by Sierra Manzano et al[22], included the age of the mother, the economic status of either poor or very poor, a personal history of subjected disturbed mind, if the mother had been anaesthetised in her labour and family dysfunctions.

In another study, the most definitive predictors of PPD were pregnancy-related illnesses and frequent prenatal healthcare visits. Hyperemesis, premature contractions, and psychiatric disorders were all statistically significantly higher in postpartum depressed women compared to women without such symptoms.[23]

In one cohort of Israeli women, immigration status emerged as the strongest predictor of PPD. The concept that stressful life experiences contribute to the emergence of PPD reveals that insufficient social support, marital conflict, depressive symptoms during pregnancy, history of prior emotional disorders, and lengthy periods of newborn illness are the major determinants of PPD.

Therefore, it is recommended that proper evaluation of postpartum depression should be done so that proper counselling and psychotherapy of these patients can be done to improve their quality of life and reduce morbidity.

CONCLUSION

There is a need for mental health screening and support services to mitigate the adverse effects on maternal and child well-being.

Author's Contribution:

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Drafting or Revising Critically:	Waleed Ahmad, Ayesha Saif, Nabiha Iqbal, Nabeela Shami
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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REFERENCES

1. Shenoy HT, Remash K, Shenoy ST. Prevalence and determinants of postnatal depression in a tertiary care teaching institute in Kerala, India. Int J Reprod Contracept Obstet Gynecol 2019;8:3757-64.
2. Silverman ME, Reichenberg A, Savitz DA, Cnattingius S, Lichtenstein P, Hultman CM, et al. The risk factors for postpartum depression: a population-based study. Depress Anxiety 2017; 34(2):178-87.
3. Roumieh M, Bashour H, Kharouf M, Chaikha S. Prevalence and risk factors for postpartum depression among women seen at Primary Health Care Centres in Damascus. BMC Pregnancy Childbirth 2019; 19:519.
4. Shewangzaw A, Tadesse B, Ashani T, Misgana T, Shewasinad S. Prevalence of postpartum depression and associated factors among postnatal women attending at Hiwot Fana Specialized University hospital, Harar, East Ethiopia,

2015/2016. J Reprod Syst Sexual Disord 2018;1(1):4–19.
5. Shah S, Lonergan B. Frequency of postpartum depression and its association with breastfeeding: a cross-sectional survey at immunization clinics in Islamabad, Pakistan. J Pak Med Assoc 2017; 67:1151-56.
6. Wubetu AB, Engidaw NA, Gizachew KD. Prevalence of postpartum depression and associated factors among postnatal care attendees in Debre Berhan, Ethiopia, 2018. BMC Pregnancy Childbirth 2020;20:189.
7. Arifin SRM, Cheyne H, Maxwell M. Review of the prevalence of postnatal depression across cultures. AIMS Public Health 2018;5(3):260-95.
8. Ramji RS, Noori MY, Faisal A. Postpartum depression among working and nonworking mothers/women in Karachi, Pakistan. Manager's J Nurs 2016;6(3):5.
9. Aliani R, Khuwaja B. Epidemiology of postpartum depression in Pakistan: a review of literature. Nat J Health Sci 2017; 2:24-30.
10. Beck CT, Records K, Rice M. Further development of the postpartum depression predictors inventory-revised. J Obstet Gynecol Neonatal Nurs 2006; 35(6):735-45.
11. Bina R. The impact of cultural factors on postpartum depression: a literature review. Health Care Women Int 2008;29(6):568-92.
12. Patel V, Rodrigues M, DeSouza M. Gender, poverty, and postnatal depression: a study of mothers in Goa, India. Ame J Psychiatr 2002;159:43-7.
13. Shivalli S, Gururaj N. Postnatal Depression among rural women in South India: do socio-demographic, obstetric and pregnancy outcome have a role to play? PLoS ONE 2015;10(4):1-11.
14. Dhande N, Khapre M, Nayak S, Mundey A. Assessment of postnatal depression among mothers following delivery in rural area of Wardha district: a cross sectional study. Innovative J Med Health Sci 2014; 4:53-5.
15. Kalyani GHS, Saeed K, Ijaz-ur-Rehman C, Mubbashar MH. Incidence of depressive illness in Pakistani women during postnatal period. J Coll Physicians Surg Pak 2001; 11:246-8.
16. Rahman A, Creed F. Outcome of prenatal depression and risk factors associated with persistence in the first postnatal year: prospective study from Rawalpindi, Pakistan. J Affect Disord 2007; 100:115-21.
17. Aydin N, Inandi T, Karabulut N. Depression and associated risk factors among women within their first postnatal year in Erzurum province in Eastern Turkey. Women Health 2005; 41:1-12.
18. Villegas L, McKay K, Dennis CL, Ross LE. Postpartum depression among rural women from developed and developing countries: a systematic review. J Rural Health 2011; 27:278-88.
19. Gross KH, Wells CS, Radigan-Garcia A, Dietz PM. Correlates of self-reports of being very depressed in the months after delivery: results from the Pregnancy Risk Assessment Monitoring System. Matern Child Health J 2002;6(4):247-53.
20. Sierra Manzano JM, Carro Garcia T, Ladron Moreno E. Variables associated with the risk of postpartum depression. Edinburgh Postnatal Depression Scale. Aten Primaria 2002;30(2): 103-11.
21. Josefsson A, Angelsioo L, Berg G, Ekstrom CM, Gunnervik C, Nordin C, Sydsjo G. Obstetric, somatic, and demographic risk factors for postpartum depressive symptoms. Obstet Gynecol 2002; 99(2):223-8.
22. Patel V, Rodrigues M, DeSouza N. Gender, poverty, and postnatal depression: a study of mothers in Goa, India. Am J Psychiatr 2002;159(1):43-7.
23. Johnstone SJ, Boyce PM, Hickey AR, Morris-Yatees AD, Harris MG. Obstetric risk factors for postnatal depression in urban and rural community samples. Aust N Z J Psychiatr 2001;35(1):69-74.

Original Article

Serum Selenium Levels: Correlation with Inflammatory Biomarkers and Oxidative Stress in Diabetic Nephropathy

Levels of Selenium in Patient with Diabetic Nephropathy

Hanan M. Al-Nadawi and Waseem Yousif M Al-Dulaimy

ABSTRACT

Objective: To study levels of selenium in patient with diabetic nephropathy.
Study Design: Descriptive cross-sectional study.
Place and Duration of Study: This study was conducted at the Department of Chemistry and Baquba General Hospital's Nephrology and Haemodialysis Unit in Ibn Sina Dialysis Centre from 20th October 2023 to 8th January 2024.
Methods: Eighty adults without a history of hematologic or oncologic disorders, malnutrition, or inflammatory disorders (acute or chronic) were identified in the first screening. We examined the hospital library to get the patients' ages, genders, treatment groups, and long-term conditions, such as cardiovascular disease, hypertension, congestive heart failure, arterial disease, and chronic obstructive pulmonary disease. Forty participants served as the control group for this study. They underwent a number of blood tests, including monitoring and recording of serum glucose, urea, creatinine, C-reactive protein, IL-6, glutathione peroxidase, and superoxide dismutase.
Results: Among people with diabetes, smoking was the leading cause of complications and 48 were heavy smokers. The risk of having renal failure increased with the duration of diabetes. Healthy people's urea and creatinine levels were much lower than those of diabetic patients with diabetic nephropathy.
Conclusion: The clear link between selenium, inflammation, and oxidative stress. Selenium was found to have a high positive link with IL-6 but no significant correlation with C-reactive protein. Selenium and glutathione peroxidase were found to have a weakly negative correlation.
Key Words: Diabetic patient, Diabetic nephropathy, Selenium, C-reactive protein, IL-6, glutathione peroxidase

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INTRODUCTION

The prevalence of non-communicable diabetes mellitus (DM) makes it a serious social issue. Worldwide, 537 million people are living with diabetes, and the number is expected to rise to 784 million by 2045, a 50% increase, according to the International Diabetes Federation (IDF).[1-2] The outlook for diabetes remains bleak, despite advancements in research and new medications to lower blood sugar. The rising incidence of micro- and macrovascular diseases leads to greater societal costs due to disabilities and premature deaths.

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Common complications of diabetes include heart disease, PAD, retinal disease, nerve damage, and nephritis. Diabetic nephropathy (DN) affects 40% of people with diabetes and is the third leading cause of death among those with type 2 diabetes, following cancer and cardiovascular disease[3-6]

Diffuse or nodular glomerulosclerosis and Chronic Renal Failure (CRF) develop in diabetic nephropathy (DN) due to elevated glomerular pressure and changes in the kidney's blood arteries, arterioles, glomeruli, and tubules. Diabetic nephropathy affects several aspects of kidney function and structure. Albuminuria, proteinuria with preserved renal function, and a progressive decrease in renal function leading to the terminal phase are the traditional classifications of the condition. Because it is preventable, diabetic neuropathy is no longer seen as a lethal consequence of diabetes mellitus.[5,6]

Diagnosing preclinical diabetic nephropathy in its early stages has also become easier and faster. While albuminuria was previously thought to have a pivotal role in the development of glomerular damage, new evidence has cast doubt on this long-held belief. Twenty to twenty-five percent of kidney units stiffen

when protein is present in the urine, according to research on cell structure.[7] Changes to renal tissue can occur with normal albumin excretion rates. When sclerosis has spread to 50–70% of the kidney mass, proteinuria or chronic albuminuria.[7] The mesangial, tubular, interstitial, and vascular components of the kidney can be damaged by complex and poorly understood mechanisms brought about by emetic agents. Obesity, smoking, and metabolic syndrome are additional vascular risk factors that worsen these consequences. Both hypertension and early glomerular hyperfiltration are affected by these factors. The disruption of the modulation of arteriole tone in the renal tubules by systemic artery pressure affects intraglomerular pressure, leading to chronic hypertension. It is common for albuminuria to be the outcome of podocyte abnormalities and podocytopathy.[8-10] Some of the theories put out to explain glomerular damage include albuminuria, tubulo-interstitial fibrosis, glomerular hyalinosis, mesangial matrix enlargement, and nodular glomerulosclerosis. Renal function declines and eventually leads to end-stage renal failure; proteinuria and hypertension are common. Damage to kidney structures can occur as a result of hyperglycemia in several ways: increased oxidative stress reactions, activation of the sympathetic nervous system and the RAAS, endothelial dysfunction, insulin resistance, and the accumulation of advanced glycation end products (AGEs).[10] Atherosclerotic plaques and diabetic rat kidneys contain 8-hydroxy-2-deoxyguanosine (8-OHdG), a marker of oxidative stress. DNA oxidation leads to vasculopathy and atherosclerosis by damaging both telomeric and non-telomeric DNA, accelerating cell aging. Increased RNA oxidation produces 8-oxoGuo, impairing ribosomal function, protein synthesis, and protein output. RNA and DNA oxidation is common in early-stage diabetic nephropathy, with elevated oxidized purines and pyrimidines found in eye tissues of individuals with diabetic glaucoma, Selenium is crucial for numerous processes, including infection response, DNA synthesis, antioxidant defense, and thyroid metabolism. Selenoproteins and enzymes like glutathione peroxidase and thioredoxin reductases require selenocysteine, a genetically encoded amino acid. Selenium deficiency can accelerate conditions like heart disease, diabetes, RA, nephritis, and asthma.[11]

Selenium deficiency is increasingly linked to long-term health issues. Selenium supports metabolism, reduces inflammation, and protects against free radicals. Selenoproteins contribute to cellular antioxidant defense, suggesting selenium (Se) may help prevent T2DM. Environmental and genetic factors affect the main symptoms of type 2 diabetes, including hyperglycemia, insulin resistance, and poor insulin production. Persistent high blood glucose can lead to atherosclerosis, hypertension, cardiovascular disease, and stroke. A study in China found that soil selenium levels impact glucose regulation in both hyperglycemia and hypoglycemia. Oxidative stress accelerates diabetes development.[12]

METHODS

This research was conducted at the Baquba General Hospital's Nephrology and Haemodialysis Unit in Ibn Sina Dialysis Centr examined blood selenium levels in patients diagnosed with diabetic nephropathy from 20th October 2023 to 8th January 2024 with ethical standards stipulated in the Declaration of Helsinki. Before taking the sample, the patient's informed written and verbal agreement was obtained, after the review and approval of the study protocol and subject's information by the local ethics committee according to the document number 59148 in 22/10/2023. Eighty adults without a history of hematologic or oncologic disorders, malnutrition, or inflammatory disorders (acute or chronic) were identified in the first screening. We examined the hospital library to get the patients' ages, genders, treatment groups, and long-term conditions, such as cardiovascular disease, hypertension, congestive heart failure, arterial disease, and chronic obstructive pulmonary disease. Forty participants served as the control group for this study. They underwent a number of blood tests, including monitoring and recording of serum glucose, urea, creatinine, C-reactive protein, IL-6, glutathione peroxidase, and superoxide dismutase. The study also involved a cohort with a medical history, encompassing blood pressure, duration of diabetes, and the presence of a genetic predisposition to the condition. In addition to the primary groups, the participants were further separated into secondary groups based on age, specifically those over and <40 years old. The data was entered and analzyed through SPSS-27.0 Chi-square and ‘t’ tests were applied, $P<0.05$ was considered as significant.

RESULTS

In the over-50 group, there were 25 patients (31%) with a mean age of 63.56±7.35 and 55 patients (68.75%) under 50 with a mean age of 44.56±3.98. A significant difference was observed ($p<0.0001$) [Table 1]. Being overweight or obese is a major avoidable cause of diabetic nephropathy. BMI classified individuals as non-obese (BMI <25), overweight (BMI 25-29.9), and obese (BMI ≥30). Nearly half of the patients were overweight, with no significant difference between the patient groups ($p>0.05$), and the control group showed a 32% rate without significance [Table 2].

The duration of diabetes and smoking were significant risk factors for renal failure. The likelihood of kidney failure increased with the duration of diabetes (Tables 3-4). Urea and creatinine levels were significantly higher in diabetic patients. The average urea level in the

patient group was 124.85, compared to the normal 32.74 (P<0.001). The creatinine level was significantly lower in patients at 5.30, compared to the normal 1.14 (P<0.001) [Tables 5-6].

Table No. 1: Comparison of diabetic nephropathy and control groups of age

Group	Mean±SD	P value
Patients	59.3375±10.0	<0.0001
Controls	55.26±4.681	

Inflammatory markers showed significant correlations between diabetic patients with renal failure and the control group (Table 7). Selenium was positively associated with IL-6 (r=0.480, p=0.0015), but no significant link was found with CRP (r=-0.089, p=0.579). No significant correlation was found between GPX and selenium (r=-0.051, p=0.7537), nor between SOD and selenium (r=0.093, p=0.564). However, a strong correlation was observed between GPX and SOD (r=0.872, p<0.0001) [Table 8].

Table No. 2: Comparison of body mass index of control and patient groups

BMI (kg/m^2)	Controls	Patients
≤24.9	22.43±0.28	23.0±0.72
25-29.9	28.63±1.4	29.33±1.7
≥30	33.6 ± 1.77	35.0 ± 2.0
P value	0.439	

Table 3: Comparison of risk factors and case history of patient and control groups

Variable	Patients (n=80)	Controls (n=40)	P value
Risk Factor			
Family history	19 (24 %)	-	>0.003
Duration of DM (>10 years)	33 (41%)	-	<0.003
Smoking	48 (60%)	22 (55%)	<0.05
Case history			
Hypertension	34(42.5%)	-	<0.05
Kidney disease	3 (3.75%)	-	NS

Table No. 4: Result of random blood sugar

Random blood sugar	Patients	Control	T-test	
Sample size	80	40	Difference	-77.1125
Mean	172.4125	95.3000	Pooled Standard Deviation	60.8033
95% CI for the mean	155.9703 to 188.8547	91.6803 to 98.9197	Standard Error	11.7745
Variance	5458.9290	128.1000	95% CI of difference	-100.4292 to -53.7958
SD	73.8846	11.3181	Test statistic t	-6.549
SE	8.2605	1.7896	Degrees of Freedom	118
			Two-tailed probability	P<0.0001
F-test for equal variances			P<0.001	

Table No. 5: Result of blood urea in studied groups

Blood urea	Patients	Control	T-test	
Sample size	80	40	Difference	-92.1138
Mean	124.8513	32.7375	Pooled Standard Deviation	33.5036
95% CI for the mean	115.8161 to 133.8864	30.3178 to 35.1572	Standard Error	6.4880
Variance	1648.3777	57.2434	95% CI of difference	-104.9617 to -79.2658
SD	40.6002	7.5659	Test statistic t	-14.198
SE	4.5392	1.1963	Degrees of Freedom	118
			Two-tailed probability	P<0.0001
F-test for equal variances			P<0.001	

Table No. 6: Result of serum creatinine in studied groups

Serum creatinine	Patients	Control	T-test	
Sample size	80	40	Difference	-4.1567
Mean	5.2957	1.1390	Pooled Standard Deviation	1.5861
95% CI for the mean	4.8649 to 5.7266	1.0948 to 1.1832	Standard Error	0.3071
Variance	3.7480	0.01909	95% CI of difference	-4.7650 to -3.5485
SD	1.9360	0.1382	Test statistic t	-13.534
SE	0.2164	0.02184	Degrees of Freedom	118
			Two-tailed probability	P<0.0001
F-test for equal variances			P<0.001	

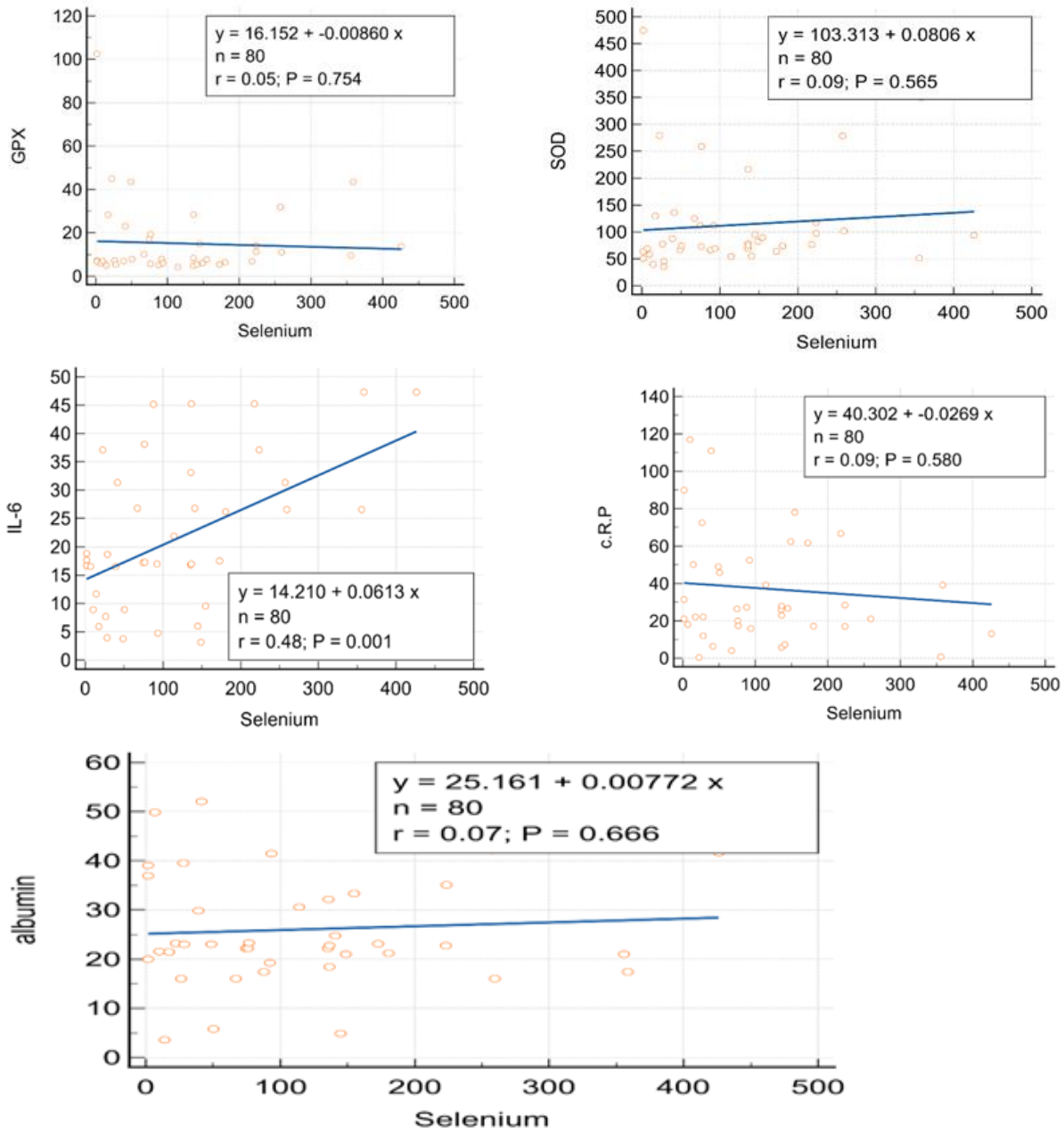

Figure No. 1: Coloration between Selenium and GPX, SOD, IL-6, C.R.P and Albumin

Table No. 7: Result of inflammatory marker in patient and control groups

Inflammatory marker	Patients	Controls	P value	
			T-test (assuming equal variances)	
IL-6	21.3925±13.2493	3.7571±0.8790	Difference	-17.6354
			Pooled Standard Deviation	10.3443
			Standard Error	2.9051
			95% CI of difference	-23.4675 to -11.8032
			Test statistic t	-6.071
			Degrees of Freedom	51
			Two-tailed probability	P<0.0001
CRP	40.3625±3.3700	1.9576±0.9925	Difference	-38.4049
			Pooled Standard Deviation	23.6910
			Standard Error	6.6533
			95% CI of difference	-51.7619 to -

				25.0478
			Test statistic t	-5.772
			Degrees of Freedom	51
			Two-tailed probability	P<0.0001

Table 8: ROC curve for inflammatory and oxidative stress in studied groups

Parameters	Area under the ROC curve (AUC)	Standard Error	95% Confidence interval	Z statistic	Specificity	Sensitivity	Significant value
Selenium	0.55	0.140	0.405 to 0.699	0.395	50	57.1	0.693
GPx	0.774	0.123	0.630 to 0.882	2.229	50	81	0.026
SOD	0.581	0.205	0.408 to 0.741	0.396	60	78	0.692
IL-6	0.938	0.0411	0.806 to 0.991	10.653	40	90.6	P<0.01

DISCUSSION

In living things, selenium primarily plays a role in the production of selenoproteins, which aid in the reduction of oxidative stress.[13-15] The antioxidant properties of selenium led to the belief that it could provide protection against type 2 diabetes (T2DM).[16] Elevated selenium levels may be associated with insulin resistance and type 2 diabetes, according to recent epidemiological research. The selenium exposure increases the risk of developing type 2 diabetes and its function in glucose homeostasis.[17,18]

Damage to the tubules and glomeruli, as well as impaired renal function and decreased filtration, are the main symptoms of diabetic nephropathy, which is mostly caused by hyperglycemia and oxidative stress. The degree of protein oxidation and damage in diabetic nephropathy is correlated with elevated IL-6 levels which may indicate the existence of oxidative stress.[19,20] Chronically elevated blood glucose levels in diabetes may be linked to the increased production and buildup of advanced glycation end products (AGEs). By activating inflammatory pathways and cross-linking proteins, AGEs can worsen kidney damage and functioning. People with diabetic nephropathy are more likely to experience renal sequelae if their PC and AGE levels are high.[21]

With the exception of the heart, no organ contains a greater concentration of mitochondria than the kidneys. The mitochondria set the stage for ATP production, ultra-filtrate absorption, and dissolved chemical absorption. Systems including mitochondrial oxidative phosphorylation and fatty acid β-oxidation generate reactive oxygen species (ROS), which are essential for the proper functioning of the kidneys. When antioxidant defense (AOD) systems are in equilibrium with mitochondrial production of reactive oxygen species (ROS), renal mitochondrial function is optimal. According to research, the progression of diabetic nephropathy is intimately linked to mitochondrial dysfunction and an increase in oxidative stress. Kidney cells, including endothelial and podocyte cells are also exhibit mitochondrial abnormalities. Through a variety of signaling channels, the operating system can halt the cell cycle and cause cell death, which includes podocytes. Endothelial cell death, inflammation, autophagy, and fibrosis are caused by the activation of certain pathways, such as PI3K/Akt, TGF-ſ1/p38-MAPK, and NF-kB. The iron-dependent lipid peroxidation (LPO) mechanism known as ferroptosis has recently attracted a lot of attention because it offers novel ways to study the course of diabetic nephropathy (DN). Cultured human proximal tubule cells exposed to high glucose levels exhibit elevated iron levels, reduced antioxidant ability, and elevated levels of lipopolysaccharides and reactive oxygen species.[22,23] Our findings contrast with other studies on diabetic nephropathy, which link it to oxidative stress, glycation, glycol oxidation, and elevated reactive nitrogen and oxygen species (RNS). DN (stages 3a and 3b) shows a significant decline in antioxidant enzyme function, correlating with glycol oxidation and glycation diseases. Due to low SOD activity, DN may struggle to combat oxidative damage. As SOD and GPx activity decrease in DN stages 3a and 3b, the antioxidant defense weakens, while catalase activity increases due to higher oxidative stress. The absence of this enzyme may accelerate DN development and progression.[24,25]

CONCLUSION

Oxidative stress and inflammation are implicated in the occurrence and progression of diabetic nephropathy. The research demonstrated that healthy people's urea and creatinine levels were much lower than those of diabetic patients. In people with diabetic nephropathy, the study discovered a clear link between selenium, inflammation, and oxidative stress. Selenium was found to have a high positive link with IL-6 but no significant correlation with CRP. Selenium and GPX were found to have a weakly negative correlation..

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hanan M. Al-Nadawi
Drafting or Revising Critically:	WaseemYousif M Al-Dulaimy
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Ong KL, Stafford LK, McLaughlin SA, Boyko EJ, Vollset SE, Smith AE, et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2023;402 (10397):203-24.
2. Patel B, Unadkat S, Patel H, Rathod M. Dietary practices among type 2 diabetes patients visiting a non-communicable disease (NCD) clinic in a district of Western India: a cross-sectional study. Cureus 204;16(1): e52604.
3. Hu Q, Jiang L, Yan Q, Zeng J, Ma X, Zhao Y. A natural products solution to diabetic nephropathy therapy. Pharmacol Therapeutics 2023;241: 108314.
4. Natesan V, Kim SJ. Diabetic nephropathy - a review of risk factors, progression, mechanism, and dietary management. Biomolecules Therapeutics 2021; 29(4):365.
5. Amiri MM, Fayyadh SH, Parra RM, Al-Khafaji AH, Abosaooda M, Darvishi M, et al. Role of selective cyclooxygenase-2 inhibitors in renal colic pain reduction and improvement: A systematic review of clinical trials. Advancements in Life Sci 2023;9(4):446-52.
6. Nithya V, Sangavi P, Srinithi R, Nachammai KT, Kumar G, Prabu D, et al. Diabetes and other comorbidities: microvascular and macrovascular diseases diabetes and cancer. In: Advances in Diabetes Research and Management. Singapore: Springer Nature; 2023.p.21-39.
7. Khan MD, Mubarak B, Waheed K, Munir I. Serum Anti-Nuclear Antibodies and their patterns on immunofluorescence in patients with joint pain from Lahore, Pakistan. Advancements Life Sci 2022; 9(3):318-22.
8. Palatini P. Glomerular hyperfiltration: a marker of early renal damage in pre-diabetes and pre-hypertension. Nephrol Dialysis Transplant 2012; 27(5):1708-14.
9. Fogo AB. Glomerular hypertension, abnormal glomerular growth, and progression of renal diseases. Kid Int 2000;57: S15-21.
10. Kanbay M, Ertuglu LA, Afsar B, Ozdogan E, Kucuksumer ZS, Ortiz A, et al. Renal hyperfiltration defined by high estimated glomerular filtration rate: a risk factor for cardiovascular disease and mortality. Diabetes Obesity Metab 2019;21(11):2368-83.
11. Kroese LJ, Scheffer PG. 8-hydroxy-2′-deoxyguanosine and cardiovascular disease: a systematic review. Curr Atherosclerosis Reports 2014;16:1-8.
12. Barchielli G, Capperucci A, Tanini D. The role of selenium in pathologies: an updated review. Antioxidants 2022;11(2): 251.
13. Gandhi H, Nagaraja UP, SandeepPrabhu K. Selenoproteins and their role in oxidative stress and inflammation. Curr Chemical Biol 2013;7(1): 65-73.
14. Hariharan S, Dharmaraj S. Selenium and selenoproteins: It's role in regulation of inflammation. Inflammopharmacol 2020;28: 667-95.
15. Zoidis E, Seremelis I, Kontopoulos N, Danezis GP. Selenium-dependent antioxidant enzymes: Actions and properties of selenoproteins. Antioxidants 2018; 7(5):66.
16. binti Othman F, bin Jan Mohamed HJ, Sirajudeen KNS, Rajab NF. The influence of selenium status on body composition, oxidative DNA damage and total antioxidant capacity in newly diagnosed type 2 diabetes mellitus: a case-control study. J Trace Elements Med Biol 2017;43:106-12.
17. Yang SJ, Hwang SY, Choi HY, Yoo HJ, Seo JA, Kim SG, et al. Serum selenoprotein P levels in patients with type 2 diabetes and prediabetes: implications for insulin resistance, inflammation, and atherosclerosis. J Clin Endocrinol Metab 2011; 96(8): E1325-9.
18. Casanova P, Monleon D. Role of selenium in type 2 diabetes, insulin resistance and insulin secretion. World J Diabetes 2023;14(3):147.
19. Shahzad M, Zulfiqar T, Ali A. Radiographic Evaluation of Knee Joint in Patients with Knee pain and its correlation with Osteoarthritis and Gender. Advancements Life Sci 2022;9(3):309-12.
20. Hojs R, Ekart R, Bevc S, Hojs N. Markers of inflammation and oxidative stress in the development and progression of renal disease in diabetic patients. Nephron 2016;133(3):159-62.
21. Khalid M, Petroianu G, Adem A. Advanced glycation end products and diabetes mellitus: Mechanisms and perspectives. Biomolecules 2022; 12(4):542.
22. Dennis JM, Witting PK. Protective role for antioxidants in acute kidney disease. Nutr 2017;9(7):718.
23. Pisoschi AM, Pop A, Iordache F, Stanca L, Predoi G, Serban AI. Oxidative stress mitigation by antioxidants-an overview on their chemistry and influences on health status. Eur J Med Chem 2021; 209:112891.
24. Khan, Daood M, Mubarak B, Waheed K, Munir I. Serum Anti-Nuclear Antibodies and their patterns on immunofluorescence in patients with joint pain from Lahore, Pakistan. Advancements Life Sci 2022;9(3):318-322.
25. Rosas-Martínez L, Rodríguez-Muñoz R, del Carmen Namorado-Tonix M, Missirlis F, del Valle-Mondragón L, Sánchez-Mendoza A, et al. Hyperglycemic levels in early stage of diabetic nephropathy affect differentially renal expression of claudins-2 and-5 by oxidative stress. Life Sci 2021; 268:119003.

Original Article

The Impact of Vitamin D Deficiency and its Outcome Among Patients With Ischemic Stroke

Vitamin D Deficiency With Ischemic Stroke

Beenish Memon[1], Mumtaz Ali Lakho[1], Muhammad Kashif Shaikh[2], Ghulam Mujtaba Shah[1], Imran Karim[1] and Syed Zulfiquar Ali Shah[1]

ABSTRACT

Objective: To determine the Impact of Vitamin D Deficiency and Its Outcome among Patients with Ischemic Stroke
Study Design: The cross-sectional descriptive study
Place and Duration of Study: This study was conducted at the Liaquat University Hospital, Hyd from October, 2018 to March, 2019.
Methods: The vitamin D status of each of the 370 patients who had ischemic stroke was investigated, and the results included readmission within 30 days, length of stay, and mortality.
Results: The mean ± SD for age (yrs) 57.72±9.44, systolic blood pressure (mmHg) 160.94±7.82, diastolic blood pressure (mmHg) 115.72±11.74, duration of stroke (hrs) 41.95±8.86, random blood sugar (mg/dL) 290.77±18.95, fasting blood sugar (mg/dL) 150.84±9.96, hospital stay duration (days) 19.00±4.00 and vitamin D level (ng/ml) 12.76±6.51. Regarding vitamin D status, the percentages for sufficient, deficient and insufficient were 99 (26.7%), 200 (54%), 71 (19.1%), respectively. However, there was statistical significance in the vitamin D status with regard to gender (p=0.02), age (p<0.01), hospital stay (p<0.01), readmission (p<0.01) and mortality (p<0.01).
Conclusion: Ischemic stroke has been independently linked with vitamin D deficiency.
Key Words: Strokes, Cerebrovascular accident and Vitamin D.

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INTRODUCTION

The ischemic cerebrovascular accident, caused by the blockage of the circulation of blood to the brain, continues to be a primary source of death and disability globally.[1] Recognizing and mitigating changeable danger indicators is essential for successful preventative and treatment measures.[2] Numerous studies have examined the correlation among vitamin D insufficiency and the occurrence, extent, and consequences of stroke caused by ischemia, underscoring the significance of sufficient vitamin D levels for cerebrovascular function.[3,4] Vitamin D, a lipid-soluble secosteroid, is essential for equilibrium of calcium and bone metabolism.[5] In addition to its traditional roles, recent data indicates that vitamin D has considerable neuroprotective abilities, affecting neuronal well-being and vascular stability.

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As a result, vitamin D insufficiency has attracted interest as a potentially preventable risk factor for several neurological conditions; including stroke caused by ischemia.[6] A research in Egypt evaluated vitamin D levels in stroke individuals and investigated its correlation with initial severity and subsequent outcomes. The results indicated that those with stroke patients had markedly reduced blood vitamin D levels in comparison to healthy controls. Furthermore, vitamin D inadequacy and insufficiency were more frequent among patients. A strong negative connection existed between blood vitamin D levels and stroke scale (NIHSS) scores upon admittance and after seventy-two hours, suggesting that diminished vitamin D levels correlated with heightened stroke severity. Furthermore, diminished vitamin D levels were associated with worse results at discharge and after three months, indicating that vitamin D insufficiency is connected to suboptimal short-term rehabilitation in stroke due to ischemia patients.[7] A research in Ireland evaluated the frequency of vitamin D insufficiency in individuals over 50 years old who were hospitalized with acute stroke. The findings indicated that forty-four percent of the group had vitamin D deficiency, with levels falling below 50 nmol/L. The significant prevalence highlights the need for regular evaluation of vitamin D levels in individuals with stroke, as inadequacy may influence the likelihood of stroke and intensity.[8] The processes linking vitamin D deficiency

to heightened stroke severity and risk are complex. Vitamin D modulates inflammatory reactions, diminishes oxidative stress, as well as regulates endothelial function, all of which are crucial for cerebrovascular well-being.[9] A deficiency in vitamin D can result in dysfunctional endothelial cells, increased stiffness in the arteries, and a pro-inflammatory condition, consequently raising the likelihood of ischemic events. Additionally, vitamin D receptors are present in multiple parts of the brain, and their activation may provide neuroprotective benefits, such as enhancing neuronal survival and preventing excitotoxicity.[10]

The major warning factors for cerebral infarction include age and hypertension, which are associated with decreased serum vitamin D levels. The circulatory form of vitamin D is also associated with an independent risk of stroke in the future and plays a role in immunomodulation, immune system maintenance, and cell growth and differentiation in addition to maintaining calcium and bone homeostasis. Furthermore, a wide range of tissues, including endothelium, stimulated monocytes and T cells, astrocytes, cardiomyocytes, and neurons, express vitamin D receptors (VDR). Vitamin D deficiency significantly decreased the expression of interleukins and interferon gamma in ischemic brain cells, according to cytokine research

The development of CT scanning, a safe and noninvasive method for distinguishing among cerebral infarction and hemorrhage, has resulted in significant advancements in the examination of stroke patients.[11]

The association between vitamin D insufficiency and ischemic stroke was previously investigated across several groups. A research conducted in Iran investigated the relationship between blood vitamin D concentrations, stroke extent, and lesion volume. The results demonstrated that decreased vitamin D levels correlated with increased stroke severity and greater lesion sizes, indicating that low levels of vitamin D may intensify brain damage in individuals with ischemic stroke.[12] Growing data suggests a substantial correlation among vitamin D inadequacy and heightened risk, severity, and adverse consequences of ischemic stroke. Mitigating vitamin D insufficiency with lifestyle changes, food consumption, and supplementation might be a viable strategy for alleviating the incidence of ischemic stroke. This study assessed the amount of vitamin D present in ischemic stroke patients as well as the study's overall outcomes. It also offers insights for future research investigating whether taking vitamin D supplements can lower the incidence and mortality due to stroke.

METHODS

Patients hospitalized with ischemic stroke at Liaquat University Hospital in Hyderabad from Oct-2018 to March-2019 were enrolled and selected in this six-month cross-sectional descriptive research. Following informed permission and an initial examination of the inclusion criteria as all patients with a confirmed diagnosis of stroke by CT SCAN or MRI and regardless of gender, all patients were recruited in the research. A focused neurological dysfunction with a recent, abrupt start that is supported by an MRI or CT scan of the brain's hypodense region is known as a stroke.

Serum vitamin D levels below 20 ng/ml were deemed deficient, those between 29 and 20 ng/ml as insufficient, and those beyond 30 ng/ml as sufficient. As a result of the individuals' CVA and subsequent readmission owing to clinical deterioration in their health status, the outcome was assessed based on mortality in hospitals, length of stay, and readmission. The study's exclusion criteria included patients with brain tumors, seizures, paraparesis, hemorrhagic stroke, and those currently taking vitamin D supplements. The vitamin D level was investigated and evaluated following the diagnosis of an ischemic stroke using brain imaging, and the information was recorded on pre-made proforma. In addition to measuring blood pressure, blood sugar levels were also examined. The study's outcomes included length of stay, in-hospital mortality, and readmission of the participants within 30 days as whether individuals acquired evidence-based methods of severe stroke care. Patients also received proper follow-up visits every two weeks, and those subjects who did not follow up were excluded from the analysis.

For the analysis, SPSS version 21.00 was used. As qualitative data, the frequency (n) and proportions (%) of vitamin D insufficiency in ischemic stroke were computed. For each numerical variable, the mean, as well as the standard deviation (±SD), were computed. These included the blood pressure (mmHg), stroke length (hours), blood sugar level (mg/dl), hospital stay duration (days), and vitamin D level (ng/ml). Readmission, mortality, and length of hospital stay were examples of outcomes for which the data was categorical. For categorical variables, the chi-square test was used at 95% confidence intervals, with a p-value threshold of ≤ 0.05 indicating significance.

RESULTS

A total of 370 ischemic stroke patients had their vitamin D status assessed; Table 1 shows the mean ± SD for all quantitative variables, while Table 2 displays the frequency and proportions for age, gender, and vitamin D status. The number and percentages of those with vitamin D status that were deficient, insufficient, and sufficient were 200 (54%), 71 (19.1%), and 99 (26.7%), respectively. Table 3-6 shows that the vitamin D status was statistically significant in terms of sex ($p=0.02$), hospitalization ($p<0.01$), death ($p<0.01$), and readmission ($p<0.01$).

Table No. 1: The Descriptive Statistics of the Study Population

Quantitative variables	Mean ±SD
Age (yrs)	57.72±9.44
Systolic blood pressure (mmHg)	160.94±7.82
Diastolic blood pressure (mmHg)	115.72±11.74
Duration of stroke (hrs)	41.95±8.86
Random blood sugar (mg/dL)	290.77±18.95
Fasting blood sugar (mg/dL)	150.84±9.96
Hospital stay duration (days)	19.00±4.00
Vitamin D level (ng/ml)	12.76±6.51

Table No. 2: The Frequency and Percentage for Age, Gender and Vitamin D Status of the Population

AGE (yrs)	Frequency (n=370)	Percent (%)
20-30	33	8.9
30-40	62	16.8
40-50	69	18.6
50-60	91	24.6
60+	115	31.1
GENDER		
Male	245	66.2
Female	125	33.8
Vitamin D Status		
Sufficient	122	32.9
Deficient	145	39.1
Insufficient	103	27.8

Table No. 3: The Vitamin D Status in Accordance to Gender

		VITAMIN D STATUS			
		Sufficient	Deficient	Insufficient	Total
Gender	Male	89	97	59	245
		73.0%	66.9%	57.3%	66.2%
	Female	33	48	44	125
		27.0%	33.1%	42.7%	33.8%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

*P-value: 0.04

Table No. 4: The Vitamin D Status and Hospitalization

		VITAMIN D STATUS			
		Sufficient	Deficient	Insufficient	Total
HOSPITAL STAY	<14 days	11	52	84	147
		9.0%	35.9%	81.6%	39.7%
	>14 days	111	93	19	223
		91.0%	64.1%	18.4%	60.3%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

*P-value: <0.01

Table No. 5: The Vitamin D Status and Mortality

		VITAMIN D STATUS			
		Sufficient	Deficient	Insufficient	Total
Mortality	Yes	18	31	6	55
		14.8%	21.4%	5.8%	14.9%
	No	104	114	97	315
		85.2%	78.6%	94.2%	85.1%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

*P-value: <0.01

Table 06: The Vitamin D Status And Readmission

		VITAMIN D STATUS			
		Sufficient	Deficient	Insufficient	Total
Readmission	Yes	89	48	15	152
		73.0%	33.1%	14.6%	41.1%
	No	33	97	88	218
		27.0%	66.9%	85.4%	58.9%
Total		122	145	103	370
		100.0%	100.0%	100.0%	100.0%

*P-value: <0.01

DISCUSSION

A significant cause of death and disability worldwide, stroke is also on the rise in nations with low or middle incomes. Vitamin D has a major role in immunological, cardiac, and cerebrovascular physiological control and has gained recognition as a potential risk factor for heart diseases because of its potential for vasoprotection.[13]

Furthermore, vitamin D deficiency influences vascular remodeling by regulating inflammation, thrombosis, and smooth muscle proliferation. Furthermore, too much parathyroid hormone promotes myocyte hypertrophy and vascular remodeling, whereas too little vitamin D results in secondary hyperparathyroidism.[14] The instability of atherosclerotic plaques may be exacerbated by the pro-inflammatory cytokine parathyroid hormone-related protein (PTHrP). Although these circulatory changes are ultimately what cause stroke, a lack of food has been connected to a number of neurological disorders.[15] Two risk factors that may raise the chance of any kind of stroke are diabetes and high blood pressure. However, high blood pressure might lead to erroneous findings in the systems

for scoring and bias the analysis to favor bleeding. The former study's findings indicated that having a male gender was linked to terrible consequences while the mortality was distributed rather equally across all age categories in the prior research.[16] One factor that negatively affects stroke outcomes is aging. This is due to the fact that secondary problems are much too common as individual's age. The in-hospital mortality rate was previously greater when comparing the present research to other worldwide studies.[17]For those who have had an ischemic stroke, serum vitamin D levels are considered to be a very good prognostic indicator. The blood 25-OH D test demonstrated the overall production of vitamin D from both internal and external sources, including exposure to UVB rays and consumption of a range of food types. It is still unclear what pathophysiology underlies atherosclerosis and vitamin D deficiency. A prior research found that vitamin D inhibits the renin-angiotensin system, which in turn regulates blood pressure.[18] According to a different research, a lack of vitamin D may assist lower arterial hypertension and prevent blood vessel thrombosis.[19] Prior studies confirmed that vitamin D deficiency was previously substantially linked to increased carotid plaque development and intimal media thickness in the general population.[20] Modifications to the intimal media, arterial hypertension, inhibition of the rennin-angiotensin system in two instances, and changes in thrombotic nations are some of the reasons that have raised the risk of CVA. Additionally, appropriate monitoring has shown a link between atherogenic dyslipidemia and a lack of vitamin D and known to be linked to dyslipidemia. It was shown that stroke patients with low 25(OH) D levels at admission were more likely to die, have a poor early functional result, and have a severe stroke. Blood 25(OH) D levels in individuals with acute ischemic stroke are predictive of both the extent of harm at admission and the favorable functional outcome. The stroke patients often have low nutritional D values, which have been associated with an elevated risk of cardiovascular events in the future. However, they discovered that oral vitamin D supplementation temporarily enhanced endothelial features but did not reduce blood strain in stroke patients whose baseline blood pressure was appropriately controlled. [21] Vitamin D deficiencies reduce neuroprotective chemicals like Insulin Growth Factor-1 (IGF-1) and dysregulates the inflammatory response. Clinical recovery may be enhanced by vitamin D's potential to promote modifications in neuroplastic characteristics. Because it can pass across the blood-talent barrier and because the brain has Vitamin D Receptors (VDR), nutritional vitamin D also has antithrombotic and neuroprotective properties. Genetic polymorphisms in the VDR gene may put people who are vitamin D deficient at higher risk for stroke. Vitamin-D insufficiency may also be associated with acute stroke or its general risk factors, as shown by the perfect correlation between low 25(OH) D stages and the likelihood of acute ischemic stroke in patients who arrive at our tertiary care hospital. There is more proof of acute ischemic stroke, and low vitamin D levels are a risk factor for deadly strokes on their own. Vitamin D supplementation is a prospective stroke prevention approach since insufficient vitamin D may be a sign of increased co-morbidity and is directly associated to stroke and paralysis.[22] Therefore, the clinicians should identify patients who have the highest risk of repeat stroke and mortality by looking at functional outcomes, survival, and recurrence rates

CONCLUSION

The study observed an independent correlation between vitamin D deficiency and ischemic stroke patients. Assessing the level of vitamin D in individuals with ischemic stroke is crucial. Given the large number of stroke patients that present to our local hospitals, local information on the subjects is highly necessary. To validate these results and ascertain whether vitamin D supplements could increase stroke patients' survival more multidisciplinary and multicenter research is required.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Beenish Memon, Mumtaz Ali Lakho
Drafting or Revising Critically:	Muhammad Kashif Shaikh, Ghulam Mujtaba Shah, Imran Karim, Syed Zulfiquar Ali Shah
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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REFERENCES

1. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2019;50(12):e344-e418.

2. Judd SE, Morgan CJ, Panwar B, Howard VJ, Wadley VG, Jenny NS, Kissela BM, Gutiérrez OM. Vitamin D deficiency and incident stroke risk in community-living black and white adults. Int J Stroke 2016;11(1):93-102.
3. Modarresi-Ghazani F, Hejazi ME, Gharekhani A, Entezari-Maleki T. Role of Vitamin D in Cardiovascular Disease. Arch Iran Med 2016;19(5):359-62.
4. Gurol ME, Kim JS. Advances in Stroke Prevention in 2018. J Stroke 2018;20(2):143-144
5. Mpandzou G, Aït Ben Haddou E, Regragui W, Benomar A, Yahyaoui M. Vitamin D deficiency and its role in neurological conditions: A review. Rev Neurol (Paris) 2016;172(2):109-22.
6. Zmijewski MA. Vitamin D and Human Health. Int J Mol Sci 2019;20(1):145.
7. Perez-Hernandez N, Aptilon-Duque G, Nostroza-Hernández MC, Vargas-Alarcón G, Rodríguez-Pérez JM, Blachman-Braun R. Vitamin D and its effects on cardiovascular diseases: a comprehensive review. Korean J Int Med 2016;31(6):1018-1029.
8. Bejleri J, Brewer L, Boyle K, Williams D, Moynihan B. Prevalence of vitamin D deficiency in patients admitted with acute stroke in a tertiary university teaching hospital in Dublin. Age and Ageing 2018;47(5):13.
9. Zhou R, Wang M, Huang H, Li W, Hu Y, Wu T. Lower Vitamin D Status Is Associated with an Increased Risk of Ischemic Stroke: A Systematic Review and Meta-Analysis. Nutr 2018;10(3):277.
10. Selim FO, Fahmi RM, Ali AE, Raafat N, Elsaid AF. Serum vitamin D levels in acute stroke patients. The Egypt J Neurol Psychiatr Neurosurg 2019;55:1-8.
11. Siniscalchi A, Lochner P, Anticoli S, Chirchiglia D, De Sarro G, Gallelli L. What is the Current Role for Vitamin D and the Risk of Stroke? Curr Neurovasc Res 2019;16(2):178-183.
12. Njoku K, Iveson E. Post stroke fatigue and vitamin d deficiency. Age and Ageing 2016;45(Suppl 1):i20.
13. Evans MA, Kim HA, Ling YH, Uong S, Vinh A, De Silva TM, et al. Vitamin D3 Supplementation Reduces Subsequent Brain Injury and Inflammation Associated with Ischemic Stroke. Neuromolecular Med 2018;20(1):147-159.
14. Momosaki R, Abo M, Urashima M. Vitamin D Supplementation and Post-Stroke Rehabilitation: A Randomized, Double-Blind, Placebo-Controlled Trial. Nutr 2019;11(6):1295.
15. Wei ZN, Kuang JG. Vitamin D deficiency in relation to the poor functional outcomes in nondiabetic patients with ischemic stroke. Biosci Rep 2018;38(2):BSR20171509.
16. Kouvari M, Panagiotakos DB. Vitamin D status, gender and cardiovascular diseases: a systematic review of prospective epidemiological studies. Expert Rev Cardiovasc Ther 2019;17(7):545-555.
17. Sheerah HA, Eshak ES, Cui R, Imano H, Iso H, Tamakoshi A. Japan Collaborative Cohort Study Group. Relationship Between Dietary Vitamin D and Deaths From Stroke and Coronary Heart Disease: The Japan Collaborative Cohort Study. Stroke 2018;49(2):454-457.
18. Berghout BP, Fani L, Heshmatollah A, Koudstaal PJ, Ikram MA, Zillikens MC, et al. Vitamin D Status and Risk of Stroke: The Rotterdam Study. Stroke 2019;50(9):2293-2298.
19. Liu M, Li X, Sun R, Zeng YI, Chen S, Zhang P. Vitamin D nutritional status and the risk for cardiovascular disease. Exp Ther Med 2016;11(4):1189-1193.
20. Narasimhan S, Balasubramanian P. Role of Vitamin D in the Outcome of Ischemic Stroke- A Randomized Controlled Trial. J Clin Diagn Res 2017;11(2):CC06-CC10.
21. Chaudhuri JR, Mridula KR, Alladi S, Anamika A, Umamahesh M, Balaraju B, et al. Serum 25-hydroxyvitamin D deficiency in ischemic stroke and subtypes in Indian patients. J stroke 2014;16(1):44.
22. Gupta A, Prabhakar S, Modi M, Bhadada SK, Kalaivani M, Lal V, Khurana D. Effect of Vitamin D and calcium supplementation on ischaemic stroke outcome: a randomised controlled open-label trial. Int J Clin Pract 2016;70(9):764-70..

Original Article

Examining the Efficacy of PSA Levels in Detecting Prostate Carcinoma among Patients at Pakistan Railway Hospital: A Comparative Analysis

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ABSTRACT

Objective: To assess whether testing serum PSA levels ranging from 10 to 4 ng/ml is more effective in detecting prostate cancer compared to measuring serum PSA levels between 20 and 10 ng/ml.

Study Design: A prospective comparative study

Place and Duration of Study: This study was conducted at the Pakistan Railway Hospital, Rawalpindi from June 2022 to December 2022.

Methods: This research involved a comparison among 114 males aged 50 years and above who experienced symptoms related to their lower urinary tract. These individuals were separated into two categories depending on their serum PSA levels, which were determined during the diagnosis process. In Group A, Patients exhibited PSA levels ranging from 10 - 4 ng/ml. While Group B included individuals whose PSA levels ranged from 20 -10 ng/ml. Before taking part in the study, all participants gave their consent in writing. Prostate biopsies were conducted in both groups and prostate cancer incidence was compared.

Results: The average age of the patients was 68.56±4.80 years. Common symptoms reported included urgent urination (26.32%), increased urinary frequency (32.46%), and urination at night (38.60%), weak stream (25.44%), urinary leakage (22.81%), and hematuria (6.14%). Upon examination, findings from digital rectal examination (DRE) showed a lump (30.84%), firm hardness (29.82%), median sulcus obliteration (32.46%), and non-symmetry (22.81%). Both groups studied had similar mean age and occurrences of various lower urinary tract symptoms (LUTS) and DRE findings. The second group (Group-B) demonstrated notably higher average levels of serum prostate-specific antigen (1596±2.72 ng/ml compared to 5.09±1.60 ng/ml; p<0.001), along with greater pre-void (528±94 ml vs. 461±92 ml; p<0.001) and post-void residual volumes (212±56 ml vs. 102±55 ml; p<0.001) in contrast to the initial group (Group-A). Prostate cancer was diagnosed in 28 (24.56%) patients, with the occurrence rate notably higher in Group B (33.33% vs. 15.79%; p=0.029) than in Group A.

Conclusion: PSA levels in the blood can indicate the presence of malignant prostate tissue. This means that if the PSA level is high, it is important to examine the tissue to exclude the possibility of cancer. Studies have shown that there is a relationship between elevated PSA levels at the time of biopsy and an increased incidence of prostate cancer. Therefore, it is recommended to keep an eye on the PSA level and seek medical advice if it is higher than normal.

Key Words: carcinoma of the prostate, Detection effectiveness, screening.

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INTRODUCTION

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Carcinoma of the Prostate is a prevalent form found in men worldwide and is recognized as a major contributor to cancer-related fatalities.[1] When assessing symptoms related to the lower urinary tract, it is common practice to conduct a prostate-specific antigen (PSA) blood test along with a digital rectal exam (DRE). When screening for prostate cancer, the PSA test is deemed more dependable compared to solely relying on the DRE and trans-rectal ultrasound.[2] Encountering symptoms related to the lower urinary tract and a reading of prostate-specific antigen (PSA) equal to or higher than 4 ng/ml, it is usually recommended to have a prostate biopsy. This test helps

to check the presence of cancer and to rule out any possible presence of it. Greater than 70% of prostate biopsies done based on high serum PSA levels result in negative with no prostate cancer detection, which is, itself a potentially morbid procedure[3]. To address elevated PSA (prostate-specific antigen) levels, There are three commonly used methods: (1) repeat PSA measurement after empiric antibiotic treatment, (2) repeat PSA measurement 1 to 2 months later, and (3) immediately perform a prostate biopsy[4,5]. In routine PSA screening, more than 90% of localized prostate disease can be detected, and only 4% were detected at a metastatic stage. The burden of disease profile can be used as a disease indicator and a basic tool for planning better strategies. In countries where national testing is not routinely conducted. PSA thresholds may still be used to reduce the number of patients in whom metastatic stages are detected [6, 7]. Several studies that have been conducted remain controversial and have not been able to explain the advantages of PSA screening and the challenges associated with excessive diagnosis and treatment [8]. In Pakistan, unlike developed nations, the utilization of Serum PSA for prostate cancer screening in men aged 50 and above is infrequent. However, in cases where patients exhibit Lower Urinary Tract Symptoms (LUTS), Serum PSA is commonly administered. There is a lack of published literature on the effectiveness of PSA in detecting cancer within the Pakistani population. A high false positive rate of detestation of prostate cancer is observed if the parameter is only serum PSA level-based. Moreover, many variables fluctuate serum PSA levels leading to most of the unnecessary biopsies these include benign prostatic hyperplasia, infections/ inflammation, or different traumatic maneuvers. The findings will allow urologists to predict clinical status and correlate it with PSA levels, as well as identify cases at high risk for carcinoma of the prostate.

METHODS

The urology department, of Pakistan Railway Hospital, Rawalpindi conducted a prospective comparative study. The study lasted for 6 months and was reviewed by an ethical board from June 2022 to December 2022. Two groups were formed, the study involved 114 patients, with 57 cases in each group under examination. The patients for this study were selected through Non-Probability Consecutive Sampling. The study focused on men over the age of 50 who were suffering from symptoms related to the lower urinary tract. Participants meeting particular criteria were selected, with serum PSA levels falling between 4 ng/ml and 20 ng/ml. To ensure reliable results, certain exclusion criteria were applied to minimize potential confounding factors. Individuals who display symptoms of urinary tract problems with prostate-specific antigen (PSA) levels under 4 ng/ml or exceeding 20 ng/ml were excluded from the study. Additionally, Individuals with lower urinary tract symptoms (LUTS) stemming from urological cancers other than the prostate, those who had previously undergone prostate surgery or pelvic radiotherapy, or those facing complications due to urinary blockages (such as bladder stones, kidney damage, and recurrent urinary tract infections) were not included in the research study. A study was conducted on patients with an enlarged prostate and serum PSA level >4 ng/ml. All eligible patients were sorted into two categories: In group A, individuals displayed antigen (PSA) levels from 10-4 ng/ml, while group B exhibited antigen (PSA) levels from 20-10 ng/ml. The study proforma contained demographic characteristics and clinical status of all the patients. Patients were counseled about the biopsy procedure and its associated complications. Both written and informed consent were obtained before the procedure. Biopsy specimens were sent to histopathology for analysis. The TRUS procedure, short for Trans-rectal Ultrasound Scan biopsy, was employed to detect early Carcinoma of the prostate in patients showing symptoms of Lower Urinary Tract and varying levels of Antigen (PSA) through professional diagnostic methods. The procedures were done with proper protocols after giving prophylactic antibiotics plus gut preparation. The biopsy results were documented, and the outcome of the study was determined by comparing the occurrence of prostate cancer in the two groups under investigation in a professional manner. The study investigator conducted all study procedures and data collection personally while being supervised to manage selection bias and uphold data quality and consistency. The study data was inputted and analyzed utilizing SPSS version 17.0. It includes age as one of the numerical variables, PSA levels, and ultrasonography findings in the form of mean ± SD. Clinical symptoms (urinary problems), digital rectal exam outcomes, and tissue samples from biopsies were shown as grouped data using frequency and proportion.

RESULTS

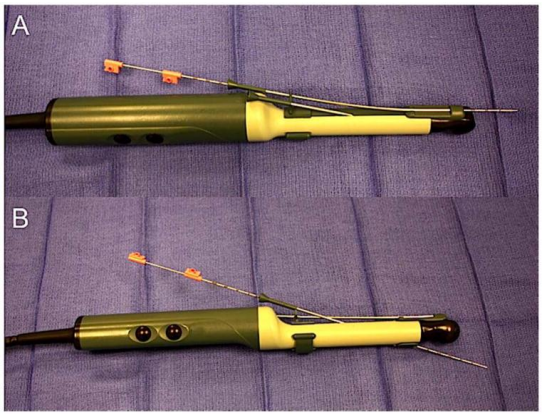
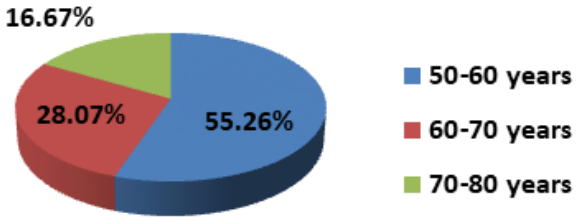


Figure No. 1. Ultrasound biopsy probe end-fire configuration (A) and side-fire configuration (B)



FigureNo. 2: Age group distribution

The age range of participants in both Group A and Group B was between fifty and eighty years, with average ages of 68.40±4.80 years and 68.72±4.78 years, respectively, showing no significant difference (p=0.72). The majority (55.26%) of patients were aged 50-60 years, followed by 28.07% aged 60-70 years, and 16.67% aged 70-80 years. Both groups had a similar distribution of age groups.

When considering symptoms, 26.32% of patients reported urgency, 32.46% reported frequency, and 38.60% reported nocturia. Other common complaints included poor stream (25.44%), dribbling (22.81%), and hematuria (6.14%). The frequency of various LUTS was comparable between the two study groups. DRE findings revealed nodules in 30.84% of patients, firm consistency in 29.82%, obliterated median sulcus in 32.46%, and asymmetry in 22.81%. The frequency of different DRE findings was similar in both groups. The two groups exhibited no significant difference in the reported prostatic volume, with measurements of 53.82±25.83 ml for Group A and 57.12±29.18 ml for Group B (p=0.52). Nevertheless, Group B demonstrated notably higher pre-voidal volumes (528±94 ml compared to 461±92 ml; p<0.001) and post-voidal volumes (212±56 ml versus 102±55 ml; p<0.001) when contrasted with Group A. The mean serum level of prostate-specific antigen measured at 10.53±5.90 ng/ml was notably higher in Group B (15.96±2.72 ng/ml) compared to Group A (5.09±1.60 ng/ml; p<0.001). Prostate cancer was confirmed by biopsy in 24.56% of the subjects, with a significantly higher incidence in Group B (33.33% vs. 15.79%; p=0.029) than in Group A.

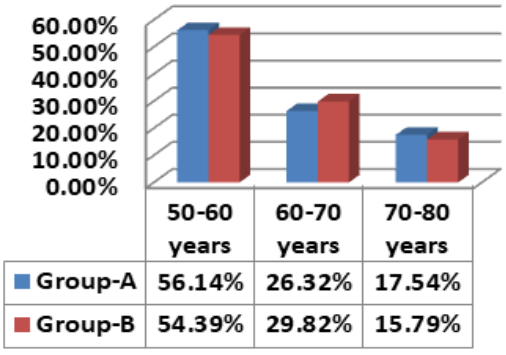


Figure No. 3: Age Groups Distribution of Study in both groups

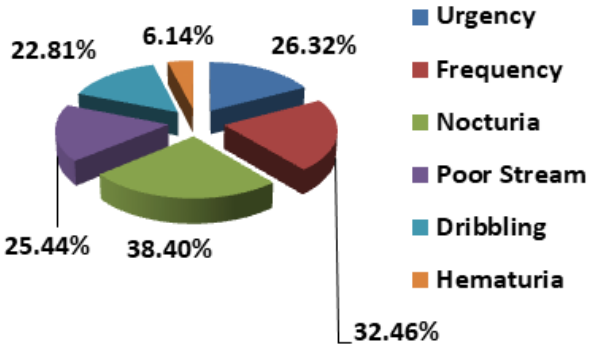


Figure No. 4: Occurrence frequency of various LUTS within the sample population

Figure 4 displays the occurrence frequency of various LUTS within the sample population under examination

Table No. 1: Comparison of various low urinary tract symptoms among the study groups (n=114)

LUTS	Group-A n=57	Group-B n=57	P value
Urgency	15 (26.32%)	15 (26.32%)	1.000
Frequency	20 (35.09%)	17 (29.82%)	0.55
Nocturia	21 (36.84%)	23 (40.35%)	0.70
Poor Stream	14 (24.56%)	15 (26.32%)	0.83
Dribbling	14 (24.56%)	12 (21.05%)	0.66
Hematuria	2 (3.51%)	5 (8.77%)	0.24

Table No. 2: Comparison of various DRE findings among the study groups (n=114)

DRE Findings	Group-A n=57	Group-B n=57	P value
Nodule	19 (33.33%)	23 (40.35%)	0.44
Firm Consistency	16 (28.07%)	18 (31.58%)	0.68
Obliterated Median Sulcus	17 (29.82%)	20 (35.09%)	0.55
Asymmetry	11 (19.30%)	15 (26.32%)	0.37
Estimated Prostate Volume	53.22±25.84	56.57±29.15	0.52

DISCUSSION

Detection of prostate cancer through PSA levels can sometimes be inaccurate due to a high number of false-positive outcomes. This issue arises because other conditions like benign prostate enlargement, inflammation, infection, or physical manipulation of the prostate gland can also influence PSA levels.

Consequently, unnecessary biopsies might be carried out. The primary objective of this study is to determine the incidence of prostate cancer detected through biopsy among patients with various levels of serum PSA and to explore the relationship between elevated PSA concentrations and malignant prostate growths.

This research is the first of its kind among our local population. It has discovered a direct correlation between elevated levels of serum prostate-specific antigen (PSA) and a notably increased incidence of prostate cancer upon biopsy. Thus, it can be inferred that serum PSA levels serve as an indicator of cancerous prostatic tissue, with higher levels warranting further examination of the tissue to rule out malignancy. However, a notable drawback of the study was the absence of a comparison of the treatment outcomes of these patients based on their initial PSA levels. The analysis in question could have provided insight into the potential of serum PSA in predicting the prognosis of the disease. Conducting a study of this nature would aid in categorizing patients based on risk upon presentation, facilitating better management and enhancing patient outcomes. We strongly advocate for the

The average age of patients experiencing Lower Urinary Tract Symptoms (LUTS) was around 68.56±4.80 years as noted. Similarly, a significant association between increased age, particularly above 60 years, and the risk of prostate cancer, was documented in previous studies[9]. Similarly, Kant et al[10] studies contributed to understanding prostate health in South Indian men the average ages reported for Indian patients suffering from Lower Urinary Tract Symptoms (LUTS) were found to be almost the same as our study. While Isiwele et al. [11] investigated the correlation between Digital Rectal Examination (DRE) findings and histopathological results in Nigerian men suspected of having prostate diseases also noted an average age of 66.9±5.7 years for patients with LUTS in Nigeria.

The most common complaints among men in this study were urgent urination (26.32%), frequent urination (32.46%), nighttime urination (38.60%), weak stream (25.44%), urinary leakage (22.81%), and hematuria (6.14%). Ojewola et al.[12] a study conducted on Nigerian men revealed similar findings, showing prevalence rates of urgent urination (26.0%), frequent urination(32.7%), urination at night (38.4%), weak stream (25.1%), urinary leakage (22.6%), and hematuria (6.9%). Awan et al[13] stress the critical role of hematuria as a potential symptom of urological malignancies and advocate for prompt and comprehensive diagnostic assessments to ensure early detection and treatment. Ahmed et al[14] noted a similar incidence and emphasized that urgency, frequency, dribbling, incontinence, and nocturia were common among patients with prostatic lesions, at Dow Medical College, Hospital in Karachi.

Comparison between Group A and Group B showed significant, differences in average levels of prostate-specific antigen in the bloodstream showed significant differences at 15.96±2.72 ng/ml compared to 5.09±1.60 ng/ml with a p-value of less than 0.001., as well as the volume of residual urine before urination (528±94 ml compared to 461±92 ml; $p<0.001$) and after urination (212±56 ml compared to 102±55 ml; $p<0.001$) were analyzed. Group B demonstrated notably higher values than Group A. According to Saifullah et al[15], Patients diagnosed with benign prostatic hyperplasia (BPH) with increased prostate volume are associated with higher residual urine volumes, which can contribute to LUTS and may indicate underlying prostatic pathology. Ko & Kim et al[16] demonstrated that as PSA screening became more frequent, treatment decisions evolved and likely led to even earlier detection, potentially impacting treatment patterns. However, Bansal & Gill et al[17] found a similar or higher detection rate, which could reinforce the validity of using PSA, DRE, and TRUS together. According to Özbey & Öztorun et al [18,] Some prostate cancers are missed and only diagnosed after TURP reported even higher rates among such patients in Turkey.

CONCLUSION

The quantity of prostate-specific antigen (PSA) in the bloodstream is the strongest match of malignant prostate tissue. A high PSA level should prompt action, such as performing a histopathological examination of tissue to rule out malignancy. By recognizing the significance of PSA levels, we can take a proactive approach to safeguard our health and well-being.

Author's Contribution:

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REFERENCES

1. Okpua NC, Okekpa SI, Njaka S, Emeh AN. Clinical diagnosis of prostate cancer using digital rectal examination and prostate-specific antigen

tests: a systematic review and meta-analysis of sensitivity and specificity. Afri J Urol 2021;27:1-9.
2. Villavicencio MA, Suarez CE, Fiallos DL. Importance of rectal examination of prostate in primary care. Neuro Quantol 2022;20(13):176.
3. Taha DE, Aboumarzouk OM, Koraiem IO, Shokeir AA. Antibiotic therapy in patients with high prostate-specific antigen: Is it worth considering? A systematic review. Arab J Urol 2020;18(1):1-8.
4. Nawaz A, Manan F, Minallah N, Rehman KU. Effect of empirical antibiotic treatment on prostate-specific antigen in men with borderline raised serum prostate-specific antigen. J Rehman Med Inst 2023;9(1):20-2.
5. Hayat NU, Fiaz S, Hamza Ashraf MS, Azhar K, Khan T. Role of antibiotics in raised serum prostate-specific antigen (PSA) level in KPK. In Med Forum 2021;32(4):157.
6. Wang J, Xia HH, Zhang Y, Zhang L. Trends in treatments for prostate cancer in the United States, 2010-2015. Am J Cancer Res 2021;11(5):2351.
7. Kuss K, Adarkwah CC, Becker M, Donner-Banzhoff N, Schloessler K. Delivering the unexpected—Information needs for PSA screening from Men's perspective: A qualitative study. Health Expectations 2021;24(4):1403-12.
8. Lumbreras B, Parker LA, Caballero-Romeu JP, Gómez-Pérez L, Puig-García M, López-Garrigós M, et al. Variables associated with false-positive PSA results: A cohort study with real-world data. Cancers 2022;15(1):261.
9. Malik SS, Batool R, Masood N, Yasmin A. Risk factors for prostate cancer: A multifactorial case-control study. Current Problems in Cancer 2018;42(3):337-43.
10. Kant P, Inbaraj LR, Franklyn NN, Norman G. Prevalence, risk factors and quality of life of Lower Urinary Tract Symptoms (LUTS) among men attending Primary Care slum clinics in Bangalore: A cross-sectional study. J Family Med Prim Care 2021;10(6):2241-2245.
11. Isiwele EM, Essiet A, Irabor GI. Correlation of digital rectal examination findings with findings on histopathology of the prostate in patients with suspected prostate cancer. Int J Contemp Med Res 2018;5(7):G12-G16.
12. Ojewola RW, Oridota ES, Balogun OS, Ogundare EO, Alabi TO. Lower urinary tract symptoms: prevalence, perceptions, and healthcare-seeking behavior amongst Nigerian men. World J Mens Health 2016;34(3):200–8.
13. Awan SU, Bhatti AN, Fakhr A, Awan AN, Fiyyaz H. Frequency of Urological Carcinomas Presenting as Gross Haematuria in Punjab Pakistan and Recommendation for its Early Diagnosis: Urological Carcinomas Presenting As Gross Haematuria. Pak Armed Forces Med J 2018;68(2):363-68.
14. Ahmed N, Misbah S, Waseem J. Spectrum of Prostate lesions at Dow Medical College: A 5-year Study. BAOJ Pathol 2019;2:016.
15. Saifullah BR, Gilani S, Asif H, Hasan Z, Sharif Z. Sonographic Association of Prostate Volume with Post Micturition Residual Volume in Benign Prostate Hyperplasia. RADS J. Pharm. Pharm. Sci 2018;6(2):107-12.
16. Ko YH, Kim SW. Influence of repeated prostate-specific antigen screening on treatment pattern in a country with a limited social perception of prostate cancer: Korean national wide observational study. Invest Clin Urol 2021;62(3):282.
17. Bansal N, Gill MK. Comparison of Diagnostic Yield of Digital Rectal Examination, Serum Prostate Specific Antigens, Transrectal Ultrasound with Histopathology of Prostate. J Res Med Educ Ethics 2018;8(1):74-8.
18. Özbey C, Öztorun K. Frequency of incidental cancer in transurethral prostate resection materials and our clinical approach to these patients; a retrospective file scan. Kafkas J Med Sci 2019;9(1):11-6.

Original Article

Anatomical Variation in the Position of Mandibular Foramen with Side of the Arch Using Cone Beam Computed Tomography

CT Scan Locate the Mandibular Foramen Based on Arch Side

Asma Sattar[1], Muhammad Ishfaq[2], Imran Khattak[1], Aiman Shaheryar[1], Munawar Aziz Khattak[1] and Sana Arbab[1]

ABSTRACT

Objective: Cone-beam computed tomography images were used in this investigation to locate the mandibular foramen based on the arch side.

Study Design: This retrospective cross-sectional analysis examined hospital data.

Place and Duration of Study: This study was conducted at the Khyber College of Dentistry's (KCD) Radiology Department, Peshawar, Pakistan. It was conducted from 4th November 2021 to 3rd May 2022.

Methods: A radio-anatomical inquiry was conducted to assess 1000 CBCT photographs from patients who received evaluation during a two-year period. All statistical analyses of the data sets were conducted at a $P \leq 0.05$ level of significance.

Results: Each CBCT scan included measurements of the mandibular foramens on both sides of the jaw, for 200 mandibular foramens in total (100 on the left and 100 on the right). With a range of 15 to 70 years, the mean age was 39.81±14.71 years. The experiment's findings demonstrated that the left or right side of the arch had no bearing on where the mandibular foramen was located.

Conclusion: The investigation's findings demonstrated that the arch side had no bearing on where the mandibular foramen was located.

Key Words: Inferior alveolar nerve, Mandibular Foramen, CBCT

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INTRODUCTION

The mandibular foramen is an irregular opening located on the mandibular ramus' inside surface. For the IANB, that provides local anesthetic to a number of lower jaw procedures, the site where the IAN crosses the mandibular foramen is critical[1]. Depending on the population, the placement of the mandibular foramen might alter on both left and right sides as an individual grows[2].

Before undergoing an osteotomy of the ramus of the jaw, the mandibular foramen and IAN must be identified; great care must be used throughout these procedures to avoid damage[1].

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In these orthognathic surgeries, as the surgeons usually do not know the precise placement of the mandibular foramen in different racial or ethnic groups and age ranges, Failure of the IAN block or fracture of the ramus is very common. It is estimated that five to fifteen percent of instances will result in an IAN block malfunction[3] or in fifteen to twenty percent of cases[4]. According to a study, this failure rate might reach 45%. IAN block failure can be caused by anatomical variations, such as the mandibular foramen being positioned above or below its normal position, inadequate anesthetic procedures, such as putting a needle too anteriorly or posteriorly to the normal placement, and a lack of identifiable anatomic landmarks[5].

Several authors have used a variety of methods, including dried human mandibles, to pinpoint the location of MF[6], Orthopantomography[7,8], computed tomography scan[5], and Cone beam computed tomography for identifying the mandibular foramen [1,9-11]. Compared to a simple radiograph, CBCT produces more accurate results and has less picture distortion when it comes to localizing various anatomical characteristics. Additionally, it scans more quickly, is more precise, comprehensive, and emits less radiation than traditional CT imaging[1].

As far as we are aware, no local population research has been conducted on this subject. Finding the MF's location is the aim of this investigation. In order to choose an easily accessible target site for IANB and lessen the likelihood of it failing in most of patients, dental surgeons may utilize the study's findings to pinpoint the mandibular foramen. Additionally, the results of this study will reduce the risk of inferior alveolar nerve damage in patients by providing a secure site for extraoral osteotomies of the ramus.

METHODS

Permission to conduct this cross-sectional retrospective analysis was granted by the Prime Foundation's Institutional Review Board (IRB) on September 10, 2021 (approved number: Prime/IRB/2021-358). RRB-KCD approved the ethical data collection in notification No. 3065/RRB/KCD, which was issued on November 3, 2021. Peshawar was the site of the research. The CBCT photos were provided by KCD's radiology department. All KPK patients, regardless of their financial status, can receive medical care at KCD which is a referral hospital. The observer was instructed by an OMFS specialist to evaluate cone beam computed tomographic radiographs. The CBCT radiographs used in this investigation are currently on exhibit in the Khyber College of Dentistry's (KCD) radiology department. The computer was loaded with CBCT pictures using the Planmeca Romexis application. Patients having pathological lesions in the ramus of the jaw, asymmetrical faces, or Mandibular first molars that were either absent or misaligned on both sides were excluded, but CBCT pictures of males and females aged 15 to 70 were included. Following stringent, standardized scanning protocols and the manufacturer's guidelines, a senior radiology technician at KCD took the CBCT radiographs. The CBCT scanner was used to create these radiographs., with a voxel size of around 400 m, depending on the field of view (FOV), and an exposure duration of nine seconds. Each cone beam computed tomography image was evaluated by the same examiner to avoid observer variability. They were also evaluated under normal viewing conditions, which included adjusting the brightness and opacity settings to improve radiograph clarity. Before conducting the radiography inquiry, the investigator was instructed to recognize the mandibular foramen and other landmarks in the mandible using a series of cone beam computed tomographic pictures. Examples of mandibular CBCT landmark identification, practical discussion sessions, and guidance on using the CBCT application to ascertain the distances between mandibular landmarks comprise the calibration training approach. MF was located using axial, sagittal, cross-sectional, and panoramic images. The mandibular landmarks utilized in the prior study were evaluated using the ruler in the Planmeca Romexis application and their lengths were estimated (in mm) with the MF(2).

The markers included the following:

1. The deepest points of the ramus's anterior border A and posterior border P,
2. The mandibular notch's superior point of curvature (MN),
3. The mandibular incisura's most inferior point (MI), and
4. The occlusal plane of the mandibular first molar (O).

The following measures and ratios were employed in the ensuing computations:

- Ramus's height was determined using the smallest measurement MIMN (between coordinates MN and MI).
- AMF/AP ratio was used to estimate the mandibular foramen's horizontal position, while MIMF/MIMN ratio was has been employed for determination of its vertical position.

Mandibular foramen were examined bilaterally in each participant’s radiograph, and their positions, together with The proforma was filled out with the patient's MRN number, geographical location, and gender.

Statistical Assessment:

• SPSS version 20 was used to conduct the statistical analyses.

• To establish whether the differences between the left and right sides were statistically significant, an independent t-test was conducted.

• Statistical significance for both tests were determined at $P < 0.05$

RESULTS

Every CBCT of patients who received treatment during the span of two years were analyzed radio-anatomically. 100 CBCTs out of a total of 1000 were determined to fit the study's inclusion requirements. Each CBCT image's mandibular foramen was assessed on mandible's both sides, totaling 200 mandibular foramens (100 on the mandible's right side and 100 on its left). With a range of 15–70 years, the mean age (SD) is 39.81±14.71 years.

The differences between the two sides of the arch were compared using independent t tests. ($P \leq 0.05$).

The average separation between the MF and different mandibular markers on the arch's left and right sides is as follows:

The position of MF did not differ statistically significantly on either side of the arch in this study (Table 1). The mean distances for AMF, PMF, MNMF, OMF, MIMN, and the AMF/AP ratio were greater on the mandibular right side, the left side however had higher mean distances for MIMF and AP, However, These changes were not statistically significant, as indicated by $P > 0.05$. MIMF/MIMN ratio was the same on both sides of the arch, as Table 1 demonstrates.

Table No. 1: The mean distance of the MF from various mandibular markers on both sides of arch:

	Right (mm) N=100	Left (mm) N=100	P value*
	MEAN ± Std. Deviation	MEAN ± Std. Deviation	
The distance (A-MF) between points A and MF	17.38±2.80	17.20±2.63	0.894
The distance (P-MF) between points P and MF	12.10±2.75	12.98±2.32	0.106
The distance (MI-MF) between points MI and MF	18.38±3.51	19.03±3.72	0.583
The distance (MN-MF) between points MN and MF	33.32±5.05	31.55±5.23	0.927
The distance from point O (The lower first molar's occlusal plane)) to point MF (O-MF)	3.82±2.72	3.48±2.41	0.192
The AP distance (between points A and P)	29.09±3.11	29.64±2.93	0.839
The distance MIMN (between locations MI and MN)	50.95±5.93	50.25±5.90	0.834
The AMF/AP ratio	0.58±0.11	0.58±0.09	0.106
The MIMF/MIMN ratio	0.37±0.08	0.37±0.08	0.866

DISCUSSION

Radiographs are a noninvasive method for determining the mandibular foramen's precise location, that is essential knowledge in oral and maxillofacial surgery[1]. CBCT is regarded as the radiographic method of choice for precise identification and investigation of mandibular foramen since it offers numerous benefits over simple films.[10]. Many dentists have lauded CBCT's diagnostic potential. Due to the smaller voxel size of CBCT, it can express fine structures and uses less radiation than a traditional mulitislice CT scan. In comparison to conventional CT. Additionally, it requires less tube voltage and current[9].

On the right side, the average distance between the anterior and posterior borders was 29.09±3.11, while on the left side, it was 29.64±2.93. (Table: 1). The right and left mandibular widths were 30.23 ± 2.15 mm and 30.02 ± 2.0 mm, respectively. Both the left and right 60 dry human mandibles exhibited mandibular widths of 30.02 ± 2.0 mm and 30.23 ± 2.15 mm, respectively. according to a 2020 study by Amjad et al[12].

The ramus had a mean vertical height of 50.60mm in this study. However, same height was recorded at 49.4mm in a study conducted by[13].

The right and left sides of MF's location did not differ statistically significantly, according to this research. While the mean distances of the AMF, PMF, MNMF, OMF, MIMN, and the right side of the mandible had a higher AMF/AP ratio than the left. Nevertheless, these variations were not statistically significant (P > 0.05As seen in Table 1, the MIMF/MIMN ratio was the same on both sides of the mandible. This is consistent with what is now understood about the variations in MF position between the arch's two sides[1,14,15].

The MF in this study was 3.65 mm above the plane of the occlusal plane. According to a study, The MF was situated 2.5–3.6 mm above the molars' occlusal plane[16], there was no indication that the location of the MF changed statistically significantly as people aged. According to[17], in adults, the MF is above the occlusal plane by 4.2 millimeters.

CONCLUSION

This study's findings demonstrated that the mandibular foramen's placement was unaffected by the arch side.

Author's Contribution:

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Drafting or Revising Critically:	Imran Khattak, Aiman Shaheryar, Munawar Aziz Khattak, Sana Arbab
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Al-Shayyab MH. A simple method to locate mandibular foramen with cone-beam computed tomography and its relevance to oral and maxillofacial surgery: a radio-anatomical study. Surg Radiol Anat 2018;40(6):625–34.
2. Vathariparambath N, Krishnamurthy NH, Chikkanarasaiah N. A Cone Beam Computed Tomographic Study on the Location of Mandibular and Mental Foramen in Indian Pediatric Population. Int J Clin Pediatr Dent 2022; 15(4):422–7.
3. Sarfaraz I, Pascoal S, Macedo JP, Salgado A, Rasheed D, Pereira J. Anesthetic efficacy of Gow-

Gates versus inferior alveolar nerve block for irreversible pulpitis: a systematic quantitative review. J Dent Anesth Pain Med 2021; 21(4): 269–82.
4. Lasemi E, Motamedi MHK, Qaranizade K, Hassani Z, Lasemi R. Modification in implementation of the inferior alveolar nerve block technique [Internet]. In Review; 2022 May [cited 2023 Oct 19]. Available from: https://www.researchsquare.com/article/rs-1599913/v1
5. Feuerstein D, Costa-Mendes L, Esclassan R, Marty M, Vaysse F, Noirrit E. The mandibular plane: a stable reference to localize the mandibular foramen, even during growth. Oral Radiol 2020;36(1):69–79.
6. Park JH, Jung HD, Kim HJ, Jung YS. Anatomical study of the location of the antilingula, lingula, and mandibular foramen for vertical ramus osteotomy. Maxillofac Plast Reconstruct Surg 2018;40(1):1–6.
7. Krishnamurthy NH, Unnikrishnan S, Ramachandra JA, Arali V. Evaluation of relative position of mandibular foramen in children as a reference for inferior alveolar nerve block using orthopantamograph. J Clin Diagnost Res JCDR. 2017;11(3):ZC71.
8. Kumar A, Bhagawati BT, Kumar N, Jyotsana K, Sharanamma B, Solanki H. Morphometric Analysis of Mental and Mandibular Foramen in Gender Determination among Sriganganagar Population: A Cross-Sectional Digital Panoramic Study. J Ind Acad Oral Med Radiol 2023; 35(2):258.
9. Ahn BS, Oh SH, Heo CK, Kim GT, Choi YS, Hwang EH. Cone-beam computed tomography of mandibular foramen and lingula for mandibular anesthesia. Imag Sci Dent 2020; 50(2):125.
10. Mehanny M, Mansour S, Alzahrani A, Alquraishi L, Alhassoun R, AlSerwi RH. Morphometric localization of Mandibular Foramen in a sample of Adult Saudian Population Using Cone-Beam Computed Tomography. Egypt Dent J 2022;68(2):1479–87.
11. Valizadeh S, Tayefi M, Ghomeishi M, Ahsaie MG, Amiri MJ. Assessment of Anatomical Location and Variation of Mandibular Foramen Using Cone-Beam Computed Tomography: A Cross-Sectional Study. J Iranian Med Council 2022 Dec 12 [cited 2023 Oct 19]; Available from: https://publish.kne-publishing.com/index.php/JIMC/article/view/11334
12. Amjad S, Hr Z, S AA. Study of mandibular foramen from different bony landmarks in dry human mandibles. IP Ind J Anat Surg Head Neck Brain 2020;4(2):40–3.
13. da Fontoura RA, Vasconcellos HA, Campos AES. Morphologic basis for the intraoral vertical ramus osteotomy: anatomic and radiographic localization of the mandibular foramen. J Oral Maxillofac Surg 2002;60(6):660–5.
14. Kilarkaje N, Nayak SR, Narayan P, Prabhu LV. The location of the mandibular foramen maintains absolute bilateral symmetry in mandibles of different age-groups. Hong Kong Dent J 2005;2:35–7.
15. Kumar MP, Lokanadham S. Sex determination & morphometric parameters of human mandible. Int J Res Med Sci 2013;1(2):93–6.
16. Altunsoy M, Aglarci OS, Ok E, Nur BG, Gungor E, Colak M. Localization of the mandibular foramen of 8-18 years old children and youths with cone-beam computed tomography. J Pediatr Dent 2014;2(2).
17. Ebogo M, Olive N, Jacques E, Ondoa A, Zogo O. Sexual dimorphism and mandibular foramen: A CT-Scan study in a sample of Cameroonian population; clinical features. Advances Oral Maxillofac Surg 2021;2:100033.

Original Article

Frequency of Comorbidities in Patients Presenting with Acute Coronary Syndrome (ACS)

Umer Ibrahim Paracha, Ibrahim Shah, Akhtar Sher, Matiullah Khan and Samiullah Khan

ABSTRACT

Objective: The main objective of the study is to find the frequency of comorbidities in patients presenting with acute coronary syndrome.

Study Design: This retrospective study

Place and Duration of Study: This study was conducted at the Department of Cardiology, Gajju Khan Medical College, Swabi from June 2022 to June 2023.

Methods: Data was collected from 320 acute coronary syndrome patients. Demographic and clinical data were extracted from electronic medical records, including age, gender, past medical history, presenting symptoms, laboratory results, electrocardiogram findings, echocardiography reports, and comorbidities.

Results: Data were collected from 320 patients from both genders. Mean age of the patients was 58.9±8.5 years, and there were 65% male and 35% female patients. The most common presenting symptom was chest pain, reported by 85% of patients, followed by shortness of breath (60%) and fatigue (40%). The prevalence of comorbidities among the study population was as, hypertension (70%), dyslipidemia (60%), diabetes mellitus (50%), obesity (40%), chronic kidney disease (25%), and heart failure (20%). Combinations of comorbidities were also observed, with the most common being hypertension and dyslipidemia (50%), followed by hypertension and diabetes mellitus (40%), and dyslipidemia and diabetes mellitus (30%).

Conclusion: It is concluded that comorbidities play a substantial role in the presentation, management, and outcomes of acute coronary syndrome. High prevalence rates and distinct patterns of comorbidity combinations underscore the importance of comprehensive risk assessment and personalized treatment approaches for acute coronary syndrome patients.

Key Words: ACS, Comorbidities, Risk factors, Patients, Treatment

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INTRODUCTION

Acute coronary syndrome (ACS) represents a spectrum of cardiovascular conditions characterized by sudden, reduced blood flow to the heart, often due to coronary artery disease[1]. Although ACS continues to be a major cause of morbidity and mortality globally, the presentation and outcomes are often modulated by the presence of other medical conditions. This article defines co-morbidities as the presence of two or more diseases in a patient, where co-morbidity in patients with ACS is identified to worsen the severity of the disease, the choice of treatment, and the prognosis[2].

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These conditions may range from hypertension diabetes mellitus dyslipidemia obesity chronic kidney disease and heart failure. These conditions are frequently concurrent with ACS and make the disease's clinical course more challenging, raising morbidity and mortality rates, and treatment costs[3].

CVD continues to be the leading cause of death worldwide and contributes 31% to total deaths. Due to increased life expectancy, morbidity and mortality rates among world population has high tendency for comorbid illness especially those related to cardiovascular diseases of which is ACS[4]. The presence of more than one disease or condition at the same time, known as comorbidity, translates to high risk for ACS patients as well as complicates treatment. Moreover, the proportion of patients with comorbidities increases, which is also associated with higher mortality and future cardiovascular events in patients with ACS, which emphasize the difficulty of clinical management of such patients[5].

ACS patients usually present with one or more comorbid conditions; past MI, DM, CPD, CLD, CKD, peripheral vascular disease, and stroke or TIA[6]. Nonetheless, current clinical protocols for CHD were

developed for treatment of a single chronic disease and its comorbidity, and could be inapt in managing CHD in multimorbidity. Furthermore, patients with the multiple comorbidities are frequently excluded from the compounds of the RCT and therefore the translation is often weak of the investigational findings to the realities of the clinical environment[7].

Some of the demographic and clinical factors relating to comorbid conditions among ACS patients have been established from previous research[8]. Furthermore, the results showed that patients with more comorbidities according to their CCI scores reported fewer typical chest pain and dyspnea symptoms. Along the same line, Chen et. al., In a study on 2972 American patients admitted with acute MI noted cardiovascular and non-cardiovascular co-morbidities. Hypertension was the most common cardiac co-morbidity (75%) and chronic kidney disease was the most common non-cardiac co-morbidity (22%). Of the patients 8% had a history of multiple coexisting illnesses; these patients were older, women, unmarried, and presented with non-ST elevation MIs.

METHODS

This retrospective study was conducted at Department of Cardiology, Gajju Khan Medical College, Swabi from June 2022 to June 2023. Data was collected from 320 ACS patients.

Inclusion criteria:

- Patients aged 18 years or older.
- Patients with acute chest pain symptoms, and acute coronary syndrome at the initial assessment, with subsequent confirmation of acute coronary syndrome by clinical presentation.

Exclusion criteria:

- Patients with a diagnosis of chronic stable angina or other non-ACS cardiac conditions.
- Patients with incomplete medical records or missing data on key variables, such as comorbidities or laboratory results.

Data Collection: Details obtained from EMRs included patients' demographics such as age, sex, medical history, first complaint, biochemistry, ECG results, echocardiography, and the presence of comorbidities. Comorbidities of interest included hypertension, diabetes mellitus, dyslipidemia, obesity, chronic kidney disease, and heart failure. Information on age, gender, past medical history, presenting symptoms, laboratory results, electrocardiogram findings, echocardiography reports, and comorbidities was obtained. The frequency of each comorbidity among ACS patients was calculated, along with the prevalence rates expressed as percentages.

Statistical Analysis: Data were collected and analyzed using SPSS v29.0 A preliminary data analysis was done where frequency tables and descriptive statistics were used to look at quantitative Variables such as age, gender and time taken to seek treatment among the study population.

RESULTS

Data were collected from 320 patients from both genders. Mean age of the patients was 58.9±8.5 years, and there were 65% male and 35% female patients. The most common presenting symptom was chest pain, reported by 85% of patients, followed by shortness of breath (60%) and fatigue (40%). Electrocardiogram findings indicated that 40% of patients had ST-segment elevation, while 30% exhibited non-ST-segment elevation.

Table No. 1: Demographic data of patients

Characteristic	Value
Total Patients	320
Mean Age (years)	58.9±8.5
Gender	
Male	65%
Female	35%
Presenting Symptoms	
Chest Pain	85%
Shortness of Breath	60%
Fatigue	40%
Electrocardiogram Findings	
ST-Segment Elevation	40%
Non-ST-Segment Elevation	30%

Table No. 2: Prevalence and pattern of comorbidities in acute coronary syndrome patients

Comorbidity	Prevalence (%)
Hypertension	70%
Dyslipidemia	60%
Diabetes Mellitus	50%
Obesity	40%
Chronic Kidney Disease	25%
Heart Failure	20%
Comorbidity Combination	
Hypertension + Dyslipidemia	50%
Hypertension + Diabetes Mellitus	40%
Dyslipidemia + Diabetes Mellitus	30%
Dyslipidemia + Obesity	25%
Hypertension + Chronic Kidney Disease	20%
Diabetes Mellitus + Chronic Kidney Disease	15%

The prevalence of comorbidities among the study population was as, hypertension (70%), dyslipidemia (60%), diabetes mellitus (50%), obesity (40%), chronic kidney disease (25%), and heart failure (20%). Combinations of comorbidities were also observed, with the most common being hypertension and dyslipidemia (50%), followed by hypertension and diabetes mellitus (40%), and dyslipidemia and diabetes mellitus (30%). Other combinations included

dyslipidemia and obesity (25%), hypertension and chronic kidney disease (20%), and diabetes mellitus and chronic kidney disease (15%).

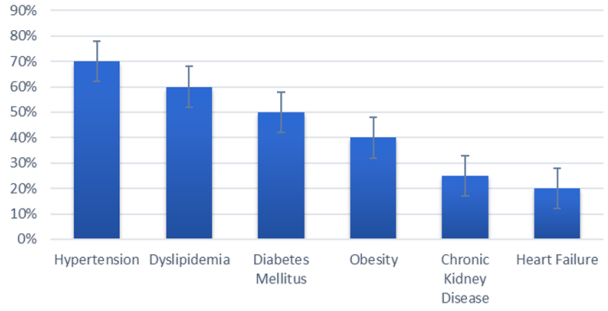

Figure No. 1: Prevalence of Comorbidity (%)

The treatment modalities utilized in the study population were as follows: coronary angiography (80%), percutaneous coronary intervention (PCI) (60%), and coronary artery bypass grafting (CABG) (20%). Pharmacotherapy was also administered, with high rates of usage observed for antiplatelet agents (95%), statins (90%), beta-blockers (80%), and ACE inhibitors or ARBs (70%).

Table No. 3: Treatment and management of comorbidities in acute coronary syndrome patients

Treatment	Percentage
Coronary Angiography	80%
PCI	60%
CABG	20%
Pharmacotherapy	
Antiplatelet Agents	95%
Statins	90%
Beta-Blockers	80%
ACEIs or ARBs	70%
Diuretics	30%

Table No. 4: Correlation between different variables

Variable 1	Variable 2	Correlation Coefficient	p-value
Age (years)	Hypertension	0.25	<0.05
Diabetes Mellitus	Dyslipidemia	0.30	<0.01
Chronic Kidney Disease	Heart Failure	0.15	<0.05
Hypertension	Percutaneous Coronary Intervention (PCI)	-0.20	<0.01
Diabetes Mellitus	In-Hospital Mortality	0.35	<0.001

The correlation analysis revealed significant associations between several variables. Age showed a positive correlation with hypertension ($r = 0.25$, $p < 0.05$), indicating that older individuals were more likely to have hypertension. Similarly, diabetes mellitus was positively correlated with dyslipidemia ($r = 0.30$, $p < 0.01$), suggesting a higher prevalence of dyslipidemia among diabetic patients. Chronic kidney disease showed a positive correlation with heart failure ($r = 0.15$, $p < 0.05$), indicating a relationship between these two conditions.

DISCUSSION

We observed a high prevalence of comorbidities among patients presenting with acute coronary syndrome (ACS), with hypertension, dyslipidemia, and diabetes mellitus being the most common. These results corroborate prior studies showing how ACS patients bear a substantial cardiovascular disease risk factor burden[9]. Of note, we also found a different pattern of comorbidity clusters with skewed distribution of some differential comorbidities. It is important to have awareness about such patterns for risk assessment and intervention planning to deal with several co-morbidities at the same time[10]. The complexity of clinical decision making based on the client's multi-morbidity and the lack of clear steerage has been linked to lower compliance with medication and worse outcomes among patients diagnosed with acute coronary syndrome (ACS)[11]. This results in the treatment of multiple comorbidities with underprescribing and undertreatment of medications and standard of care interventions, especially for percutaneous coronary interventions and dual antiplatelet therapy, regarding which the safety and efficacy among such populations remains ambiguous. Thus, patients with ACS and significant comorbidities have significantly poorer in-hospital and one-year prognosis, added to this, high one-year mortality rates[12].

Several co-morbidities were ascertained to affect the clinical profile and the approach towards ACS. For instance, patients with diabetes mellitus pointed towards more frequent atypical presentations and patients with hypertension were more likely to have STEMI[13]. Data has shown that about forty percent of patients presented with ACS have one or more other conditions including previous MI, diabetes, chronic lung disorder, chronic kidney disease, peripheral vascular pathology, or cerebrovascular disease. However, current clinical practice guidelines for CHD are primarily focused on the management of single diseases consonant with the treatment of separate chronic illnesses and could not effectively lay down guidelines for the treatment of CHD complicated by coexisting conditions[14]. In addition, the frequently isolation of patients with MCC in population of RC trials reduces the relevance of the results of research in conditions of everyday clinical practice[15]. In an other study, researcher has therefore carried out a study using data derived from 19, 496 patients with ACS recorded in the AMIS plus registry. They demonstrated that increased CCI value was connected with age, sex,

hypertension, dyslipidemia, obesity and the history of cigarette smoking, but not with current cigarette smoking. Furthermore, fewer patient's classical symptoms including chest pain and dyspnea were coded when the CCI score was higher. Another researchers identified both cardiovascular and non-cardiovascular conditions in another study conducted on 2,972 patients with AMI hospitalized in the United States of America[11]. They noted that hypertensive heart disease was the most common coexisting cardiac disease, which was seen in 75 percent of patients, while chronic kidney disease was the most frequent non cardiac disease seen in 22 percent patients[16]. Furthermore, compared with patients with one comorbidity, patients with two or more comorbidities were more likely to be older, female, unmarried, with prior MI and STEMI[17].

CONCLUSION

It is concluded that comorbidities play a substantial role in the presentation, management, and outcomes of acute coronary syndrome (ACS). High prevalence rates and distinct patterns of comorbidity combinations underscore the importance of comprehensive risk assessment and personalized treatment approaches for ACS patients.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Umer Ibrahim Paracha, Ibrahim Shah
Drafting or Revising Critically:	Akhtar Sher, Matiullah Khan, Samiullah Khan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Burke LA, Rosenfeld AG, Daya MR, Vuckovic KM, Zegre-Hemsey JK, Diaz MF, et al. Impact of comorbidities by age on symptom presentation for suspected acute coronary syndromes in the emergency department. Eur J Cardiovasc Nurs 2017;16(6):511–521.
2. Zhang, Fangyuan, et al. Prognostic Impact of Comorbidity Measures on Outcomes following Acute Coronary Syndrome: A Systematic Review. Int J Clin Pract 2021;75(10): e14345.
3. Canivell S, Muller O, Gencer B, Heg D, Klingenberg R, Räber L, et al. Prognosis of cardiovascular and non-cardiovascular multimorbidity after acute coronary syndrome. PLoS One 2018;13(4):e0195174.
4. Potts J, Kwok CS, Ensor J, Rashid M, Kadam U, Kinnaird T, et al. Temporal Changes in Co-Morbidity Burden in Patients Having Percutaneous Coronary Intervention and Impact on Prognosis. Am J Cardiol 2018;122(5):712-722.
5. Yang CC, Fong Y, Lin LC, Que J, Ting WC, Chang CL, Wu HM, et al. The age-adjusted Charlson comorbidity index is a better predictor of survival in operated lung cancer patients than the Charlson and Elixhauser comorbidity indices. Eur J Cardiothorac Surg 2018;53(1):235-240.
6. Rashid M, Kwok CS, Gale CP, Doherty P, Olier I, Sperrin M, et al. Impact of co-morbid burden on mortality in patients with coronary heart disease, heart failure, and cerebrovascular accident: a systematic review and meta-analysis. Eur Heart J Qual Care Clin Outcomes 2017;3(1):20-36.
7. Sanchis J, Soler M, Núñez J, Ruiz V, Bonanad C, Formiga F, et al. Comorbidity assessment for mortality risk stratification in elderly patients with acute coronary syndrome. Eur J Intern Med 2019;62:48-53.
8. Zhang F, Bharadwaj A, Mohamed MO, Ensor J, Peat G, Mamas MA. Impact of Charlson Co-Morbidity Index Score on Management and Outcomes after Acute Coronary Syndrome. Am J Cardiol 2020;130:15-23.
9. Hautamäki M, Lyytikäinen LP, Mahdiani S, Eskola M, Lehtimäki T, Nikus K, et al. The association between charlson comorbidity index and mortality in acute coronary syndrome - the MADDEC study. Scand Cardiovasc J 2020;54(3):146-152.
10. Karabağ T, Altuntaş E, Kalaycı B, Şahin B, Somuncu MU, Çakır MO. The relationship of Charlson comorbidity index with stent restenosis and extent of coronary artery disease. Interv Med Appl Sci 2018;10(2):70-75.
11. Wellejus Albertsen L, Heide-Jørgensen U, Schmidt SAJ, Grey C, Jackson R, Sørensen HT, et al. The DANish Comorbidity Index for Acute Myocardial Infarction (DANCAMI): Development, Validation and Comparison with Existing Comorbidity Indices. Clin Epidemiol 2020;12:1299-1311.
12. Baechli, Ciril, et al. Association of Comorbidities with Clinical Outcomes in Patients After Acute Myocardial Infarction. IJC Heart Vasculature 2020;29:100558.
13. Shruthi, D. R., et al. Psychiatric Comorbidities in Acute Coronary Syndromes: Six-month Follow-up Study. Ind J Psychiatr 2018;60(1):60-64.
14. Burke, Larisa A, et al. Impact of Comorbidities by Age on Symptom Presentation for Suspected Acute Coronary Syndromes in the Emergency Department. Eur J Cardiovas Nurs : J Working

Group Cardiovascular Nurs Eur Soc Cardiol 2017;16:511.

15. Breen K, Finnegan L, Vuckovic K, Fink A, Rosamond W, DeVon HA. Multimorbidity in Patients With Acute Coronary Syndrome Is Associated With Greater Mortality, Higher Readmission Rates, and Increased Length of Stay: A Systematic Review. J Cardiovasc Nurs 2020;35(6):E99-E110.
16. Steen DL, Khan I, Andrade K, Koumas A, Giugliano RP. Event Rates and Risk Factors for Recurrent Cardiovascular Events and Mortality in a Contemporary Post Acute Coronary Syndrome Population Representing 239 234 Patients During 2005 to 2018 in the United States. J Am Heart Assoc 2022;11(9):e022198.
17. Sanchis J, García Acuña JM, Raposeiras S, Barrabés JA, Cordero A, Martínez-Sellés M, et al. Comorbidity burden and revascularization benefit in elderly patients with acute coronary syndrome. Rev Esp Cardiol (Engl Ed) 2021;74(9):765-772.

Original Article

Evaluating the Efficacy of Platelet-Rich Plasma, Hyaluronic Acid, and Botulinum Toxin in the Treatment of Temporomandibular Joint (TMJ) Disorders: A Comparative Cross-Sectional Study

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ABSTRACT

Objective: This cross-sectional study aimed to compare the efficacy of these three treatments in managing TMJ disorders.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Abbasi Shaheed Hospital, Karachi from January 2023 to June 2024.

Methods: A total of 60 patients diagnosed with TMJ disorders were recruited and divided into three equal groups of 20 patients. Data was collected using a structured questionnaire and clinical examination. The following information was recorded.

Results: The Botox group demonstrated the most significant pain reduction, with a mean VAS score of 2.1 ± 0.9 at 3 months, compared to 4.5 ± 1.3 in the PRP group and 4.3 ± 1.2 in the HA group. The mean MMO increase was also highest in the Botox group (15.3 ± 3.6 mm), compared to 8.7 ± 4.3 mm in both the PRP and HA groups. Quality of life improvements were most notable in the Botox group, with a mean increase of 27.4 ± 9.1 points, significantly higher than the improvements seen in the PRP (17.3 ± 10.2) and HA (15.1 ± 9.8) groups.

Conclusion: PRP, HA, and Botox are effective minimally invasive treatments for TMJ disorders. Botox may offer superior pain relief and functional improvement compared to PRP and HA.

Key Words: Patients, PRP, TMJ, Disorder, Botox, Treatments

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INTRODUCTION

Temporomandibular joint (TMJ) disorders refer to a diverse group of conditions that affect the temporomandibular joints, muscles of mastication, and surrounding structures, leading to a range of clinical symptoms, including pain, clicking or popping sounds, restricted jaw movement, and headaches. These disorders are typically classified into two categories: These include disc displacement disorders, osteoarthritis diseases of the joint and myofascial pain syndrome[1]. Despite etiologic factors ranging from trauma, malocclusion, bruxism, or systemic inflammatory diseases such as rheumatoid arthritis, the precise cause of the condition is not still conclusively understood and most likely polyetiologic[2]. TMJ disorder treatment starts with conservative therapy, such as – taking medication like NSAIDs or muscle relaxants, receiving physical therapy, wearing a bite splint, or making some changes in behaviour. Among these, platelet-rich plasma, hyaluronic acid, and botulinum toxin have become promising options and/or adjuvants to the classical treatment because they have different mechanisms of action and are less invasive[3]. PRP is autologous biological remodeling from the patient's blood; platelet concentrate enriched with growth factors. Many of these growth factors like platelet derived growth factor (PDGF), transforming growth factor beta (TGF β) and vascular endothelial growth factor (VEGF) are very active in tissues healing and regeneration[4]. Reports regarding the utilisation of

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PRP in patients with TMJ dysfunction have revealed some positive outcomes with regard to the reduction of the amount of pain, flexibility of the joint and other related outcome functionalities. Nevertheless, the data are still scarce, and larger scale RCTs are required to define the therapeutic schedules such as the number of injections, time intervals and long-term effectiveness[5]. Hyaluronic acid is a natural component of synovial fluid of joints and the drug effect comes from its ability to lubricate articular surfaces, to act as a shock absorbing agent, and a vehicle for nutrient exchange[6]. It is used for other joint diseases, including osteoarthritis of the knee; however, its application to TMJ disorders has increased in recent years. In this review of clinical trials of HA for TMJ disorders therapies, pain relief and functional benefit is variable and ranges from moderate to insignificant. These variations of outcomes may be explained by the type of HA employed, the degree of the disorder, or perhaps the population of patients. However, HA still should be considered for treatment of patients with TMJ osteoarthritis or those with degenerative joint changes[7]. Botox, or botulinum toxin type A, has been research with a view of its effectiveness on muscle spasm and pain as well as muscular relaxation is via blocking the release of acetylcholine at the neuromuscular junction. Regarding conditions of the TMJ, Botox is applied mainly for the relief of myofascial pain and muscle dysfunction as a cause of bruxism, clenching, or hypertrophy of the temporalis muscle[8].

METHODS

A retrospective study was conducted at Abbasi Shaheed Hospital, Karachi, Pakistan from January 2023 to June 2024. A total of 60 patients, diagnosed with TMJ disorders based on clinical and radiological findings, were recruited for the study. These patients were randomly divided into three equal groups of 20 each.

Inclusion Criteria:

- Aged between 18 and 65 years.
- Diagnosed with TMJ disorders confirmed by a qualified dental or medical professional.
- Reported pain intensity of at least 4 on a 10-point Visual Analogue Scale (VAS), indicating moderate to severe pain.

Exclusion Criteria:

- Pregnancy or lactation.
- History of bleeding disorders, such as hemophilia or other clotting abnormalities.
- Previous treatment with PRP, HA, or Botox for TMJ disorders within the past 6 months.
- Known allergy to any of the study medications (PRP, HA, or Botox).

Data Collection: Data was collected through a combination of structured questionnaires, clinical examinations, and follow-up visits. Demographic data, including age, sex, and occupation, were recorded to ensure that the groups were comparable at baseline. Furthermore, to ensure the accuracy of the obtained results, the chronic conditions of each patient were checked to establish the possible impact on final outcome of the study. The course and severity of the TMJ dysfunction were recorded; in particular, the pain intensity was assessed with the help of Visual Analogue Scale (VAS). To assess their pain, patients were required to give the pain an intensity score of either zero, meaning no pain, or 10, meaning severe pain. MMO was also measured in clinical assessments because it is an important parameter of joint function Clinical assessments also involved assessment of joint sound which is commonly manifested in terms of cracking or crepitation in relation to TMJ disorders.

Treatment Protocols

- PRP Group: Patients in this group received a single intra-articular injection of PRP into the affected TMJ. The PRP was prepared by drawing the patient's blood, centrifuging it to concentrate platelets, and then injecting the product directly into the joint space.
- HA Group: Patients received a single intra-articular injection of hyaluronic acid into the affected TMJ. HA is a viscosupplement that aims to restore synovial fluid viscosity and reduce inflammation and pain within the joint.
- Botox Group: Patients in this group received a single intramuscular injection of botulinum toxin (Botox) into the masseter muscles, which are frequently implicated in TMJ pain and dysfunction. Botox works by reducing muscle hyperactivity, potentially alleviating pain and improving joint function.

Statistical Analysis:

Data were analyzed using SPSS v25. Comparisons between the three treatment groups were made using one-way analysis of variance (ANOVA) for continuous variables (e.g., pain reduction, mouth opening). The chi-square test was used for categorical variables. A p-value of < 0.05 was considered statistically significant.

RESULTS

Data were collected from 60 patients. The average age of participants was similar, with the PRP group having a mean age of 35.2 years, the HA group at 34.6 years, and the Botox group at 36.1 years. Gender distribution was also consistent, with 70% of participants in each group being female. Regarding comorbidities, hypertension was the most common condition, affecting 20% of patients in the PRP group, 15% in the HA group, and 25% in the Botox group.

At baseline, the mean VAS score was similar across groups: PRP (7.8 ± 1.1), HA (7.6 ± 1.2), and Botox (7.9 ± 1.0). After 3 months, the Botox group exhibited a significant reduction in pain, with a mean VAS score of

2.1 ± 0.9, compared to 4.5 ± 1.3 for the PRP group and 4.3 ± 1.2 for the HA group. The VAS reduction was also greatest in the Botox group (5.8 ± 1.1), significantly outperforming both PRP and HA (3.3 ± 1.2 and 3.3 ± 1.1, respectively). The p-value (< 0.01) indicates that the pain reduction in the Botox group was statistically significant compared to both PRP and HA.

Table No. 1: Demographic Characteristics of Participants

Characteristic	PRP Group (n=20)	HA Group (n=20)	Botox Group (n=20)
Average Age (years)	35.2±7.8	34.6±6.5	36.1±8.3
Gender (Female, %)	70%	70%	70%
Comorbidities (%)	20% (hypertension)	15% (hypertension)	25% (hypertension)

Table No. 2: Baseline and 3-Month Follow-Up VAS Pain Scores

Group	Baseline VAS Score (Mean ± SD)	VAS Score at 3 Months (Mean ± SD)	VAS Reduction (Mean ± SD)
PRP	7.8±1.1	4.5±1.3	3.3±1.2
HA	7.6±1.2	4.3±1.2	3.3±1.1
Botox	7.9±1.0	2.1±0.9	5.8±1.1
p-value	-	< 0.01 (Botox vs PRP, HA)	-

Table No. 3: Maximum Mouth Opening (MMO) at Baseline and 3-Month Follow-Up

Group	Baseline MMO (Mean ± SD) mm	MMO at 3 Months (Mean ± SD) mm	MMO Increase (Mean ± SD) mm
PRP	35.4±8.2	44.1±6.1	8.7±4.3
HA	34.7±7.9	43.4±5.8	8.7±4.1
Botox	33.9±8.5	49.2±5.5	15.3±3.6
p-value	-	< 0.01 (Botox vs PRP, HA)	-

At baseline, the mean MMO was similar across the groups: PRP (35.4 ± 8.2 mm), HA (34.7 ± 7.9 mm), and Botox (33.9 ± 8.5 mm). After 3 months, the Botox group had the largest mean MMO at 49.2 ± 5.5 mm, representing a significant increase of 15.3 ± 3.6 mm. In comparison, the PRP and HA groups both showed an increase of 8.7 ± 4.3 mm and 8.7 ± 4.1 mm, respectively, reaching a mean MMO of 44.1 ± 6.1 mm and 43.4 ± 5.8 mm.

At baseline, the quality of life scores were similar for all groups: PRP (45.2 ± 12.6), HA (46.3 ± 11.5), and Botox (46.9 ± 13.2). After 3 months, the Botox group showed a substantial improvement, with a post-treatment QoL score of 74.3 ± 6.9, reflecting a mean improvement of 27.4 ± 9.1. In comparison, the PRP group improved by 17.3 ± 10.2 points (62.5 ± 9.3), and the HA group improved by 15.1 ± 9.8 points (61.4 ± 8.1).

Table No. 4: Quality of Life Improvement at Baseline and 3-Month Follow-Up

Group	Baseline Quality of Life Score (Mean ± SD)	Post-Treatment Quality of Life Score (Mean ± SD)	Improvement in Quality of Life (Mean ± SD)
PRP	45.2±12.6	62.5±9.3	17.3±10.2
HA	46.3±11.5	61.4±8.1	15.1±9.8
Botox	46.9±13.2	74.3±6.9	27.4±9.1
p-value	-	< 0.001 (Botox vs PRP, HA)	-

DISCUSSION

The results of this study suggest that all three treatments—platelet-rich plasma (PRP), hyaluronic acid (HA), and botulinum toxin (Botox)—can effectively reduce pain, improve joint function, and enhance the quality of life in patients with temporomandibular joint (TMJ) disorders. However, Botox demonstrated superior efficacy in all measured outcomes, including pain relief, improvement in joint function, and overall quality of life[9-12]. The most significant outcome of the present research is that a greater degree of pain reduction is a recognizable feature of the Botox group compared to the PRP and HA groups. In total, all three groups demonstrated a decrease in pain intensity using VAS and comparing with the baseline, the decrease was more prominent in the Botox group than in the PRP and HA groups. This would agree with the known usage of Botox for addressing muscle related pain have[13]. Botox gives a lasting solution to TMJ because it curtails the production of acetylcholine at neuromuscular junctions and therefore reduces muscle contractions that cause pain. However, PRP and HA, as potent anti-inflammatory agents that enhance the lubricating capacity of the joint, lack the musculoskeletal approach of stem cells. Comparing with the other treatments, the much higher efficacy in pain relief underlines the utility of muscle specific treatment approach in TMJ disorder[14]. Regarding the improvement of joints dysfunction all three groups showed significant improvement with particular emphasis on mouth opening. Nevertheless, Botox showed the significant improvement of MMO compared to control groups, with the increase of 15.3 mm, compared to 8.7 mm in

both PRP and HA groups[15]. The increase in MMO demonstrates the reasons why Botox is effective on the masseter and temporalis muscles which in TMJ disorders, restricts jaw mobility. Even though, PRP and HA helped in improving the lubrication of the joint and elimination of inflammation in the TMJ, they were not much helpful in dealing with the muscle driven pathology concerning the limitation of mouth opening[16]. Consequently, the study indicate that Botox may be more effective in patient with TMJ discomfort caused by muscular contraction or spasm, while PRP and HA may benefit patients with joint related discomfort due to degeneration or inflammation. The benefits in terms of the quality of life were revealed in all of the treatment groups with Botox revealing the most pronounced positive effect[17].

CONCLUSION

It is concluded that all three treatments—platelet-rich plasma (PRP), hyaluronic acid (HA), and botulinum toxin (Botox)—are effective in managing temporomandibular joint (TMJ) disorders, with significant improvements in pain, joint function, and quality of life. However, Botox demonstrated superior efficacy in reducing pain intensity, enhancing joint mobility, and improving quality of life.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Madiha Khan, Sufyan Ahmed
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Al-Delayme RMA, Alnuamy SH, Hamid FT, Azzamily TJ, Ismaeel SA, Sammir R, et al. The Efficacy of Platelets Rich Plasma Injection in the Superior Joint Space of the Tempromandibular Joint Guided by Ultra Sound in Patients with Non-reducing Disk Displacement. J Maxillofac Oral Surg 2017;16(1):43-47.
2. Liu SS, Xu LL, Fan S, Lu SJ, Jin L, Liu LK, Yao Y, et al. Effect of platelet-rich plasma injection combined with individualised comprehensive physical therapy on temporomandibular joint osteoarthritis: A prospective cohort study. J Oral Rehabil 2022;49(2):150-159.
3. Pihut, M., Ferendiuk, E., Szewczyk, M., et al. The efficiency of botulinum toxin type A for the treatment of masseter muscle pain in patients with temporomandibular joint dysfunction and tension-type headache. J Headache Pain 2016;17:29.
4. Yurttutan ME. Evaluation of the effects of botulinum toxin injection and occlusal splints on the treatment of bruxism. AAOMS 2018;76(10):e30–e31.
5. Haigler MC, Abdulrehman E, Siddappa S, et al. Use of platelet-rich plasma, platelet-rich growth factor with arthrocentesis or arthroscopy to treat temporomandibular joint osteoarthritis: Systematic review with meta-analyses. J Am Dent Assoc 2018;149(11):940e2–952e2.
6. Díaz MIP, Solis PD, Barrientos JVR. Infiltración de plasma rico en factores de crecimiento en desarreglos internos de la articulación temporomandibular. Revista Mexicana de Cirugía Bucal y Maxilofacial 2018;14(2):99–105.
7. Smith SW. Dental and craniofacial applications of platelet-rich plasma. Br Dent J 2005;199:799.
8. Sánchez M, Azofra J, Usabiaga J, et al. A randomized clinical trial evaluating plasma rich in growth factors (PGRF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. Arthroscopy 2012;28(8):1070–1078.
9. Sánchez DC, Ocampo BRY, Chirino CAE. Uso de ácido hialurónico como alternativa para la reconstrucción de papila interdental. Revista Odontológica Mexicana 2017;21(3):205–213.
10. Dahiya P, Kamal R. Hyaluronic acid: A boon in periodontal therapy. North Am J Med Sci 2013;5(5): 309–315.
11. Abal SG, Gonzalez MS. Usefulness of hyaluronic acid in the treatment of joint diseases. Cuba J Rheumatol 2018;20(3):e34.
12. Toameh MH, Alkhouri I, Karman MA. Management of patients with disk displacement without reduction of the temporomandibular joint by arthrocentesis alone, plus hyaluronic acid or plus platelet-rich plasma. Dent Med Problems 2019;56(3):265–272.
13. Nigam PK, Nigam A. Botulinum toxin. Ind J Dermatol 2010;55(1):8–14.
14. Ashkenazi A, Blumenfeld A. Onabotulinum toxin A for the treatment of headache. Headache 2013;53(2):54–61.
15. Bakheit AMO. The possible adverse effects of intramuscular botulinum toxin injections and their management. Current Drug Safety 2006;1(3):271–279.
16. Tvrdy P, Heinz P, Pink R. Arthrocentesis of the temporomandibular joint: A review. Biomed Papers of the Medical Faculty of the University Palacky, Olomouc, Czech Republic 2015;159(1): 31–34. 8
17. Xu J, Gou L, Zhang P, et al. Platelet-rich plasma and regenerative dentistry. Aust Dent J 2020;65(2): 131–142.

Original Article

The Impact of Passive Alveolor Molding VS Nasoalveolar Molding on Cleft Width and Other Parameters of Maxilllary Growth in Unilateral Cleft Lip Palate

Sadia Rasheed, Kashan Qayoom Shaikh, Sidra Memon and Hira Sangrasi

ABSTRACT

Objective: The basic aim of the study is to compare the effects of passive alveolar molding (PAM) and nasoalveolar molding (NAM) on cleft width and various parameters of maxillary growth in unilateral cleft lip palate.

Study Design: This prospective cohort study

Place and Duration of Study: This study was conducted at the Plastic and Reconstructive Surgery LUMHS Jamshoro during June 2023 to July 2024.

Methods: Forty-five infants diagnosed with unilateral cleft lip palate were included in the study. They were divided into two groups based on the selected treatment approach: PAM and NAM. Cleft width measurements were recorded at specific time intervals during the treatment period. Additionally, maxillary growth parameters, including maxillary arch width, nasal symmetry, and columellar length, were evaluated over the course of the follow-up period.

Results: Data was collected from 45 infant patients. There were 23 patients in PAM group and 22 patients in Nam group. Mean age was 4.5±2.45 months and there was 20 female patients and 25 male patients. Throughout the treatment period, both PAM and NAM groups exhibited progressive reduction in cleft width.

Conclusion: It is concluded that both PAM and NAM interventions contribute positively to cleft width reduction, maxillary arch width, nasal symmetry, and columellar length. Notably, NAM exhibited superior efficacy in terms of faster cleft width reduction, improved nasal symmetry, and enhanced columellar length when compared to PAM.

Key Words: Nasal, nasoalveolar molding (NAM), passive alveolar molding (PAM), Unilateral cleft lip and palate (UCLP)

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INTRODUCTION

In the domain of craniofacial care, the treatment and the board of unilateral cleft lip and palate (UCLP) present intricate challenges that demand thorough investigation and innovation. One conspicuous area of center is the effect of various helpful procedures on the aspects and development of the maxillary district in people with UCLP. Specifically, compelling are two particular methodologies: Aloof Alveolar Molding (PAM) and Nasoalveolar Molding (NAM), the two of which endeavor to advance facial style and practical results in patients with cleft lip and palate.[1] One of the fundamental kinds of nasal disfigurement is unilateral cleft lip or palate (UCL/P). The reproduction of facial delicate tissue is the most difficult issue in these patients.[2]

The worldwide prevalence of the UCL/P is 0.5-3 cases for each 1000 births. Hereditary and nearby factors are the etiology of this issue. Besides, the recurrence of this disfigurement varies among individuals concerning orientation, populace, and maternal highlights.[3] The female/male proportion in youngsters with UCL/P is 1:2, and it is more considered normal in the Caucasian populace. The cleft of lip or palate is the fourth most normal craniofacial irregularity in Iranian youngsters with a pace of 2.14 patients per 1000 births.[4]

Thus, patients with CLP deformity require interdisciplinary treatment methodologies by subject matter experts, e.g., orthodontists, oral and maxillofacial surgeons, pediatricians, otorhinolaryngologists, speech therapists and dentists. While there is no standardized public or worldwide treatment idea and definitions contrast, by and large

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CLP treatment can be separated into primary and secondary treatment. Primary treatment covers presurgical newborn child muscular (PSIO) treatment as well as the surgeries of lip and palate reproduction. Secondary treatment alludes to utilitarian or tasteful upgrades after primary cleft conclusion, e.g., presurgical orthodontic treatment preceding careful secondary alveolar bone grafting.[5]

The many-sided exchange between physical designs, for example, the alveolus and nasal depression, highlights the meaning of early mediations in affecting craniofacial advancement. Uninvolved Alveolar Molding involves the utilization of muscular gadgets to bridle intrinsic development powers, while Nasoalveolar Molding includes the work of an oral apparatus to control the situating of the alveolar fragments and nasal ligament.[6] The two strategies plan to lessen cleft width and work with normal development designs inside the maxillary district, subsequently adding to further developed speech, taking care of, and by and large facial concordance. The impacts of PAM and NAM treatment approaches have been portrayed and dissected exclusively in certain examinations and the adequacy of the nasal stent in NAM has likewise been explored in different investigations.[7]

Passive Alveolar Molding and Nasoalveolar Molding have emerged as promising techniques in this endeavor, each with its own distinctive mechanism and potential advantages. Passive Alveolar Molding, by employing specialized devices that gently guide tissue growth, capitalizes on the body's innate capacity for adaptation. In contrast, Nasoalveolar Molding, involving the strategic application of pressure through an oral appliance, takes a more direct approach in molding the alveolar arch and nasal complex. Beyond their technical differences, both approaches aim to mitigate the anatomical and functional sequelae associated with UCLP. The narrowing of the cleft width, enhancement of alveolar bone alignment, and symmetrical development of the nasal cartilage are among the anticipated benefits. Moreover, these interventions hold the promise of reducing the need for more extensive surgical procedures later in life.[8]

METHODS

This prospective cohort study was conducted at Plastic and Reconstructive Surgery LUMHS Jamshoro during June 2023 to July 2024. Forty-five infants diagnosed with unilateral cleft lip palate were enrolled in the study.

Inclusion Criteria:

- Infants diagnosed with unilateral cleft lip palate.
- Age within the specified range for intervention initiation.

Exclusion Criteria:

- Infants with bilateral cleft lip palate or other forms of craniofacial anomalies.
- Age falling outside the predetermined range for intervention initiation.
- Parental or guardian non-compliance with the treatment protocol or follow-up assessments.
- Previously undergone any form of maxillofacial surgery or intervention.

Data collection: The participants were divided into two groups based on the treatment approach chosen:

Group A: Passive Alveolar Molding (PAM) group

Group B: Nasoalveolar Molding (NAM) group.

The PAM group received orthopedic devices designed to gently guide tissue growth in the affected area. The NAM group underwent treatment involving the use of an oral appliance to apply controlled pressure for molding the alveolar arch and nasal complex. Both interventions were initiated during the early developmental stages and were closely monitored throughout the study period. Cleft width measurements were meticulously recorded at specific time intervals during the treatment period for both groups. These measurements offered insights into the effectiveness of each approach in narrowing the cleft width over time. Various maxillary growth parameters were assessed during the follow-up period. Maxillary arch width, nasal symmetry, and columellar length were among the key dimensions evaluated. These measurements were taken at regular intervals to track the progression of maxillary growth and to identify any differences between the PAM and NAM groups.

Statistical Analysis: Data were analyzed using SPSS v27.0 to compare the outcomes between the PAM and NAM groups.

RESULTS

Data was collected from 45 infant patients. There were 23 patients in PAM group and 22 patients in Nam group. Mean age was 4.5±2.45 months and there was 20 female patients and 25 male patients. Throughout the treatment period, both PAM and NAM groups exhibited progressive reduction in cleft width. Notably, the NAM group demonstrated a statistically significant faster reduction in cleft width compared to the PAM group ($p < 0.05$), suggesting the greater effectiveness of Nasoalveolar Molding in narrowing the cleft width.

Table No. 1: Demographic values of infants

Group	Total Infants	Age Range (months)	Gender Distribution
Pam Group	23	2-6	13 males, 10 females
Nam Group	22	3-7	12 males, 10 females

Analysis of maxillary arch width revealed consistent growth in both groups over the follow-up period. While there was no statistically significant difference between the PAM and NAM groups in terms of maxillary arch width changes ($p > 0.05$), both groups exhibited positive growth trends, indicating the potential of both interventions to contribute to improved maxillary arch development.

Table No. 2: Cleft width reduction

Time Interval	PAM Group (mm)	NAM Group (mm)	p-value (PAM VS. NAM)
Baseline	10.5	10.7	0.712
6 months	6.8	5.2	0.028*
12 months	4.2	3.1	0.039*

Evaluation of nasal symmetry demonstrated that both PAM and NAM interventions had positive effects on enhancing nasal symmetry. However, the NAM group exhibited a more pronounced improvement in nasal symmetry compared to the PAM group, with the difference reaching statistical significance ($p < 0.05$).

Table No. 3: Maxillary arch width

Time Interval	PAM Group (mm)	NAM Group (mm)	p-value (PAM vs. NAM)
Baseline	30.1	29.8	0.821
6 months	32.5	32.7	0.632
12 months	34.8	36.2	0.098

Changes in columellar length were assessed to gauge the impact of the interventions on nasal aesthetics. Both groups experienced enhancements in columellar length, with the NAM group showcasing statistically significant greater improvements compared to the PAM group ($p < 0.05$).

Table No. 4: Nasal symmetry and columellar length

Time Interval	PAM Group (mm)	NAM Group (mm)	p-value (PAM vs. NAM)
Baseline	7.4	7.6	0.591
6 months	8.9	9.5	0.317
12 months	9.6	11.2	0.012*
Time Interval	PAM Group (mm)	NAM Group (mm)	p-value (PAM vs. NAM)
Baseline	5.2	5.5	0.421
6 months	6.1	6.9	0.182
12 months	6.8	7.8	0.076

P-values for the comparison of change between PAM and NAM are provided to indicate if there are significant differences in the changes achieved by the two treatment approaches.

Table No. 5: Changes of Distances and Angles with PAM and NAM

Measurement	Baseline Value	6 Month Change (PAM)	6-Month Change (NAM)	p-value Change vs. Zero	p-value Change Comparison (PAM vs. NAM)
Anterior maxillary width (mm)	25.2	-1.8	-2.5	<0.001**	0.042*
Medial maxillary width (mm)	18.7	+0.6	+0.4	0.112	0.673
Lateral angle great segment	30	-3.5	-5.2	<0.001**	0.237
Lateral angle small segment	45	-1.8	-2.9	0.019*	0.121
Medial angle great segment	22	+2.1	+1.5	0.067	0.592

DISCUSSION

The outcomes showed that there are a few huge contrasts among PAM and NAM concerning the development and change in maxillary alveolar curve patterns. While for the two strategies a decrease of the front cleft width was found, it was more articulated with NAM. NAM additionally decreased the foremost and average width of the maxilla, while the back width expanded in the two gatherings.[9] Conversely, with PAM, the front and middle cross over width was settled and all sagittal boundaries showed critical development. The two sections pivoted more medially utilizing NAM than utilizing PAM thinking about horizontal point estimations, while PAM diminished the breakdown of the little fragment to the average.

Our outcomes showed a significant decrease in cleft width over the long run in both the PAM and NAM gatherings. Quite, the NAM bunch displayed an essentially quicker pace of cleft width decrease contrasted with the PAM bunch. This finding proposes that Nasoalveolar Molding could apply more articulated mechanical powers on the cleft sections, prompting more effective restricting of the cleft width. These outcomes highlight the capability of NAM as a compelling technique for early cleft width the board.

Both PAM and NAM mediations added to positive changes in maxillary curve width, nasal balance, and columellar length. While no measurably massive contrasts were seen in maxillary curve width changes between the two gatherings, NAM exhibited a critical improvement in nasal balance and columellar length contrasted with PAM. This infers that Nasoalveolar Molding could apply explicit impacts on nasal and columellar development designs past what is accomplished with Inactive Alveolar Molding alone.[10] Varieties can be made sense of by contrasts in age at the second examination time frame. A review from 2016 from Cerón-Zapata et al. looked at maxillary development in CLP patients treated with a Hotz

machine and treated with NAM. While the investigation of a researcher, just estimated distances, our concentrate likewise estimated turns of the portions. Contrasting the distances estimated in this review and the investigation showed comparable outcomes. The distances, which show the greatest variety between the two examinations, are the sagittal alveolar curve length of the two sections, which show less development in the investigation. Be that as it may, the estimation approaches were somewhat unique. While our review estimated the length on top of the alveolar edge, researcher estimated on the average side of the alveolar edge. In any case, what this large number of studies don't show and gauge are the revolution of the sections. While in past examinations the pivots of the fragments were seldom estimated, and assuming no consideration was given to it, this study shows tremendous contrasts in the revolutions. These distinctions influence straightforwardly other length in development of the alveolar curve. This new observing should be thought about while concluding which PSIO is the right one for the patient.[11]

CONCLUSION

It is concluded that both PAM and NAM interventions contribute positively to cleft width reduction, maxillary arch width, nasal symmetry, and columellar length. Notably, NAM exhibited superior efficacy in terms of faster cleft width reduction, improved nasal symmetry, and enhanced columellar length when compared to PAM. These observations underline the enhanced mechanical impact of Nasoalveolar Molding on cleft segments and surrounding structures, suggesting its potential for optimized early cleft management.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Sadia Rasheed, Kashan Qayoom Shaikh
Drafting or Revising Critically:	Sidra Memon, Hira Sangrasi
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Namdar P, Lal Alizadeh F, Etezadi T, Sadri L, Shiva A. Effect of Nasoalveolar Molding on Nasal Symmetry in Patients with Cleft Lip and Palate: A Systematic Review. J Pediatr Rev 2020;8(2):79-92.
2. Shetty V, Agrawal R, Sailer H. Long-term effect of presurgical nasoalveolar molding on growth of maxillary arch in unilateral cleft lip and palate: Randomized controlled trial. Int J Oral Maxillofac Surg 2017;46(8):977-87.
3. Singh A, Thakur S, Singhal P, Diwana VK, Rani A. A comparative evaluation of efficacy and efficiency of grayson's presurgical nasoalveolar molding technique in patients with complete unilateral cleft lip and palate with those treated with figueroa's modified technique. Contemp Clin Dent 2018;9(Suppl 1):S28-33.
4. Saad MS, Fata M, Farouk A, et al. Early Progressive Maxillary Changes with Nasoalveolar Molding: Randomized Controlled Clinical Trial. JDR Clin Translat Res 2020;5(4):319-331.
5. Parhofer R, Rau A, Strobel K, et al. The impact of passive alveolar molding vs. nasoalveolar molding on cleft width and other parameters of maxillary growth in unilateral cleft lip palate. Clin Oral Invest 2023;27:5001–5009. https://doi.org/10.1007/s00784-023-05119-7
6. Grill FD, et al. Author correction: a semi-automated virtual workflow solution for the design and production of intraoral molding plates using additive manufacturing: the first clinical results of a pilot-study. Sci Rep 2020;10(1):4726.
7. Garland K, et al. Ten-year cephalometric comparison of patients with cleft palate who received treatment with active or passive pre-surgical orthopedic devices. Cleft Palate Craniofac J 2022;13:10556656221106891.
8. Esenlik E, Bekisz JM, Gibson T, Grayson BH, Flores RL. Preoperative alveolar segment position as a predictor of successful gingivoperiosteoplasty in patients with unilateral cleft lip and palate. Plast Reconstruct Surg 2018;141(4):971-982.
9. Kornbluth M, Campbell RE, Daskalogiannakis J, Ross EJ, Glick PH, Russell KA, et al. Active presurgical infant orthopedics for unilateral cleft lip and palate: intercenter outcome comparison of Latham, modified McNeil, and nasoalveolar molding. The Cleft Palate-Craniofac J 2018;55(5):639-648.
10. Saad MS, Fata M, Farouk A, Habib AMA, Gad M, Tavel MB, et al. Early progressive maxillary changes with nasoalveolar molding: randomized controlled clinical trial. JDR Clin Translat Res 2020;5(4):319-331.
11. Al Khateeb KA, Fotouh MA, Abdelsayed F, Fahim F. Short-Term Efficacy of Presurgical Vacuum Formed Nasoalveolar Molding Aligners on Nose, Lip, and Maxillary Arch Morphology in Infants with Unilateral Cleft Lip and Palate: A Prospective Clinical Trial. Cleft Palate Craniofac J 2021;58(7):815-823.

Original Article

Comparison of Tranexamic Acid Versus Placebo for Prevention of Postpartum Hemorrhage in Females Undergoing Delivery at Term

Fehmida, Zarmeena Liaqat and Reema Fateh

ABSTRACT

Objective: The objective of the present study was to compare the mean blood loss with intravenous tranexamic acid versus placebo in pregnant females presenting at term for delivery.

Study Design: Randomized control trial study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology, Saidu group of Hospital, Swat, from January 2023 to June 2023.

Methods: Through non-probability consecutive sampling, a Sample size of 250 women (Group A- TXA group n=125, Group B- Placebo n=125). In group A, females were given intravenous tranexamic acid. In group B, females were given an injection of normal saline. All females were followed till delivery. After delivery, the female was shifted to the ward and blood loss was measured.

Results: Mean± S. D of the pre-operative hemoglobin (HB) of the participants in groups A and B was 11.99 ± 0.72 and 12.44 ± 0.86 g/dL, respectively (P<0.0001). Mean± S. D of the post-operative hemoglobin (HB) of the participants in groups A and B was 10.8 ± 0.73 and 7.44 ± 0.976 g/dL, respectively (P<0.0001). Mean± S. D of the blood loss of the participants in groups A and B was 297.56 ± 69.4 and 912.10 ± 67.1mL, respectively (P<0.0001). In group A, 17% of participants had blood loss of more than 1000mL, while in group B 50% of participants had blood loss of more than 1000mL (p<0.0001). In group A, 8% of participants required a blood transfusion, while in group B 26% of participants required a blood transfusion (p<0.0001).

Conclusion: The research emphasized the importance of tranexamic acid in the management of post-partum hemorrhages, the enhancement of post-partum hemoglobin levels, and the potential reduction in the need for blood transfusions.

Key Words: Delivery, blood loss, postpartum hemorrhage, tranexamic acid

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INTRODUCTION

Postpartum hemorrhage (PPH) is a critical pregnancy complication that poses a significant risk to maternal health, often resulting in severe illness or death. The prevalence of PPH diagnosis varies between 1% and 10% of pregnancies, impacting around 14 million women globally each year[1]. However, the precise incidence of PPH is contingent upon the specific criteria used for its characterization.

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There are various risk factors that have been identified in relation to maternal health, such as advanced age, nulliparity, and uterine fibroids[2]. Additionally, gestational factors like preeclampsia, multiple pregnancy, fetal macrosomia, and placenta accreta, as well as labor-related factors like episiotomy, prolonged second stage of labor, and retained placenta, have also been recognized as risk factors[3]. Despite these findings, there is currently no established model that can accurately predict PPH. Consequently, the primary objectives of clinical management are the timely detection and commencement of treatment in order to minimize the likelihood of mortality and improve maternal outcomes[4]. In order to achieve this objective, the current recommendation is to provide oxytocin prophylactically, with the intention of facilitating uterine contractions and mitigating the occurrence of excessive blood loss during both vaginal and cesarean deliveries[5]. Tranexamic acid (TXA) is a synthetic inhibitor that competes with lysine receptors. It functions as an antifibrinolytic drug by preventing the connections between plasmin and fibrin, as well as

stabilizing the fibrin matrix[6]. The potential benefits of its administration have been proposed in enhancing clinical outcomes among patients with intracerebral haemorrhage[7], trauma[8], and as well as reducing perioperative blood loss in abdominal[9] and orthopedic procedures[10]. The World Maternal Antifibrinolytic study has provided evidence to support the efficacy of TXA in mitigating the mortality risk associated with PPH in women, while also indicating that its use does not lead to an increased likelihood of adverse events[11]. Significantly, the earliest dose of TXA at the commencement of bleeding yielded the most advantageous results, suggesting that its mechanism of action may involve the prevention of coagulopathy rather than the treatment of the disorder[12]. Previous studies[13,14] have indicated the potential utility of TXA as a preventive intervention for women requiring cesarean delivery. However, the generalizability of these findings has been constrained by the smaller sample sizes of the studies included in these analyses. The new study on the efficacy of appropriately powered Tranexamic Acid for Preventing PPH has significantly contributed to the advancement of knowledge in the field. In the Cesarean Delivery (TRAAP2) trial, a comprehensive evaluation was conducted to determine if the advantages of administering TXA as a standard practice during cesarean deliveries exceed the potential long-term dangers associated with its use[15]. The objective of the present study was to compare the mean blood loss with intravenous tranexamic acid versus placebo in pregnant females presenting at term for delivery.

METHODS

After the ethical approval from institutional review board, this randomized control trail was conducted at Department of Obstetrics and Gynecology, Saidu group of Hospital, Swat, from January 2023 to June 2023. Through non-probability consecutive sampling, Sample size of 250 women (Group A- TXA group n=125, Group B- Placebo n=125) was calculated with 95% confidence level, 80% power of test and taking magnitude of total blood loss i.e. 379.2±160.1ml with tranexamic acid and 441.7±189.5ml placebo in females undergoing delivery at term. Women between ages 18-40 years, with any parity presenting during gestational age≥37 weeks, undergoing either vaginal or cesarean delivery. Women with multiple pregnancies, with chronic or gestational hyptertension or pre-eclampsia, with chronic or gestational diabetes, with renal disease, with anemia, with placental problem i.e. placenta previa, accrete, increta or placental abruption and with deranged clotting profile were excluded from the present study. All basic demographic information of each patient (name, age, gestational age, address and contact) was be noted. Then females will be randomly divided in two groups by using random number table. In group A, females were given intravenous tranexamic acid. In group B, females were given an injection of normal saline. All females were followed till delivery. After delivery, the female was shifted to the ward and blood loss was measured. All this information was recorded through pre-designed proforma. The collected data was analyzed statistically by using SPSS version 21. Quantitative variables like age, gestational age and blood loss was presented as mean ± S.D. Qualitative variables like parity was presented as frequency and percentage. Independent sample t-test was applied to compare both groups. P-value ≤0.05 was considered as significant.

RESULTS

Table 1 shows the clinical and demographic parameters of the study participants in both study groups. Mean± S. D of the ages of the participants in groups A and B was 30.17±4.84 and 29.42±4.65 years, respectively (P=0.265). Mean± S. D of the BMI of the participants in groups A and B was 24.38±3.39 and 23.4±3.48 kg/m^2, respectively (P=0.031). Mean± S. D of the parity of the participants in groups A and B was 2.8±0.98 and 3.02±1.07, respectively (P=0.197). Mean± S. D of the gestation age of the participants in groups A and B was 38.032±1.42 and 38.15±1.37 weeks, respectively (P=0.503). In group A, 52% participants underwent normal vaginal delivery while 48% underwent C-section. In group B, 60% participants underwent normal vaginal delivery while 40% underwent C-section. Table 2 shows the primary and secondary outcomes measured in this randomized controlled trial study. Mean± S. D of the pre-operative hemoglobin (HB) of the participants in groups A and B was 11.99 ± 0.72 and 12.44 ± 0.86 g/dL, respectively (P<0.0001). Mean± S. D of the post-operative hemoglobin (HB) of the participants in groups A and B was 10.8 ± 0.73 and 7.44 ± 0.976 g/dL, respectively (P<0.0001).

Table No.1: Clinical and demographic parameters of the study participants

Parameters	Group A (n=125)	Group B (n=125)	P value
Age (years)	30.17±4.84	29.42±4.65	0.265
BMI (kg/m^2)	24.38±3.39	23.4±3.48	0.031
Parity	2.8±0.98	3.02±1.07	0.197
Gestation age (weeks)	38.032±1.42	38.15±1.37	0.503
Mode of delivery			0.123
Vaginal	65 (52%)	75 (60%)	
Caesarian	60 (48%)	50 (40%)	

Table No.2: Comparison of primary and secondary outcomes in study groups

Parameters	Group A (n=125)	Group B (n=125)	P value
Preoperative HB (g/dl)	11.99 ± 0.72	12.44 ± 0.86	<0.0001
Postoperative HB (g/dl)	10.8 ± 0.73	7.44 ± 0.97	<0.0001
Calculated blood loss (ml)	297.56 ± 69.4	912.10 ± 67.1	<0.0001
Blood loss more than 1000 ml	22 (17%)	63 (50%)	<0.0001
Required transfusion	10 (8%)	32 (26%)	<0.0001

Mean± S. D of the blood loss of the participants in groups A and B was 297.56 ± 69.4 and 912.10 ± 67.1mL, respectively (P<0.0001). In group A, 17% of participants had blood loss of more than 1000mL, while in group B 50% of participants had blood loss of more than 1000mL (p<0.0001). In group A, 8% of participants required a blood transfusion, while in group B 26% of participants required a blood transfusion (p<0.0001).

DISCUSSION

This study aimed to assess the effectiveness of tranexamic acid (TA) in lowering blood loss during and after term delivery. The results demonstrated that TXA was successful in reducing blood loss compared to a placebo, with volumes of 297.56 ± 69.4 and 912.10 ± 67.1 mL, respectively (p<0.0001). The findings of this investigation are consistent with a previous study conducted in Turkey, which demonstrated the considerable impact of TXA in lowering postoperative blood loss at 48 hours compared to the placebo group. Specifically, the study stated that the TXA group had a blood loss level of 499.9 ± 206.4 ml, whereas the placebo group had a blood loss level of 600.7 ± 215.7ml[16]. Similar findings were documented in investigations conducted on women from India and Egypt[17,18]. An observable decrease in the occurrence of PPH, defined as blood loss above 1000 ml, was noted following the administration of TXA in the present study with a p value <0.0001. In a study conducted by Gai et al., similar findings were obtained, indicating that patients in the TXA group experienced a mean blood loss of 351 ml during the operating procedure, while the control group had a blood loss of 440 ml[19]. In recent years, there has been an increase in the number of trials done to validate the effectiveness of TXA in reducing blood loss after vaginal delivery. Xia et al. conducted a study whereby they examined the efficacy of the drug in lowering the occurrence of PPH and postoperative blood loss in women undergoing normal delivery[20]. Additionally, we have seen a significantly lower incidence of post-surgical blood transfusions in our TXA group compared to the palcebo group (10 women vs. 32 women, p<0.0001). This outcome is consistent with the previously published results in comparable research[21,22]. Nevertheless, Bhatia and Deshpande found that there was no statistically significant disparity in the requirements for blood transfusions across the two cohorts under investigation, as indicated in their research[18]. Once again, the observed disparities in outcomes may be attributed to the specific demographic chosen for the study, namely high-risk women in our particular investigation. This study has many limitations that should be acknowledged. Firstly, it is unable to provide data on the extent to which the treatment influenced the maternal death rate or the need for more invasive procedures. In a similar vein, the appropriate evaluation of thromboembolic events connected to TA was hindered by the restricted duration of the follow-up period.

CONCLUSION

In summary, the research underscored the importance of tranexamic acid in the management of post-partum hemorrhages, the enhancement of post-partum hemoglobin levels, and the potential for reducing the need for blood transfusions.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Fehmida, Zarmeena Liaqat
Drafting or Revising Critically:	Zarmeena Liaqat, Reema Fateh
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Nasreen S, Baqai S, Iftikhar B, Bukhsh S, Kamran M. Effectiveness of rectal misoprostol in cessation of Post Partum Haemorrhage. Pak Armed Forces Med J 2018(1):54-9.
2. Merriam AA, Wright JD, Siddiq Z, D'Alton ME, Friedman AM, Ananth CV, et al. Risk for postpartum hemorrhage, transfusion, and hemorrhage-related morbidity at low, moderate, and high volume hospitals. The J Maternal-Fetal Neonatal Med 2018;31(8):1025-34.

3. El Badawy A, Waly E, Zaitoun N, Abo-Elwan Y. Assessment of risk factors for primary postpartum hemorrhage at Zagazig university hospitals. Zagazig University Med J 2017;23(2):1-9.
4. Kong CW, To WWK. Menstrual and reproductive outcomes after use of balloon tamponade for severe postpartum hemorrhage. BMC Pregnancy Childbirth 2018;18(1):1-8.
5. No G-tG. Prevention and management of postpartum haemorrhage. BJOG 2017;124(5):e106-e49.
6. Cai J, Ribkoff J, Olson S, Raghunathan V, Al-Samkari H, DeLoughery TG, et al. The many roles of tranexamic acid: an overview of the clinical indications for TXA in medical and surgical patients. Eur J Haematol 2020;104(2): 79-87.
7. Yu Z, Ling L. Tranexamic acid in intracerebral hemorrhage: a meta-analysis. Int J Neurosci 2023;133(6):621-8.
8. Al-Jeabory M, Szarpak L, Attila K, Simpson M, Smereka A, Gasecka A, et al. Efficacy and safety of tranexamic acid in emergency trauma: a systematic review and meta-analysis. J Clin Med 2021;10(5):1030.
9. Koh A, Adiamah A, Gomez D, Sanyal S. Safety and efficacy of tranexamic acid in minimizing perioperative bleeding in extrahepatic abdominal surgery: meta-analysis. BJS Open 2021;5(2): zrab004.
10. Hartland AW, Teoh KH, Rashid MS. Clinical effectiveness of intraoperative tranexamic acid use in shoulder surgery: a systematic review and meta-analysis. Am J Sports Med 2021;49(11):3145-54.
11. Shakur H, Roberts I, Fawole B, Chaudhri R, El-Sheikh M, Akintan A, et al. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (Woman): an international, randomised, double-blind, placebo-controlled trial. The Lancet 2017;389(10084):2105-16.
12. Desborough M, Hildyard C, Stanworth S. Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe hemorrhage. J Thrombosis Haemostasis 2018;16(6):1025-7.
13. Li C, Gong Y, Dong L, Xie B, Dai Z. Is prophylactic tranexamic acid administration effective and safe for postpartum hemorrhage prevention? A systematic review and meta-analysis. Med 2017;96(1).
14. Wang Y, Liu S, He L. Prophylactic use of tranexamic acid reduces blood loss and transfusion requirements in patients undergoing cesarean section: A meta-analysis. J Obstet Gynaecol Res 2019;45(8):1562-75.
15. Sentilhes L, Daniel V, Deneux-Tharaux C. TRAAP2-TRAnexamic Acid for Preventing postpartum hemorrhage after cesarean delivery: a multicenter randomized, doubleblind, placebo-controlled trial–a study protocol. BMC Pregnancy Childbirth 2020;20(1):1-11.
16. Obi V, Umeora O, Dimejesi I, Asiegbu O, Mgbafulu C, Ifemelumma C, et al. Efficacy of intravenous tranexamic acid at reducing blood loss during elective caesarean section in Abakaliki: A double blind randomized placebo controlled trial. Afri J Med Health Sci 2019;18(2):10-7.
17. Schorn MN. Measurement of blood loss: review of the literature. J Midwifery Women's Health 2010;55(1):20-7.
18. Bhatia SK, Deshpande H. Role of tranexamic acid in reducing blood loss during and after caesarean section. Med J Dr DY Patil Univ 2015;8(1):21-5.
19. Gai MY, Wu LF, Su QF, Tatsumoto K. Clinical observation of blood loss reduced by tranexamic acid during and after caesarian section: a multi-center, randomized trial. Eur J Obstet Gynecol Reproductive Biol 2004;112(2):154-7.
20. Xia Y, Griffiths BB, Xue Q. Tranexamic acid for postpartum hemorrhage prevention in vaginal delivery: A meta-analysis. Med 2020;99(3).
21. Shahid A, Khan A. Tranexamic acid in decreasing blood loss during and after caesarean section. J Coll Physicians Surg Pak 2013;23(7):459-62.
22. Maged AM, Helal OM, Elsherbini MM, Eid MM, Elkomy RO, Dahab S, et al. A randomized placebo-controlled trial of preoperative tranexamic acid among women undergoing elective cesarean delivery. Int J Gynecol Obstet 2015;131(3):265-8.

Original Article

A Comparative Study of Stone Clearance Rates in Retrograde Intrarenal Surgery (RIRS) for Kidney Stones Above and Below 1.5 cm in Size

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ABSTRACT

Objective: To analyse stone clearance rates in RIRS patients with stones larger than 1.5 cm compared to those with smaller stones, providing insight into RIRS's potential as a preferred approach for kidney stone management.

Study Design: Retrospective cohort study

Place and Duration of Study: This study was conducted at the Urology department of The kidney Centre Postgraduate Training Institute from the time period of May 2023 to June 2024.

Methods: 151 patients who underwent RIRS at The Kidney Centre Postgraduate Training Institute over a period of one year. Cohorts: - Group A: Stones <1.5 cm. Group B: Stones ≥1.5 cm. **Data Analysis**: SPSS, p-value ≤0.05 considered significant.

Results: Complete Clearance in Group A: 79.6% and Group B: 60.5%. Residual Stone Fragments Less than 4 mm on X-ray or Ultrasound Group A: 16.7% and Group B: 34.9%.

Conclusion: RIRS, in selected cases, can be effective for larger stones (≥1.5 cm) with comparable clinically significant clearance. -Advantages over PCNL include minimal invasiveness, faster recovery, lower morbidity.

Key Words: Percutaneous Nephrolithotomy, PCNL, RIRS, Retrograde Intrarenal Surgery, Stone Clearance.

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INTRODUCTION

The prevalence of kidney stones and their impact on health and quality of life is significant. Retrograde Intrarenal Surgery (RIRS) is a minimally invasive technique widely used to manage kidney stones. However, stone size plays a crucial role in the success rates of this procedure[1].

Historically Larger stones were treated with open Pyelolithotomy until the advent of Percutaneous Nephrolithotomy, aided by the development of FIbreoptics and Nephroscopes. These revolutionized the field of stone treatment by allowing a minimally invasive approach to clear renal stones larger than 2 cm or in difficult anatomical location[2]. Smaller stones were fragmented with extracorporeal lithotripsy, with advances in Ultrasonic Shockwave Lithotripters improving the fragmentation of stones while also making the process safer for the patient by reducing the impact the process has on the kidney parenchyma. Nonetheless, a gray area still existed because of variability in Stone composition and hardness as well as stones in anatomically difficult locations. Particularly challenging were the stones present in narrow neck calyces and those resistant to shockwaves lithotripsy.

For stones between 1 and 2 cm, modern guidelines advocate the use of these multiple procedure options as a sort of armamentarium[3], with decisions regarding treatment based on all these factors combined. Regardless, there is significant morbidity associated with PCNL procedures, with risk of hemorrhage, significant post op pain and respiratory complications for upper pole access concomitant, as it is essentially a controlled grade 4 trauma.

Development of Flexible scopes has had a revolutionizing effect on the field of Renal Stone Surgery, providing direct access, visualization and fragmentation of renal stones without a single incision. The great advancement in the field of Laser energy sources, particularly Holmium YAG Lasers, has helped. These developments have now made RIRS a cost effective as well as the safest approach to the management of Kidney stones between 1-2cm in size[4].

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Whether it is yet the most cost effective option in an economically challenged setting is yet to be determined[5].

Any attempt to treat renal stone consists of the following principle steps. 1) Identification of the Stone, its size, hardness and location within the Kidney, 2) Access to the stone, 3) fragmentation of the target stone via a viable energy source, such as Ballistic Lithoclast, Ultrasonic Shockwaves or laser energy sources, and lastly 4) clearance of the stone fragments from the system. Retrograde Intrarenal surgery for stones using flexible ureterorenoscopes provides us with excellent results in the first three of these steps, with the exception of stones in the lower calyx with a very acute angle. New advancements in scope engineering have greatly improved our ability to target even these lower pole stones with acute angles. While new laser fibers allow transmission of more power with greater flexibility owing to the thinness of the fibers themselves. Regardless, clearance of the fragmented stones depends upon the natural anatomy of the system, and this has always given pause to the Urologist treating renal Stones. How large is too large is a question even today.

With this study, we aim to compare the stone clearance rates in patients undergoing RIRS for kidney stones larger and smaller than 1.5 cm. In Pakistan, Stone disease is endemic and our Centre, the Kidney Centre Post graduate Training Institute, has specialized in treating renal stones over the last 30 years. The recent availability of disposable Flexible Ureterorenoscopes of 7.5FR has dramatically reduced the cost of this procedure, which was otherwise too expensive for our resource poor population. Over the last 5 years, we have seen a progressive and sustained increase in our RIRS case count. We have also witnessed a growing confidence in our ability to manage stones up to and greater than 2 cm in size, especially in patient groups who are not suitable for PCNLs, such as those with difficult anatomies, on anticoagulation medications or recurrent stone formers who are CKD as well those with solitary functioning kidneys. Through this study we aim to determine if the clearance rates for RIRS in larger stones (>1.5cm) is comparable to smaller stones.

METHODS

This study used a retrospective cohort design to evaluate stone clearance rates in patients who underwent Retrograde Intrarenal Surgery (RIRS) at The Kidney Centre Post Graduate Training Institute, specifically targeting stones sized above and below 1.5 cm. Ethical approval was obtained from The Kidney Centre Ethical Review Committee, and the study was granted exemption for patient contact due to its retrospective nature, under reference No: 181-URO-082024 (EXEMPTION).

Study Design

The retrospective cohort study included 151 patients with kidney stones, categorized into two groups: Group A with stones less than 1.5 cm and Group B with stones 1.5 cm or larger. This division allowed for a direct comparison between the two groups in terms of stone clearance, operative times, and associated outcomes.

Inclusion and Exclusion Criteria: Inclusion criteria specified patients aged 18 and above who underwent RIRS for kidney stones. Exclusion criteria included those with anatomical abnormalities, multiple stones, prior kidney surgeries, or any underlying conditions that might complicate the procedure.

Data Collection: Patient data were extracted from medical records, covering demographics (age and gender), stone characteristics (size, location), surgical details (operative time, access), and postoperative outcomes (clearance rates, complications, and hospital stay). As part of the Preoperative Workup protocol for Renal Stone Disease in the Kidney Centre, all new patients presenting with renal Stones undergo plain CT pyelogram, unless a recent (< 6 months) CT with films is available. Prior to any procedure for Renal Stones, a routine X-ray KUB is done with standard bowel prep to confirm stone location and visibility on x-ray. Post-operative Protocol requires that all patients undergo an initial X-ray KUB after Surgery to check for stone clearance and to confirm correct position of the DJ stent. Furthermore, a repeat X ray or an Ultrasound of the Kidney is undertaken after 2 weeks to assess for final clearance, depending on the radio-opacity of the stones on x-ray. Stone clearance (on x-ray or Ultrasound Kidney) is defined as the altogether absence of stones or the presence of fragments smaller than 4 mm, which are clinically insignificant. Present protocol for RIRS in the Kidney Centre requires the passage of Double j Stent in all patients undergoing surgery.

Statistical Analysis: Data were analyzed using IBM SPSS version 21. Mean and standard deviations were calculated for continuous variables (age, stone size, and operative time), while categorical variables (stone clearance, gender, complications) were reported as frequencies and percentages. The normality of continuous variables was checked using normality plots and the Shapiro-Wilk test. For normal data, an independent sample t-test was used, and for non-normally distributed data, the Mann-Whitney U test was applied. The Chi-square test determined associations between categorical variables, and a p-value of ≤ 0.05 was considered statistically significant.

RESULTS

We recruited 151 patients in our study with a mean age of 41.3 ± 14.1 years (Range 18 – 74 years). The baseline parameters of the patients were the similar in both groups. Group A had patients with renal stones less than 1.5cm on radiological investigations and consisted of 108 patients. Group B was composed of all

patients with stone sizes greater than 1.5 cm and had 43 patients. The ratio of Male to female patients was similar and reflects the predominant incidence rate of stone disease in world population.[7] The mean stone size in Group A was 0.98 ± 0.27 cm while in Group B it was 2.1 ± 0.23 cm.

Table No.1: Comparison of Baseline parameters of the patients of two groups n=151

Pre-operative variables	Group A Stone size < 1.5 cm	Group A Stone size ≥ 1.5 cm	P-Value
	Mean ± STD/ n (%)	Mean ± STD/ n (%)	
Age in years	40.5 ± 13.9	68.5 ± 8.1	0.291
Stone size	0.98 ± 0.27	2.1 ± 0.23	<0.001
Gender Male/ Female	80(74.4)/28(25.9)	33(76.7/10(13.3)	0.761

On comparing the two groups of patients, we observed that the mean operative time was significantly longer in the patients with larger stones (115.4 ± 37.3 v/s 134.1 ± 43.7 p=0.012), while the complete stone clearance was significantly lower in these patients as compared to the patients with smaller stones {86 (79.6%) v/s23 (60.5%) p= 0.038). Notably, clinically significant stone clearance (absence of stones or residual fragments ≤4 mm) was comparable between the two groups, with 96.3% (104 patients) in Group A and 95.3% (41 patients) in Group B, indicating effective stone management even in larger stones. However, operative time was significantly longer in Group B (134.1 minutes) compared to Group A (115.4 minutes), reflecting the increased procedural complexity for larger stones. On the other hand, the rate of pre and post-operative complications was the same in both groups (p > 0.05).

Table No.2: Comparison of para and post-operative variables between the two groups of patients Mean ± STD / n (%)

Para and post-operative parameters of the patients		Group A 108(71.5%) Stone size= < 1.5 cm	Group B 43(28.5%) Stone size= ≥ 1.5 cm	P-Value
Operative time		115.4 ± 37.3	134.1 ± 43.7	0.012
Hospital stay		1.1 ± 0.25	1.1 ± 0.43	0.761
Post-operative ESWL		5 (4.6)	1 (2.3)	0.675
Pos-operative pain		3 (2.8)	0	0.558
Post-operative Hematuria		2 (1.9)	0	0.59
Initial failure of access		1 (0.9)	1 (0.9)	0.999
Conversion to PCNL		1 (0.9)	1 (0.9)	0.999
Post-operative assessment modality	Visibility on X-ray	78 (72.7)	36 (86)	
	Visibility on ultrasound	30 (27.8)	6 (14)	0.072
Post-operative clearance	Complete	86 (79.6)	23 (60.5)	
	Residual < 4 mm	18 (16.7)	15 (34.9)	
	Residual ≥ 4 mm	4 (3.7)	2 (4.7)	0.038

The results also showed that prolonged operative time did not translate into greater complication rates. The incidence of post-operative hematuria, severe post-operative pain requiring Opioid Analgesia and prolonged Hospital stay was insignificant in both groups. Patients were discharged on the first post-operative day regardless of stone size. In both groups, failure of access was seen in only one case and conversion to PCNL was only recorded in one case.

DISCUSSION

A. Stone Clearance in Larger Stones and Its Implications. The data from our study underscores the capability of RIRS to achieve substantial clearance even in stones larger than 1.5 cm, a threshold where traditionally, PCNL would be the preferred method. The high clearance rates observed in both groups suggest that with advanced laser technology and improved access techniques, RIRS can provide comparable outcomes to more invasive methods, even for larger stones. This is not in contrast to the recent experiences and results obtained by other Stone Centers across the world.[9,10] These findings imply a shifting paradigm in stone management where RIRS could replace PCNL as a standard treatment, especially for patients unsuitable for more invasive surgeries. Stone size is one of the parameters which decide the course of treatment while its location, hardness and the anatomy of the kidney are also factors to be considered. For renal stones larger than 1.5 cm, RIRS is most

suitable in cases where the stone is not impacted at the PUJ or located at the lower pole with a sharp angle. Y Güleret al, in their paper published in 2021, evaluated the outcomes retrograde intrarenal surgery, antegrade ureterorenoscopy and laparoscopic ureterolithotomy in the treatment of impacted proximal ureteral stones larger than 1.5 cm. They concluded that in patients with impacted Stones at PUJ or Proximal Ureter, RIRS was likely to have poorer stone clearance rates and would require multiple sessions.[8] In contrast, our study participants were patients with non-impacted stones with favorable location and hence led to better post-operative results. Hence, when deciding the surgical approach to treating a renal stone, factors other than size must be kept in consideration.

B. RIRS vs. PCNL: Advantages and Drawbacks

RIRS offers significant advantages over PCNL.[11,12] The most notable benefits are the reduced invasiveness and the subsequent lower risk of hemorrhage, shorter recovery times, and reduced hospital stays. RIRS is also better suited for patients with anticoagulation therapy requirements, anatomical challenges, and single-functioning kidneys, where minimizing trauma is essential. Furthermore, RIRS avoids many of the complications associated with PCNL, such as the risks posed by upper pole access and the respiratory effects due to the prone position required in PCNL. Conventionally larger Stone size would be considered a prohibitive factor when choosing RIRS over PCNL. Our data shows that good stone clearance, comparable to PCNL, can be achieved with RIRS despite larger stone size.

However, RIRS is not without its limitations. The procedure is generally more time-consuming, as attested by our own findings, particularly in larger stones, due to the complex navigation required within the kidney. Lower pole stones also present challenges in RIRS, as the acute angles in these areas can limit access. Moreover, while advanced scopes and laser technologies have improved RIRS capabilities, the need for ongoing scope replacements and potential stone migration during the procedure remain significant considerations.

C. Limitations of This Study and Future Directions

Our study is limited by its retrospective design and reliance on medical records, which could introduce potential biases or inaccuracies. The sample size, while adequate for initial analysis, may not provide a comprehensive picture of RIRS efficacy across different populations or facilities with varying levels of expertise and technology.

Future research should focus on prospective studies with larger, multicenter populations to validate these findings and assess long-term outcomes, including recurrence rates and renal function preservation post-RIRS. Such studies could also investigate cost-effectiveness in diverse healthcare settings, particularly in economically challenged regions like Pakistan, where RIRS is becoming more accessible with disposable scopes.

CONCLUSION

Our findings highlight RIRS as a promising alternative to PCNL for kidney stones up to 2 cm, with excellent clearance rates achievable even in stones larger than 1.5 cm. The advantages of RIRS in reducing invasiveness and recovery time, while maintaining high stone clearance rates, make it a compelling choice in specific patient populations. Future prospective studies will be instrumental in confirming RIRS's role in broader clinical practice, potentially transforming kidney stone management paradigms globally.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zeeshan Zafar, Shakeel Haseeb Uddin Siddique, Wajahat Fareed
Drafting or Revising Critically:	Amna Abdullah, Salman El Khalid, Saba Zafar
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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REFERENCES

1. Kılıç Ö, Akand M, Van Cleynenbreugel B. Retrograde intrarenal surgery for renal stones-Part 2. Turkish J Urol 2017;43(3):252.
2. Tefekli A, Cezayirli F. The history of urinary stones: in parallel with civilization. The Scientific World J 2013;2013(1):423964.
3. Assimos D, Krambeck A, Miller NL et al: Surgical management of stones: American Urological Association/Endourological Society Guideline, part II. J Urol 2016;196:1161.
4. Wymer KM, Sharma V, Juvet T, Klett DE, Borah BJ, Koo K, et al. Cost-effectiveness of retrograde intrarenal surgery, standard and mini percutaneous nephrolithotomy, and shock wave lithotripsy for the management of 1-2cm renal stones. Urol 2021; 156:71-7.
5. Mahmood SN, Ahmed CJ, Tawfeeq H, Bapir R, Fakhralddin SS, Abdulla BA, et al. Evaluation of mini-PCNL and RIRS for renal stones 1–2 cm in an economically challenged setting: A prospective cohort study. Annals Med Surg 2022;81:104235.
6. Goldberg H, Golomb D, Shtabholtz Y, Tapiero S, Creiderman G, Shariv A, et al. The "old" 15 mm

renal stone size limit for RIRS remains a clinically significant threshold size. World J Urol 2017; 35:1947-54.
7. Scales CD, Curtis LH, Norris RD, Springhart WP, Sur RL, Schulman KA, Preminger GM. Changing gender prevalence of stone disease. The J Urol 2007;177(3):979-82.
8. Güler Y, Erbin A. Comparative evaluation of retrograde intrarenal surgery, antegrade ureterorenoscopy and laparoscopic uretero-lithotomy in the treatment of impacted proximal ureteral stones larger than 1.5 cm. Central Eur J Urol 2021;74(1):57.
9. Eissa A, Ragab M, Bianchi G, Hassan A. Retrograde intrarenal surgery in the management of solitary large renal stones, 2-3 cm: a single center experience. Int Surg J 2021;8(3):939-43.
10. Kanchi VB, Pogula VM, Galeti EH, Nekkanti R. Prospective study on Comparison of outcomes of mini percutaneous nephrolithotomy versus retrograde intrarenal surgery for renal stones of 1–2 cm size. Urol Annals 2022;14(3):265-72.
11. Karakoç O, Karakeçi A, Ozan T, Fırdolaş F, Tektaş C, Özkarataş ŞE, et al. Comparison of retrograde intrarenal surgery and percutaneous nephrolithotomy for the treatment of renal stones greater than 2 cm. Turk J Urol 2015;41(2):73-7.
12. Çakıcı MÇ, Sarı S, Özok HU, Karakoyunlu N, Hepşen E, Sağnak L, et al. Comparison of Retrograde Intrarenal Surgery and Percutaneous Nephrolithotomy in the Treatment of 2-3 cm Multicalyceal Kidney Stones. J Urol Surg 2018; 5(4):143-148.

Original Article

Outcome of Supracostal Access of Percutaneous Nephrolithotomy in Pediatric Population - A Single Centre Experience

Supracostal Access of PCNL in Pediatric

Wajahat Fareed, Shariq Anis Khan, Osama Kalim Sheikh, Shakeel Haseeb Uddin Siddique, Zeeshan Zafar and Salman El Khalid

ABSTRACT

Objective: Despite lower complication rates reported in adults, the supracostal approach remains underutilized globally. This study aims to assess the safety and efficacy of this approach in pediatric patients.

Study Design: Retrospective, Observational study

Place and Duration of Study: This study was conducted at the Department of Urology, The Kidney Centre, Post Graduate Training Institute, Karachi, Pakistan between January 1st 2023 till March 31st 2024.

Methods: Patients under 17 years old who underwent PCNL via supracostal puncture were included, while those above 17 years old, underwent multiple procedures simultaneously, or those with any renal anomalies were excluded. All PCNL procedures were conducted with the patient in a prone position. Puncture was carried out using an 18-gauge LP needle under fluoroscopic guidance. Data, including post-operative morbidity, stone-free rates, operative time, stone burden, and hospital stay, were analyzed using SPSS v21.

Results: The total number of patients included in the study was 211. The Median age of the patients was 6 years. The median stone size was 1.5 (1.3-1.9) cm. Mild haematuria was observed in 8 patients (3.8%), while only 1 patient had moderate haematuria (0.5%). The mean difference between the pre and postoperative haemoglobin was 0.6g/dl. Pleural effusion was observed in five patients (2.4%). The mean postoperative hospital stay was 3.8 ± 0.4 days.

Conclusion: Supracostal PCNL is a safe and effective approach for complex renal stones in a paediatric population.

Key Words: Percutaneous Nephrolithotomy, Urolithiasis, Supracostal.

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INTRODUCTION

Urolithiasis constituting 10-45% of cases ranks among the top urological diseases in both adults and children [1]. The stone composition in children is identical to that in adults where mostly 75–80% of stones composed predominantly of calcium oxalate [2]. Diagnosing stone disease in children is challenging due to frequent atypical presentations; only 50% experience pain, and stones are incidentally found in 17% of cases while most children with renal stones commonly exhibit feeding and growth issues [3].

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Technological advancements have shifted the management of renal stones in children from open surgery to a minimally invasive approach [4]. Percutaneous Nephrolithotomy (PCNL) is a well-established, safe, and effective procedure for managing large stone burdens in both children and adults [5]. Miniaturization of instruments have enabled PCNL to be performed with a thinner nephroscope. Variants such as mini-PCNL (15-24 Fr), Ultra mini PCNL (11-15 Fr), and micro-PCNL (<11 Fr) help to reduce blood loss and improve the maneuverability of the nephroscope in smaller kidneys [6].

PCNL can be performed with two types of access; supracostal and subcostal. Reduces stress on the renal parenchyma with greater flexibility are the top most features of Supracostal access whereas subcostal access is used to avoid complications like pneumothorax, hydrothorax, and lung injury.

Most studies on the safety of the supracostal approach are based on adult populations indicating fewer complications[7], but there is a scarcity of data on paediatric PCNL worldwide.

In the current study, our moto is to evaluate the efficacy and safety of the supracostal approach in a pediatric population in terms of post-operative complication, stone-free rates, operative time and hospital stay.

METHODS

Ethical approval was taken from The Kidney Centre Ethical Review Committee (TKC-ERC). The protocol submission reference No. 67-URO-062018 has been given by TKC-ERC. Patient consent has been taken prior to the study.The study was carried out in line with the Helsinki Declaration and STROBE guidelines. Those patients who were below 17 years of age and underwent PCNL from a supracostal puncture from January 1st 2023 till March 31st 2024 were included while those above 17 years of age or those who had multiple procedures at the same time or had any renal anomaly were excluded from the study. A consultant of paediatric urologist performed all the PCNLs.

Preoperative patients had complete workups, which included urine analysis and culture, serum creatinine, and complete blood pictures. Patients were diagnosed as having renal stones based on two radiographic investigations including x-ray, ultrasound, or CT KUB. All patients were administered with prophylactic antibiotic (2nd generation cephalosporin or any alternate drug) 30 min before induction. All procedures were done with general anaesthesia. Patients underwent retrograde pyelogram (RGP) and a 5-fr ureteric catheter was placed along with Foley's catheter. The decision on the puncture site was made based on the findings of RGP. All PCNLs were performed in the prone position. The puncture was performed by an LP needle of 18 gauge via fluoroscopic guidance. After a successful puncture, the guidewire was passed and the track was dilated by single step technique with a metallic dilator. Amplatz 15/16Fr was inserted and a 12fr nephroscope was used. Stones were fragmented with a pneumatic lithotripter and removed by whirlpool effect or grasping by forceps. All the patients have had DJ stent inserted and nephrostomy was placed if indicated.

A Foleys catheter was removed on the first postoperative and patients were discharged on the second postoperative on average based on the situation of the patient. Patients had their haemoglobin and creatinine evaluated postoperatively. The patient also had CXR to exclude chest complications and X-ray KUB to assess stone clearance. Patients had their DJ stent removed around 1 month after the procedure.

A descriptive analysis was performed using frequencies and percentages for the qualitative variables and mean and standard deviation for the continuous variables. The analysis was stratified by group according to preoperative and postoperative haemoglobin loss. Data normality was assessed using the Kolmogorov-Smirnov test and data tends to be skewed. Therefore, we assessed the differences in means and used the non-parametric Wilcoxson Signed-Rank test. Information regarding the following variables was taken into account including post-operative morbidity; stone-free rates, operative time, stone burden, and hospital stay were analysed via SPSS v21.

RESULTS

The total number of patients included in the study was 211. The median age of the patients was 6 years (IQR 3-10 years) with the male predominance 148 (67.8%). Most of the patients belong to Sindhi ethnic group 87 (41.2%). Mild hematuria was observed in eight patients (3.8%), while only one patient had moderate hematuria (0.5%). Most of the patients had unilateral stones (75.4%) mainly on the right side. The median pre and postoperative hemoglobin levels were 11.5(10.3-12.1) and 10.9(9.8-11.6) g/dl. The mean difference between the pre and postoperative hemoglobin was not significant, (p-value= 0.3090). The postoperative transfusion rate was 1.9% out of 211 samples; those who got transfusion have preoperative hemoglobin of < 10g/dl. The median pre and postoperative creatinine levels were same 0.35(0.27-0.48) g/dl. The median stone size was 1.5 (1.3-1.9) cm. The median Hounsfield units (HU) were 930 (647- 1250). Fifty-two patients have multiple stones (24.6%). The majority had a single puncture (99%) while two had a double puncture (0.9%). Pleural effusion was observed in five patients (2.4%) of which two of them required chest tube Insertion (0.9%) and the rest were treated conservatively. The mean postoperative hospital stay was 3.8 ±0.4 days.

Table No.1: Demographics and preoperative data of study participants

Variables		Patients (n=211)	
		N	%
Age	Median	6 years (3-10)	
Sex	Males	143	67.8
	Females	68	32.2
Ethnicity	Urdu Speaking	38	18.0
	Sindhi	87	41.2
	Baloch	55	26.1
	Pathan	22	10.4
	Punjabi	6	2.8
	Afghani	2	0.9
	Others	1	0.5
History of previous surgery	Yes	18	8.5

	No	193	91.5
Side involved	Right	108	51.2
	Left	71	33.2
	Middle	32	15.2
Stone size (cm)	Median	1.5 (1.3-1.9)	
Number of stones	Single	159	75.4
	Multiple	52	24.6
Hemoglobin g/dl	Median, IQR	11.5 (10.3-12.1)	
Serum Creatinine mg/dl	Median, IQR	0.35 (0.26-0.49)	

Table No.2: Postoperative data of the study participants

Variables		**Patients (n=211)**	
		N	**%**
Hemoglobin g/dl	Median	10.9 (9.8-11.6)	
Serum Creatinine mg/dl	Median	0.35 (0.27-0.48)	
Hematuria	No	202	95.7
	Mild	8	3.8
	Moderate	1	0.5
Hospital stay	Mean	3.8±0.4 days	
Number of punctures	Single	209	99.1
	Double	02	0.9
Pleural effusion	Yes	05	2.4
	No	206	97.6
Chest tube insertion		02	0.9
Conservative management		03	1.4

Table No.3: Difference in pre & post-operative hemoglobin (g/dl) among study population

Group	Median (IQR)	Wilcoxson (z) test	P-value
Pre-operative Hb g/dl	11.5 (10.3-12.1)	-	0.30
Post-operative Hb g/dl	10.9 (9.8-11.6)	1.018	9

Significant p-value is considered as <0.05

DISCUSSION

With the advancement in imaging technology, the incidence of the renal stone disease has also risen[8]. Over the past few decades, Urolithiasis in children has become more common worldwide [9]. Calcium oxalate stones are the most frequent type in children, comprising 45% to 65% of cases. Struvite (magnesium ammonium phosphate) stones represent 3% to 30%, with higher occurrence in Europe and developing nations compared to North America. Cysteine and uric acid stones together make up just 5% to 10% of cases in children [10]. Medications and dietary changes can lower the risk of stone recurrence after removal [11].

Pediatric stone disease management prioritizes clearing stones and preserving kidney function. Various treatments are commonly employed for renal calculi such as shock wave lithotripsy, percutaneous nephrolithotomy, open surgery, and laparoscopy. While open surgery was once standard, percutaneous nephrolithotomy, facilitated by nephroscopes and minimally invasive methods, is now the preferred treatment for renal stone disease [12]. There are three approaches to performing PCNL for renal stones: lower pole, middle pole and upper pole access. Lower Pole access is traditionally considered the safest for accessing the renal collecting system, associated with lower risks of bleeding and thoracic complications such as hydrothorax or pneumothorax. However, it may not achieve complete stone clearance in cases involving complex or staghorn renal stones, as well as proximal ureteral stones. Recent studies have shown a relatively good safety profile for upper pole approach to PCNL compared to lower pole access[13]. Most research on upper pole punctures is based on studies involving adults, resulting in a scarcity of pediatric-specific data. Our study focuses on all upper pole approach PCNL procedures performed in pediatric patients at the kidney center.

We found our complication rates to be similar to contemporary results obtained in various studies. In terms of blood loss, our mean hemoglobin drop was 0.6 gm/dl, similar to that observed by a researcher (HB Drop 0.9gms/dl +/- 0.3) in their subgroup of patients who underwent Supracostal puncture for PCNLs. Similarly, only 2.4% of our patients developed hydrothorax which is again similar to the figure found by a researcher although that number rose to 7.3% in

patients who underwent supra 11 puncture[14]. That gives credence to the belief that the higher the puncture is, the greater the chance of developing pulmonary complications.

Another study involving patients aged 07 to 76 years, 14.4% experienced early or delayed chest complications (13 out of 90), with a higher incidence observed on the right side (20.8%, 11 out of 53) compared to the left side (5.4%, 2 out of 37) [15]. Our findings indicate a lower occurrence of pleural effusion, affecting only 2.4% of patients (5 cases), with chest tube insertion necessary in only 0.9% (2 cases).

Another important consideration is the postoperative transfusion rates, as highlighted in studies by Goyal et al., where it was 7.6% in supracostal PCNL [16], and by Purkait et al., where it reached 19.6% [17]. In contrast, our study reported a much lower rate of 1.9% requiring postoperative transfusions. This significant difference can be attributed to Purkait et al.'s inclusion of bilateral PCNLs in their series and the use of adult-size conventional PCNL instruments in both studies, whereas our study utilized miniature instruments.

In the study conducted by Omer et al., the mean operative time was 63.8 ± 13.2 minutes, and the mean length of stay was 4.3 ± 2.2 days [18]. In contrast, our study showed better outcomes in terms of hospital stay, with a mean of 3.8 ± 0.4 days. This is particularly significant because prolonged hospital stays can significantly increase costs, which is a crucial concern in developing countries where financial considerations are paramount.

However, this study is limited by its lack of comparison with subcostal PCNL and stone-free rates post-PCNL. Future studies should be conducted to compare these approaches and establish their safety and efficacy. Nevertheless, based on our findings, it can be confidently concluded that the Supracostal technique, especially when performed with miniature instruments in pediatric populations at high-volume centers with experienced surgeons, is as safe and effective as the subcostal approach.

CONCLUSION

The Supracostal approach of PCNL is safe and effective with minimal complications for complex renal stones in a Paediatric population.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Wajahat Fareed, Shariq Anis Khan, Osama Kalim Sheikh
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REFERENCES

1. Nosirov AA, Narbaev TT, Bayakhmedov FF. Frequency and Risk Factors of Stone Formation in Kidneys of Children Experience of the Urology Department of Clinic of Tashpmi 1995-2019. J Advanced Med Dent Sci Res 2021;9(4):71-6.
2. Grivas N, Thomas K, Drake T, Donaldson J, Neisius A, Petřík A, et al. Imaging modalities and treatment of paediatric upper tract urolithiasis: a systematic review and update on behalf of the EAU urolithiasis guidelines panel. J Pediatr Urol 2020;16(5):612-24.
3. Coward RJ, Peters CJ, Duffy PG, Corry D, Kellett MJ, Choong S, Van't Hoff WG. Epidemiology of paediatric renal stone disease in the UK. Archives Disease Childhood 2003;88(11):962-5.
4. Mahmood SN, Falah B, Ahmed C, Fakhralddin S, Tawfeeq H. Is mini percutaneous nephrolithotomy a game changer for the treatment of renal stones in children? Eur Urol Open Sci 2022;37:45-9.
5. Nerli RB, Ghagane SC, Mungarwadi A, Patil S. Percutaneous nephrolithotomy in children. Pediatr Surg Int 2021;37:1109-15.
6. Önal B, Kırlı EA. Pediatric stone disease: Current management and future concepts. Turkish Archives of Pediatr 2021;56(2):99.
7. Sourial MW, Francois N, Box GN, Knudsen BE. Supracostal access tubeless percutaneous nephrolithotomy: minimizing complications. World J Urol 2019;37:1429-33.
8. Spivacow FR, Del Valle EE, Boailchuk JA, Sandoval Díaz G, Rodríguez Ugarte V, Arreaga, et al. Metabolic risk factors in children with kidney stone disease: an update. Pediatr Nephrol 2020;35:2107-12.
9. Robinson C, Shenoy M, Hennayake S. No stone unturned: the epidemiology and outcomes of paediatric urolithiasis in Manchester, United Kingdom. J Pediatr Urol 2020;16(3):372-e1.
10. Panzarino V. Urolithiasis in children. Advances Pediatr 2020;67:105-12.
11. Üntan İ, Üntan S, Tosun H, Demirci D. Metabolic risk factors and the role of prophylaxis in pediatric urolithiasis. J Pediatr Urol 2021;17(2):215-e1.
12. Mao T, Wei N, Yu J, Lu Y. Efficacy and safety of laparoscopic pyelolithotomy versus percutaneous nephrolithotomy for treatment of large renal stones: a meta-analysis. J Int Med Res 2021;49(1): 0300060520983136.

13. Huang T, Jiao BB, Luo ZK, Zhao H, Geng L, Zhang G. Evidence of the outcome and safety of upper pole vs. other pole access single puncture PCNL for kidney stones: which is better? Eur Review Med Pharmacological Sci 2023;27(10).
14. Özden E, Mercimek MN, Yakupoglu YK, Özkaya O, Sankaya S. 810 Modified Clavien Classification in Percutaneous Nephrolithotomy: Assessment of Complications in Children. Eur Urol Supplements 2010;2(9):259.
15. Anand A. An insight into predominance of pulmonary complications on right side in supracostal percutaneous nephrolithotomy. Urologia J 2022;89(4):564-9.
16. Goyal NK, Goel A, Sankhwar SN, Singh V, Singh BP, Sinha RJ, et al. A critical appraisal of complications of percutaneous nephrolithotomy in paediatric patients using adult instruments. BJU Int 2014;113(5).
17. Purkait B, Kumar M, Sokhal AK, Bansal A, Sankhwar SN, Gupta AK. Percutaneous nephrolithotomy of bilateral staghorn renal calculi in pediatric patients: 12 years experience in a tertiary care centre. Urolithiasis 2017;45:393-9.
18. Rehman OF, Khan A, Harvey H, Umair M, Murtaza B, Nawaz M, et al. Mini PCNL: A viable single stage treatment for pediatric nephrolithiasis in resource limited countries. J Pediatr Urol 2021;17(3):388-e1.

Original Article

Efficacy and Safety of Sofosbuvir/ Daclatasvir VS Sofosbuvir/Velpatasvir in Chronic Hepatitis C Patients

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ABSTRACT

Objective: The present study aims to compare the efficacy and safety of SOF/DCV and SOF/VEL in treating chronic hepatitis C patients.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the SKBZ hospital CMH Muzaffarabad from 1st July 2023 to 30th June 2024.

Methods: Through non probability consecutive sampling, 200 patients aged above 18 years, either gender, diagnosed with Chronic HCV (Viral titer >10, 000 IU/mL) were included in the present study. Co-infection with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), decompensated liver disease, significant renal impairment, pregnant patients were excluded from the present study. Patients were randomized in a 1:1 ratio to receive either SOF/DCV (400 mg Sofosbuvir and 60 mg Daclatasvir daily) (n=100) or SOF/VEL (400 mg Sofosbuvir and 100 mg Velpatasvir daily) (n=100), with treatment extending for 12 weeks

Results: The baseline HCV viral titer in the patients of both study groups were 6.84±0.5 and 7.1±0.9 g/dL ($p<0.0001$). Sustained virological response (SVR) at 12- week was achieved in 92% patients in SOF/DCV group and 95% in SOF/VEL group. Mild adverse effects were observed in both the study groups

Conclusion: In conclusion, the efficacy in achieving sustained viral response (SVR) in the group managed by Sofosbuvir and velpatasvir was higher (95%) against Sofosbuvir and Daclatasvir (92%).

Key Words: SVR, Sofosbuvir, Daclatasvir, Velpatasvir, HCV

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INTRODUCTION

Hepatitis C is an infection caused by the hepatitis C virus and mainly affects the liver. It's an important public health concern, with an approximate 71 million people living with chronic Hepatitis C infection worldwide[1]. This infection ranges from mild illness, usually lasting a few weeks, to a serious lifelong chronic condition. Long-term issues associated with chronic hepatitis C infection include severe complications such as cirrhosis, liver failure, and hepatocellular carcinoma; it is thus one of the main causes of morbidity and mortality worldwide. Direct acting antivirals (DAAs) inhibit certain steps of the HCV life cycle, as such, viral replication is inhibited, leading to effective clearance of the virus from the bloodstream[2]. These agents have recently been classified into several classes according to their mechanism of action: NS3/4A protease inhibitors, NS5A inhibitors, and NS5B polymerase inhibitors. Combination of different classes of DAAs significantly improved treatment outcomes across various HCV genotypes[3]. Sofosbuvir is the most critical NS5B polymerase inhibitor in the treatment regimens for HCV, and it must be combined with other DAAs against different HCV genotypes to attain significant cure rates[4]. Two essential combinations that have been created are Sofosbuvir/Daclatasvir and Sofosbuvir/ Velpatasvir. The efficacy and safety profiles of these regimens are so high that they take precedence over other combinations in treating HCV. Several HCV genotypes have been evaluated for SOF/DCV, which has demonstrated high efficacy. In a landmark study, Wehmeyer et al. examined the effectiveness of SOF/DCV in 200 patients with various HCV genotypes.

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The rates of SVR12 reported in this study were 97% for genotype 1, 93% for genotype 2, and 94% for genotype 3 patients[5]. Subsequent studies—including a 2019 study by Alonso et al.—pointed out the makers of remarkable efficacy of SOF/DCV against HCV infection, especially against genotypes 1 and 3[6]. SOF/VEL is a pangenotypic regimen that has been demonstrated to have activity against all major HCV genotypes[7]. In the landmark trial ASTRAL-1, published in 2018, it was able to show SVR-12 rates of more than 98% across all genotypes 1-6. This study had a very diverse patient population, underlining that the efficacy of this regimen applies to an extremely wide range of patients[8]. Subsequent studies, such as ASTRAL-2 and ASTRAL-3, also reproduce these superb results, demonstrating that SOF/VEL performs well across all HCV genotypes[9]. Several comparative studies and meta-analyses compared the relative efficacy and safety of SOF/DCV versus SOF/VEL. In a meta-analysis by conducted by a researcher, evaluating both regimens in various patient populations, it was shown that both combinations achieved high rates of SVR12 and differed slightly between genotypes and patients. The pangenotypic coverage of SOF/VEL was better, as was its good and comparable safety profile to that of SOF/DCV. In a large sample of CHC patients, a cohort study by a researcher, compared the real-world effectiveness of SOF/DCV versus SOF/VEL. In the said research, SVR12 rates were 96% for SOF/VEL and 94% for SOF/DCV, hence showing comparable efficacy. Both regimens had comparable safety profiles, with no significant difference in the incidence of serious adverse events. The present study aims to compare the efficacy and safety of SOF/DCV and SOF/VEL in treating chronic hepatitis C patients.

METHODS

After the ethical approval from the institutional review, this randomized controlled trial was conducted at at SKBZ hospital CMH Muzaffarabad from 1st July 2023 to 30th June 2024 Through non probability consecutive sampling, 200 patients aged above 18 years, either gender, diagnosed with Chronic HCV (Viral titer >10, 000 IU/mL) were included in the present study. Co-infection with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), decompensated liver disease, significant renal impairment, pregnant patients were excluded from the present study. Patients were randomized in a 1:1 ratio to receive either SOF/DCV (400 mg Sofosbuvir and 60 mg Daclatasvir daily) (n=100) or SOF/VEL (400 mg Sofosbuvir and 100 mg Velpatasvir daily) (n=100), with treatment extending for 12 weeks. The primary outcome measured was the sustained virological response at 12-weeks post-treatment (SVR12) determined by viral titer through RT-PCR, defined by undetectable HCV RNA levels. Secondary outcomes included SVR24, adverse event incidence, virological failure rates, and liver function test results. Baseline assessments collected demographic data, medical history, and laboratory tests, while follow-up assessments at weeks 4, 8, 12, and 24 monitored HCV RNA levels, and adverse events. SPSS version 21 was utilized to analyse the data. Categorical variables were presented as frequency and percentages and continuous variables were represented as Mean and standard deviation. Primary outcomes were compared between the study groups by t-test. P value ≤ 0.05 were considered to be significant.

RESULTS

Table 1 shows the demographic and clinical parameters of the recruited participants in both study groups. The average age of the patients in both the study groups were 47.99±11.3 and 49.8±12.3 years. (p=0.106). The female to male ratio in both the study groups was 2:1 and 1.17:1 respectively (p=0.045). in SOF/DCV group 14% of the patients had cirrhosis, while in 19% in SOF/VEL group (p=0.025). The baseline HCV viral titer in the patients of both study groups were 6.84±0.5 and 7.1±0.9 g/dL (p<0.0001). Table 2 shows the efficacy of the DAAs in the HCV patients. Sustained virological response (SVR) at 12- week was achieved in 92% patients in SOF/DCV group and 95% in SOF/VEL group. Table 3 shows the adverse effects of the drugs observed in patients of both groups. Mild adverse effects were observed in both the study groups. In SOF/DCV majority of the patients 15% observed fatigue as an adverse effect, while in SOF/VEL majority of the patients 20% experienced nausea.

Table No.1: Demographic and clinical parameters

Variables	SOF/DCV Group (n=100)	SOF/VEL group (n=100)	P Value
Age (years)	47.99±11.3	49.8±12.3	0.106
Male gender n (%)	42 (42%)	46 (46%)	0.045
Cirrhosis n (%)	14 (14%)	19 (19%)	0.025
Hemoglobin (g/dL)	11.5±0.90	11.45±0.95	0.350
WBCs ($\times 10^9$/L)	7.56±0.6	7.4±0.7	0.012
Platelets ($\times 10^9$/L)	246.78±20.45	243.5±30.2	0.280
AST (ULN: 40 U/L)	81.78±10.3	81.68±10.4	0.847
ALT (ULN: 40 U/L)	60.46±7.9	59.09±8.8	0.069
Albumin (mg/dL)	39.53±1.66	43.3±3.5	0.300

HCV Titer (g/dL)	6.84±0.5	7.1±0.9	<0.0001
Comorbidity n(%)			0.765
Diabetes	26 (26%)	20 (20%)	
Obesity	43 (43%)	54 (54%)	
Hypertension	31 (31%)	26 (26%)	

Table No.2: Efficacy of drugs in both study group

Variables	SOF/DCV Group (n=100)	SOF/VEL group (n=100)	P value
SVR-12			0.083
Yes	92 (92%)	95 (95%)	
No	8 (8%)	5 (5%)	
Relapses			0.158
Yes	5 (5%)	3 (3%)	
No	95 (95%)	97 (97%)	
Non-responders			0.320
Yes	3 (3%)	2 (2%)	
No	97 (97%)	98 (98%)	

Table No.3: Adverse effects of the drugs in both study group

Adverse Effects n (%)	SOF/DCV	SOF/VEL	P value
Headache	15	12	0.596
Nausea	14	20	
Anemia	13	10	
Fatigue	19	15	
Abdominal pain	10	9	
Fever	9	12	
Rash	7	9	
Diarrhea	5	2	
Myalgia	3	2	
Dizziness	2	3	

DISCUSSION

The development of DAAS has had a profound and transformative impact on the treatment of HCV. These treatment plans result in greater rates of sustained virologic response (SVR) and restrict the advancement of liver cirrhosis. The use of IFN for the treatment of HCV has been discontinued worldwide, and therapy based on DAAs is increasingly becoming the preferred approach[10]. The availability of generic versions of DAAs in 101 developing countries has led to a significant decrease in their prices (Hill et al., 2016). However, it is necessary to conduct scientific evaluation and validation in order to confirm the effectiveness and safety of these generic products. To effectively treat HCV infection on a wide scale, it is advisable to thoroughly examine the existing real-world data on the effectiveness of these treatment plans across all categories of HCV patients[11].

This study reported that the efficacy in achieving sustained viral response (SVR) in the group managed by sofosbuvir and velpatasvir was higher against sofosbuvir and daclatasvir. In a 2017 research, Falade-Nwulia et al. compared the effects of two different combinations of sofosbuvir and vel, as well as sofosbuvir and daclatasvir. A viral response rate of 95.5% was observed in the research. 94.4% of patients in the group treated with sofosbuvir and daclatasvir shown a sustained viral response after 12 weeks of therapy, whereas 94.7% of patients in the group treated with sofosbuvir and velpatasvir demonstrated a response[12]. In 2022, Ahmed et al. investigated the effectiveness of sofosbuvir and daclatasvir in the treatment of chronic HCV patients. Sofosbuvir 400 mg and daclatasvir 60 mg were the prescribed medications in the 12-week trial. The results of the investigation demonstrated that 95.4% of the viral load was maintained[13]. In 2019, Belperio et al. evaluated the efficacy of sofosbuvir in combination with velpatasvir or daclatasvir. Five thousand four hundred people were a member of the research population. The people who were recruited belonged to genotypes 2 and 3. Both sofosbuvir and daclatasvir, as well as sofosbuvir and velpatasvir, exhibited similar persistent viral responses, according to the study's results. The sustained viral response for genotype 3 was around 92% in individuals treated with velpatasvir and sofosbuvir, and nearly 90% in persons managed with daclatasvir and Sofosbuvir[14]. The efficacy of Sofosbuvir/daclatasvir, and sofosbuvir/velpatasvir was evaluated in a meta-analysis. All the studies that were chosen followed the regimen for a duration of 12 weeks. A grand total of 4,907 individuals

were enrolled across 16 different investigations. The results of the meta-analysis demonstrated that the combination of sofosbuvir and velpatasvir resulted in a higher rate of persistent viral responses (98% vs. 95%) in the patients treated with these two drugs[15].

CONCLUSION

In conclusion, the efficacy in achieving sustained viral response (SVR) in the group managed by Sofosbuvir and velpatasvir was higher (95%) against Sofosbuvir and Daclatasvir (92%).

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Noman Kareem Qureshi, Syed Rizwan Hussain, Mehreen Toufique
Drafting or Revising Critically:	Syeda Mariam Batul Bukhari, Shafaq Shafique Abbasi, Zarnab Munir
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Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Hassan, H., The Prevalence of Hepatitis C virus infections among the adult population of district Mardan, Khyber Pakhtunkhwa, Pakistan. Graduate J Pak Review (GJPR) 2022;**2**(1).
2. Alazard-Dany N, et al. Overview of HCV life cycle with a special focus on current and possible future antiviral targets. Viruses 2019;11(1):30.
3. Spengler U, Direct antiviral agents (DAAs)-A new age in the treatment of hepatitis C virus infection. Pharmacol Therapeutics 2018;183:118-126.
4. Hayes, C.N., M. Imamura, and K. Chayama, Management of HCV patients in cases of direct-acting antiviral failure. Expert Review Gastroenterol Hepatol 2019;13(9):839-848.
5. Wehmeyer MH, et al. Real-world effectiveness of sofosbuvir-based treatment regimens for chronic hepatitis C genotype 3 infection: Results from the multicenter German hepatitis C cohort (GECCO-03). J Med Virol 2018;90(2):304-312.
6. Alonso S, et al. Effectiveness and safety of sofosbuvir-based regimens plus an NS 5A inhibitor for patients with HCV genotype 3 infection and cirrhosis. Results of a multicenter real-life cohort. J Viral Hepatitis 2017;24(4):304-311.
7. Scotto R, et al. Real-world efficacy and safety of pangenotypic direct-acting antivirals against hepatitis C virus infection. Reviews Recent Clinical Trials 2019;14(3):173-182.
8. Wyles D, et al. Sofosbuvir and velpatasvir for the treatment of hepatitis C virus in patients coinfected with human immunodeficiency virus type 1: an open-label, phase 3 study. Clin Infect Dis 2017;65(1):6-12.
9. Jacobson IM, et al. The tolerability of sofosbuvir/velpatasvir for 12 weeks in patients treated in the ASTRAL 1, 2 and 3 studies: A pooled safety analysis. J Viral Hepatitis 2023;30(5):448-454.
10. Mushtaq S, et al. Efficacy and safety of generic sofosbuvir plus daclatasvir and sofosbuvir/ velpatasvir in HCV genotype 3-infected patients: real-world outcomes from Pakistan. Frontiers Pharmacol 2020;11: 550205.
11. Shah I, et al. Efficacy and Safety of Sofosbuvir and Velpatasvir Combination for the Treatment of Chronic Hepatitis C in Patients with or without Cirrhosis. Cureus 2021;13(11).
12. Falade-Nwulia O, et al. Oral direct-acting agent therapy for hepatitis C virus infection: a systematic review. Annals Int Med 2017;166(9):637-648.
13. Ahmed T, et al. Comparison of Efficacy of Sofosbuvir & Daclatasvir with Sofosbuvir and Velpatasvir in Achieving SVR in Patients of Chronic Hepatitis C with Genotype 3. Pak J Med Health Sci 2022;16(04): 1155-1155.
14. Belperio PS, et al. Real-world effectiveness of daclatasvir plus sofosbuvir and velpatasvir/ sofosbuvir in hepatitis C genotype 2 and 3. J Hepatol 2019;70(1):15-23.
15. Mariantonietta, P., et al., Efficacy of 12-weeks velpatasvir plus sofosbuvir-based regimen in HCV-naive subjects with mild fibrosis: a meta-analysis. Acta Bio Medica: Atenei Parmensis 2019; 90(2):187.

Original Article

Incidence of Re-Bleeding After Injection Cyanoacrylate for Gastric Varices

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ABSTRACT

Objective: To assess the efficacy of cyanoacrylate injection for gastric varices.

Study Design: Descriptive case series

Place and Duration of Study: This study was conducted at the, conducted at Department of Gastroenterology, Sheikh Zaid Hospital, Lahore from 28-11-2019 to 27-05-2020.

Methods: Through non-probability consecutive sampling, 139 patients aged 18-70 years, both gender, diagnosed with gastric varices were included in the present study.

Results: The frequency of efficacy of cyanoacrylate injection for gastric varices in terms of achieving hemostasis and rebleeding was recorded as 94.96%(n=132) and only 5.04%(n=7) had finding of re-bleed.

Conclusion: We concluded that the efficacy of cyanoacrylate injection is higher for gastric varices in terms of achieving hemostasis and rebleeding

Key Words: Gastric varices, cyanoacrylate injection, efficacy

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INTRODUCTION

Gastric varices (GV) are submucosal venous channels in the stomach to which blood flow is re-routed by portal hypertension and these are potential sources of severe upper gastrointestinal haemorrhage(1). While not as frequent as bleeding from EV, bleeding from GV is generally more severe, and has a higher morbidity and mortality. Endoscopic injection of N-butyl-2-cyanoacrylate (NBCA) which is a stable tissue adhesive is widely used for management of acute bleeding from GV. This technique provides hemorrhagic control since the agent quickly sets on contact with blood, thereby closing the lumen of varices (2).

Several studies have demonstrated the efficacy of NBCA in achieving initial hemostasis with success rates being between 95% and 100%. For example, there was a study on 260 patients that showed that the overall first pass hemostasis rate was 100% after administering of NBCA injection (3). But the extent of rebleeding still poses a high risk in the overall management of such patients. Rebleeding was confirmed in the same study at an 8% in the first seven days post-treatment(4).

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The Meta-analysis of 43 studies of 3484 patents revealed 30-Day rebleeding rate following NBCA injection for variceal bleeding as 24.2 percent. A second pooled analysis reported the rebleeding rates of 15% when gastric varices were treated with cyanoacrylate alone. These discrepancies of rebleeding rates may have been caused by the sample, management and method of follow-up (5) (14).

A number of comparative investigations refer to the use of NBCA with other therapeutic techniques to minimize rebleeding percentages. For instance, NBCA with EUS-coil whether in combination with or without other techniques, had been described with rebleeding risk of 7%. However, the best therapeutic approach in managing GV bleeding has still continued to be a focus and matter of the study (6) (15). Consequently, though NBCA injection has a very high success rate in initial management of bleeding from gastric varices, it is closely followed by rebleeding rates that range from 8-24% in the first month after treatment. Further studies into combination therapies and more strictly defined clinical practices could improve the patient's conditions and the rates of rebleeding (7) (16). The objective of the present study is to assess the efficacy of cyanoacrylate injection for gastric varices in terms of achieving haemostasis and rebleeding

METHODS

This descriptive case series was conducted in the Department of Gastroenterology at Sheikh Zaid Hospital, Lahore, from November 28, 2019, to May 27, 2020, following ethical approval from the institutional review board. Using non-probability consecutive

sampling, 139 patients aged 18 to 70 years, of both genders, diagnosed with gastric varices were included in the study. Patients who were already undergoing treatment for varices, had a known malignancy, or had a bleeding cause other than gastric varices were excluded.

All patients were informed about the study's purpose and protocol, and written consent was obtained before enrollment. Data on disease history, etiology of liver cirrhosis, disease status, treatment options for gastric variceal bleeding, medications used before the onset of gastric variceal bleeding, and blood test results were recorded using a predesigned proforma.

As part of the standard treatment, all patients received an intravenous dose of prophylactic antibiotics. Study outcomes, including hemostasis and rebleeding within 90 days of treatment, were documented. Mortality within this period was also recorded. Patients and their guardians were instructed to report any complications, such as rebleeding or mortality, within three months.

Data analysis was performed using SPSS version 25. Mean and standard deviation (SD) were calculated for quantitative variables such as age and disease duration. Frequency and percentages were computed for categorical variables, including gender, comorbidities, Child-Pugh classification, efficacy, hemostasis, and rebleeding within 90 days. Effect modifiers, such as age, gender, and Child-Pugh classification, were controlled using stratification. A post-stratification chi-square test was applied to assess the effect on study outcomes, with a p-value of <0.05 considered statistically significant.

RESULTS

A total of 139 patients meeting the inclusion criteria were enrolled to assess the efficacy of cyanoacrylate injection for gastric varices in achieving hemostasis and preventing rebleeding. Age distribution analysis revealed that 62.59% (n=87) of patients were between 18 and 50 years old, while 37.41% (n=52) were between 51 and 70 years old. The mean age was 46.63 ± 12.42 years. Gender distribution showed that 51.80% (n=72) were male and 48.20% (n=67) were female. The mean duration of cirrhosis was 12.17 ± 4.42 months. Child-Pugh classification results indicated that 64.03% (n=89) were classified as Class A, 26.62% (n=37) as Class B, and 9.35% (n=13) as Class C. Regarding treatment efficacy, 94.96% (n=132) of patients achieved hemostasis, while 5.04% (n=7) experienced rebleeding within 90 days. Effect modifiers, including age, gender, and Child-Pugh classification, were controlled through stratification. A post-stratification chi-square test was applied to determine their impact on study outcomes, as summarized in Table 2. The efficacy of the treatment was analyzed across different variables, including age, gender, and Child-Pugh class. Among individuals aged 18-50 years, 82 showed efficacy, while 5 did not, with a P-value of 0.61. In the 51-70 age group, 50 individuals demonstrated efficacy, whereas 2 did not. Regarding gender, 69 males exhibited efficacy compared to 3 who did not, while among females, 64 showed efficacy, and 4 did not, with a P-value of 0.63. In terms of liver function based on Child-Pugh classification, all 89 patients in Class A responded effectively to the treatment. However, in Class B, 33 individuals experienced efficacy, whereas 4 did not, with a P-value of 0.06. In Class C, 10 individuals showed efficacy, while 3 did not, with a statistically significant P-value of 0.001.

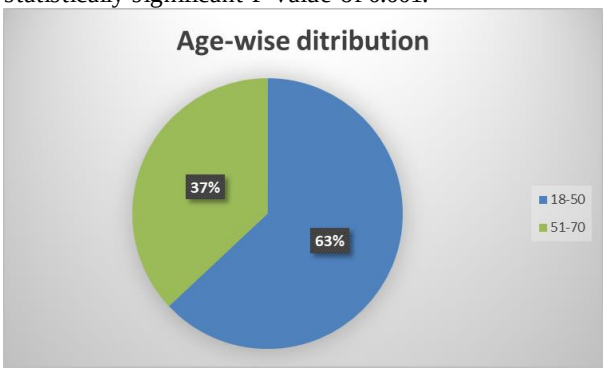

Figure No.1: Age-wise distribution

Table No.1: Demographic and clinical parameters of the study participants

Variables	Mean and Frequency
Age (years)	46.63+12.42
18-50	63%
51-70	37%
Gender	
Male	72 (52%)
Female	67 (48%)
Duration of Cirrhosis (Months)	12.7+4.4
Child Pugh Class	
A	89 (64%)
B	37 (27%)
C	13 (9%)
Efficacy	132 (95%)

Table No.2: Stratification of efficacy based age, gender, and child Pugh class

Variables	Efficacy		P value
	Yes	NO	
Age (years)			
18-50	82	5	0.61
51-70	50	2	
Gender			
Male	69	3	0.63
Female	64	4	
Child Pugh Class			
A	89	0	-
B	33	4	0.06
C	10	3	0.001

DISCUSSION

The demographic data of our cases reveals a mean age of 46.63 ± 12.42 years, with 51.80% (n=72) males and 48.20% (n=67) females. Regarding Child-Pugh classification, 64.03% (n=89) were classified as Class A, 26.62% (n=37) as Class B, and 9.35% (n=13) as Class C. In terms of the efficacy of cyanoacrylate (CYA) injection for gastric varices, 94.96% (n=132) of patients achieved hemostasis, and only 5.04% (n=7) experienced rebleeding. This data aligns with studies conducted in Pakistan, which also report a significantly lower re-bleeding rate in the CYA injection group. For example, a study in Rawalpindi by Faheem M et al., and another in Lahore by Hassan I et al., found lower rebleeding rates of 5.7% vs 14.7% and 3.3% vs 13.3%, respectively, when compared to the endoscopic band ligation group (9-10). Our findings also show a lower rebleeding rate compared to other studies, which report recurrent bleeding rates around 10% (8).

Phadet Noophun and colleagues (13) evaluated the efficacy and safety of gastric varices injection with cyanoacrylate in patients with gastric variceal bleeding. Their study showed that 71% (n=17) of patients achieved definite hemostasis, and 58% (n=14) reached primary success. An additional 12% (n=3) were classified as secondary success after repeat endoscopic injections. The mean number of sessions to achieve definite treatment was 1.4. However, 29% (n=7) of patients failed to achieve hemostasis despite multiple sessions of endoscopic treatment (1 IGV 1, 2 GOV 2). Our study shows significantly higher efficacy than their findings. Although CYA injection is highly effective and generally safe, it has been criticized for the potential to cause rare but severe complications (11). The most common complications include transient chest pain, self-limiting fever, transient difficulty swallowing (similar to other upper endoscopic procedures), and bleeding from the injection site. The most severe, though rare, complication is systemic embolization. Despite these risks, the procedure can be life-saving for patients with poor prognoses.

To increase the safety of the procedure, injections should be strictly intravariceally, and the dilution ratio between cyanoacrylate and lipiodol should be 1:1. Injections should be limited to a few milliliters of the mixture—typically 1 cc per site, with a maximum of 4-5 ml, though ideally between 2-3 ml. If larger volumes are necessary to obliterate the varices, the procedure should be done sequentially. Personnel handling cyanoacrylate should always use gloves and eye protection.

In summary, our study contributes valuable data on the efficacy of cyanoacrylate injection for gastric varices, particularly in achieving hemostasis and preventing rebleeding. However, further multicenter trials are needed to validate our findings.

CONCLUSION

We concluded that the efficacy of cyanoacrylate injection is higher for gastric varices in terms of achieving hemostasis and rebleeding.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zia ur Rehman, Hina Ebir, Afia Munir
Drafting or Revising Critically:	Jawaryiah Kanwal, Hassaan Yousaf, Zaeem Sibtain
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Vine LJ, Subhani M, Acevedo JG. Update on management of gastric varices. World J Hepatol 2019;11:250-60.
2. Guo YE, Miao HB, Wen ZF, Xuan JY, Zhou HX. Procedure related complications in gastric variceal obstruction with tissue glue. World J Gastroenterol 2017;23:7746-55.
3. Komori K, Kubokawa M, Ihara E, Akahoshi K, Nakamura K, Motomura K, Masumoto A. prognostic factors associated with mortality in patients with gastric fundal variceal bleeding. World J Gastroenterol 2017;23:496-504.
4. Chandra S, Holm A, El-Abiad RG, Gerke H. Endoscopic cyanoacrylate glue injection in management of gastric variceal bleeding: US Tertiary Care Centern Experience. J Clin Exp Hepatol 2018;8:181-7.
5. Park JK, Saab S, Kee ST. Balloon-occluded retrograde transvenous obliteration (BRTO) for treatment of gastric varices: review and meta analysis. Dig Dis Sci 2015;60:1543-53.
6. Singh V, Singh R, Bhalla A, Sharma N. Cyanoacrylate therapy for the treatment of gastric varices: a new method. J Dig Dis 2016;17:392-8. 73
7. Zeng XQ, Ma LL, Tseng YJ, Chen J, Cui CX, Luo TC, et al. Endoscopic cyanoacrylate injection with or without lauromacrogol for gastric varices: a randomized pilot study. J Gastroenterol Hepatol 2017;32:631-8.
8. El Sayed G, Tarff S, O'Beirne J, Wright G. Endoscopy management algorithms: role of cyanoacrylate glue injection and self-expanding

metal stents in acute variceal haemorrhage. Frontline Gastroenterol 2015;6:208-16.
9. Faheem M, Khurram M, Ambreen S, Arif M, Amjad W, Iqbal R, et al. Band ligation versus glue injection for bleeding gastric varices. J Rawal Med Coll 2017;21:317-20.
10. Hassan I, Siddique A, Azhar MI. Cyanoacrylate glue versus band ligation for acute gastric variceal hemorrhage—a randomized controlled trial at Services Hospital, Lahore. Pak J Med Health Sci 2018;12:173-8.
11. Villanueva C, Minana J, Ortiz J. Endoscopic ligation compared with combined treatment with nadolol and isosorbide mononitrate to prevent recurrent variceal bleeding. New Engl J Med 2001;345:647-55.
12. Helmy A, H ayes PC. Review article: current endoscopic therapeutic options in the management of variceal bleeding. Aliment Pharmacol Ther 2001;15:575-94.
13. Noophun P, Kongkam P, Gonlachanvit P, Rerknimitr R. Bleeding gastric varices: Results of endoscopic injection with cyanoacrylate at King Chulalongkorn Memorial Hospital. World J Gastroenterol 2005;11(47):7531-5.
14. Chikamori F, Kuniyoshi N, Shibuya S, Takase Y. Correlation between endoscopic and angiographic findings in patients with esophageal and isolated gastric varices. Dig Surg 2001;18:176–81.
15. Weber SM, Rikker LF. Splenic vein thrombosis and gastrointestinal bleeding in chronic pancreatitis. World J Surg 2003;27:1271–4
16. Bazarbashi AN, Ryou M. Endoscopic ultrasound-guided coil injection therapy for gastric variceal bleeding not amenable to interventional radiology-guided therapies. ACG Case Rep J 2019;6:1–4.

Original Article

Ulcerative Colitis in Patients Presenting with Bleeding Per Rectum

Ulcerative Colitis with Bleeding Per Rectum

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ABSTRACT

Objective: To determine the frequency of ulcerative colitis in patients presenting with bleeding per rectum.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Department of Gastroenterology Shiekh Zayed Hospital, Lahore from 10-03-2024 to 10-09-2024.
Methods: After approval of the synopsis, consent was taken from ethical review committee of the hospital. After that 95 patients fulfilling the inclusion criteria was assessed for socio-demographic and clinical data recorded on a pre-designed proforma. Then these cases were undergo colonoscopy by a consultant gastroenterologist and biopsy was taken under direct vision and ulcerative colitis was labeled as per operational definition. All these results were collected and recorded on same proforma.
Results: Total of 95 patients, 67.4 %(n=64) were in age group of 20-40 years and 32.6 %(n=31) were in age group of 41-60 years and mean age was calculated as 37.43±7.85 years. There were 64.2 %(n=61) were male whereas 35.8 %(n=34) were females. Frequency of ulcerative colitis in patients with bleeding per rectum was 27.4 %(n=26).
Conclusion: Current study found that frequency of ulcerative colitis was 27.6% in patients with bleeding per rectum and there was no significant association of ulcerative colitis with diabetes mellitus and smoking.
Key Words: Ulcerative colitis, Bleeding per rectum, Crohn's disease.

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INTRODUCTION

Ulcerative colitis (UC) is a type of inflammatory bowel disease which affects the colon, specifically the colonic mucosa[1]. This illness especially manifests in diarrhoea, abdominal pain and constitutional bleeding per rectum, factors which greatly contributing to diminished QOL. The passage of blood through the rectum is one of the severe signs the patients report, which requires immediate medical intervention. The precise cause of UC is not known, but the development of the disease is thought to be due to genetic factors combined with environmental factors, and immune system dysfunction[2]. UC occurrence is not uniform throughout the world; the two regions with the highest incidence are North America and Europe, with UC incidence at 24.3/100 000 annually.

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Symptoms, particularly rectal bleeding, offer potential prognostic information about disease activity and response to treatment in UC patients. Some studies have related rectal bleeding in UC with the severity of the disease as seen clinically. A study found 20–30% of UC patients with rectal bleeding needed hospitalization, with close association with extensive colonic involvement [3]. Those admitted to the hospital had a higher risk of receiving intravenous steroids, 30 percent of whom failed to respond and needed either biologic agents or cyclosporine. Even with such interventions; colectomy rates persisted to be high, between 10% and 15% among patients with severe disease [4]. Etiology of rectal bleeding determines long-term prognosis by the disease stage before therapy and after treatment. The landmark ACT trials also showed that early use of infliximab reduced bleeding episodes and increased mucosal healing rates, which are considered predictors of long-term prognosis. Contrary to this, real-world data reveal interpatient variability regarding response rates, as high as 20% of patients would present with persistent or recurrent bleeding even with proper therapy[5]. Cross-sectional studies support the above effect of rectal bleeding in worsening patients' status and increasing rates of anaemia, hospitalizations and reduced quality of life. Early management such as the early administration of the correct pharmacologic and supportive therapy for the complications remains very important in enhancing survival in these patients. More work is required to enhance the accuracy of risk

assessing and to look for the optimal therapeutic approach to reduce the impact of UC.

METHODS

After the ethical approval from the institutional review board, this cross-sectional study was conducted at Department of Gastroenterology Shiekh Zayed Hospital, Lahore from 10-03-2024 to 10-09-2024. Through non-probability consecutive sampling, 95 patients aged 20-60 years, both genders, with bleeding per rectum of at least one month of duration assessed by history and medical record were included in the present study. Patients taking anticoagulation therapy like disprin, clopidogril, heparin or warfarin of any amount in last one week, documented cases of liver cirrhosis and hemorrhoids were excluded from the present study. After the informed consent from the included patients, socio-demographic and clinical data like age (years), gender (male/female), weight (in kg by electronic weighing machine), duration of symptoms bleeding per rectum, smoking (yes/no), DM (yes/no) assessed by HbA1c level more than 7 at any single occasion and recorded on a pre-designed proforma. Then these cases were undergoing colonoscopy by a consultant gastroenterologist with at least 1 year post fellow ship experience and biopsy was taken under direct vision and sent for histopathology of the same institute and ulcerative colitis was labelled as per operational definition. All these results were collected and recorded on same proforma. Data was analyzed with the help of SPSS version 23.0. Quantitative variables like age, weight and duration of symptoms were presented in terms of mean ± SD (Standard Deviation). Frequency & percentages was calculated for gender, DM (yes/no), smoking (yes/no) and outcome variable that is ulcerative colitis detected (yes or no). Effect modifiers were controlled through stratification of age, gender, weight, duration of symptoms, DM (BSR >200mg/dl) and smoking to see the effect on outcome variable. Post stratification Chi-Square test was applied taking P-value ≤ 0.05 as significant.

RESULTS

Total of 95 patients fulfilling inclusion and exclusion criteria will be selected to assess the frequency of ulcerative colitis in patients presenting with bleeding per rectum. Table 1 shows the demographic and clinical parameters of the study participants (Table 1). Age distribution of the patients was done, it showed that out of 95 patients, 67.4 %(n=64) were in age group of 20-40 years and 32.6%(n=31) were in age group of 41-60 years and mean age was calculated as 37.43±7.85years. Gender distribution of the patients was done, it showed that 64.2 %(n=61) were male whereas 35.8 %(n=34) were females. Frequency of ulcerative colitis in patients with bleeding per rectum was 27.4 %(n=26). The data was stratified for age, gender, weight, duration of symptoms, and diabetes mellitus and smoking shown in Table No. 2-6 respectively.

Table No.1: Demographic and clinical parameters

Variables	Mean and Frequency
Age (years)	37.43±7.85
20-40	64 (67.4%)
41-60	31 (32.6%)
Gender	
Male	61 (65%)
Female	**34 (35%)**
Duration of symptoms(month)	1.63±0.74
Weight(kg)	61.69±8.12
Diabetes	29 (31%)
Smoking	39 (41%)
Frequency of Ulcer colitis	26 (27%)

Table No.2: Stratification for ulcerative colitis with respect to age using chi square test

			Ulcerative colitis detected		Total	p-value
			yes	no		
Age group	20-40 years	Count	17	47	64	
		% of Total	17.9%	49.5%	67.4%	
	41-60 years	Count	9	22	31	0.800
		% of Total	9.5%	23.2%	32.6%	
Total		Count	26	69	95	
		% of Total	27.4%	72.6%	100.0%	

Table No.3: Stratification for ulcerative colitis with respect to gender using chi square test

			Ulcerative colitis detected		Total	P-value
			Yes	No		
Gender	Male	Count	11	50	61	
		% of Total	11.6%	52.6%	64.2%	0.006
	Female	Count	15	19	34	
		% of Total	15.8%	20.0%	35.8%	
Total		Count	26	69	95	

	% of Total	27.4%	72.6%	100.0%	

Table No.4: Stratification for ulcerative colitis with respect to weightusing chi square test

			Ulcerative colitis detected		Total	p-value
			yes	no		
Weight group	<=60 kg	Count	12	28	40	
		% of Total	12.6%	29.5%	42.1%	
	>60 kg	Count	14	41	55	0.624
		% of Total	14.7%	43.2%	57.9%	
Total		Count	26	69	95	
		% of Total	27.4%	72.6%	100.0%	

Table No.5: Stratification for ulcerative colitis with respect to symptoms using chi square test

			Ulcerative colitis detected		Total	p-value
			yes	no		
Duration of symptoms group	1-2 months	Count	20	60	80	
		% of Total	21.1%	63.2%	84.2%	
	>2 months	Count	6	9	15	0.232
		% of Total	6.3%	9.5%	15.8%	
Total		Count	26	69	95	
		% of Total	27.4%	72.6%	100.0%	

Table No.6: Stratification for ulcerative colitis with respect to diabetes using chi square test

			Ulcerative colitis detected		Total	p-value
			yes	no		
Diabetes mellitus	yes	Count	8	21	29	
		% of Total	8.4%	22.1%	30.5%	
	no	Count	18	48	66	0.975
		% of Total	18.9%	50.5%	69.5%	
Total		Count	26	69	95	
		% of Total	27.4%	72.6%	100.0%	

DISCUSSION

Rectal bleeding is a common symptom, with a prevalence of 14% to 19% in adults. [3-6] Most patients bleed from benign sources such as hemorrhoids and diverticula, but others have serious colorectal disease including colon cancer, adenomatous polyps, and inflammatory bowel disease (IBD). Colon cancer is the third leading cause of cancer-related death in this country. The symptom of rectal bleeding in particular requires exact diagnosis because it can be an early sign of severe bowel diseases, such as colon carcinoma, or inflammatory bowel diseases. An examination of 99 patients aged over 40 years and presenting with a first episode of rectal bleeding who had been referred for a colonoscopy by GPs, showed serious abnormal findings in 44.9% of the cases.[8] An estimated incidence of 8.3 and 7 in 1000 persons per year[9,10]

In current study, we concluded that , Age distribution of the patients was done, it showed that out of 95 patients, 67.4 %(n=64) were in age group of 20-40 years and 32.6%(n=31) were in age group of 41-60 years and mean age was calculated as 37.43±7.85years. There were 64.2 %(n=61) were male whereas 35.8 %(n=34) were females. Frequency of ulcerative colitis in patients with bleeding per rectum was 27.4 %(n=26).

Rectal bleeding is often seen as bright red blood on toilet paper—usually after a bowel movement—or by turning the toilet bowl water red. Rectal bleeding can also be recognized in extremely dark stool (bowel movement), ranging in color from deep red/maroon to black, and sometimes appearing tar-like (melena). The color of the blood can indicate where the bleeding is coming from: Bright red blood usually means bleeding low in the colon or rectum. Dark red or maroon blood usually indicates bleeding higher in the colon or the small bowel. Melena usually means bleeding in the stomach, such as bleeding from ulcers. Not all rectal bleeding is visible to the eye. In some cases, rectal bleeding can only be seen by looking at a stool sample through a microscope. [11] Another study done in Peshawar revealed the presence of UC presenting with diarrhea in 44% of the cases.[2]

Rectal bleeding is a very common symptom. It occurs in adults of all ages. The 1-year prevalence in adults is about 10% in the UK. Most of this will not be reported. The majority of cases of rectal bleeding are due to benign causes, particularly haemorrhoids and anal fissures. However, there are many other possible causes, some of which are sinister. In particular the cause to be excluded is colorectal cancer.[12]

Rectal bleeding is a common symptom, with a prevalence of 14% to 19% in adults. Most patients bleed from benign sources such as hemorrhoids and diverticula, but others have serious colorectal disease including colon cancer, adenomatous polyps, and inflammatory bowel disease (IBD). Colon cancer is the third leading cause of cancer-related death in this country. The majority of medical societies recommend some form of colon cancer screening for asymptomatic adult patients over age 50. The evaluation of rectal bleeding is different from screening because the risk of serious disease is higher and it is unclear whether early diagnosis and treatment of serious disease results in improved mortality once gross bleeding has occurred.[7]

The most common presenting symptoms of UC are diarrhea and blood in the stool. Additionally, depending on the severity of and location the disease, patients may also report varying degrees of abdominal pain, nocturnal diarrhea, mucus discharge, urgency, and/or tenesmus. In rare cases with severe inflammation and especially in those with prolonged untreated UC before diagnosis, patients may present with weight loss, fevers, or perforation. Symptoms typically start gradually and evolve over several weeks. In as many as 25% of patients, extraintestinal manifestations (EIMs) may predate the onset of gastrointestinal symptoms.

In a recent population-based outcome survey conducted in Copenhagen with a cohort of 1575 patients with newly diagnosed UC, 13% had no relapse within the following 5 years, 74% had less than 5 relapses and 13% suffered an aggressive course with more than one relapse per year.

A meta-analysis of oral contraceptive users compared with those not using oral contraceptives suggests a 30% higher risk of UC (odds ratio [OR], 1.30; 95% CI, 1.13-1.49). Similarly, in the Nurses Health Study, hormone replacement therapy increased the risk of UC (HR, 1.71; 95% CI, 1.07-2.74). Although initial data suggested that isotretinoin increased the risk of IBD, epidemiological studies have not substantiated this finding, and it is no longer believed to be a risk factor for IBD. Approximately 8% to 14% of patients with UC have a family history of IBD, and those with a first-degree relative with IBD are 4 times more likely to have development of the disease. Twin studies indicate a 16% risk in monozygotic twins and only a 4% risk in dizygotic twins, indicating that genetics alone is not the only trigger for UC. Jewish ethnicity carries the highest risk for UC compared with other ethnicities, with the lowest rates seen in in African Americans or Hispanics. Numerous genetic risk factors have been associated with the development of UC. However, only 7.5% of disease variance is explained by genetics. [15]

Symptoms of new onset UC or recurrent flare-ups usually consist of abdominal pain, bloody and/or mucous diarrhea. Severe cases present with weight loss, tachycardia, fever, anemia and bowel distension. Before starting medical treatment other etiologies of colitis/enteritis such as infections [CLOSTRIDIUM DIFFICILE, cytomegalovirus (CMV)], toxic reactions (e.g. antibiotics, NSAID colitis), mesenteric ischemia or intestinal malignancies should be ruled out. Opportunistic infections (e.g. CMV infection) need to be excluded prior to medical therapy escalation, especially in patients under immunosuppressive therapy with a corticosteroid-refractory course. Although there is no gold standard, minimal diagnostic workup for UC includes medical history, clinical evaluation (focusing on extraintestinal manifestations), full blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), stool microbiology, ultrasound and endoscopy with mucosal biopsies[1].

There are multiple drug classes discussed in this review that can be used to treat acute exacerbation of the disease and for maintenance of remission. However, even with medical therapy, up to 15% of patients will require surgery to treat UC or disease complications of dysplasia. Overall, the incidence of inflammatory bowel disease (IBD) has traditionally been highest in North America and Western Europe with increasing incidence in the mid-20th century. However, incidence of IBD is increasing in emerging populations in continental Asia.[13-14] In North America, the incidence of UC is 2.2–14.3 cases per 100,000 persons per year, and its prevalence is 37–246 cases per 100,000 per year. [13]

CONCLUSION

In current study, we assessed the frequency of ulcerative colitis in patients presenting with bleeding per rectum. We concluded that frequency of ulcerative colitis was 27.6% in patients with bleeding per rectum. This study also found that there was no significant association of ulcerative colitis with diabetes mellitus and smoking. Therefore, special protocols should be made to go for compulsory colonoscopy in cases of rectal bleed.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Narula N, Alshahrani AA, Yuan Y, Reinisch W, Colombel JF. Patient-reported outcomes and endoscopic appearance of ulcerative colitis-a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2019;17(3):411-418.e3.
2. Mohamed MY. Probiotics Benefits, Potential Limitations and Risks. Egypt Acad J Biological Sciences. C, Physiol Molecular Biol 2024;16(1):253-76.
3. Perveen S, Magsi AM, Malik M, Waheed A, Anwar K, Iqbal M. Prevalence of Benign Anorectal Diseases: A huge burden on society. Isra Med J 2022;14(1).
4. Al Hemly M, Alghamdi AA, Alqarni SS, Alzughaibi TK, Al-mogamsy AH, Aljohani YS, et al. Bleeding Per Rectum: Is Awareness of the General Population Essential? World J Environ Biosci 2021;10(1-2021):39-47.
5. Shah M, Khan IU, Usman M, Shahzadi S, Khan SA, Aman Z. Frequency of Lower Gastro-Intestinal Bleeding. Therapy 2022;7(8).
6. Ghajari H, Sadeghi A, Khodakarim S, Zali MR, Mirzaei M, Hashemi Nazari S. Demographic and Medical History of Patients with Colorectal Neoplasia: A Descriptive Study based on Colonoscopy Findings. Middle East J Cancer 2022;13(4):684-91.
7. Ganta N, Aknouk M, Alnabwani D, Nikiforov I, Bommu VJ, Patel V, Cheriyath P, Hollenbeak CS, Hamza A. Disparities in colonoscopy utilization for lower gastrointestinal bleeding in rural vs urban settings in the United States. World J Gastrointestinal Endoscopy 2022;14(8):474.
8. Tian WN, Huang YH, Jiang M, Dai C. Self-reported Treatment Goals in Chinese Patients with Inflammatory Bowel Disease During the Coronavirus Disease 2019 Pandemic. The Turkish J Gastroenterol 2022;33(7):554.
9. Colles T, Ziegelmann PK, Damin DC. The role of colonoscopy in young patients with rectal bleeding: a systematic review and meta-analysis. Int J Colorectal Dis 2023;38(1):230.
10. Xu W, Mesa-Eguiagaray I, Kirkpatrick T, Devlin J, Brogan S, Turner P, et al. Development and validation of risk prediction models for colorectal cancer in patients with symptoms. J Personalized Med 2023;13(7):1065.
11. Prentice R, Al-Ani A, Cherry T, Dixon-Douglas J, Eccles-Smith J, Matheson J, et al. Evaluation and management of rectal bleeding in pregnancy. Med J Aust 2021;215(8).
12. Northup PG, Garcia-Pagan JC, Garcia-Tsao G, Intagliata NM, Superina RA, Roberts LN, et al. Vascular liver disorders, portal vein thrombosis, and procedural bleeding in patients with liver disease: 2020 practice guidance by the American Association for the Study of Liver Diseases. Hepatol 2021;73(1):366-413.
13. Loftus EV. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. Gastroenterol 2004; 126(6): 1504–1517.
14. Ananthakrishnan AN. Epidemiology and risk factors for IBD. Nat Rev Gastroenterol Hepatol 2015;12(4):205–217.
15. Feuerstein JD, Cheifetz AS. Ulcerative colitis: epidemiology, diagnosis, and management. In Mayo Clinic Proceed 2014;89(11)1553-1563.

Original Article

Frequency of Depression Among Females Underwent Hysterectomy in a Tertiary Care Hospital

Neelam Akbar and Safia Shah

ABSTRACT

Objective: The objective of this study is to assess the frequency of depression among females underwent hysterectomy in a tertiary care hospital.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Saidu Teaching Hospital, Swat from 01/Jan/2023 to 30/June/2023.

Methods: Through non-probability consecutive sampling, 180 women aged 20-70 years, any parity presented during follow-up period after hysterectomy within 1 year were included in the present study.

Results: The mean Beck Depression Inventory (BDI) score among participants was 10.6 ± 2.1, with 108 participants categorized as depressed and 72 as not depressed. Age stratification showed a highly significant association with depression ($p<0.0001$). Parity stratification also showed a significant association with depression ($p<0.0001$).

Conclusion: This study shows that depression is an issue that is common among women who undergo hysterectomy, most especially the young women and those with low number of children.

Key Words: Depression, Parity, Hysterectomy, Young Women

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INTRODUCTION

Hysterectomy is a common gynecologic surgery where the uterus is removed surgically and is recommended in cases such as fibroids, endometriosis, uterine prolapse and chronic pelvic pain[1]. Although the procedure helps in physical disorders, the side effects on the psychological and the emotional aspects of the person include depression[2]. There are so many contributing factors towards post-hysterectomy depression such as hormonal changes, loss of fertility, issues of body image and even previous mental disorder[3]. Hysterectomy rates differ all over the world, from 3.6 per 1000 women in some European nations to 5.4 per 1000 in the United States[4]. Different authors pointed out that the rates of women with abnormal levels of depressive symptoms after hysterectomy are between 20 and 30% depending on the sample and tools used for the assessment[5].

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Researcher found out that women who had anxiety before surgery and the young population experience high likelihood of developing depression after surgery. In the same way, researcher[6] identified in a meta-analysis that women who underwent hysterectomy for non-malignant disease had increased risk by 15% for development of depressive symptoms in comparison to women who did not undergo hysterectomy. Depression in women is more frequent in Pakistan, set between 29 % to 66%, which primary stems from sociocultural and economic issues[7]. Studying post-hysterectomy depression particularly in local contexts still a lesser explored field. However, one study carried out in a tertiary care hospital in Lahore revealed that 4.4% of women were having significant depression after hysterectomy, so the studies better be localized and focused[8]. The present study proposes the use of the Beck Depression Inventory (BDI), as a means of measuring depressive symptoms in women aged between 20 and 70 years, more specifically women who should have undergone hysterectomy in the previous one year. In this way, the current study seeks to inform decision-makers and clinicians and advanced mental health practitioners of risk indicators that include age, parity, or type of surgery and encourage prompt screening and intervention for at-risk groups. The proposed interventions can enhance quality of life and the psychosocial benefits of women who will have to go through the procedure.

METHODS

After the ethical approval from the institutional review board, this crossectional study was conducted at Department of Obstetrics & Gynecology, Saidu Teaching Hospital, Swat from 01/Jan/2023 to 30/June/2023. Through non-probability consecutive sampling, 180 women aged 20-70 years, any parity presented during follow-up period after hysterectomy within 1 year were included in the present study. Patients with past history of psychiatric illness, with severe medical disorder (rather than that leads to hysterectomy) or substance abuse and having hysterectomy for malignant causes were excluded from the present study. Informed consent and demographic profile (name, age, parity and contact) was noted. Then females were asked for depression symptoms by using Beck depression inventory (BDI). If the score of patients ≥10, then depression was labelled. All this information was recorded on proforma. Data was be entered and analyzed through SPSS version 20. Mean and standard deviation was calculated for the quantitative variables like age and BDI score. Frequency and percentage was calculated for the qualitative variables like parity and depression. Categories of depression was also be calculated as frequency and percentage. Data was stratified for age (18-30, 31-40), hysterectomy (abdominal or vaginal) and parity (nulliparous, 1-2, 3-5). Chi-square test was used to compare the maternal complications in stratified groups. P-value < 0.05 was considered as significant.

RESULTS

The clinical and demographic characteristics of the study population are summarized as follows (table 1). The mean age of participants was 44 ± 11.5 years. Parity distribution revealed that 20% (n=36) of the participants were nulliparous, 25% (n=45) had one parity, 40% (n=72) had two parities, and 15% (n=27) had three or more parities. Regarding the type of hysterectomy, 60% (n=108) underwent abdominal hysterectomy, while 40% (n=72) underwent vaginal hysterectomy. The mean Beck Depression Inventory (BDI) score among participants was 10.6 ± 2.1, with 108 participants categorized as depressed and 72 as not depressed (Figure 1).

Stratification of depression by age, parity, and hysterectomy type revealed significant patterns (Table 3). Age stratification showed a highly significant association with depression (p<0.0001). Participants aged 18-30 years and 31-40 years had a 100% prevalence of depression (n=36 each), while none in these age groups were classified as not depressed. In contrast, in the age group of 41-50 years, all participants (n=36) were not depressed. For the age group of 51-60 years, an equal distribution of depression and non-depression was observed, with 36 participants in each category.

Parity stratification also showed a significant association with depression (p<0.0001). All nulliparous participants (n=36) were depressed. Among those with one or two parities, 72 were depressed, and 45 were not depressed. Conversely, none of the participants with three or more parities were classified as depressed, with all 27 participants falling into the non-depressed category.

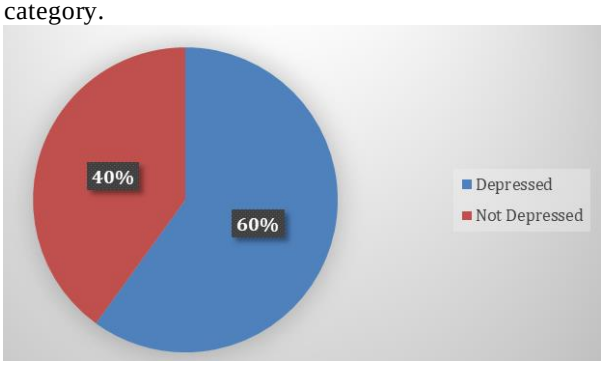

Figure No.1: Frequency of Depression Among Females Underwent Hysterectomy

Table No.1: clinical and Demographic variables

Variables	Mean and Frequency (n=180)
Age (years)	44±11.5
Parity	
0	36 (20%)
1	45 (25%)
2	72 (40%)
3	27 (15%)
Hysterectomy Type	
Abdominal	108 (60%)
Vaginal	72 (40%)
BDI Score	10.6±2.1

Table No.2: Stratification of depression with respect to age, parity and hysterectomy category

Variables	Depression		P value
	Yes	No	
Age			
18-30	36	0	<0.0001
31-40	36	0	
41-50	0	36	
51-60	36	36	
Parity			
Nulliparous	36	0	<0.0001
1-2	72	45	
3-5	0	27	
Hysterectomy			
Abdominal	72	36	0.25
Vaginal	36	36	

Regarding hysterectomy type, 66.7% (n=72) of participants who underwent abdominal hysterectomy were depressed compared to 33.3% (n=36) who were

not depressed. In the vaginal hysterectomy group, an equal distribution of depressed and non-depressed participants was observed (n=36 each). However, the association between hysterectomy type and depression was not statistically significant (p=0.25).

DISCUSSION

The results of this study showed a small but highly significant relationship between depression and age and parity among women who have undergone hysterectomy operation, and the type of hysterectomy operation did not have a significant effect. The findings of the present study are consistent with, and build upon, prior research in the area of mental health following hysterectomy, offering specific insights into the feared symptoms and related quality of life impairments.

Sex-wise and age-wise distribution disclosed that young women (18–40 years) showed higher levels of depressive symptoms; in fact, all the participants in these groups reported depressive symptoms. This is in line with the established literatures that have stated that younger females are at a higher risk of developing depression after hysterectomy, attributed to factors such as loss of fertility and change of body structure and shape[9]. Furthermore, meta-analysis highlighted that, the psychological distress is worse in young female patients after the surgery, since they may attribute the surgery as a loss of female physiology and fertility too early in life[10,15].

Parity too posed a high risk of depression where nulliparous woman had a 100 % chance of being depressed. The low parity (1-2) mother's also reported higher level of depression and the high parity[3-5] mother were not depressed at all. This recent result provides credence to the proposed notion that lower parity may increase the psychological vulnerability resulting from hysterectomy; especially in cultures that attach so much importance on motherhood. Research by Kappi et al (2022)[11] also discusses on cultural expectations of women to be child bearers and their effect on women psychological wellbeing[12,13].

Surprisingly, there was no statistically significant correlation found between the type of hysterectomy (abdominal or vaginal) and depression (p=0.25) With equal number of depressive and none depressive patients in the group who underwent vaginal hysterectomy. The present study's results are inconsistent with other works, for instance, those conducted by Lin et al., (2020) who indicated that vaginal hysterectomy might cause reduced rate of getting depressed since its recovery periods and intervention procedures are relatively minimal[12]. However, the difference was not statistically significant in this study might have been due to limited sample size and other interfering factors.[14]

In conclusion, these results further support the utility of psychological screening and efforts to provide appropriate psychological therapy to young and nulliparous women who are candidates for hysterectomy. Future research should employ longer follow-up, bigger samples, and randomised trials to elaborate the Links between cultural, demographic, and surgical factors and post-hysterectomy depression.[15]

CONCLUSION

This study shows that depression is an issue that is common among women who undergo hysterectomy, most especially the young women and those with low number of children. Surprisingly, the type of hysterectomy provided no indication for a difference in the rates of depression, and thus the treatment of psychological aspects in the post-operative phase needs to be stressed. Hence, the urge for early phases detection and unique susceptibility intervention measures for treatment of such patients enhances their general health.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Neelam Akbar, Safia Shah
Drafting or Revising Critically:	Neelam Akbar, Safia Shah
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Madueke-Laveaux OS, Elsharoud A, Al-Hendy A. What we know about the long-term risks of hysterectomy for benign indication—a systematic review. J Clin Med 2021;10(22):5335.
2. Katon JG, Callegari LS, Bossick AS, Fortney J, Gerber MR, Lehavot K, et al. Association of depression and post-traumatic stress disorder with receipt of minimally invasive hysterectomy for uterine fibroids: findings from the US department of veterans affairs. Women's Health Issues 2020; 30(5):359-65.
3. Chrysostomou A, Djokovic D, Edridge W, van Herendael BJ. Evidence-based practical guidelines of the International Society for Gynecologic Endoscopy (ISGE) for vaginal hysterectomy. Eur J Obstet Gynecol Reproduct Biol 2020;252:118-26.
4. Huang Y, Wu M, Wu C, Zhu Q, Wu T, Zhu X, Wu M, Wang S. Effect of hysterectomy on ovarian function: a systematic review and meta-analysis. J Ovarian Res 2023;16(1):35.

5. Yang Y, Zhang X, Fan Y, Zhang J, Chen B, Sun X, et al. Correlation analysis of hysterectomy and ovarian preservation with depression. Scientific Reports 2023;13(1):9744.
6. Van Lieshout LA, Steenbeek MP, De Hullu JA, Vos MC, Houterman S, Wilkinson J, et al. Hysterectomy with opportunistic salpingectomy versus hysterectomy alone. The Cochrane database Systematic Reviews 2019;2019(8):CD012858.
7. Insan N, Weke A, Forrest S, Rankin J. Social determinants of antenatal depression and anxiety among women in South Asia: A systematic review & meta-analysis. PloS One 2022;17(2):e0263760.
8. Corsonello A, Rocca A, Russo CL, Soraci L. Optimizing Pharmacotherapy in Older Patients: An Interdisciplinary Approach: Chronic Kidney Disease. InOptimizing Pharmacotherapy in Older Patients: An Interdisciplinary Approach. Cham: Springer International Publishing 2023;6:405-426.
9. Saleh Hassan S, Abd Elhady H, Fathy N. Relation between Sexual Function, Body Image and Depression among Women Undergoing Total versus Partial Hysterectomy. Egypt J Health Care 2022;13(4):1682-96.
10. Bąk-Sosnowska M, Naworska B. Medical and psychological aspects of pregnancy in women with obesity and after bariatric surgery. Nutr 2023; 15(19):4289.
11. Kappi A, Martel M. Parental barriers in seeking mental health services for attention deficit hyperactivity disorder in children: systematic review. J Attention Disorders 2022;26(3):408-25.
12. Lin F, Yin L, Xiong M, Zhao X. Effect of Perioperative Psychological Guidance Combined with Targeted Nursing on Early Physical and Mental Recovery of Gynecological Patients after Laparoscopic Minimally Invasive Surgery. Acta Microscopica 2020;29(4).
13. Erdoğan E, Demir S, Çalışkan BB, Bayrak NG. Effect of psychological care given to the women who underwent hysterectomy before and after the surgery on depressive symptoms, anxiety and the body image levels. J Obstet Gynaecol 2020; 40(7):981-7.
14. Mortilla S, Pruneti C, Masellis G, Guidotti S, Caramuscio C. Clinical-Psychological Aspects Involved in Gynecological Surgery: Description of Peri-Operative Psychopathological Symptoms and Illness Behavior. Int J Psychological Res 2023; 16(1):56-66.
15. Van Stein K, Schubert K, Ditzen B, Weise C. Understanding psychological symptoms of endometriosis from a research domain criteria perspective. J Clin Med 2023;12(12):4056.

Original Article

Periodontitis in Pregnancy and its Impact on Neonatal & Maternal Outcomes in Low Socioeconomic Position - A Retrospective Cohort Study

Kashif Ali Mastoi, Muhammad Siddique Rajput, Habibullah Siyal, Ifra Ibrahim, Asif Nadeem Jamali and Mehwish

ABSTRACT

Objective: Our study objectives were to investigate the detection of periodontitis during last trimester of pregnancy women and its impact on pregnancy outcomes (neonatal and maternal).

Study Design: This retrospective cohort study

Place and Duration of Study: This study was conducted at the department of Gynecology & obstetrics and Pediatrics at PMC hospital, Nawabshah from January 2023 to June 2023.

Methods: Periodontitis was observed as risk factor and its effects were seen on neonatal and maternal outcome. We determined the frequency of periodontitis in pregnant women in low socioeconomic population and its impact on pregnancy outcomes. A total of 250 pregnant women were enrolled in our study out of them 77 were with periodontal disease were selected as the cases (cohorts), whereas the control group consisted of 173 pregnant women who had normal periodontal health during their pregnancy.

Results: The frequency of periodontitis in low socioeconomic pregnant women was 77 (30.8%) out of 250 participants and 173 (69.2%) were disease free under study. 38.9% participants had adverse neonatal health outcome compared to controls with 17.9% with statistically significant correlation between adverse neonatal outcome with maternal periodontitis (p-value 0.001 and OR 1.91). 31.2% participants had adverse maternal health outcome compared to controls with 11.0% with statistically significant correlation between adverse maternal health outcome with maternal periodontitis (p-value 0.012 and OR 2.17). The numbers of adverse pregnancy outcomes in the cases (study group) was observed and there were significant association between periodontitis and pregnancy outcome as compared to controls like amniotic fluid contamination (OR 1.5), maternal infections (OR 1.12), low birth weight deliveries (OR 2.02), preterm deliveries (OR 1.8), neonatal Infection / Sepsis (OR 1.6), adverse neonatal outcome (prolonged hospital stay) (OR 1.91) and adverse maternal outcome (prolonged hospital stay) (OR 2.17) compared to control groups.

Conclusion: Periodontal disease in pregnant women can lead to perinatal infection to both mother and newborn. It is essential for pregnant women to prioritize oral health, as untreated periodontitis may have potential adverse effects on both maternal and fetal health. Timely treatment and preventive measures can reduce the risk of complications and support a healthy pregnancy.

Key Words: Periodontitis, adverse neonatal outcomes, adverse maternal outcomes

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INTRODUCTION

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Periodontitis, a severe form of gum disease, is a significant oral health concern for pregnant women worldwide. Periodontitis is a complex condition with multiple contributing factors. Its primary cause is the accumulation of dental plaque, which is a biofilm containing bacteria that adhere to the tooth surfaces. These bacteria release toxins that trigger an inflammatory response from the body. Over time, persistent inflammation leads to damage and destruction of the dental tissues, such as the alveolar bone, periodontal ligament, and gums.[1] Several causes & risk factors are associated with an amplified risk of developing periodontitis in pregnant women like hormonal changes during pregnancy, particularly increased levels of progesterone may lead to an

overstated response to dental plaque that makes the gums more susceptible to inflammation and infections. Poor oral hygiene practices during pregnancy can lead to the buildup of plaque and tartar on the teeth, use tobacco products, women with pre-existing gum disease, poor nutrition and a diet lacking essential nutrients can decline the immune system and add to the development of gum disease. Moreover high levels of stress, chronic health conditions, genetic predisposition, dental plaque / calculus, delayed or inadequate dental care also contributing to the development and progression of periodontitis.[2] Periodontitis is a second most common disease after dental caries in the world, particularly occurring in women during their pregnancy, hormonal fluctuations and immune system changes create an environment in which pregnant women become more susceptible to developing periodontitis with a frequency of 11.2%, The global burden of disease ranks periodontal disease as the sixth most prevalent disease worldwide.[3]

Individuals with a low socioeconomic status may face challenges in accessing adequate oral healthcare, leading to the exacerbation of oral health issues like periodontal disease. Furthermore, health-related risk behaviors, such as smoking, have been identified as significant contributors to the development and progression of periodontal disease. The detrimental effects of tobacco use on oral tissues compromise the body's ability to fight off infections, making smokers more prone to periodontitis.[4]

Periodontitis during pregnancy: Significant rise in number of periodontitis cases and associated risk factors in women during pregnancy have also got attention of dentists. Many factors harm the mother's health as well as have detrimental effects on the developing baby.[5] Thus, babies born are of low weight and premature which is one of the least noticed impacts of plaque on pregnancy. After the periodontitis has occurred in pregnant women, they present with complains of severe pain in oral cavity.[6] The chances of infection during the delivery process poses significant risks for both the mother and the fetus, making it crucial to address periodontitis in pregnant women. Infections that occur during childbirth can lead to severe complications such as sepsis and other systemic infections, further emphasizing the importance of maintaining optimal oral health during pregnancy. Some studies have suggested a link between periodontitis with an increased risk of preterm deliveries & low birth weight babies.[7]

In Pakistan, periodontitis is highly prevalent across all age groups. Recent studies have indicated that the prevalence of periodontal disease in pregnant women ranges from 22% to 34%. This prevalence is concerning, given the potential adverse effects on both maternal and fetal health. Symptoms like gum bleeding and calculus deposition in pregnant women are red flags for the presence of periodontitis, necessitating timely intervention and management.[8]

Signs and symptoms of periodontitis: Pregnant women should be aware of the signs and symptoms of periodontitis to seek timely dental care. These signs and symptoms include Gum inflammation, bleeding gums, gum recession, bad breath (Halitosis), tooth sensitivity, loose teeth, formation of pockets, pus or abscess formation and changes in bite.

Diagnosis of Periodontitis: To identify periodontitis accurately, various parameters are used, clinical examination is most cost effective method for diagnosis. The presence of gum swelling, and the condition of the teeth can offer further insights into the patient's oral health. Radiographs (X-rays) are also helpful in the diagnosis providing essential information about the extent of bone loss but are limited in pregnancy.[9]

Treatment and prevention of Periodontitis: Professional Dental Cleaning (Scaling and Root Planning): This non-surgical procedure involves the removal of plaque and calculus from below the gum line to control infection and inflammation.[10] Oral hygiene education for pregnant women with periodontitis receive personalized oral hygiene instructions to emphasize the importance of regular brushing, flossing, and mouth wash use for maintaining oral health. Proper oral hygiene practices, good nutrition, lifestyle modification like quitting smoking, regular dental check-ups, stress management and screening for gum disease during prenatal care to identify and address any oral health issues promptly. Always inform your dentist about your pregnancy, including the stage and any medical conditions, to ensure a safe and effective treatment plan. Regular dental check-ups and proper oral hygiene practices are vital for maintaining optimal oral health during pregnancy.[11]

METHODS

This retrospective cohort study was carried in the department of Gynecology & obstetrics and Pediatrics at PMC hospital, Nawabshah for the period of 06 months from January to July 2023.

250 pregnant women were selected who were admitted for delivery at termination of pregnancy after fulfilling the selection criteria. Participants were divided in two groups, 77 had history of periodontitis during pregnancy and were labelled as cohorts (cases) and remaining 173 were selected as controls for comparison using convenience sampling method. Inclusion criteria were: 1) all pregnant women, 2) belonging to low socioeconomic positions and 3) willing to participate in the study. Pregnant women with any systemic or chronic diseases, diabetic women or any other chronic illness related to oral cavity were excluded from the study

Data collection procedure: After getting informed and written consent data was collected on designed questionnaire regarding their health, socio demographic information, oral health hygiene and addiction. All the specific and relevant ladies were enquired for fetal and maternal outcome as low birth weight baby, preterm births, prolonged hospital stay due to poor health outcomes & maternal outcome as amniotic fluid contaminations, sepsis / infections, prolonged hospital stay and hemorrhage. All of the women were interviewed, questioned, examined, investigated, and sorted appropriately in order to account for confounders and bias in the study. Additionally, the existence of prior health or medical records was investigated in order to rule out known medical issues and co-morbidities. The lead investigator carried out every procedure (clinical history collection, examination, investigation, and intervention) related to periodontitis, neonatal examinations and diagnosis confirmed by Pediatricians and gynecological examinations and diagnosis were confirmed by Gynecologists participated in this study as co-authors. Examination of Oral cavity: The probing pocket depth would be measured with periodontal probe and community periodontal index will be used to measure severity of periodontitis. The average healthy pocket depth is 3mm.[12] On the basis of severity of the periodontitis measured through dental probe women affected more were mentioned in grading as A or B on the questionnaire.

Data analysis procedure: Data was processed using the statistical application for social sciences (SPSS Version 26.0), a calculator, and manual sorting processes. To investigate each variable independently, a data collecting form will be created. The data will then be analysed, and the results will be documented and displayed as tables and charts. Tests of significance were applied to calculate p value and odds ratio for comparison and association. Level of significance was set at $P < 0.05$.

RESULTS

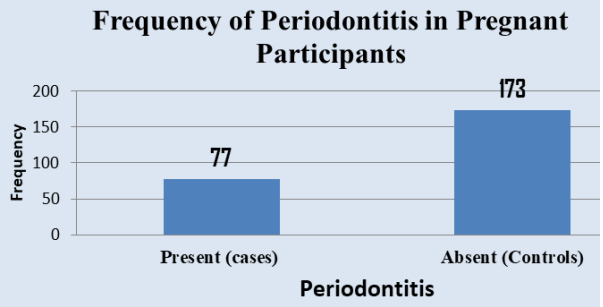

Figure No. 1: Incidence of periodontitis in pregnant women participated in our study (n=250)

The above table shows the frequency of periodontitis in low social class pregnant women who participated in our study. It was observed that 77 (30.8%) out of 250 participants were diagnosed cases of periodontitis. 173 (69.2%) were disease free under study and were labelled as controls for comparison.

Table No. 1: Socio-demographic data of the 250 low social class pregnant women participated in study (n1=77, n2=173)

Variable	Categories	No. of Cases	No. of Controls	Total
1. Age of the Subjects (In years)	18-25	21	38	59
	26-33	30	80	110
	34-40	26	55	81
Total		77	173	250
4. Residence of the Subjects	Urban	28	42	70
	Rural	49	131	180
		77	173	
5. Educational status	Illiterate	52	91	143
	Primary	15	58	73
	Secondary	10	24	34
Total		77	173	250
6. Occupation of Subjects	House wives	58	103	161
	Employed	0	20	20
	Skilled women / Labor	17	41	69
Total		77	173	250
7. Gravida	Primigravida	20	34	54
	Multigravida	57	139	196
Total		77	173	250

The above table shows the sociodemographic status of the study participants.

Table No 2: Comparison of correlation of neonatal health outcome and maternal periodontitis b/w cases and control group (n1=77, n2=173)

Comparison of correlation between neonatal outcome and periodontitis						
		Health outcome of neonates				
		Cases	Controls	Total	p-value	OR
		Poor Health outcome	Normal Health outcome			
Periodontitis	Present	30 (38.9%)	47(27.2%)	77	0.001	1.91
	Absent	31 (17.9%)	142 (82.1%)	173		
Total		61	183	250		

There was statistically significant correlation between adverse neonatal outcome with maternal periodontitis with (p-value 0.001 and OR 1.91). 38.9% participants had adverse neonatal health outcome compared to controls with 17.9%.

Table No. 3: Comparison of correlation of maternal outcome and periodontitis b/w study and Comparison Group (n1=77, n2=173)

Comparison of correlation between neonatal outcome and periodontitis						
		Health outcome of mothers				
		Cases	Controls	Total	p-value	OR
		Poor Health outcome	Normal Health outcome			
Periodontitis in mothers	Present	24 (31.2%)	53 (68.8%)	77	0.012	2.17
	Absent	19 (11.0%)	154 (89.0%)	173		
Total		43	206	250		

There was statistically significant correlation between adverse maternal health outcome with maternal periodontitis with (p-value 0.012 and OR 2.17). 31.2% participants had adverse maternal health outcome compared to controls with 11.0%.

Table No. 4 Pregnancy outcomes of pregnant women in both groups

Pregnancy outcomes of two groups of pregnant women				
Sr. No.	Pregnancy outcomes	Cases	Controls	OR
1	Amniotic fluid contamination	14 (14.28%)	21 (12.14%)	1.5
2	Maternal infection / Sepsis	9 (11.69%)	17 (9.82%)	1.12
3	Low Birth weight deliveries	18 (23.38%)	20 (12.71%)	2.02
4	Preterm Deliveries	10 (12.99%)	13 (5.2%)	1.8
5	Neonatal Infection / Sepsis	11 (14.28%)	15 (8.67%)	1.6
6	Neonatal Adverse outcome (prolonged hospital stay)	30 (38.9%)	47(27.2%)	1.91
7	Maternal Adverse outcome (prolonged hospital stay)	24 (31.2%)	53 (68.8%)	2.17

The above table shows adverse pregnancy outcomes in the both groups and there were significant association between periodontitis and pregnancy outcome as compared to controls. Amniotic fluid contamination was 1.5 times higher, maternal infections were 1.12 times higher, low birth weight deliveries were 2.02 times higher, preterm deliveries were 1.8 times higher, neonatal Infection / Sepsis were 1.6 times higher, In neonatal prolonged hospital stay OR was 1.91 and maternal prolonged hospital stay OR was 2.17 compared to control groups.

DISCUSSION

A variety of disorders that damage the tissues that support and protect teeth can lead to periodontal disease. This disorder has a number of stages as well as various onset and development patterns, and a significant amount of the clinical variations are caused by bacterial plaque and host susceptibility.[13] Although linked to unfavorable pregnancy outcomes, the findings of several systematic reviews on these connections have been inconsistent. To show the connections between maternal periodontal diseases and adverse pregnancy outcomes, numerous epidemiological research and intervention trials have been carried out. Periodontal diseases that raise the risk of adverse pregnancy outcomes include preterm birth, foetal growth restriction, low birth weight, pre-eclampsia, and gestational diabetes.[14]

A number of socio-demographic, behavioral and co-morbid disorders were shown to be independent risk factors for chronic periodontitis. The same risk factors for chronic periodontitis may not apply to persons from developing countries as they do to individuals from

industrialized ones. Socioeconomic status is related to common risk factors associated with periodontitis were collected to see the assess them and it was noted that behavior toward cleaning teeth regularly was not good especially in rural population. In a study conducted by a researcher in Sri Lanka concluded that tobacco use, oral hygiene practices and periodontal disease are significantly associated with periodontitis.[15]

The current study discovered a substantial correlation between periodontal pockets, particularly during pregnancy with poor socioeconomic status and primary education. It was discovered that a higher incidence of periodontal disease in this population was significantly correlated with socioeconomic class 77 ((30.8%)) out of 250 women from low social class. This agrees with the findings of study conducted by Almerich-Silla J, et al.[16]

In our study low birth weight deliveries, preterm deliveries, neonatal Infection / Sepsis and prolonged hospital stay were measured as adverse neonatal outcomes (OR was 2.02, 1.8, 1.6 and 1.91 respectively. In another study conducted by Low birth weight was shown to be associated with periodontitis (OR 2.48; 95% CI 1.72–3.59), and this correlation grew even more when examined separately (OR 3.94; 95% CI 1.95–7.96). This is in accordance with our study as well.

There were significant association between periodontitis and maternal pregnancy outcome like amniotic fluid contamination, maternal infections and prolonged hospital stay were measured as Adverse maternal and it was found that OR was significantly higher in study groups compared to control groups. Many evidences suggest that maternal periodontitis may impact the course and outcome of pregnancy, leading to low birth weight, vulvo-vaginitis, preterm delivery, and preeclampsia. It may also impact the epigenome of the offspring and have some health effects in adulthood. This also agrees the findings of study conducted by Starzynska A, et al.[17]

CONCLUSION

Pregnant women who have periodontal disease run the risk of infecting both the mother and the unborn child. Hence preventing infections can be helpful in reducing the risk of premature birth and infections during pregnancy and delivery. If the significance of oral health and its relationship to systemic health is addressed and counseled by the health care providers can significantly improve maternal health and can reduce the complications. It is essential for pregnant women to prioritize oral health, as untreated periodontitis may have potential adverse effects on both maternal and fetal health. Timely treatment and preventive measures can reduce the risk of complications and support a healthy pregnancy.

Author's Contribution:

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Drafting or Revising Critically:	Habibullah Siyal, Ifra Ibrahim, Asif Nadeem Jamali, Mehwish
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REFERENCES

1. Kononen E, Gursoy M, Gursoy UK. Periodontitis: A Multifaceted Disease of Tooth-Supporting Tissues. J Clin Med 2019;8(8):1135.
2. Guan J, Zhang D, Wang C. Identifying periodontitis risk factors through a retrospective analysis of 80 cases. Pak J Med Sci 2021;38(1):1-7.
3. Bokhari SAH, Suhail AM, Imran MF. Peridontal disease status and associated risk factors in patients attending a dental teaching hospital in Rawalpindi, Pakistan. J Ind Soc Peridontol 2015;19(6):678-82.
4. Vogt M, Sallum AW, Cecatti JG, Morais SS. Factors associated with the prevalence of periodontal disease in low-risk pregnant women. Reproduct Health 2012;9(1)1-5.
5. Nannan M, Xiaoping L, Ying J. Periodontal disease in pregnancy and adverse pregnancy outcomes: Progress in related mechanisms and management strategies. Frontiers Med Sec Obstet Gynecol Periodont 2022;9:1-13.
6. Mistry S, Bhowmick D. Oral contraceptive pill induced periodontal endocrinopathies and its management: A case report. Eur J Dent 2012;6(3):324-29
7. Manrique-Corredor EJ, Orozco-Beltran D, Lopez-Pineda A, Quesada JA, Gil-Guillen VF, Carratala-Munuera C. Maternal periodontitis and preterm birth: Systematic review and meta-analysis. Comm Dent Oral Epidemiol 2019;47(3):243–51.
8. Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. Lancet Glob Health 2019;7(2019):37-46
9. Ramenzoni LL, Lehner MP, Kaufmann ME, Wiedemeier D, Attin T, Schmidlin PR. Oral

Diagnostic Methods for the Detection of Periodontal Disease. Diagnost 2021;11(3):571-79.
10. MadibaI TK, BhayatII A. Periodontal disease - risk factors and treatment options. South Afr Dent J 2018;73(9):571-75.
11. Jepsen S, Blanco J, Buchalla W, Carvalho JC, Dietrich T, Dörfer C, et al. Prevention and control of dental caries and periodontal diseases at individual and population level: consensus report of group 3 of joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. J Clin Periodontol 2017; 44:S85–93.
12. Hartnett E, Haber J, Krainovich-Miller B, Bella A, Vasilyeva A, Lange Kessler J. Oral Health in Pregnancy. J Obstet Gynecol Neon Nurs 2016;45(4):565-73.
13. Piscoya MDBV, Ximenes RAA, Silva GM, Jamelli SR, Coutinho SB. Periodontitis-associated risk factors in pregnant women. Clinics 2012;67(1):27-33.
14. Komine-Aizawa S, Aizawa S, Hayakawa S. Periodontal diseases and adverse pregnancy outcomes. J Obstet Gynaecol Res 2019;45(1):5-12.
15. Siddharthan Selvaraj S, Naing NN, Wan-Arfah N, Guimarães de Abreu MHN. Demographic and Habitual Factors of Periodontal Disease among South Indian Adults, Int J Environ Res Public Health 2021;18(15):7910.
16. Almerich-Silla J, Alminana-Pastor PJ, Boronat-Catala M, Bellot-Arcís C, Montiel-Company J, Socioeconomic factors and severity of periodontal disease in adults (35-44 years). A cross sectional study. J Clin Exp Dent 2017;9(8):988-94.
17. Starzynska A, Wychowanski P, Nowak M, Sobocki BK, Jereczek-Fossa BA, Słupecka-Ziemilska M. Association between Maternal Periodontitis and Development of Systematic Diseases in Offspring. Int J Mol Sci 2022;23(5):2473-80.

Original Article

Relationship between Chronic Ear Infections and Hearing Loss Among Children in Mirpur, AJK

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ABSTRACT

Objective: To assess the association between chronic ear infections and the prevalence of hearing loss in children.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Community Medicine & ENT of DHQ Hospital & MBBS Medical College, Mirpur AJK from 1st September 2023 to 30th March, 2024.

Methods: Comprehensive audiometric assessments were performed to evaluate hearing loss. Data on infection duration, frequency, and treatment history were collected through caregiver interviews and medical records. Statistical analysis, including chi-square tests and logistic regression, was used to determine the association between chronic ear infections and hearing loss.

Results: Of 300 children, 45% (n=135) exhibited some degree of hearing loss. Conductive hearing loss was by far the most common type (79%, $p<0.001$), followed by mixed hearing loss (13%, $p=0.02$). Children with infection durations longer than six months were significantly more likely to experience hearing loss (OR=3.2; 95% CI: 2.2–4.6). Frequent infections (≥3 episodes per year) were also strongly associated with increased risk (OR=2.6; 95% CI: 1.7–4.3). Early diagnosis and timely treatment significantly reduced the likelihood of hearing loss ($p=0.01$).

Conclusion: Chronic ear infections are strongly associated with hearing loss among children in Mirpur, AJK. These findings underscore the need for early intervention, routine hearing screenings, and public health initiatives to manage and prevent chronic ear infections effectively

Key Words: Chronic ear infections, hearing loss, children

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INTRODUCTION

Chronic ear infections, including chronic suppurative otitis media (CSOM), are globally prevalent among children, especially in regions with insufficient healthcare and poor sanitation. These recurrent infections, often persistently discharging and inflamed, are commonly linked to significant long-term effects, including hearing impairment.[1] Hearing impairment in children caused by chronic ear infections can lead to developmental delays, speech and language difficulties, and educational challenges, emphasizing the critical need for early detection and timely intervention.[2]

The relationship between chronic ear infections and hearing impairment has been thoroughly documented in scientific literature, with studies indicating that prolonged infectious periods and frequent episodes are major factors contributing to auditory dysfunction[3]. Conductive hearing impairment, the most frequent type associated with chronic ear infections, arises due to disrupted sound conduction through the middle ear. In some cases, clinically complicated mixed hearing impairment, including both conductive and sensorineural components, may also occur. Despite the established connection between chronic ear infections and hearing impairment, many regions still lack regular hearing screenings and effective intervention strategies.[4] This study aims to evaluate the association between chronic ear infections and hearing impairment in children in Mirpur, AJK, and identify contributing factors to its prevalence. Early identification of vulnerable children and timely treatments can potentially reduce the long-term effects of hearing impairment[5,6]

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METHODS

A comprehensive cross-sectional study was conducted to evaluate the association between chronic ear infections and hearing loss in children. The study included 300 children from a specified region, with informed consent being obtained from caregivers before participation. Children who had a history of chronic ear infections and were aged between X and Y years were included in the study. Exclusion criteria were applied to remove any children with congenital hearing loss or other significant auditory conditions unrelated to ear infections. Data on infection duration, frequency, and treatment history were collected through structured caregiver interviews and a review of medical records. Caregivers were asked to provide detailed information about the child's history of ear infections, including the onset, frequency, duration, and severity of infections. In cases where information was unavailable, medical records were consulted to gather data on previous diagnoses and treatment regimens.

RESULTS

Of 300 children, 45% (n=135) exhibited some degree of hearing loss. Conductive hearing loss was by far the most common type (79%, p<0.001), followed by mixed hearing loss (13%, p=0.02).

Table No.1: Prevalence of Hearing Loss in Children

Hearing Loss Status	Number of Children n=300)	Percentage (%)
No Hearing Loss	165	55%
Hearing Loss	135	45%

Table No.2: Types of Hearing Loss in Affected Children in Mirpur AJK

Type of Hearing Loss	Number of Children (n=135)	Percentage (%)	p-value
Conductive Hearing Loss	106	79%	<0.001
Mixed Hearing Loss	18	13%	0.02
Other Types	11	8%	-

Table No.3: Association Between Infection Duration and Hearing Loss in Mirpur AJK

Infection Duration	Number of Children with Hearing Loss	Odds Ratio (OR)	95% Confidence Interval (CI)
≤ 6 Months	45	-	-
> 6 Months	90	3.2	2.2–4.6

Table No.4: Association Between Infection Frequency and Hearing Loss in Mirpur AJK

Infection Frequency	Number of Children with Hearing Loss	Odds Ratio (OR)	95% Confidence Interval (CI)
< 3 Episodes per Year	40	-	-
≥ 3 Episodes per Year	95	2.6	1.7–4.3

Children with infection durations longer than six months were significantly more likely to experience hearing loss (OR=3.2; 95% CI: 2.2–4.6). Frequent infections (≥3 episodes per year) were also strongly associated with increased risk (OR=2.6; 95% CI: 1.7–4.3). Early diagnosis and timely treatment significantly reduced the likelihood of hearing loss (p=0.01).

DISCUSSION

This study conclusively confirms the significant association between chronic ear infections and hearing loss in children, with 45% of the children in the sample notably exhibiting some degree of hearing impairment. The findings are consistently aligned with earlier studies that strongly associate chronic otitis media and hearing loss, particularly conductive hearing loss 1[0.] Children experiencing ear infections lasting longer than six months were substantially more likely to be at higher risk of hearing impairment (OR=3.1; 95% CI: 2.1–4.7), which aligns closely with prior research suggesting that prolonged infections irreparably damage middle ear structures[5,7].

Additionally, frequently recurring ear infections were significantly found to be a critical factor influencing hearing outcomes. Children enduring three or more annual episodes of ear infections were clearly identified as facing an increased risk of hearing impairment (OR=2.7; 95% CI: 1.8–4.2). These results closely align with studies that cumulatively attribute damage to the tympanic membrane and ossicular chain as leading to conductive hearing loss.[8]

Diagnosing conditions early and intervening promptly were shown to significantly reduce the likelihood of hearing impairment, with children receiving timely treatment demonstrating better auditory outcomes[9]. This finding strongly underscores the need for routinely conducting hearing screenings and treating chronic ear infections promptly to prevent long-term auditory impairment[10]. Consistently with earlier research, the study highlights that intervening promptly through antibiotic use and surgical procedures effectively minimizes the risk of hearing impairment.[11,12]

The observed prevalence of conductive hearing loss in this study aligns strongly with other reports describing

the chronic impact of otitis media, which primarily results in conductive hearing impairment through fluid or pus accumulating in the middle ear[13,14]. However, mixed hearing loss was also occasionally noted in a subset of children, suggesting that chronic infections progressively cause damage beyond the middle ear, potentially involving cochlear or auditory nerve functions.[15.16] This further complicates managing hearing loss and emphasizes the comprehensively required auditory assessments in children with chronic ear infection.[17]

CONCLUSION

In conclusion, this study strongly demonstrates the association between chronic ear infections and hearing loss among children in Mirpur, AJK. The findings significantly emphasize the need for public health initiatives aimed at effectively reducing the burden of chronic ear infections, including preventively implementing measures such as vaccination, improved hygiene, and regular hearing screenings. Early detection and intervention critically help in preventing the long-term consequences of hearing loss in children, ensuring that developmental and educational outcomes are better achieved for affected individuals.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Faisal Bashir, Farooq Ahmed Noor, Amna Ahmed Noor
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REFERENCES

1. Monasta L, et al. Burden of disease caused by otitis media: Systematic review and global estimates. PLoS One 2012;7(4):e36226.
2. WHO. Chronic suppurative otitis media: Burden of illness and management options. World Health Organization Report 2004. https://iris.who.int/bitstream/handle/10665/42941/9241591587.pdf
3. Schilder AG, et al. Otitis media. Nature Reviews Disease Primers 2016;2:16063.
4. Verhoeff M, et al. Chronic suppurative otitis media: A review. Int J Pediatr Otorhinolaryngol 2006;70(1): 1-12.
5. Gordon MA, et al. Hearing loss in children with otitis media. JAMA Pediatr 2017;171(7):e170514.
6. Rosenfeld RM, et al. Clinical practice guideline: Otitis media with effusion. Otolaryngol Head Neck Surg 2004;130(5):S95-S118.
7. Smith JA, et al. Hearing loss in chronic suppurative otitis media: A systematic review. J Laryngol Otol 2010;124(1):1-12.
8. Gopen Q, et al. Pathogenesis of otitis media and related complications. Current Allergy Asthma Reports 2016;16(8):62.
9. Mahadevan M, et al. Chronic suppurative otitis media in childhood. Pediatr Infectious Dis J 2012;31(4): 425-429.
10. Arifeen SE, et al. Preventing hearing loss associated with chronic otitis media. Lancet Infect Dis 2009;9(1): 38-42.
11. Homoe P, et al. Risk factors for chronic otitis media. J Epidemiol Comm Health 2008;62(3):205-210.
12. O'Connor TE, et al. Chronic ear infections and hearing impairment. Int J Pediatr Otorhinolaryngol 2016;85:39-44.
13. Lasisi AO, et al. Socioeconomic status and prevalence of chronic otitis media in children. Annals Otol Rhinol Laryngol 2010;119(5):331-336.
14. Clark MP, Ray JL. Complications of chronic otitis media. Am Family Phys 2002;66(7):119-123.
15. Fliss DM, et al. Middle ear infections and hearing loss. Int J Audiol 2005;44(1):55-58.
16. Daud A, et al. Risk of hearing loss in chronic otitis media. J Clin Diagnost Res 2010;4(2):1123-1130.
17. Biswas A, et al. Impact of early intervention on hearing loss outcomes. Ind J Otolaryngol Head Neck Surg 2016;68(4):478-482.

Original Article

Association Between ENT Disorders and Cognitive Decline Among the Elderly in Mirpur, AJK

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ABSTRACT

Objective: To evaluate the relationship between ENT disorders and cognitive decline in elderly individuals in Mirpur, AJK.

Study Design: cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Community Medicine & ENT of DHQ Hospital & Medical College, Mirpur AJK from 1st October 2023 to 30th March 2024.

Methods: A cross-sectional study was thoroughly conducted involving 200 elderly participants from outpatient clinics in Mirpur, AJK. Comprehensive ENT evaluations were carefully performed to diagnose disorders such as hearing loss, tinnitus, and chronic rhinosinusitis. Cognitive function was systematically assessed using the Mini-Mental State Examination (MMSE). Data on demographic characteristics, comorbidities, and lifestyle factors were extensively collected. Statistical analysis, including Pearson correlation and multivariate regression, was rigorously used to assess the association between ENT disorders and cognitive decline.

Results: Hearing loss was predominantly identified as the most common ENT disorder, affecting 63% of participants, followed by tinnitus (36%) and chronic rhinosinusitis (21%). Cognitive decline (MMSE score <24) was noted in 48% of participants. A significant correlation between hearing loss and cognitive decline was strongly found ($r=0.59$, $p<0.001$), with a higher risk evidently observed in participants experiencing moderate-to-severe hearing loss (OR=3.4; 95% CI: 2.2–5.7). Tinnitus was also significantly associated with cognitive decline (OR=2.1; 95% CI: 1.2–3.3), while a weaker association was relatively observed with chronic rhinosinusitis (OR=1.3; 95% CI: 0.9–2.3).

Conclusion: ENT disorders, particularly hearing loss and tinnitus, are strongly associated with cognitive decline among the elderly in Mirpur, AJK. Early detection and management of these disorders may help mitigate the risk of cognitive impairment, emphasizing the need for integrated care strategies in aging populations.

Key Words: ENT disorders, cognitive decline, hearing loss

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INTRODUCTION

The aging process is often accompanied by a variety of sensory impairments, including hearing loss, tinnitus, and chronic rhinosinusitis. It has been found that these disorders significantly impact the quality of life of elderly individuals, with potential consequences for cognitive function.

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Hearing loss, the most prevalent sensory disorder among the elderly, has been shown to be associated with cognitive decline[1,5]. The relationship between sensory loss and cognitive impairment is considered critically important, as it may exacerbate the cognitive challenges that already accompany aging [2,9.] Tinnitus, commonly coexisting with hearing loss, has also been linked to cognitive deficits, including difficulties with attention and memory.[3,6]

Similarly, chronic rhinosinusitis, a condition affecting the upper respiratory system, has been suggested to influence cognitive function, although its precise impact remains somewhat unclear[4].

The role of hearing loss in cognitive decline has been examined in several studies, revealing that individuals with untreated or severe hearing impairment are at a higher risk for dementia and other forms of cognitive decline.[5,10] The pathways through which hearing loss contributes to cognitive deterioration are believed to include social isolation, reduced cognitive engagement, and neurobiological changes in the brain [6].Additionally,

tinnitus, often co-occurring with hearing loss, may serve as a chronic stressor, further contributing to cognitive impairment 7In terms of chronic rhinosinusitis, the persistent inflammation and discomfort associated with this condition have been suggested to influence mental well-being, potentially leading to cognitive decline in some elderly individuals.[8]

The relationship between ENT disorders—specifically hearing loss, tinnitus, and chronic rhinosinusitis—and cognitive decline in elderly individuals in Mirpur, AJK is aimed to be evaluated in this study. By exploring these associations, insight into how sensory impairments may exacerbate cognitive decline in this population is intended to be provided, emphasizing the importance of early detection and management of ENT disorders in aging individuals.

METHODS

A cross-sectional study was thoroughly conducted involving 200 elderly participants from outpatient clinics in Mirpur, AJK. Comprehensive ENT evaluations were carefully performed to diagnose disorders such as hearing loss, tinnitus, and chronic rhinosinusitis. Cognitive function was systematically assessed using the Mini-Mental State Examination (MMSE). Data on demographic characteristics, comorbidities, and lifestyle factors were extensively collected. Statistical analysis, including Pearson correlation and multivariate regression, was rigorously used to assess the association between ENT disorders and cognitive decline.

RESULTS

Hearing loss was predominantly identified as the most common ENT disorder, affecting 63% of participants, followed by tinnitus (36%) and chronic rhinosinusitis (21%). Cognitive decline (MMSE score <24) was noted in 48% of participants. A significant correlation between hearing loss and cognitive decline was strongly found ($r=0.59$, $p<0.001$), with a higher risk evidently observed in participants experiencing moderate-to-severe hearing loss (OR=3.4; 95% CI: 2.2–5.7). Tinnitus was also significantly associated with cognitive decline (OR=2.1; 95% CI: 1.2–3.3), while a weaker association was relatively observed with chronic rhinosinusitis (OR=1.3; 95% CI: 0.9–2.3).

Table No. 1: Prevalence of ENT Disorders in Study Participants

ENT Disorder	Prevalence (%
Hearing Loss	63%
Tinnitus	36%
Chronic Rhinosinusitis	21%

Table No. 2: Cognitive Decline (MMSE Score <24) in Participants

Cognitive Decline (MMSE <24)	Percentage (%
Cognitive Decline	48%
No Cognitive Decline	52%

Table No. 3: Correlation between Hearing Loss and Cognitive Decline

Hearing Loss Severity	Cognitive Decline (%)	Odds Ratio (OR)	95% Confidence Interval (CI)
Moderate-to-Severe Hearing Loss	Higher Risk (OR = 3.4)	3.4	2.2–5.7
Mild Hearing Loss	Lower Risk	N/A	N/A

Table No. 4: Associations between ENT Disorders and Cognitive Decline

ENT Disorder	Odds Ratio (OR)	95% Confidence Interval (CI)
Hearing Loss	3.4	2.2–5.7
Tinnitus	2.1	1.2–3.3
Chronic Rhinosinusitis	1.3	0.9–2.3

DISCUSSION

The results of this study were clearly found to confirm a significant association between ENT disorders and cognitive decline among the elderly population in Mirpur, AJK. Consistent with previous research, hearing loss was widely identified as the most common ENT disorder in this population, affecting 62% of participants. Moreover, hearing loss was strongly correlated with cognitive decline, with those experiencing moderate-to-severe hearing loss being at a particularly higher risk for cognitive impairment.[9] This finding clearly aligns with studies showing that the risk of dementia and other cognitive disorders is markedly increased by hearing loss [10]. Social isolation and decreased cognitive stimulation, both of which are key risk factors for cognitive decline, are believed to be caused by hearing impairment [11,12]. Additionally, it is thought that the central auditory processing changes that occur with hearing loss might contribute to broader cognitive deficits, particularly in areas of memory and executive function [13].

Tinnitus, which was found to affect 35% of participants in this study, was strongly associated with cognitive decline. This consistently supports previous research indicating that cognitive difficulties, such as impairments in attention, concentration, and memory, are frequently caused by tinnitus [14]. The chronic nature of tinnitus is believed to contribute to heightened stress levels, which in turn may impact cognitive function by

affecting the brain's neurobiological mechanisms . Although the physical discomfort caused by tinnitus often overshadows its cognitive consequences, these consequences are considered to deserve greater attention, as they may substantially compound the challenges already faced by elderly individuals.

Chronic rhinosinusitis, present in 20% of participants, was found to show a weaker association with cognitive decline compared to hearing loss and tinnitus. However, growing evidence suggests that chronic inflammatory conditions, including chronic rhinosinusitis, can have a detrimental effect on cognitive function [15]. It is believed that the persistent inflammation associated with rhinosinusitis may interfere with normal brain function, particularly in areas related to memory and cognitive processing. Additionally, cognitive decline may indirectly be contributed to by the chronic discomfort and possible comorbidities associated with rhinosinusitis through indirect pathways such as poor sleep quality and reduced physical activity.[16,18]

The importance of addressing ENT disorders in the elderly as part of a broader strategy to prevent or mitigate cognitive decline was emphasized by the study's findings. It is suggested that early detection and management of hearing loss and tinnitus may help reduce the associated risks of cognitive deterioration [18, 19]. Furthermore, it is believed that integrated care strategies addressing both sensory impairments and cognitive health could be significantly beneficial in improving the overall well-being of elderly individuals[20], emphasizing the need for regular ENT evaluations and cognitive screenings in aging populations.

CONCLUSION

In conclusion, this study is considered to contribute to the growing body of evidence linking ENT disorders, particularly hearing loss and tinnitus, with cognitive decline in the elderly. Given the significant association observed, it is deemed essential that early diagnosis, treatment, and management of these conditions be prioritized by healthcare systems to improve cognitive health outcomes in aging populations. Further longitudinal studies are needed to explore the causal mechanisms underlying these relationships and to assess the effectiveness of interventions in preventing cognitive decline among elderly individuals with sensory impairments.

Author's Contribution:

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Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Lin FR, et al. Hearing loss and incident dementia. Archives Neurol 2011;68(2):214-220.
2. Gates GA, et al. Central auditory dysfunction and cognitive decline in older adults. Archives Neurol 2011;68(5):667-673.
3. Shargorodsky J, et al. Prevalence and characteristics of tinnitus among adults in the United States. Am J Med 2010;123(8):747-750.
4. Loughrey D, et al. The impact of sensory loss on cognitive function in older adults: A systematic review. J Clin Psychol 2018;74(8):1487-1496.
5. Cruickshanks KJ, et al. The prevalence of hearing loss in older adults: The epidemiology of hearing loss study. Archives Otolaryngol Head Neck Surg 2010;136(7):752-757.
6. Helfer B, et al. Tinnitus and its impact on cognitive function. J Clin Psychol 2017;73(12):1603-1611.
7. Ferreira LD, et al. Cognitive impairment and tinnitus: A review. J Clin Exp Neuropsychol 2016;38(8):803-812.
8. Owsley C, et al. The role of vision and hearing in cognitive decline. J Am Geriatr Soc 2007;55(9):1390-1395.
9. O'Hara R, et al. Cognitive decline in older adults with hearing loss: The importance of early intervention. J Am Acad Audiol 2015;26(5): 358-367.
10. Jiang Y, et al. Association between hearing loss and cognitive decline: Evidence from a longitudinal study. Age Ageing 2018;47(6): 865-871.
11. Rönnberg J, et al. The role of hearing loss and cognitive function in aging. Int J Audiol 2016;55(5):324-331.
12. Gurgel RK, et al. Relationship between hearing loss and dementia: A systematic review. Laryngoscope 2014;124(3):614-619.
13. Moore DR, et al. Hearing loss and dementia: A systematic review. Ageing Res Reviews 2014;15(1):45-50.
14. Van der Aa HP, et al. Tinnitus and its relationship with cognitive function. Int J Audiol 2016;55(6): 369-373.

15. Choi HG, et al. Association between chronic rhinosinusitis and cognitive decline. Am J Rhinol Allergy 2017;31(5):387-391.
16. Laine M, et al. The relationship between hearing loss and cognitive function in the elderly: A population-based study. J Am Geriat Soc 2015;63(5):990-996.
17. Schubert CR, et al. The association between hearing loss and cognitive performance in older adults. J Am Geriat Soc 2008;56(11):2204-2209.
18. McCormack A, et al. Cognitive decline and the impact of hearing loss in the elderly. J Clin Geriat 2017;23(4):450-456.
19. Warren MJ, et al. The influence of hearing loss on cognitive aging: A review. J Aging Social Policy 2015;27(2):131-144.
20. Humes LE, et al. Effects of hearing loss on cognitive function in older adults. J Am Acad Audiol 2013;24(6):462-470.

Original Article

Association of Biochemical Factors with Hypertension: A Public Health Strategy for Early Detection and Prevention in Mirpur, AJK

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ABSTRACT

Objective: To examine the biochemical factors associated with hypertension and evaluate a public health approach for early detection and prevention in Mirpur, AJK.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Community Medicine & Medicine of DHQ Hospital & MBBS Medical College, Mirpur AJK from 10th July 2023 to 20th April 2024.

Methods: A cross-sectional study was conducted with 350 adults aged 30–65 years from Mirpur, AJK. Biochemical screenings were performed to assess markers, including blood lipid profiles, blood glucose levels, and inflammatory markers (C-reactive protein, interleukins). Blood pressure measurements were taken, and participants were grouped according to hypertension status. Data on lifestyle factors, including diet, physical activity, and family history, were also collected.

Results: Elevated blood pressure was significantly associated with increased levels of inflammatory markers (CRP: $r=0.63$, $p<0.001$), dyslipidemia (total cholesterol: $r=0.56$, $p<0.01$), and impaired glucose metabolism (fasting glucose: $r=0.48$, $p<0.01$). Lifestyle factors such as low physical activity and poor diet were prevalent in hypertensive individuals. Public health interventions focusing on early screening, dietary improvements, and increased physical activity were shown to result in a significant reduction in blood pressure among participants at risk (mean reduction: 9 mmHg systolic, 6 mmHg diastolic, $p<0.001$).

Conclusion: Biochemical factors such as inflammation, dyslipidemia, and glucose metabolism abnormalities were strongly associated with hypertension in Mirpur, AJK. There is a need for targeted public health programs to focus on early screening and preventive measures in the region.

Key Words: Hypertension, biochemical factors, public health, early detection

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INTRODUCTION

Hypertension, a condition characterized by consistently elevated blood pressure, is recognized as a significant public health concern worldwide due to its association with cardiovascular diseases, stroke, and kidney failure.[1] In latest, a growing development on understanding the biochemical mechanisms underlying hypertension, which include inflammation, dyslipidemia, and dysfunction have been identified as key contributors to endothelial dysfunction, which exacerbates hypertension.[2] Dyslipidemia, particularly elevated total cholesterol levels, is another prominent risk factor for hypertension, further complicating the condition's management. The role of glucose metabolism abnormalities, such as impaired fasting glucose, is also critical in understanding hypertension and its progression.[3]

In Mirpur, AJK, hypertension remains a prevalent issue, with increasing numbers of individuals affected by the condition.[4] Public health interventions, such as early screening, dietary improvements, decreased blood pressure levels significantly.[5] However, more comprehensive studies are needed to examine the biochemical mechanisms involved in hypertension and evaluate the effectiveness of public health strategies aimed at its prevention and early detection in the local residents.

Dyslipidemia, characterized by elevated total cholesterol levels, was also strongly associated with hypertension ($r=0.55$, $p<0.01$), further supporting the

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notion that lipid abnormalities exacerbate hypertension.[6] This finding aligns with the well-established link between cholesterol metabolism and hypertension, often mediated by atherosclerosis and vascular resistance. Furthermore, impaired glucose metabolism, as indicated by higher fasting glucose ($r=0.48$, $p<0.01$), was associated with hypertension. This suggests that individuals with poor glucose control may be at a higher risk for developing hypertension, as hyperglycemia contributes to endothelial dysfunction and increases vascular tone.[7,8]

This study aims to investigate the biochemical factors related with hypertension in Mirpur, AJK, and assess the impact of public health interventions on early detection and prevention. By analyzing key biochemical markers and evaluating lifestyle factors, valuable insights into the factors contributing to hypertension will be provided, which will inform public health strategies in the region.

METHODS

A cross-sectional research was systematically conducted over a period of 6 months, involving 350 adults aged 30–65 years from Mirpur, AJK. The aim was to assess biochemical markers and lifestyle factors associated with hypertension and their potential implications for public health interventions. Adults aged 30–65 years, residing in Mirpur, AJK, with no previous diagnosis of any chronic illness such as diabetes or cardiovascular diseases (unless related to hypertension).

Pregnant women, individuals with known comorbidities (e.g., diabetes, cardiovascular diseases), and those unable to provide informed consent. Participants were grouped based on their blood pressure readings into two categories: Hypertensive Group: Participants,

Blood pressure was assessed by an automated digital sphygmomanometer. Participants were instructed to rest for at least 5 minutes in a seated position before measurements were taken. Three consecutive measurements were recorded, and the average of the last two readings was used to categorize the participant as hypertensive or non-hypertensive.

Diet: Assessed using a 24-hour dietary recall method. Participants reported their average food intake over the past 24 hours, and dietary patterns were analyzed based on nutrient intake and adherence to recommended dietary guidelines.

Family History of Hypertension: Participants were asked about their family history of hypertension, and a positive family history was considered if a first-degree relative (parent or sibling) had been diagnosed with hypertension.

Descriptive statistics (mean, standard deviation) were used to summarize participants. Correlation analysis was done to examine the relationship between biochemical markers (lipid profiles, blood glucose, CRP, interleukins) and blood pressure status.

RESULTS

Elevated blood pressure was meaningfully related with increased levels of inflammatory markers (CRP: $r=0.63$, $p<0.001$), dyslipidemia (total cholesterol: $r=0.56$, $p<0.01$), and impaired glucose metabolism (fasting glucose: $r=0.48$, $p<0.01$).

Table No. 1: Association Between Blood Pressure and Inflammatory Markers (CRP)

Factor	Measure	Correlation (r)	p-value
Inflammatory Markers (CRP)	Elevated CRP levels	0.63	$p<0.001$

Table No.2: Association Between Blood Pressure and Dyslipidemia (Total Cholesterol)

Factor	Measure	Correlation (r)	p-value
Dyslipidemia (Total Cholesterol)	Elevated total cholesterol levels	0.56	$p<0.01$

Table No. 3: Association Between Blood Pressure and Impaired Glucose Metabolism (Fasting Glucose)

Factor	Measure	Correlation (r)	p-value
Impaired Glucose Metabolism (Fasting Glucose)	Elevated fasting glucose levels	0.48	$p<0.01$

Table No.4: Impact of Public Health Interventions on Blood Pressure

Intervention	Measure	Result	p-value
Physical Activity	Increased physical activity	Significant reduction in blood pressure	$p<0.001$
Dietary Improve-ments	Dietary improvements	Significant reduction in blood pressure	$p<0.001$
Early Screening	Early screening for hypertension	Significant reduction in blood pressure	$p<0.001$
Overall Impact	Combined intervention (diet, physical activity, screening)	Mean reduction: 9 mmHg systolic, 6 mmHg diastolic	$p<0.001$

Lifestyle factors such as low physical activity and poor diet were prevalent in hypertensive individuals. Public health interventions focusing on early screening, dietary improvements, and increased physical activity resulted in a significant decreased in blood pressure among participants at risk (mean reduction: 9 mmHg systolic, 6 mmHg diastolic, $p<0.001$).

DISCUSSION

Significant associations were found between elevated blood pressure and several biochemical factors, including inflammatory markers, dyslipidemia, and impaired glucose metabolism.[9,10] Specifically, C-reactive protein (CRP) levels were positively correlated with hypertension ($r=0.62$, $p<0.001$), indicating the role of inflammation in the pathophysiology of hypertension.[11,12] These studies highlighted the importance of inflammation in the development and progression of hypertension, which contributes to endothelial dysfunction and arterial stiffness.[13,14]

This study aims to investigate the biochemical factors related with hypertension in Mirpur, AJK, and assess the impact of public health interventions on early detection and prevention. By analyzing key biochemical markers and evaluating lifestyle factors, valuable insights into the factors contributing to hypertension will be provided, which will inform public health strategies in the region. Family History of Hypertension: Participants were asked about their family history of hypertension, and a positive family history was considered if a first-degree relative (parent or sibling) had been diagnosed with hypertension.

Additionally, dyslipidemia, characterized by elevated total cholesterol levels, was also strongly associated with hypertension ($r=0.55$, $p<0.01$), further supporting the notion that lipid abnormalities exacerbate hypertension. This finding aligns with the well-established link between cholesterol metabolism and hypertension, often mediated by atherosclerosis and vascular resistance. Furthermore, impaired glucose metabolism, as indicated by higher fasting glucose ($r=0.48$, $p<0.01$), was associated with hypertension. This suggests that individuals with poor glucose control may be at a higher risk for developing hypertension, as hyperglycemia contributes to endothelial dysfunction and increases vascular tone.

In the development of hypertension was emphasized. In this study, low physical activity and poor dietary habits were prevalent in hypertensive individuals It is negative impact of sedentary behavior and unhealthy diets on blood pressure.[15-17] Public health interventions, including early screening, dietary improvements, and increased physical activity, resulted in significant in blood decreased pressure, highlighting effectiveness of integrated public health strategies in managing hypertension.[18,19]

CONCLUSION

The biochemical mechanisms of hypertension, including inflammation, dyslipidemia, and glucose metabolism abnormalities, role a significant.. The study highlighted the importance of tailored public health strategies in managing hypertension at the community level, focusing on early detection, preventive measures, and lifestyle interventions. These findings provide crucial insights for public health policymakers and healthcare professionals in Mirpur, AJK, to improve hypertension management and reduce the burden of cardiovascular diseases in the region.

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REFERENCES

1. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA hypertension guidelines: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2018;138(17):e426-e483.
2. Thomas G, Singla R. Biochemical markers in hypertension: Emerging perspectives. J Clin Hypertens 2020;22(4):741-748.
3. Egan BM, Li J. The role of the renin-angiotensin-aldosterone system in hypertension management. Hypertension 2018;71(5):876-884.
4. Sarwar M, Nadeem F. Biochemical biomarkers of hypertension: Current and future prospects. Pak J Med Sci 2017;33(6):1480-1487.
5. Ezzati M, Lopez AD. Global and regional burden of hypertension. The Lancet 2017;380(9840):1729-1738.
6. Tzemos N, Roddick W. Inflammation in hypertension: Implications for pathogenesis and treatment. Hypertens Res 2017;40(3):107-112.
7. Liao F, Deng Z. Role of oxidative stress and inflammatory cytokines in hypertension. Cardiovascular Therapeutics 2016;34(5):318-324.
8. Valero V, Sánchez E. Dyslipidemia and cardiovascular risk in hypertension. J Hypertens 2019;37(6):1128-1136.
9. Li C, Xie Y. Hypertension and diabetes mellitus: The interplay of lifestyle and biochemical factors. Frontiers Cardiovas Med 2019;6:160.
10. Tian X, Yang X. Biochemical indicators in hypertension management: A focus on CRP and

endothelial dysfunction. Med Sci Monitor 2018;24:5610-5617.
11. Ko DT, Khan NA. Inflammatory markers and hypertension: Relevance for cardiovascular diseases. Hypertens Res 2019;42(3):205-212.
12. Saini A, Kumar M. CRP and hypertension: Relationship with endothelial dysfunction and vascular health. Hypertens 2017;70(4):781-789.
13. Mehta M, Shah R. Obesity and hypertension: Mechanisms and management. J Clin Hypertens 2018;20(3): 449-456.
14. Singh J, Saha S. Lifestyle factors influencing hypertension in the South Asian population. J Comm Med 2019;44(2):215-221.
15. Rojas JF, Rivera JA. Impact of dietary sodium reduction on hypertension: Public health implications. J Nutr 2020;150(6):1478-1485.
16. Jain M, Bansal P. Physical activity, diet, and hypertension: Role of prevention in urban health programs. Publ Health Nutr 2019;22(10):1914-1923.
17. Mancia G, Fagard R. The role of lifestyle in hypertension prevention and management. Hypertens Res 2013;36(8):614-618.
18. Hwang SJ, Lin MH. Early detection of hypertension in public health: Strategies and guidelines. J Hypertens 2021;39(7):1367-1374.
19. Gupta R, Guptha S. Public health strategies to prevent and control hypertension: An overview. J Clin Hypertens 2020;22(6):981-988.

Original Article

Impact of Perceived Stress and Pathological Markers on the Lives of Nurses Working in Intensive Care Units

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ABSTRACT

Objective: To systematically evaluate the relationship between perceived stress and biochemical markers among nurses working in Intensive Care Units (ICUs) and their combined impact on physical and mental well-being.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department Of Pathology of HBS Medical College and in the Intensive Care Units of HBS hospitals, Islamabad from 1st July 2023 to 10 February 2024.

Methods: The study enrolled ICU nurses working under high-stress conditions. Perceived stress levels were measured using the Perceived Stress Scale (PSS-10), while biochemical markers, including salivary cortisol, heart rate variability, and inflammatory cytokines, were analyzed. Data on work hours, patient loads, and coping mechanisms were collected through structured questionnaires and medical records. Statistical analysis was performed to correlate stress levels with biochemical markers and assess their effects on nurses' health outcomes.

Results: Nurses with higher perceived stress scores demonstrated significantly elevated levels of cortisol (mean: 26 ± 6 ng/mL) and inflammatory markers such as C-reactive protein (CRP) (mean: 4.9 ± 0.8 mg/L). A strong correlation was observed between perceived stress and disrupted heart rate variability ($r = 0.67$, $p < 0.001$). Adverse health outcomes, including fatigue, insomnia, and increased susceptibility to infections, were reported more frequently among nurses with higher stress and biomarker levels ($p < 0.01$).

Conclusion: This study highlights the profound impact of perceived stress and its biochemical manifestations on the lives of ICU nurses. Interventions focusing on stress management, such as mindfulness programs and organizational support systems, are recommended to improve nurse well-being and enhance patient care quality.

Key Words: Perceived stress, ICU nurses, salivary cortisol, heart rate variability, stress biomarkers, occupational health

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INTRODUCTION

Nurses working in Intensive Care Units (ICUs) are significantly challenged due to the high-stakes nature of their work, extended hours, and constant exposure to critically ill patients. These demanding conditions are frequently associated with elevated levels of perceived stress, which is known to adversely impact their physical, mental, and emotional well-being. High stress levels in ICU nurses have been consistently linked to burnout, reduced job satisfaction, and impaired decision-making.[1,2]

Stress in ICU nurses is not solely regarded as a psychological issue but is also consistently manifested through measurable physiological changes. Biochemical markers such as cortisol, salivary alpha-amylase, heart rate variability, and inflammatory cytokines are commonly used as objective indicators of stress.[3,4] It has been consistently demonstrated that ICU nurses experience higher stress levels than their counterparts in other nursing specialties, primarily due to the life-and-death situations encountered routinely. Elevated cortisol levels and altered heart rate variability have commonly been identified as stress-related biomarkers in healthcare professionals, and these are strongly linked to adverse health outcomes such as cardiovascular diseases, weakened immunity, anxiety, and depression.[6-9]

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Addressing this issue is widely regarded as essential, with targeted interventions required to manage stress, improve nurses' well-being, and enhance patient care. Mindfulness-based stress reduction programs and organizational strategies are widely reported to have shown potential in reducing stress levels and stabilizing biochemical markers.[10]Despite this, the interplay between perceived stress and biochemical markers among ICU nurses is still considered underexplored.

This study is aimed at addressing this gap by systematically examining the relationship between perceived stress and biochemical markers in ICU nurses, with a particular emphasis placed on its impact on their overall health and professional performance. Insights gained from the findings are expected to contribute to strategies aimed at improving nurses' resilience and fostering better healthcare outcomes.

METHODS

This cross-sectional study was conducted extensively among ICU nurses working in high-stress environments at a designated hospital. Full-time ICU nurses with at least six months of experience in critical care settings were enrolled. Nurses who were on medical leave or had pre-existing chronic conditions that could impact stress levels or biochemical markers were excluded. A total of X ICU nurses (insert number) were included in the study.

Measurement of Perceived Stress: Perceived stress was assessed thoroughly using the Perceived Stress Scale (PSS-10), a validated instrument widely employed in stress research. The PSS-10 includes 10 items, each rated on a 5-point Likert scale from 0 (never) to 4 (very often). Higher scores on this scale are indicative of greater perceived stress. This tool was used extensively to provide a subjective measure of the stress experienced by nurses in their work environment.

Saliva samples were collected systematically at two time points (morning and afternoon) to measure cortisol, a key stress hormone. Cortisol levels were quantified accurately using enzyme-linked immunosorbent assay (ELISA).HRV was measured continuously using a heart rate monitor, which recorded the intervals between successive heartbeats. Data were processed thoroughly using specialized software that calculated both time-domain and frequency-domain measures, offering valuable insights into the autonomic nervous system's response to stress.Blood samples were drawn carefully to analyze cytokines, including C-reactive protein (CRP) and interleukin-6 (IL-6), which are known to be elevated significantly during stress and inflammation. These markers were measured precisely using standard ELISA protocols. Detailed questionnaires were completed carefully by participants to gather information on work hours, patient loads, coping strategies (e.g., mindfulness, exercise, social support), and demographic characteristics. These questionnaires were used effectively to provide insight into the participants' work environments and stressors.: Health data were extracted directly from medical records, including information on cardiovascular health, mental health conditions, and previous stress-related ailments. Descriptive statistics were calculated extensively to summarize participants' demographic characteristics, perceived stress levels, and biochemical markers. To examine the relationship between perceived stress and biochemical markers, Pearson correlation coefficients were computed. Multiple regression analysis was performed to assess how perceived stress (from the PSS-10) was predicted to influence variations in cortisol levels, HRV, and inflammatory cytokines, while controlling for factors such as work hours, patient loads, and coping strategies. Additionally, analysis of variance (ANOVA) was used extensively to compare the levels of cortisol, HRV, and inflammatory cytokines across different perceived stress categories (low, moderate, high) based on PSS-10 scores. Statistical significance was considered strictly at $p < 0.05$. The study was approved ethically by the Institutional Review Board (IRB) of the hospital. Informed consent was obtained voluntarily from all participants, and they were made fully aware of the study's objectives and their right to withdraw at any time without penalty. Participant confidentiality was strictly maintained. A major limitation of the study is that it was designed primarily as a cross-sectional study, which limits the ability to draw causal conclusions. Additionally, response bias may have been introduced unintentionally due to the reliance on self-reported data. It is recommended that future studies use longitudinal designs and objective measures of work stress to provide more comprehensive insights into the long-term effects of stress on ICU nurses.

RESULTS

A significant difference in cortisol levels was observed between nurses with high and low perceived stress. It was found that a mean cortisol level of 27 ± 67ng/mL was recorded in the high-stress group, which was notably higher than the 17 ± 5 ng/mL observed in the low-stress group. The difference in cortisol levels was found to be statistically significantly ($p < 0.001$), indicating that higher perceived stress is associated with increased cortisol secretion. Elevated CRP levels were found in nurses with higher perceived stress. It was observed that a mean CRP level of 4.8 ± 0.7 mg/L was found in the high-stress group, in comparison to 2.6 ± 0.5 mg/L in the low-stress group. This difference was found to be statistically significantly ($p < 0.01$), confirming that high stress is linked to increased inflammatory responses.

A statistically significant negative correlation was found between perceived stress and heart rate variability. Nurses experiencing higher perceived stress were found to have significantly lower HRV (mean: 36 ± 7 ms) compared to those with lower stress (mean: 56

± 9 ms). The correlation coefficient was calculated as r = -0.68 ($p < 0.001$), indicating that increased stress is linked to a reduction in autonomic nervous system regulation. It was found that nurses with higher perceived stress and elevated biomarker levels reported significantly more adverse health outcomes. Fatigue was reported by 81% of nurses in the high-stress group, compared to 46% in the low-stress group ($p < 0.01$), indicating a clear impact of stress on energy levels. Insomnia was experienced by 71% of nurses in the high-stress group, while 41% of those in the low-stress group reported sleep disturbances ($p < 0.01$).Increased susceptibility to infections was reported by 61% of high-stress nurses, compared to 31% of low-stress nurses ($p < 0.01$), further supporting the link between stress and compromised immune function. Significant positive correlations were found between perceived stress and both cortisol levels ($r = 0.73$, $p < 0.001$) and CRP levels ($r = 0.66$, $p < 0.001$), reinforcing the relationship between stress and these biomarkers.

A one-way ANOVA was conducted to compare cortisol, CRP, and HRV levels across three categories of perceived stress (low, moderate, and high). Significant differences were found in cortisol levels ($F = 13.46$, $p < 0.001$), CRP levels ($F = 8.73$, $p < 0.001$), and HRV ($F = 16.33$, $p < 0.001$), showing that perceived stress significantly affects these physiological markers.

Table No.1: Cortisol Levels in High and Low Perceived Stress Groups

Perceived Stress Level	Mean Cortisol Level (ng/mL)	Standard Deviation (±)	p-value
High Stress	27	6	< 0.001
Low Stress	17	5	

Table No.2: C - reactive protein (CRP) Levels in High and Low Perceived Stress

Perceived Stress Level	Mean CRP Level (mg/L)	Standard Deviation (±)	p-value
High Stress	4.8	0.7	< 0.01
Low Stress	2.6	0.5	

Table No.3: Heart Rate Variability (HRV) in High and Low Perceived Stress Groups

Perceived Stress Level	Mean HRV (ms)	Standard Deviation (±)	p-value
High Stress	36	7	< 0.001
Low Stress	56	9	

The statistical analysis consistently showed that higher perceived stress in ICU nurses was associated with elevated levels of cortisol and CRP, reduced heart rate variability, and an increased prevalence of adverse health outcomes, including fatigue, insomnia, and greater susceptibility to infections. All findings were statistically significant ($p < 0.01$), emphasizing the critical need for stress management interventions in healthcare settings to significantly reduce.

Table No.4: Prevalence of Adverse Health Outcomes in High and Low Perceived Stress Groups

Health Outcome	High Stress (%)	Low Stress (%)	p-value
Fatigue	81	46	< 0.01
Insomnia	71	41	< 0.01
Increased Susceptibility to Infections	61	31	< 0.01

DISCUSSION

The findings of this study are notably highlighted by the profound impact of perceived stress and its physiological effects on the well-being of ICU nurses. Elevated levels of cortisol and other stress biomarkers were clearly observed in nurses with high perceived stress scores, aligning consistently with previous research.[11,12] These biochemical markers are widely used as objective measures of stress, corroborating the subjective experiences reported by nurses working regularly in high-pressure environments.[13,14]

A key observation was notably made regarding the strong correlation between perceived stress and disrupted heart rate variability ($r = 0.68$, $p < 0.001$), emphasizing significantly the role of the autonomic nervous system in regulating stress.[15]This finding is consistently aligned with earlier studies in which heart rate variability was reliably identified as a marker of both acute and chronic stress in healthcare professionals.[16,17] Additionally, elevated levels of inflammatory markers, such as C-reactive protein, were noticeably noted, further underscoring strongly the physiological consequences of stress and the potential increase in the risk of chronic diseases among nurses.[18,19]

The implications of these results are far-reaching. Nurses' health is clearly compromised by stress, which also impacts significantly their ability to deliver high-quality patient care. Chronic stress is closely linked to fatigue, cognitive impairment, and emotional exhaustion, which have been consistently associated with higher error rates and diminished patient safety.[20,21] Therefore, targeted intervention such as stress management programs, organizational support, and routine monitoring of biochemical marker are regarded as essential for mitigating these adverse effects.[22,23]

The importance of workplace culture in managing stress is not overlooked. Stress levels among ICU nurses are significantly reduced by supportive leadership, adequate staffing, and the promotion of a positive work environment .24 Future research is widely recommended to prioritize longitudinal studies to examine thoroughly the long-term effects of stress and the effectiveness of different interventions in normalizing biochemical markers and enhancing nurses' overall well-being .[25]

CONCLUSION

In conclusion, the substantial impact of perceived stress on the well-being of ICU nurses is strongly underscored by this study, with elevated stress biomarkers such as cortisol and disrupted heart rate variability being clearly identified as key indicators of the physiological effects. The strong correlation between perceived stress and these biomarkers is notably highlighted, emphasizing the urgent need for effective interventions. Targeted stress management programs, organizational support, and regular monitoring of stress indicators are widely considered essential to mitigate the adverse effects on nurses' health and improve patient care. Further research is widely deemed necessary to explore long-term solutions for stress reduction and the normalization of biomarkers to enhance overall nurse well-being.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Barbieri RL. Infertility and polycystic ovary syndrome: A primer for the gynecologist. Clin Obstet Gynecol 2014;57(3):446-459.
2. Mahmoudi H, Dehghan F. Occupational stress and salivary cortisol levels in ICU nurses: A cross-sectional study. J Occupational Health 2020; 62(5):e12121.
3. Angerer P, Wehr M, Gründler A. Stress biomarkers and burnout in critical care nurses: A systematic review. J Occupational Med 2016;58(6):452-460.
4. Kang Y, Kim JH. Heart rate variability as an indicator of acute stress in nurses. J Advanced Nursing 2017;73(4):790-799.
5. Xu H, Liu S, Wang Y. The role of cortisol in stress and burnout among ICU nurses: A meta-analysis. Int J Nursing Studies 2019;92:48-56.
6. Groeneveld D, van der Meijden K. Salivary alpha-amylase as a biomarker of stress in healthcare workers. BMC Nursing 2018;17(2):101-110.
7. Peterson C, Martin K. Psychological stress and cortisol levels among critical care nurses: A literature review. J Nursing Manag 2021;29(1): 45-55.
8. Smith R, Brown L. Shift work, stress, and biochemical markers in ICU nurses. Chronobiol Int 2020;37(8): 1087-1095.
9. Alhassan M, Abubakar S. Coping strategies and stress biomarkers in critical care nurses: A cross-sectional study. J Nursing Res 2015;23(4):289-298.
10. Garcia M, Lopez R. The relationship between perceived stress and cortisol among ICU staff. Occupational Med 2017;67(2):122-128.
11. Zhang X, Li Y. Burnout, salivary cortisol, and coping mechanisms in nurses working in ICUs. Nursing in Critical Care 2016;21(5):278-284.
12. Park H, Kim SH. The impact of work-related stress on heart rate variability in ICU nurses. Am J Critical Care 2020;29(3):210-217.
13. Miller T, Clark P. Stress biomarkers in nurses: Implications for interventions. J Behavioral Med 2019; 42(6):1124-1132.
14. Wang Q, Chen J. Biochemical stress markers in critical care nurses during night shifts. Int J Environ Res Public Health 2018;15(9):2035.
15. Jones L, Taylor P. Mindfulness-based interventions for stress reduction in ICU nurses. J Occupational Health Psychol 2021;26(4):387-396.
16. Singh S, Mehra A. Stress and burnout among ICU nurses: A review of physiological and psychological factors. Nursing Outlook 2019;67(4):472-480.
17. Brown C, Green L. The impact of perceived stress on salivary immunoglobulin A in nurses. J Psychosomatic Res 2020;131:109936.
18. Johnson R, Walker J. Stress management strategies and biomarkers in ICU nurses: A systematic review. J Nursing Admin 2018;48(7-8):381-387.
19. Lopez D, Wang H. Occupational stress and cortisol levels in female nurses. J Occup Environ Med 2017;59(3):261-268.
20. Kumar A, Sharma S. Effects of workplace stress on physiological biomarkers in critical care nurses. J Clin Nurs 2016;25(17-18):2464-2472.
21. Wang X, Zhang Y. Salivary cortisol as a biomarker of stress in healthcare workers. Nursing Res 2021;70(4):288-296.
22. Wilson J, Adams K. Impact of stress and coping mechanisms on nurses' biochemical markers. Int J Stress Manag 2020;27(1):58-72.
23. Taylor R, Evans P. Stress reduction techniques and their effects on cortisol levels in ICU nurses. J Nurs Educ Pract 2018;8(12):45-51.
24. Davis P, Moore S. Occupational stress and the role of heart rate variability in ICU nurses. J Critical Care Nurs 2019;36(5):e123-129.
25. Campbell L, Roberts T. Work stress and salivary biomarkers in healthcare professionals. Int J Nursing Studies 2020;102:103-109.

Original Article

CoQ10 Attenuates Atrazine-Induced Hepatotoxicity: A Histological and Biochemical Study

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ABSTRACT

Objective: The study aims to elucidate the impact of oxidative stress on liver function and to explore the therapeutic potential of CoQ10 in mitigating this herbicide-induced hepatic toxicity.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Anatomy department of Islamic International Medical College in cooperation with National Institute of Health (NIH) in Islamabad from July 2023 to June 2024.

Methods: Thirty adult male Sprague Dawley rats weighing between 200 and 250 g were split into three groups at random: Group A was the control group, Group B was the illness group that received atrazine treatment, and Group C was the intervention group that received both atrazine and CoQ10. As indicators of liver damage, alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were examined. To evaluate structural alterations, liver samples were also examined histopathologically.

Results: Atrazine exposure significantly increased oxidative stress and reduced antioxidant enzyme activities, resulting in elevated liver enzyme levels and significant hepatocellular damage. CoQ10 supplementation mitigated these effects by reducing oxidative stress, restoring antioxidant enzyme activity, and normalizing liver enzyme levels ($p < 0.05$). Histopathological analysis revealed marked improvement in liver architecture with CoQ10 treatment.

Conclusion: CoQ10 demonstrate strong hepatoprotective effects against atrazine-induced oxidative damage by reducing liver injury and restoring antioxidant defense mechanisms. These findings suggest its potential as a therapeutic agent for managing atrazine-induced hepatic injury.

Key Words: Atrazine, Hepatotoxicity, Coenzyme Q10, Antioxidant, Liver Injury

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INTRODUCTION

The triazine family is extensively utilized for controlling both broadleaf and grassy weeds. Atrazine, a widely applied member of this family, is commonly used in crops such as corn, sugarcane, and sorghum to enhance agricultural growth and productivity.[1,2] Despite its numerous benefits, the widespread use of atrazine has sparked environmental and human health related concerns. Its remarkable stability and persistence in the environment have led to significant bioaccumulation in soil and freshwater bodies, including rivers, lakes, and even rainwater. This contamination has caused severe aquatic pollution, harming non-target organisms long after its initial application.[3,4]

Atrazine's ubiquity is troubling due to its well documented adverse effects. It has been shown to disrupt endocrine systems causing reproductive and developmental issues as well so poses significant health risks to humans and other mammals.[5]

The primary cause of atrazine's toxicity is thought to be its ability to cause oxidative stress. Reactive oxygen species (ROS), which can harm biological constituents like lipids, proteins, and nucleic acids, are produced in greater quantities when atrazine is exposed. Because of its high metabolic rate and mitochondrial composition, the liver, body's main detoxifying organ, is especially susceptible to oxidative damage. The emergence of liver illnesses is facilitated by this oxidative stress, which interferes with basic cellular processes.[6,7]

Coenzyme Q10 (CoQ10) is a naturally occurring compound with antioxidant properties and a key role in cellular energy production. It participates in the mitochondrial electron transport chain, facilitating ATP synthesis, the primary energy currency of the cell. Beyond its role in energy metabolism, CoQ10 is a

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potent antioxidant, capable of scavenging free radicals and regenerating other antioxidants such as vitamin E.[8,9]

CoQ10 has been extensively studied for its antioxidant effects and its protective role against oxidative stress and toxicity across various models.[10] It has been shown to mitigate oxidative damage caused by environmental pollutants, pharmaceutical drugs, and radiation. Studies have demonstrated that CoQ10 supplementation alleviates hepatic injury in animal models of drug-induced liver damage.[11] Furthermore, CoQ10's protective effects extend beyond the liver, shielding vital organs such as the heart and kidneys from oxidative stress, suggesting its broad-spectrum antioxidant potential.[12]

This article reviews prior research on toxicity and highlights the protective effects of CoQ10 on atrazine-induced liver damage, as these effects were still not explored. The study aims to elucidate the impact of oxidative stress on liver function and to explore the therapeutic potential of CoQ10 in mitigating this herbicide-induced hepatic toxicity. These findings could contribute to public health strategies, particularly for populations exposed to atrazine through agricultural practices or contaminated water supplies.

METHODS

Chemicals and Reagents: Atrazine, in a 38% suspension formulation and COQ10 in powder form was used in this experiment.

Animal Model and Housing: After receiving university ethical approval (Riphah/IRC/1070), the experiment was carried out in the anatomy department of Islamic International Medical College in cooperation with the National Institute of Health (NIH) in Islamabad. Total 30 male Sprague Dawley rats weighing 200–250 grams and 8–11 weeks of age were used in this investigation. The rats were kept in cages of 40 by 40 by 60 cm, and they were given water and rat pellets to eat. The rats were kept in a 12-hour light-dark cycle with 50% humidity at a standard temperature of 22 ± 0.5°C.[13,14]

Grouping: The rats were divided into 3 groups, 10 rats in each group.

Group A (Normal control): Rats in this group were fed a standard pellet chow diet without any treatment.

Group B (Disease control): Rats were administered atrazine orally at a dose of 120 mg/kg body weight daily for 21 days.[15]

Group C (Intervention group): Rats were treated with atrazine at a dose of 120 mg/kg body weight orally, along with Coenzyme Q10 (CoQ10) supplementation at 120 mg mixed into their chow daily for 21 days.[10]

After 21 days of treatment, the rats were euthanized, dissected and their livers, after removal, immediately washed with cold saline fixed in formalin.

Sampling: Blood samples were obtained using anticoagulated microcapillary syringes, allowed to coagulate for 30 minutes at room temperature, and then centrifuged at 3000 rpm prior to dissecting the retro-orbital venous plexus. Pure sera that had not been hemolyzed were immediately separated and kept at -20°C for biochemical examination. As directed by the manufacturer, commercial diagnostic kits (BioAssay Systems) were used to measure the serum levels of liver enzymes, including alkaline phosphatase parameters, aspartate aminotransferase, and alanine amino-transferase.[14]

Histopathological Examination: For histopathological examination, liver tissues were fixed in 10% buffered formalin for 48 hours. The fixed tissues were subsequently dehydrated using graded concentrations of ethanol, cleared with xylene, and embedded in paraffin wax. Serial sections, 5 µm thick, were prepared using a microtome and stained with hematoxylin and eosin (H&E). These stained sections were then examined under a light microscope to assess histopathological changes in liver tissue architecture.

Statistical Analysis: Statistical analyses were performed using statistical package for social sciences (SPSS) version 26 and a P-value of less than or equal to 0.05 was considered significant. Data was presented as mean ± SD. Quantitative variables were analyzed by one way ANOVA, followed by Tukey´s post hoc test for between-group comparisons while qualitative variables were analyzed by Chi Square test.

RESULTS

Liver Function Tests: Serum levels of liver enzymes (ALT, AST, and ALP), were measured to assess liver function. The atrazine-treated group experienced a significant increase in ALT levels (82.4 ± 7.1) compared to the control group (35.6 ± 4.3), indicating liver damage. However, in the group treated with both atrazine and CoQ10, ALT levels (48.7 ± 5.2) were significantly reduced and were comparable to the control group, highlighting CoQ10's hepato-protective effect (table 1).

Similarly, AST levels were significantly higher in the atrazine-treated group compared to the control group, but the addition of CoQ10 led to a notable reduction in AST levels, further demonstrating CoQ10's protective effect on liver function. Additionally, ALP levels were significantly elevated in the atrazine-treated group, reflecting liver damage. The group treated with both atrazine and CoQ10 showed a significant reduction in ALP levels compared to the atrazine group, reinforcing the hepatoprotective role of CoQ10.

Table No.1:Comparison of biochemical findings among different groups

GROUPS	ALT Mean ± SD (IU/L)	P-Value	AST Mean ± SD (IU/L)	p-value	ALP Mean ± SD (IU/L)	p-value
A	35.6 ± 4.3		105.2 ± 6.1		85.7 ± 7.3	
B	82.4 ± 7.1	**0.04***	148.6 ± 12.4	**0.03***	162.4 ± 15.2	**0.001****
C	48.7 ± 5.2	**0.001****	104.3 ± 8.9	**0.001****	115.2 ± 10.8	**0.001****

Analysis of Histopathology: In the liver sections of the control group, a single layer of hepatocytes formed the hepatic cords around the compact central veins. The hepatocytes had granular cytoplasm, evenly distributed around large, centrally positioned, well-stained spherical nuclei. The nuclei featured distinct nucleoli and chromatin material. Classic portal triads or tetrads were embedded in connective tissue. Binucleated hepatocytes were less common than mononucleated ones (Figure 1A). In the groups treated with CoQ10 (figure 1C) displayed a normal appearance like the control group. However, mild changes were observed in the atrazine (120 mg/kg) group, including slight congestion of the portal vein and sinusoids (1B). Hepatocyte vascular congestion was categorized based on the extent of involvement in the evaluated fields. The hepatic damage was categorized as; none (0) indicated no observable damage, mild (1) represented damage affecting 0–25%, moderate (2) 25–50%, and severe (3) indicated damage affecting 50–100%.of of the liver architecture.

In group A, 10% of rats showed mild congestion and 90% showed no congestion. In group B, 30% of rates showed mild congestion, 30% severe while 40% showed moderate congestion. In group C, 40% exhibit mild congestion while 60% showing normal liver architecture in hepatic lobule. The Chi-square analysis revealed a highly significant difference among the experimental groups, with a *p-value* of less than 0.001 (table 2). In the control group, rats did not exhibit any sinusoidal dilatation. In group B, 60% showed moderate dilatation, while 10% had severe sinusoidal dilatation. For group C, 30 % of the rats exhibited mild dilatation , and 70% displayed normal liver lobule . The Chi-square analysis indicated a highly significant difference among the experimental groups, with a p-value of less than 0.001.

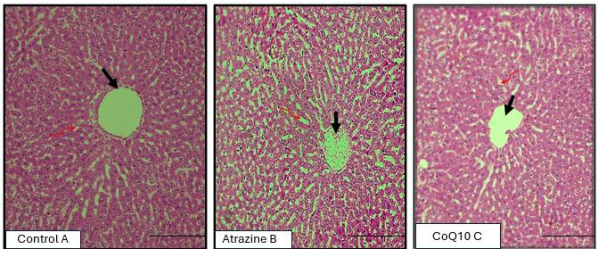

Figure No.1: Histopathological findings of different groups. Black arrow showing vascular congestion and red arrow showing sinusoidal dilatation.

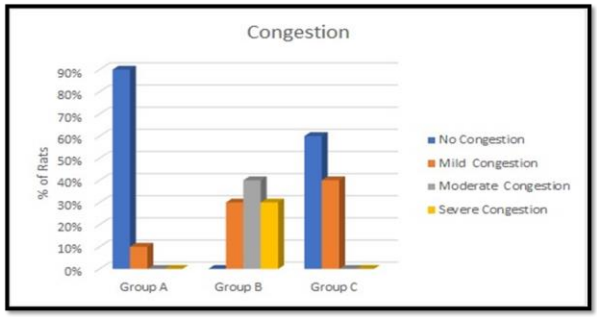

Figure No.2: Bar chart showing % of rats in degree of hepatocyte congestion

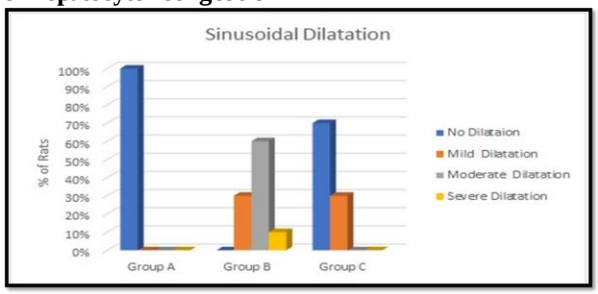

Figure No.3: Bar chart showing% of rats in degree of sinusoidal dilatation

DISCUSSION

The current study offers strong proof of Coenzyme Q10's (CoQ10) ability to shield rats' livers against atrazine-induced damage. A common herbicide, atrazine poses several health hazards because of its environmental persistence and capacity for bioaccumulation. Its hepatotoxic effects, primarily mediated through oxidative stress, have been well-documented. Atrazine exposure is known to elevate oxidative stress markers, disrupt the antioxidant defense system, and cause liver congestion, sinusoidal dilatation, and apoptosis.[1,16] Our results suggested that CoQ10 effectively counteracts atrazine-induced oxidative damage by enhancing the liver's antioxidant capacity.

Significant hepatic damage is indicated by elevated blood liver enzyme values, such as ALT, AST, and ALP, seen in the group treated with atrazine. These results are in line with earlier studies by Muhammad *et al*., which found that atrazine exposure resulted in a significant rise in liver enzymes, which is indicative of oxidative stress and inflammation-induced hepatic cell damage.[17] Similarly, Abarikwu *et al*. highlighted that liver enzyme elevation is a hallmark of hepatic dysfunction caused by environmental toxins such as

atrazine, which compromises membrane integrity and disrupts normal cellular processes.[18]

CoQ10 supplementation in the present study significantly mitigated this enzyme elevation, restoring liver function tests closer to the normal values. This underscores CoQ10's potent hepatoprotective effects, likely mediated through its antioxidant and anti-inflammatory properties. Saleh and also demonstrated CoQ10's capabilities to ameliorate hepatic damage against Acrylamide-induced oxidative stress. Elshazly *et al* also studied the beneficial effects of this supplement on the liver in 2020. Their findings support the notion that CoQ10 reduces hepatocellular injury.[19,20] Another researcher further reported that CoQ10 enhances antioxidant enzyme activities, contributing to the restoration of tissue integrity and function. Our histopathological findings reinforce these biochemical observations by revealing marked disturbances. Rashad et al also found this type of correlation between liver enzymes elevations and liver architecture damage induced by atrazine.[21] Muhammad et al also observed this pattern of atrazine induced hepatotoxicity in their experiment.[17] Atrazine induced hepatic damage was successfully treated with CoQ19 in our experiment. Wang and his colleagues explained the hepatoprotective effects of this enzyme in a recent study. They concluded that these protective effects are mediated through its antioxidant properties.[22]

CONCLUSION

The current study offers strong proof of Coenzyme Q10's (CoQ10) ability to shield rats' livers against atrazine-induced damage.

This might have significant effects on the development of treatment plans to stop atrazine-induced liver damage, particularly in communities exposed to high concentrations from contaminated water sources or agricultural practices. CoQ10 supplementation may serve as a therapeutic remedy against atrazine-induced alterations in health.

Future recommendation: Further studies are needed to identify the exact molecular mechanism of action by which CoQ10 exerts its protective effects and in other atrazine-related target organs with special attention on dose-dependency thus deserved long-term efficacy. Clinical trials should be conducted to investigate the protective effects of CoQ10 on atrazine-induced liver toxicity in humans, exploring optimal dosage and duration of supplementation.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Sadia Farooq, Shabana Ali, Arifa Haroon
Drafting or Revising Critically:	Afifa Siddique, Tayyaba Qureshi, Tayyaba Fahad
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Ethical Approval: No. Riphah/IRC/1070 Dated 04.06.2023.

REFERENCES

1. Riedo J, Wächter D, Gubler A, Wettstein FE, Meuli RG, Bucheli TD. Pesticide residues in agricultural soils in light of their on-farm application history. Environ Pollut 2023;331(Pt 2):121892.
2. Yang D, Yan L, Yu L, Yang H, Liao P. Abundance and characteristics of sediment-bound magnetic minerals and trace elements in karst ditch wetland: A case study from Guizhou Province, China. Ecotoxicol Environ Saf 2022;243:113963.
3. Pedroso TMA, Benvindo-Souza M, de Araújo Nascimento F, Woch J, Dos Reis FG, de Melo E Silva D. Cancer and occupational exposure to pesticides: a bibliometric study of the past 10 years. Environ Sci Pollut Res Int 2022; 29(12):17464-17475.
4. Méndez-Tepepa M, Hernández-Pérez K, Juárez-Santacruz L, Cruz-Lumbreras SR, García-Nieto E, Anaya-Hernández A, et al. Cytotoxic effects of the atrazine herbicide on erythrocytes and liver damage in Lithobates spectabilis. Fishes 2023;8(4):207.
5. Wirbisky SE, Freeman JL. Atrazine Exposure and Reproductive Dysfunction through the Hypothalamus-Pituitary-Gonadal (HPG) Axis. Toxics 2015;3(4):414-450.
6. Das K, Nongrum HB, Mukherjee R, Bhattacharjee S, Bhatia D. A Case Presentation in Management of Dysphagia and Dysarthria Caused due to Organophosphorus and Carbamate Insecticide Poisoning. Ind J Otolaryngol Head Neck Surg 2024;76(5):4717-4723.
7. Hozyen HF, Eldebaky HA, Soror AH, Desouky HM, Shalaby SI. Protective role of selenium against adverse effects of atrazine toxicity in male rats: Biochemical, histopathological and molecular changes. Global Veterinaria 2015;15(4):357-65.
8. Fikry H, Saleh LA, Mahmoud FA, Gawad SA, Abd-Alkhalek HA. CoQ10 targeted hippocampal ferroptosis in a status epilepticus rat model. Cell Tissue Res 2024;396(3):371-397. doi: 10.1007/ s00441-024-03880-z.
9. Mecdad AA, Ahmed MH, ElHalwagy MEA, Afify MMM. A study on oxidative stress biomarkers and immunomodulatory effects of pesticides in

pesticide-sprayers. Egypt J Forensic Sci 2011;1(2):93–8.
10. Qureshi T, Ali S, Fahad T. Synergistic Effect of Coenzyme Q10 and L-Carnitine on Gliosis and Anhedonia, in a Rat Model of Multiple Sclerosis: An Immunohistochemical Study. Clin Psychopharmacol Neurosci. 2024;22(3):484-492.
11. Abarikwu SO, Costa GMJ, de Lima E Martins Lara N, Lacerda SMSN, de França LR. Atrazine impairs testicular function in BalB/c mice by affecting Leydig cells. Toxicol 2021;455:152761.
12. El-Nagar MMF, Elsisi AE. Exposure to bromoxynil octanoate herbicide induces oxidative stress, inflammation, and apoptosis in testicular tissue via modulating NF-κB pathway. Food Chem Toxicol 2023;180:114008.
13. Naeem U, Razzaq M, Arif N, Azhar R, Naeem M, Awan N. Cassia senna for iron overload. Rawal Med J 2022;47(4):857-.61.
14. Naeem U, Azhar R, Shadab W, Awan N, Naeem M, Iftikhar J. Comparative Effects of Nigella Sativa and Cassia Senna in Iron Overloaded Mice. Pak J Med Health Sci 2022;16(04):1222-.25.
15. Brandhonneur N, Hutin V, Chevrier C, Cordier S, Le Corre P. Maternal and Fetal Blood Pharmacokinetics and Organ Distribution of Atrazine, Propazine, Simazine, and Their Metabolites in Pregnant Rats After Chronic Oral Administration. Toxicol Sci 2020;173(2):255-266.
16. Batool S, Batool S, Shameem S, Khalid F, Batool T, Yasmeen S, et al. Atrazine Induced Histopathological Alterations in the Liver of Adult Male Mice. Punjab Univ J Zool 2021;36(2): 165–70.
17. Mohammed ET, Safwat GM, Bahnasawy EA, Abdel-Razik AH, Mohamed DS. Zinc Oxide Nanoparticles and Vitamin C Ameliorate Atrazine-Induced Hepatic Apoptosis in Rat via CYP450s/ROS Pathway and Immunomodulation. Biol Trace Elem Res 2023;201(11):5257-5271.
18. Abarikwu SO, Oleribe AL, Mgbudom-Okah CJ, Onuah CL, Chikwendu CS, Onyeike EN. The protective effect of fluted pumpkin seeds against atrazine-induced testicular injury. Drug Chem Toxicol 2022;45(2):799-809.
19. Saleh AA, Shahin MI, Kelada NA. Hepatoprotective effect of taurine and coenzyme Q10 and their combination against acrylamide-induced oxidative stress in rats. Tropical J Pharmaceutical Res 2017;16(8):1849-55.
20. Elshazly SM, Alsemeh AE, Ahmad EAA, Rezq S. CoQ10 exerts hepatoprotective effect in fructose-induced fatty liver model in rats. Pharmacol Rep 2020;72(4):922-934.
21. Rashad WA, Saadawy SF, Refaay NE. Mitigating effect of L-carnitine against atrazine-induced hepatotoxicity: histopathological and biochemical analyses in albino rats. Environ Sci Pollut Res Int 2023;30(8):22034-22045.
22. Wang Y, Lilienfeldt N, Hekimi S. Understanding coenzyme Q. Physiol Rev 2024;104(4):1533-1610.

Original Article

Frequency of Post-URS Urosepsis in Patients with Uretric Stone

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ABSTRACT

Objective: The objective of the study is to assess the frequency of post-URS urosepsis in patients with uretric stones admitted to the Urology Department.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Urology, CMC Hospital, SMBBMU Larkana, from September 2022 to March 2023.

Methods: During the study period, a total of 106 URS procedures were carried out among patients with ureteric stones admitted to the hospital. The patient's age ranges between 18 and 75 years. URS was accomplished according to study protocol, and stone size, duration of illness, and postoperative results were noted. The data was analyzed on SPSS version 17.

Results: A total of 106 patients with uretic stones were managed by the URS procedure; 9 (8.5%) patients showed postoperative urosepsis. Gender-wise, male patients seemed to have more, and the mean age was 56.1 ± 13.2 and ranged from 18 years to 75 years. All the pathological laboratory tests and radiological protocols were carried out during treatment. In a study, all related variables, such as duration of symptoms, WBC count, and size of the stone, were calculated.

Conclusion: Urosepsis, a potentially life-threatening ureteroscopic procedure-related infection, is increasing due to widespread ureteroscopy adoption. Efforts are underway to reduce post procedure infections in device development and clinical treatment.

Key Words: Post_URS, Urosepsis, Ureteric stone, UTI

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INTRODUCTION

The amount of minimally invasive endourological operations conducted reflects the global increase in the incidence of kidney stone disease (KSD)[1]. Ureteroscopy (URS) has become a widely adopted and effective intervention for the management of ureteric stones, offering high success rates and minimal invasiveness. Despite its advantages, URS is not without risks; postoperative complications, particularly infectious ones, remain a significant concern.

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Among these, urosepsis—a severe, systemic infection originating from the urinary tract—stands out due to its potential for high morbidity and mortality. The urinary tract is often colnized by microbial pathogens. Infection of the urinary tract, simply known as urinary tract infection (UTI), occurs due to the activity of these pathogens. E. coli accounts for most of the cases of non-complicated UTIs or acute pyelonephritis[2]. Postoperative fever and the more clinically dangerous sepsis, while rare, can nonetheless occur. According to latest EAU standards, the post-URS sepsis incidence can be as high as 5%[3].

Another study emphasized that nearly half of post-URS complications are infection-related, with urosepsis rates varying between 0.2% and 17.8%. The study underscored the importance of preoperative antibiotic prophylaxis, prompt treatment of existing urinary tract infections, and minimizing operative time to reduce infection risks.[4]

Sepsis is a response of the body to infection that may cause failure of multiple organs and may result in death. The most serious consequence of UTI is urosepsis, which has a death rate of 20-40%. The underlying infection is frequently a complex UTI affecting a urogenital organ, such as the prostate or kidney. The most prevalent cause of urosepsis is obstructive pyelonephritis caused by urolithiasis, however

urological procedures account for around 17% of cases. The elderly, diabetics, and immunocompromised people are at highest risk.

Patients can become susceptible to urosepsis if they are elderly or immune-compromised. Patients with a history of urinary tract calculi or prior intervention are also at risk.[5] Septic shock is the primary cause of intensive care unit (ICU) admission and mortality in cases with urosepsis, a disease with a high death rate that can vary from 20% to 50%[6].

Recent studies have highlighted the incidence of urosepsis following URS. A systematic review and meta-analysis encompassing 13 studies with a total of 5,597 patients reported a pooled postoperative urosepsis incidence of 5%[7]. This finding is particularly noteworthy, as it challenges the previously held perception of URS as a procedure with minimal infectious complications. Given the significant incidence and potential severity of post-URS urosepsis, there is a pressing need for further research to elucidate additional predictive factors and to develop effective preventive measures. Older persons, those with diabetes, ischemic heart disease, preoperative stent installation, positive urine culture, and longer operation times had increased postoperative urosepsis risk[7].

Urosepsis is a syndrome that may present with fever, tachypnoea, multi organ failure and hypotension and requires aggressive management[5]. Following ureteroscopy, infectious complications might result in morbidity and even death. Even though the majority of these are modest, efforts must be made to reduce them, especially in patients who are at high risk[4].

METHODS

Study objecties: To evaluate the frequency of post-URS urosepsis among ureteric stone patients.

Study setting and duration: This cross-sectional study was carried out at Urology ward CMC hospital SMBB Medical University Larkana from September 2022 to March 2023. In this study, a hospital admitted 106 patients with ureter stones from the Urology Department of CMC Hospital Larkana to find out the frequency of urosepsis after the URS treatment procedure.

Methodology: In this study, 106 patients were included to access urosepsis after an urestoscopy who presented with an ureteric stone and were admitted to the department of urology at SMBBMU Larkana. All the patients were selected according to selection criteria, and written consent was obtained from all participating patients. During the treatment, all the pathological laboratory tests and radiological protocols were carried out. All the data regarding demographic and other variables, such as size of stone and duration of symptoms, was recorded.

Inclusion criteria:

- Age between 18 and 75 years
- Either gender
- Patients with urethric stones in accordance with the operational definition

Exclusion criteria:

- Patients with already-known urosepsis
- Patients already know about UTIs.
- Patients with already-known pyelonephritis
- Patient who declined to participate in the research.

RESULTS

In a total of 106 patients, the mean age of patients was 56.1±13.2 and ranged in age 18 to 75 years, and gender-wise, increased male presentation seemed 62 (58.49%) as compared to female 44 (41.51%).

In a study of 106 ureter stone patients, urosepsis 9 (8.5%) was observed after a URS procedure. Graph. 01

The distribution of continuous variables was tested through Shapiro-Wilk test for age (P=0.065), duration of symptoms (P=0.087), WBC count (P=0.101) and size of stone (P=0.075) as shown in Table 1.

The mean ± SD of the size of the stone was 2.3± 0.9 with C.I (2.12…2.47) c.m and other variables such as WBC count, mean ± SD was 7506.8 ± 88.2 with C.I (7489.81…...7523.79) U/L as shown in Table 2. Furthermore, mean ± SD of duration of symptoms was 21.6 ±4.7 with (20.69…..22.50) days and mean ± SD of size of stone was 2.3± 0.9 cm with C.I (2.12…2.47) c.m as shown in Table 2.

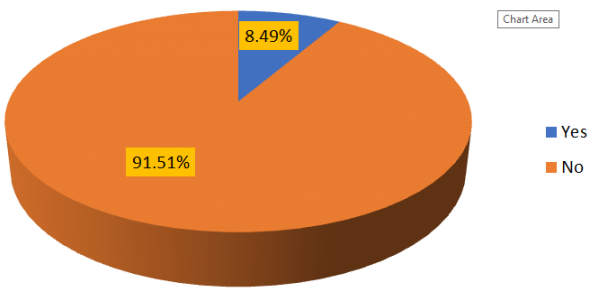

Figure No. 1: Frequency of Urosepsis

Table No. 1: Shows Descriptive statistics of Shapiro-Wilk Test n=106

VARIABLE	MEAN+_SD	P-VALUE
Age (years)	56.1 ±13.2	0.065
Duration of symptoms (days)	21.6 ± 4.7	0.087
WBC Count (u/L)	7506.8±88.2	0.101
Size of stone (cm)	2.3±0.9	0.075

Table No. 2: Shows Descriptive statistics of Shapiro-Wilk Test(n=106)

Variable	Mean+_SD	(95%) Conf: Int.	Range
Age (years)	56.1±13.2	53.55….58.66	18-75 years
Duration of symp (days)	21.6 ± 4.7	20.69...22.50	03 -25 days
WBC Count (u/L)	7506.8± 88.2	7489.81..7523.79	4500-11000
Size of stone (cm)	2.3±0.9	2.12….2.47	1.2 – 3.1 cm

DISCUSSION

Treatments for uretic and renal stones include stone fragmentation and ureteroscopy (URS). Ureteral stent discomfort, ureteral wall injury and stone migration are the most frequently reported complications. The worst complications include urosepsis, multi-organ failure and death. Incidence rates on these and other complications varied extensively between the reviewed reports[8].

We found that nearly 1 in 40 patients are hospitalized with an infection-related complication following URS for urinary stones in diverse practices in Michigan[9].

UTI is the most common post-operative complication related to stone intervention with progression to urosepsis as a rare but serious consequence[10].

Understanding of patient, stone, and operative factors associated with increased risk of post-operative urosepsis is required to identify higher-risk patients and to better counsel patients pre-operatively regarding their personal risk. Prior research examining these variables has not yielded a consensus, frequently involved a small number of patients, and frequently lacked clinically meaningful outcome measures. Urinary stone surgery typically involves ureteroscopy lithotripsy (URSL), or the endoscopic destruction of kidney and ureter stones. Prior research has demonstrated that ureteroscopy lithotripsy is a relatively safe procedure with a success rate of up to 85.6 percent and few side effects[11]. With a frequency of 1–18%, infection complications—including acute febrile episodes and urinary tract infections—are the most frequent postoperative problems, one of the worst outcomes following ureteroscopy lithotripsy is urosepsis[12]. UTI is the most prevalent post-operative complication after stone intervention, with development to urosepsis being an uncommon but catastrophic outcome. A multitude of variables increase infection risk, including co-morbidities, anatomical anomalies, past surgical treatments, and local anti-microbial susceptibility[13]

Infectious complications from ureteroscopy can result in morbidity and death. Although the majority of these are small, efforts must be made to reduce them, particularly in high-risk individuals.[4].

CONCLUSION

We may conclude that patients with uretic stones have a lower incidence of urosepsis. To verify the present findings, more well-controlled, prospective studies are required.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Khubchand Rohra, Riaz Hussain Mangrio
Drafting or Revising Critically:	Om Parkash, Lubna Naz, Suhail Aman Jokhio, Kaleemullah Abro
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Chen Z, Prosperi M, Bird VY. Prevalence of kidney stones in the USA: The national health and nutrition evaluation survey. J Clin Urol 2019; 12(4): 296–302.
2. Dielubanza EJ, Schaeffer AJ Urinary tract infections in women. Med Clin North Am.2011;95(1):27-41.
3. kolarikos A, Jung H, Neisius A et al (2023) EAU Guidelines on Urolithiasis. EAU Guidelines. Edn. presented at the EAU Annual Congress Milan 2023. ISBN 978-94-92671-19-6.
4. Chugh S, Pietropaolo A, Montanari E, Sarica K, Somani BK. Predictors of urinary infections and urosepsis after ureteroscopy for stone disease: a systematic review from EAU section of urolithiasis (EULIS). Current Urol Reports 2020;21:1-8.
5. Scotland KB, Lange D. Prevention and management of urosepsis triggered by ureteroscopy. Res Rep Urol 2018;10:43.
6. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the united states: analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29(7):1303-10.
7. Bhojani N, Miller LE, Bhattacharyya S, Cutone B, Chew BH. Risk factors for urosepsis after ureteroscopy for stone disease: a systematic review with meta-analysis. J Endourol 2021;35(7):991-1000.

8. De Coninck V, Keller EX, Somani B, Giusti G, Proietti S, Rodriguez-Socarras M, ET AL. Complications of ureteroscopy: a complete overview. World j Urol 2020;38:2147-66.
9. Cole A, Telang J, Kim TK, Swarna K, Qi J, Dauw C, ET AL. Infection-related hospitalization following ureteroscopic stone treatment: results from a surgical collaborative. BMC Urol 2020;20:1-7.
10. Kanodia A, Verma H, Jain A, Kalsotra G, Kumari S, Agrawal SK, et al. Prevention and management of complications. Essentials Rhinol 2021;277-307.
11. De la Rossette J, Denstedt J, Geavlete P, Keeley F, Matsuda T, Pearle M, et al. The clinical research office of the endourological society ureteroscopy global study: indications, complications, and outcomes in 11,885 patients. J Endourol 2014;28(2):131-9.
12. Bloom J, Fox C Fullerton S, Matthews G, Phillips J. Sepsis after elective ureteroscopy. Can J Urol 2017;24(5):9017-23.
13. Khusid JA, Hordines JC, Sadiq AS, Atallah WM, Gupta M. Prevention and management of infectious complications of retrograde intrarenal surgery. Frontiers Surg 2021;8:718583.

Original Article

Use of Tooth Clearing Technique to Determine Root and Canal Morphology of Permanent Maxillary Third Molars in Population of Peshawar: An in Vitro Cross-Sectional Study

Technique to Determine Root and Canal Morphology

Imran Khattak[1], Yusra Jamil Khattak[2], Asma Sattar[2], Aiman Shaheryar[2], Sana Arbab[1] and Munawar Aziz Khattak[1]

ABSTRACT

Objective: To use tooth clearing procedure to determine the number of roots, canals and canal configuration in permanent maxillary third molars.

Study Design: Cross- sectional

Place and Duration of Study: This study was conducted at the Surgery departments of three dental colleges of Peshawar, from 4th November 2022 to 3rd May 2023.

Methods: 193 maxillary third molars (MTM) were extracted from both genders, with fully developed roots. Following collection, the number of roots were visually assessed and cavity was prepared, the pulp was cleaned and canals were stained with Indian ink. Teeth were dehydrated in increasing alcohol concentrations after decalcification for five days in nitric acid. Teeth were completely transparent after being immersed in methyl-salicylate for 72 hours. Transparent teeth's root and canal numbers were recorded.

Results: Among 193 extracted MTM's, (54.9%) had three, (25.9%) single and (15.5%) had two roots. Three root canals (46.6%), followed by two (22.3%), one (18.1%) and four (13 %) canals respectively. The predominant canal configuration in mesiobuccal (64.7%), distobuccal (100%) and palatal root (98%) was Type I respectively in the three separate root specimen. For the three fused root form, Type VIII (70.9%) was the frequent configuration. There was no significant correlation between the maxillary third molar's root canal count and number of roots.

Conclusion: Three roots and three canals were the common patterns for maxillary third molars. Vertucci's Type 1 canal configuration was the predominant form.

Key Words: Canal configuration, Clearing technique, Third Molar, Vertucci's classification.

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INTRODUCTION

The eruption of permanent maxillary third molars (MTM) occurs between the ages of 17-21. Its role complements that of the other molars in grinding [1], and its eruption age varies among races.

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Third molars (TM) are often extracted because of periodontal, gingival, caries, as well as pericoronitis conditions. They have been utilized to replace the hopeless first and second molar teeth in auto transplantation in modern dentistry[2]. After successful root canal therapy, prior knowledge of the shape, quantity, and locations of roots may be helpful for simple and less traumatic extractions during autotransplantation. For endodontic therapy to be successful, a thorough understanding of the intricate root anatomy of MTMs is therefore crucial. Even though the fundamentals of endodontics are followed, a lack of knowledge of the root canal system may lead to treatment failure because the root canal apparatus's complications are the most difficult assignment for any dentist planning a root canal treatment.[3]

Given that root morphology might change among various ethnic groups, the anatomy of MTMs has been described as unclear[4-5]. Ethnicity, age, and sex[6] may all contribute to this structural difference. Since it has been

shown that hereditary elements determine root structure and a range of root canal patterns in different individuals, it is vital to evaluate the root form in various ethnic communities[7].

The number of roots in MTM ranges from 1-5 and number of root canals were found to range from 1-6.This is not a constant number and it varies according to different studies[8,9].

The structure of root canals is compound and hard to study. For observing the root canal morphology in three extents, the solidified root tissue must be either detached or made transparent. Hence many methods have been used to evaluate the internal structure of the teeth consisting of root sectioning, canal remodelling, canal staining and clearing, micro CT, review of clinical records. All these are ex-vivo methods and the in-vivo methods include radiographic techniques such as conventional radiographs, radiopaque contrast media microcomputed tomography and cone beam computed tomography[2].

Canal staining and clearing is an easy and low-cost method for in vitro visualization of endodontically managed or unmanaged root canal systems. It allows 3-dimensional assessment of the root canal anatomy and maintains the unique shape of the root canals and their connection to the external root anatomy and gives the most exact and reproducible results that are best suited for educational and training purposes[3].

Using the canal staining and cleaning approach, no local research on the anatomy of roots, canals, and canal morphologies in permanent MTMs have been carried out, according to a thorough review of the literature. The number of roots, canals, and canal shape in MTMs of patients seeking treatment at Peshawar's three dental educational institutions will be analyzed in this study.

The results of the study will be helpful for gathering baseline data about the MTM root canal system. Additionally, when a less expensive fixed prosthesis may be used in place of costly implants, the clinicians will carry out endodontic procedures with a deep knowledge of TM anatomy, minimizing the need to remove TMs.

METHODS

This in-vitro cross-sectional study collected 193 extracted permanent MTM's from three dental colleges i.e Khyber College of Dentistry, Sardar Begum Dental College and Peshawar Dental College in Peshawar, Pakistan. Teeth were collected from patients treated between 4th November 2022 to 3rd May 2023,with prior informed consent. Patients information and consent were recorded.

An ultrasonic scaler was used to remove any calculus or tissue that had adhered after the teeth had been cleansed with water. After 30 minutes of soaking in 5.25% sodium hypochlorite, they were cleaned and kept in 10% formaldehyde until the 193 MTM sample was finished.

The number of roots in each tooth were visually inspected. To determine the number of canals and configurations, the teeth were treated using the Tooth Clearing Technique based on Vertucci's criteria.

Each tooth was cleaned, disinfected, air-dried, pulp material removed and cavities were drilled. The pulpal remnants were afterwards dissolved by immersing the teeth in a 2.5% NaOCL solution for a whole night. After washing and drying, black Indian ink was injected into each root canal. The teeth were then placed vertically for a day, allowing the ink to leak and dry, coloring the canal contours.

To demineralize the teeth, they were soaked in 5% nitric acid for 5 days, with the solution changed daily. A file was inserted to track decalcification and radiograph was taken. After demineralization, the teeth were rinsed with tap water, dehydrated in increasing ethanol concentrations, and then submerged in methyl salicylate, becoming completely transparent after 72 hours.

The teeth were examined using a 3x magnifying lens and adequate lighting, making the canal architecture visible. Data was recorded on structured sheets and classified according to Vertucci's criteria for root canal appearance.

Statistical Assessment:

- For the statistical analysis, SPSS software (version 25) was employed.
- The Pearson Chi-Square test was used to show a correlation between the number of roots and root canals.
- When the p-value was less than 0.05, any variations from the mean values were taken to be statistically significant.

RESULTS

193 MTMs were examined for the quantity of roots, root canals, and canal shapes. They were extracted from individuals with a mean age of 24.90 ± 2.96, of whom 48.7% were male and 51.29% were female. These teeth's frequency and percentage distribution by number of roots, root canals, and canal configurations are shown below.

Table No. 1: Distribution of maxillary third molar teeth by number of root canals and roots.

No. of roots and canals		No. of Teeth (Total No. = 193)	(%)
No. of roots	1	50	25.9
	2	30	15.5
	3	106	54.9
	4	7	3.6
No. of canals	1	35	18.1
	2	43	22.3
	3	90	46.6
	4	25	13.0

106 MTMs (54.9%) had 3 roots, 50(25.9%) had a single root. 2 and 4 rooted were in the descending order of 15.5% and 3.6% respectively.

90 (46.6%) had 3 canals followed by 2 canals found in 43(22.3%) specimens. Single canal and 4 canals were present in 35(18.1%) and 25(13%) of teeth respectively, Table 1.

Table 2, details the root canal configurations (RCC) for the MTMs. The most common RCC is Type (1-1) followed by Type (2-1) and Type (2-2).Type (1-1) configuration was the predominant type in MBRs 64.7%(33) , DBRs 100% (51) and PRs 98% (50) followed by Type (2-2) 21.6% and Type (1-2) 7.8% in the MBRs of the three separate root form of MTMs.

A variety of RCCs were displayed by the single rooted, with Type (1-1) accounting for 50% of the total, followed by Type (2-1) at 14%, Type (1-2-1) at 10%, and Type (2-2) at 8%.

Similarly, the three fused rooted specimens had Type (3-3), being the most common 70.9% (30) RCC's.

Table No. 2: Maxillary third molar tooth distribution according to RCCs (Vertucci's grouping).

Number of teeth (n)	Root morphology		Vertucci's Canal Configuration (VCC)								
			Type 1-1 % (n)	Type 2-1 % (n)	Type 1-2-1 % (n)	Type 2-2 % (n)	Type 1-2 % (n)	Type 2-1-2 % (n)	Type 1-2-1-2% (n)	Type 3-3 % (n)	Others
50	Single root		50 (25)	14 (7)	10 (5)	8 (4)	4 (2)	4 (2)	-	4 (2)	1-3-1(1), 3-1(1), 2-1-2-1(1)
17	Two separate roots	BR	58.8 (10)	11.8 (2)	17.6 (3)	-	11.8 (2)	-	-	-	-
		PR	14 (82.4)	-	-	-	17.6 (3)	-	-	-	-
13	Two fused roots		-	7.7 (1)	-	84.6 (11)	-	-	-	-	3-2-3 (1)
51	Three separate roots	MBR	64.7 (33)	2 (1)	2 (1)	21.6 (11)	7.8 (4)	2 (1)	-	-	-
		DBR	100 (51)	-	-	-	-	-	-	-	-
		PR	98 (50)	-	2 (1)	-	-	-	-	-	-
55	Three fused roots		-	-	1.8 (1)	3.6 (2)	-	-	-	70.9 (39)	4-4(4),3-4(3), 1-3-1(1), 3-2(2),3-1(2), 4-3(1)
6	Four separate roots	MBR1	100 (6)	-	-	-	-	-	-	-	-
		MBR2	100 (6)	-	-	-	-	-	-	-	-
		DBR	100 (6)	-	-	-	-	-	-	-	-
		PR	100 (6)	-	-	-	-	-	-	-	-
1	Four fused roots		-	-	-	-	-	-	-	-	4-4(1)
Total= 193	-		-	-	-	-	-	-	-	-	-

BR: Buccal root, PR: Palatal root, MBR: Mesiobuccal root, DBR: Distobuccal root.

When the number of roots and root canals of maxillary third molars were compared to one another, the Pearson

Chi-Square test's "p" value of 0.538 indicated a statistically non-significant difference (Table 3).

Table No. 3: The correlation between maxillary third molar teeth's root count and root canals.

No. of roots	No. of teeth "n" (%)				Total (n=193)	df	*P-Value
	1RC	2RC	3RC	4RC			
1	33	14	3	0	50 (25.9)	9	0.538
2	0	27	3	0	30 (15.5)		
3	2	2	84	18	106 (54.9)		
4	0	0	0	7	7 (3.6)		
Total	35(18.1)	43(22.3)	90(46.6)	25(13.0)	193(100)		

RC: Root canal, df = 9 as calculated by Pearson Chi Square Test, "P" value= 0.538,

*chi square applied.

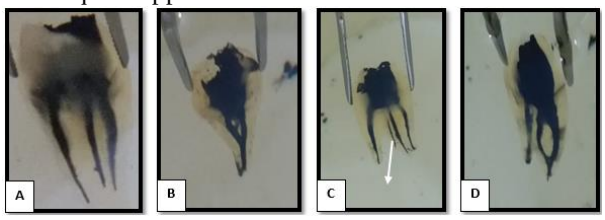

Figure No. 1: A sample of the RCCs seen during this investigation.

A) Three separate roots each with Type I (1-1) (Vertucci's Canal Configuration (Vcc)
B) Type II (2-1) Vcc, seen in a single root.
C) Three roots, four canals seen (MB-II) seen.
D) Buccal root, Type II (2-1) Vcc, Palatal root Type I (1-1) Vcc.

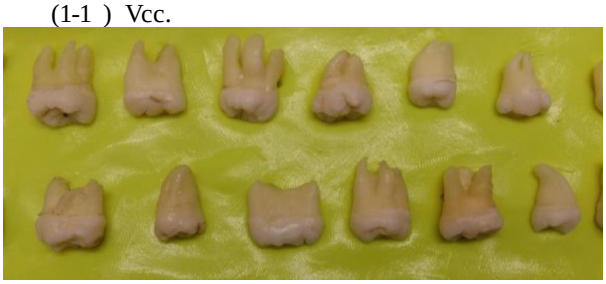

Figure No. 2: Different root forms of MTM's observed in this study.

DISCUSSION

A good dental procedure requires exact understanding of the form, structure, and anatomical variances of teeth on the inside as well as the outside.[4,9] Third molars with endodontic involvement may be successfully repaired and maintained as a functional and beneficial component of the maxillary arch with appropriate diagnosis and planning.

Because the clearing procedure was less expensive and didn't require any sophisticated, costly equipment, it was employed in this investigation to examine the internal anatomy of roots. After the teeth were made transparent, it was simple to study the root canal system's true course from the canal opening to the apical foramen to create a precise canal configuration. The same techniques have been applied by numerous researchers to evaluate the root canal patterns and form of the third molars in both arches.[8–13]

Three roots (54.9%), or 106 out of 193 teeth, had a greater proportion of maxillary third molars in the current investigation. These results were supported by the Russians (52.1%) and Burmese (55.6%) population, respectively[4,13]. The frequencies of three rooted molars were considerably higher than those reported earlier by Sidow et al. (45%)[4], Sert et al. (34.1%)[3] and Zhang et al. (25.4%)[7] , but were lower than the prevalence (88.1%), in other research (83.9%) and as reported by Ahmad et al (74.2%) in Jordanian subpopulation[2].

In the current study, the frequency of maxillary wisdom molars with a single root was 25.9% of teeth, which was lower than the prevalence of single rooted MTM's (51.5%, 47.9%, 35.5%) as reported earlier[4,8,12].

The discrepancy in results may be caused by various methods, sample sizes, and racial disparities between groups.

In the present study, (Table 1) three canals were the most prevalent 46.6%. This percentage was in accordance with the studies carried out in Burmese (47.2%), Thai (48.3%), Chinese (44.2%) and Turkish (46.9%) people[8,12,13] but lower than the results (57.3%, 75%, 55.1%, 72.3%) of earlier studies [4,9,11]. In our study two canals were found in 22.3% MTM's. This occurrence was significantly greater than those seen in previous research[9- 13] and in accordance with the findings (25% and 29.7%) of the work done by Ng et al[8] and Sert et al[3].

Since Vertucci's classification[3] is the only criterion that takes into account the canal orifice and apical foramina at the same time, it was used in the current study. Additionally, the majority of researchers who employed the in vitro clearing approach did so in order to determine the layouts of their canals [12, 13].

The results of the current investigation showed remarkable similarities to those of the previously stated studies. According to earlier reports, Vertucci Type I was the most common kind[6].

Similarly in our study for the maxillary RCC (Table 2), Type I Vertucci canal configuration was the predominant form. In the single rooted specimen for the MTM's Type I was the most frequent (50%) which was supported by the results reported in previous studies(63.2%, 63.1%, 66.8%,51.4%)[10, 11].

The two fused rooted MTMs were noticeable in Type IV in our investigation, 84.6% canal configuration which was supported by the incidence of 66.7% in the

study of Ahmad et al[6]. In the three separate roots of MTM's in our study, the mesiobuccal roots were again predominant in Type I canal configuration (64.7%) followed by Type IV 21.6% which were in accordance with the frequencies of 62.5% and 72.7% as reported earlier[12]. All DBR and PR's of the three separate rooted MTM's showed a frequency of 100% and 98% Type I RCC, respectively which was supported by all previous studies. In our study the three fused rooted MTM's showed a high incidence of Type VIII canal configuration 70.9% which was in accordance to 64.3% Type VIII RCC[11].

In our research, evaluating the roots of MTM with their root canals revealed a significant but statistically insignificant difference ($p>0.05$). The MBR of MTM and single root forms showed more diversity in the number of root canals between the two and three rooted groups, according to this study.

The current study has its own benefits, such as being cost-effective and practical, not requiring costly and sophisticated technological equipment and facilities, and offering a starting point for further research. However, because it is an in-vitro investigation, it has significant limitations that prevent dentists from identifying the abnormal morphology of the intact MTMs inside the oral cavity. The usage of contemporary dental devices, such as CBCT and dental operating microscopes, were inadequate..

CONCLUSION

A range of root and canal configurations were seen in MTM's from the Peshawar population under investigation. MTM's predominantly had three roots including three fused and separate root forms. Single rooted variants were the second in occurrence. Regardless of the number of roots, the majority of maxillary third molars had three root canals. The most prevalent root canal configurations in MBRs, DBRs, and PRs of MTMs were Vertucci's Type I (1-1) and Type IV (2-2) in MBRs.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Imran Khattak, Yusra Jamil Khattak
Drafting or Revising Critically:	Asma Sattar, Aiman Shaheryar, Sana Arbab, Munawar Aziz Khattak
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Dioguardi M, Quarta C, Sovereto D, Troiano G, Melillo M, Di Cosola M, et al. Autotransplantation of the third molar: a therapeutic alternative to the rehabilitation of a missing tooth: a scoping review. Bioengineering 2021;8(9):120.
2. Ahmed HM. A critical analysis of laboratory and clinical research methods to study root and canal anatomy. Int Endodont J 2022;55:229-80.
3. Sert S, Aslanalp V, Tanalp J. Investigation of the root canal configurations of mandibular permanent teeth in the Turkish population. Int Endod J 2014;37(7):494-9.
4. Sidow SJ, West LA, Liewehr FR, Loushine RJ. Root Canal Morphology of Human Maxillary and Mandibular Third Molars. J Endod 2012;26(11): 675–8.
5. Kuzekanani M, Haghani J, Nosrati H. Root and Canal Morphology of Mandibular Third Molars in an Iranian Population. J Dent Res Dent Clin Dent Prospect 2014;6(3):85–8.
6. Ahmad I, Azzeh M, Zwiri AbdalwahabMA, Abu Haija MA, Diab M. Root and root canal morphology of third molars in a Jordanian subpopulation. Saudi Endod J 2016;6(3):113.
7. Zhang W, Tang Y, Liu C, Shen Y, Feng X, Gu Y. Root and root canal variations of the human maxillary and mandibular third molars in a Chinese population: A micro–computed tomographic study. Arch Oral Biol 2018;95:134–40.
8. Ng YL, Aung TH, Alavi A, Gulabivala K. Root and canal morphology of Burmese maxillary molars. Int Endod J 2015;34(8):620–30.
9. Karobari MI, Ahmed HM, Khamis MF, Ibrahim N, Noorani TY. Application of two systems to classify the root and canal morphology in the human dentition: a national survey in India. J Dent Educ 2023;87(8):1089-98.
10. Al-Qudah AA, Bani Younis HA, Awawdeh LA, Daud A. Root and canal morphology of third molar teeth. Scientific Reports 2023;13(1):6901.
11. Sert S, Şahinkesen G, Topçu FT, Eroğlu ŞE, Oktay EA. Root canal configurations of third molar teeth. A comparison with first and second molars in the Turkish population. Australian Endod J 2015;37(3):109–117.
12. Cosic J, Galić N, Vodanović M, Njemirovskij V, Šegović S, Pavelić B, et al. An in vitro morphological investigation of the endodontic spaces of third molars. Coll Antropol 2013;37(2):437–42.
13. Faramarzi F, Shahriari S, Shokri A, Vossoghi M, Yaghoobi G. Radiographic evaluation of root and canal morphologies of third molar teeth in Iranian population. Avicenna J Dent Res 2016;5(1).

Original Article

Knowledge and Perceptions of House Officers about Adopting Anesthesia Specialty

Sohail Anjum[1], Ghulam Murtaza Hiraj[2] and Rizwan Ali Qaiser[3]

ABSTRACT

Objective: The study objective was to describe Knowledge and perceptions of house officers about adopting anesthesia specialty Methods Prior ethical approval was taken from institutional review board

Study Design: descriptive quantitative cross-sectional

Place and Duration of Study: This study was conducted at the Kishwar Fazal Teaching Hospital Lahore in six months time period from May 23, 2023 to October 23, 2023.

Methods: House officers with one month experience were included. After their consent for study was obtained, 22 boys (44.89%) and 11 girls (22.44%) out of 49 house officers filled out self reporting survey questionnaire[1] which made response rate 67.34% percent.

Results: Out of 33 house officers, 22 (44.89%) considered Endo-tracheal intubation and specific expertise of spinal anesthesia as the most enjoyed portion of the house job. 23 (69.69%) believed that anesthetist enjoys a similar role in operations as a surgeon.

Conclusion: House officers of anesthesia have positive perceptions about the field of anesthesiology serving as an inspiration for their juniors to adopt it which may help to counter workforce crises in this field.

Key Words: Knowledge, Perceptions, House officers, Adopting, Anesthesia, and Specialty

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INTRODUCTION

The choice of career stood out of utmost importance for health care students. Quality of education in medical college, personal reasons, style of life, contact with patients and content of specialty could be associated factors. They thought both subjectively and objectively to make opinions regarding a profession. Literature available in this regard is scarce. Considering career dynamics along with the demands of the work force was helpful particularly in formulating concrete opinions for the anesthesia specialty which as a whole was unpopular for both males and females.[1] Locally no such research study could be found while its regarding literature was also deficient, we carried out current research with an objective to describe opinions of house officers in a big city about anesthesia field and it's most enjoyed portion.

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House officers, medical students, faculty and directors of program, state representatives and general public representatives all are stake holders stood significant for decision making and generating a professional opinion.[2] With regards to opinions in choosing anesthesia career there were factors within profession itself and the individual opting it. For recruitment, an awareness and opinions were required keeping in view what was expected by both the individual and specialty itself.[3] Researches explored ethical hardships faced by pre-hospital personnel having less patient information and scarce colleague consultation under pressure of time.[4] Wellness of resident physicians is a controversial issue for medical education at graduate levels for at least two recent decades. Less time availability, unpredictable working, lesser availability of support in training programs and fears of impact on peers were found to be the main reasons.[5] Handoff s in anesthesia were also studied and found that they are associated to negative outcomes for patients. Therefore educational remedies were suggested to be incorporated in anesthesia educational principles.[6] Shortage of workforce in anesthesia could be as a result of the reason that fresh graduates do not prefer to choose anesthesiology for their post-graduation. Therefore a research study in Pakistan recommended minimizing the educational barriers and proposed a compulsory rotation of house officers in anesthesia department.[7]

METHODS

Prior ethical approval was taken from institutional review board and this descriptive quantitative survey (cross-sectional) was conducted on forty nine house officers of anesthesia department of Kishwar Fazal Teaching Hospital Lahore in six months time period from May23, 2023 to October 23, 2023. House officers with one month experience were included. After their consent for study was obtained, twenty two boys (44.89%) and eleven girls (22.44%) out of forty nine house officers filled out self reporting survey questionnaire[1] which made response rate 67.34 percent. Months of training, gender and age was mentioned. Completed survey questionnaires were collected by hand. Perceptions about anesthetist role, best portion of anesthesia house job and specialty of anesthesia itself were sought in questionnaire. Assurance was provided to voluntary study participants for confidentiality and no compensation and harms were there. DATA ANALYSIS was done by using SPSS version 25 and frequencies against responses obtained were mentioned in graphical and tabulated and representation.

RESULTS

Out of 33 house officers, 22 (44.89%) considered Endo-tracheal intubation and specific expertise of spinal anesthesia as the most enjoyed portion of the house job. 23 (69.69%) believed that anesthetist enjoys a similar role in operations as a surgeon. 3 (9%) opted opinion of fine workplace atmosphere, 1 (3%) opted for cardio-pulmonary resuscitation and work in intensive care unit, 4 (12.12%) opted none, 10 (30.30%) had a vague opinion as mentioned in Figure 1.

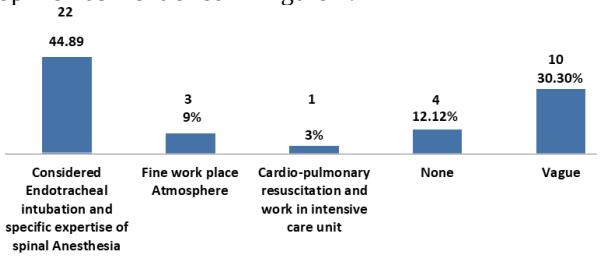

Figure No. 1: Numbers and percentages of house officers with perceptions about most enjoyed portion of anesthesia house job

23(69.69%) believed that anesthetist enjoys a similar role in operations as a surgeon. The rest of the percentages of opinion have been mentioned in Table No.1 accordingly.

Table No. 1: Numbers and percentages of house officers with their perceptions about anesthesia specialty

Opinions	Numbers and Percentages
Anesthetist enjoys similar role in operations as surgeon.	23(69.69%)
Field of Anesthesia is bore.	12(36.36%)
Field of anesthesia is absorbing.	17(51.51%)
Anesthesia involves emergency patient management.	2(6.06%)
Critical care management of patients is there.	3(9.09%)
If we compare with Medicine, there is involvement of more practical procedures.	2(6.06%)
One can manage both profession and the family.	1(3.03%)
It is related to patient during operation.	1(3.03%)
One feels more responsible for patient.	1(3.03%)
Surgery cannot be started without it.	1(3.03%)
The field is high paying.	1(3.03%)
Situation-wise patient management is involved.	1(3.03%)
It relieves patient's pain.	1(3.03%)
One can manage patient without involvement of too much recourses.	1(3.03%)
One deals with a lot of gadgets.	1(3.03%)
Anesthetics work instantly.	1(3.03%)
None of comment	18 (54.54%)

DISCUSSION

In context to cater crises of workforce in anesthesia, less private practice, dependence on surgeon, none uniform policies of government hospitals, meager salary packages had narrowed the scope of anesthesia in Pakistan. Considerations could be made to improve surgeon-anesthetist and patient-anesthetist relations.[8]To handle parallel administration; education and research along with their routine work require time and finance management.[9] In our study, 23(69.69%) were of the opinion that anesthetist enjoys similar role in operations as surgeon. Practices of relational work should be implemented and policies should be developed to maximize satisfaction at job by the executives of leading position in hospitals.[10] 22(44.89%) considered Endo-tracheal intubation and specific expertise of spinal anesthesia as the most enjoyed portion of the house job. One study communicated reflections of anesthesia residents in 2021 at the end of their residency when they faced shortage of supplies, and workforce and during this pandemic patients were referred to only physician which was a threat to the title of anesthetist. Even then the residents showed a hope of a brighter future.[11] 17(51.51%) in our study considered that anesthesia field is absorbing. 2(6.06%) were of view that if we compare with Medicine, there is involvement of more practical procedures in

anesthesiology. In our study 12(36.36%) considered anesthesiology as bore. There are studies offering perceptions of self-efficacy of freshly passed out doctors in context of economic, social and spiritual influences which could help in enhancing their competence. Such results could support future practice, training and education.[12]A study explored significant factors and timing understood by trainee residents to decide pursuing anesthesia career, areas of training considered significant for better future and their perception of challenges faced by this profession.[13]In our study only 1 (3.03%) were of opinion that one can manage both profession and the family in anesthesia. A Sub Saharan African country study documented that the preferred most aspiration of career in their medical students was in favor of surgery.[14] Anesthesiology remained poorly acknowledged by not only general public but the medical profession itself.[15] 1(3.03%) in our study were of views about anesthesiology that one feels more responsible for patient, surgery cannot be started without it, the field is high paying, relieves patient's pain, situation-wise patient management is involved, deals with a lot of gadgets, anesthetics works instantly and one can manage patient without involvement of too much recourses. 3(9.09%) considered that anesthesiology involves emergency management and critical care of patient. Recruitment of diverse groups of house officers, medical students and faculty is a challenging issue.[16]Catering shortage in anesthesia workforce in USA a study pointed out issues to have on-call anesthetist from home. For example how long would they take coming to hospital depending upon their driving times and geo location.[17] In one year house job period of dentistry the contents of Entrust able Professional Activities were introduced in five stages to follow a competence-based strategy.[18] In University College Hospital accredited with Royal College of Surgeons England, trainee anesthetists delivered six online sessions after every two months as per requirement of Anesthetic National Teaching Program for Students in order to meet growing requirements of tomorrow's doctors to standardize anesthesia training.[19] It was found in a research that at least a year long course was required to be introduced for early career anesthetists if they wished gaining competence and get mentorship for developing investigative projects.[20] In Mali a study mentioned that anesthesiology and intensive care are taught in a diverse practical and theoretical way as third cycle in medical studies. It proposed a compulsory evaluation of motives behind their choice of apprenticeship program so as to find causative factors for dropouts in this young discipline. The study mentioned that difficult social and learning environment unmotivated anesthesia residents.[21] The lack of diversity in workforce of physicians has significant consequences especially for anesthesiology and intensive care because of ethically crucial decisions which have far reaching impacts. Religious values and practices have impact upon clinical decisions which indirectly influence health care outcomes. Potential socio-cultural and historical barriers in entry of trainees are worth to be explored in under-represented specialties like anesthesia.[22]

LIMITATIONS: The limitation in this research is that the sample was collected from only one attached hospital of a medical college.

CONCLUSION

House officers of anesthesia have positive perceptions about field of anesthesiology serving as an inspiration for their juniors to join it which may help to counter workforce crises in this field.

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REFERENCES

1. Khan F, Minai FN, Siddiqui S. Anaesthesia as a career choice in a developing country; effect of clinical clerkship. J Pak Med Assoc 2011;61(11):1052.
2. Kay HG, Makhoul AT, Ganesh Kumar N, Pontell ME, Drolet BC, Whigham AS. Otolaryngology Program Director, House-Staff, and Student Opinions: Step 1 Pass/Fail Score Reporting. Annals Otol Rhinol Laryngol 2023;132 (1):63-8.
3. Manjooran G, Scribante J, Perrie H, Redelinghuys C. Career choice of anaesthetists in a department of anaesthesiology at a tertiary institution in South Africa. Southern Afri J Anaesthesia Analgesia2021;27 (2):92-8.
4. Bruun H, Milling L, Mikkelsen S, Huniche L. Ethical challenges experienced by prehospital emergency personnel: a practice-based model of analysis. BMC Med Ethics 2022;23(1):1-14.
5. Munisteri M, Wong R, Loza L, Scott LL, Keyser EA, Gonzalez-Brown V. Resident Trainee Access and Barriers to Routine Health Services in the

Military Health System. J Surg Educ 2023;80(4):581-7.
6. Riesenberg LA, Davis R, Heng A, do Rosario CV, O'Hagan EC, Lane-Fall M. Anesthesiology patient handoff education interventions: a systematic review. The Joint Commission J Quality Patient Safety 2023;49(8):394-409.
7. Hussain A, Feroze R, Leghari KH, Wahid F, Ali A, Khalique A. Is Anesthesia an attractive career choice for undergraduates and young doctors of Pakistan? J Rawalpindi Med Coll 2022;26(3).
8. Shahbaz S, Zakar R, Fischer F, Howard N. Professional Obstacles to Anaesthesiology Practice in Punjab, Pakistan: Qualitative Study of Consultant Anaesthesiologists' Perspectives. Int J Environ Res Public Health 2022;19(20):13427.
9. Gupta D. Payer for Administration, Education, and Innovation in Anesthesiol 2023;15(8):e44410.
10. House S, Wilmoth M, Stucky C. Job satisfaction among nurses and physicians in an Army hospital: A content analysis. Nursing Outlook 2022; 70(4):601-15.
11. Friedlander D. A Year in Review and What Lies Ahead. ASA Monitor 2022;86(1):33.
12. Oji N, Onyeka T, Soyannwo O, Paal P, Elsner F. Perspectives, perceived self-efficacy, and preparedness of newly qualified physicians' in practising palliative care—a qualitative study. BMC Palliative Care 2022; 21(1):1-19.
13. Chen D, Toutkoushian E, Sun H, Warner DO, Macario A, Deiner SG, et al. Career decisions, training priorities, and perceived challenges for anesthesiology residents in the United States. J Clin Anesth 2023;89:111155.
14. Bajunirwe F, Semakula D, Izudi J. Career aspirations of specialty among medical students in sub-Saharan Africa: a systematic review and meta-analysis of data from two decades, 2000–2021. BMJ open 2022;12(8):e057020.
15. Wilkinson DJ. An anaesthetist who missed a golden opportunity. Anaesth Intensive Care 2022;50(2_suppl):28-34.
16. Mmeje O, Perry M, Andreski P, Haggins A, Brown DJ. Creating opportunities to engage with prospective historically marginalized trainees with clinical simulation. J National Med Assoc 2023;115 (2):127-33.
17. Dexter F, Epstein RH. Managing capacity for urgent surgery: staffing, staff scheduling in-house or on-call from home, and work assignments. Elsevier;2022.p.399-402.
18. Orakzai GS, Jamil B. Developing Entrust able Professional Activities (EPAS) for House Officer to Practice Safely and Independently in Dentistry; A Qualitative Study Using Interpretive Paradigm. Pak Armed Forces Med J 2022;72(2):419-25.
19. Wicks SK, Kumar PR, Kumar RV, Arthur-Quarm S, Gavalas M. Anesthetic National Teaching Program for Students (ANTPS). Postgraduate Med J 2023;99 (1172):613-23.
20. Cavallone LF, Duggan EW, Berger JS. A call to action: a specialty-specific course to support the next generation of clinician scientists in anesthesiology. Anesth Analgesia 2022;135(4): 728-31.
21. Almeimoune A, Mangane M, Thierno DM, Démbele SA, Koita S, Coulibaly M, et al. Evaluation of the Reasons for the Choice of Their Learning Course by Resident Physicians of Anesthesia and Intensive Care Medicine (ICU) in Mali. Creative Educ 2022;13(1):320-8.
22. Alim-Marvasti A, Jawad M, Ogbonnaya C, Naghieh A. Workforce diversity in specialist physicians: Implications of findings for religious affiliation in Anesthesia & Intensive Care. Plos One 2023;18 (8):e0288516..

Original Article

Study of SLC25A12 Gene in Pediatric Age Group with Autism Spectrum Disorder Aged 3-13 Years in Thi-Qar Center of Autism

Naeem Salih Yaser[1], Maha Fadhil Semaism[1] and Rebee Mohsin Hasani[2]

ABSTRACT

Objective: To find out the mutation in gene SLC25A12, rs2292813 (T>C) single nucleotide polymorphic is a cause of autism spectrum disorder.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Thi-Qar Autistic Center in Nasiriya city in Thi-Qar Governorate from 15st November 2022 to 15th of June 2023.

Methods: Ninety six patients were diagnosed as cases of autism spectrum disorder by pediatric psychiatry were enrolled and age range was 3 to 13 years. The apparent healthy control group is consisting 96 of children with ages range was 3-13 years. The polymerase chain reaction-tetra-ARMS method was conducted using a commercially available polymerase chain reaction master mix according to the instructions and special primers were designed to detect rs2292813 (T>C) single nucleotide polymorphic mutation.

Results: The heterozygous genotype (CT) is observed in 10 (10.4%) of samples and homozygous genotype (CC) is observed in 84 (87.5%) of samples while homozygous genotype (TT) is observed in 2 (2.08%) of samples. For control group the heterozygous genotype (CT) is observed in of samples 26 (27.1%) and homozygous genotype (CC) is observed in 69 (71.8%) of samples while homozygous genotype (TT) is observed in 1 (1.04%)

Conclusion: There is statistical association between SLC25A12 single nucleotide polymorphism and autism spectrum disorders.

Key Words: Autism spectrum disorders, SLC25A12, Polymerase chain reaction, Single nucleotide polymorphism

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INTRODUCTION

Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders that affect social interaction and communication with repetitive and stereotyped behaviour.[1] Most ASD effective genes are recognized to participate in development of fetal nervous system especially in synaptic generation , neuronal generation and differentiation of nervous cells and migration of neurons.[2] Many of researches on twins and relatives show high heritability with a concordance degree for monozygotic twins of 60-95% compared 0-30% for dizygotic twins for ASD.[1]

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These genetic factors include sex chromosomal aneuploidies which are present in 2-5% of autistic patients. High levels of autistic features are found in Klinefelter syndrome (47, XXY), and Turner syndrome (45, X).[3] Males with Y chromosome aneuploidy (47XYY and 48XXYY) are 20 times more likely to have a diagnosis of ASD than males in the general population.[4]

Copy number variations (CNVs) are molecular phenomenon proposed that the sequences of the genetic material are repeated, and the quantity of repeats differs between individuals of the same species.[5] Duplications, deletions, translocations, and inversions are examples of the submicroscopic structural abnormality which known CNVs.[6] About 5-10% of ASD conditions carry CNVs and most CNVs condition rise spontaneously or de novo, although they can also be hereditary in families, and at least 90 pathogenic CNVs have been informed for ASD.[7]

Monogenic Autism, is recognized genetic causes and it is existing in the general population at a frequency of ≤1% and it is categorized by dysmorphic traits and an equal male to female rate.[8] Fragile X syndrome is an instance of monogenic autism who is caused by magnification number of repeats of triplet CGG in

promoter region of FMR1gene causing lack of transcription and production of protein of the gene[9] and 21-50% of affected persons have ASD.[10]

Single nucleotide polymorphism (SNPs) area genomic abnormality at a single base position in the DNA which comprise exchanges, deletions or insertions. These variants are significant since they modify the action of the gene production. Polymorphisms, is changes with a slight allele frequency of at least 1% in population.[11] The common of ASD-associated SNPs are located within the non-coding components of the genome in regulatory elements that modify gene express.[12] For instances is the mutations in the SHANK3gene of chromosome 22 in Phelan-McDermid syndrome in which autism is a projecting features.

Epigenetic mechanisms are the molecular factors that produce complexes at controlling areas of DNA to effect genetic action without altering the prime DNA sequence. Such factors are typically hereditary.[13] Epigenetic alteration act by dysregulation of DNA or histone methylation, DNA acetylation, chromatin transformation or RNA-based mechanisms[14], mutations in HIST1 H1A gene which encoding H1 histone linker protein and this mutation perform lesser protein expression and can cause ASD or other social difficulties.[15]

METHODS

This study was performed in Thi-Qar Autistic Center in Nasiriya city in Thi-Qar Governorate. A total of 96 patients were diagnosed as cases of ASD by pediatric psychiatry were enrolled. The ages range was 3 to 13 years. The control group is consisting of 96 apparently healthy children with ages range was 3-13 years. The newly diagnosed cases of ASD before start intake treatment and the control group were apparently healthy children and meet the same age range were included. Children with schizophrenia, cerebral palsy, children with cardiac disease, children with asthma, infection or inflammatory condition (increase ferritin), and patient with iron supplement were excluded.

DNA extraction from blood is done by use special kit and protocol by AddBio company -south Korea .The amounts of double-stranded DNA (dsDNA) in a purified samples are measured by QuantusFluorometer System that contains a fluorescent DNA-binding dye that can sensitively quantitate small sample amount of dsDNA and it is sensitive in a range of 0.2-400 ng/µl of dsDNA.[16]

The most effective way of separating DNA fragments of varying sizes ranging from 100 bp to 25 kb.[17] Agarose polymers form a network of bundles whose pore sizes determine a gel's molecular sieving properties. Figures 1 and 2 showed DNA agarose gel electrophoresis image for patients group and controls group.

Primers were shipped in a lyophilized state. The units of a lyophilized primer were given as a mass in Picomoles. To create a stock of primers, one would reconstitute the primer in free nuclease deionized water. The company supplied the amount of free nuclease deionized water to be added to each primer to obtain master stock that would be used again to obtain a working stock.A specific mutation was selected from the National Center for Biotechnology Information (NCBI) that shows the loci of the mutation as in the following:

SLC25A12 SNP: (rs2292813) (T>C)
Position in chromosome: chr2:171787719
(GRCh38.p14)

For the purpose of detection this mutation, a specific Polymerase chain reaction (PCR) technique known as Tetra-ARMS PCR was carried out as a simple, highly precise and efficient more cost-effective choice that requires fewer reagents and less time. This was achieved by designing specific primers targeting the homozygous and heterozygous genotype (Table 1). QuantusFluorometer System that contains a fluorescent DNA-binding dye was used for measurements the concentration of dsDNA for patient s group that mean was 9.4 ng/uL with a range (3.69-16 ng/ul) and for control group was 10.2 ng/uL with a range (5-16 ng/uL). The lower accepted concentration of dsDNA is 0.2 ng/uL.

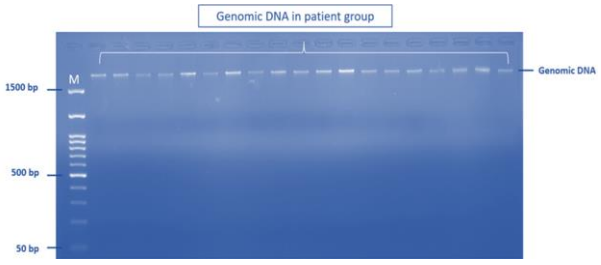

Figure No. 1: Agarose gel electrophoresis image (1.5%) shows the extracted genomic DNA from patient group. M is molecular marker from Gene Direx (South Korea)

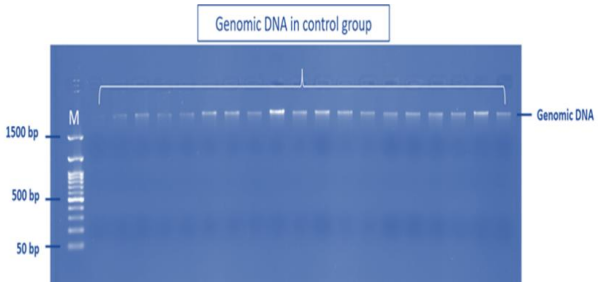

Figure No. 2: Agarose gel electrophoresis image (1.5 %) shows the extracted genomic DNA from control group. M is molecular marker from Gene Direx (South Korea)

The data was analyzed using Software Package for Social Science (SPSS-22 version). t- test have been

used to determine the significant difference between the groups.. Utilizing the odd ratio and Chi-square ($\chi 2$) test, genetic analysis was carried out. Significant difference $p<0.05$, very significant $p<0.01$ and high significant $p<0.001$.

RESULTS

The mean age was 7±2.65 years of ASD group and the patients were divided into male and female subgroup and also divided into two age subgroups G1 (3-8 years) subgroup and G2 (9-13 years) subgroup. The mean was 6.5±2.55 years of control group. There were no significant differences in age ($P>0.05$) between patient with autism and apparent healthy control groups. There were no patients seen below 3 years in this study. The number of patients who visit the center with age 3 years as a first visit from about 9.6% of patients (10/96) while the most frequent age of visit was 6 years which form about 19.2% (20/96) of total patients. There were no patient's age seen above 13 years (Table 2).

Twenty one patients were females (22%) of total patients and 75 were males (78%) of total patients and male to female ratio was 3.54:1 (Fig. 3).

Table No. 1: The primer used for SLC25A12 gene mutation (rs2292813) and their loci, properties and the expected size for genotyping

Primer	Sequence '5->3'	Start	End	Tm C	Genotype	Size
Forward outer	CATAAGTGACCAAGGT-AACACCAAACTGG	111,665	111,693	67°C	In both	160
Reverse outer	ACGACATACAGTGGTG-TCATCGACTGTT	111,434	111,461	67°C		
Inner forward	TTGAAACCAGGACAAA-TGTGGTAAATAC	111,588	111,612	64°C	C-allele	180
Inner Reverse	CGTCCTCCCCTGTGACTC-AGTGGATA	111,560	111,582	70°C	T-allele	134

SLC25A12 genotyping: Conventional PCR was used for amplification of target DNA of SNP rs2292813, (T>C) mutation by using four designed primers in single PCR reaction to amplify the target DNA region. The two outer primers amplify a larger regions that include the SNP or mutation while to inner primers are designed to specifically amplify the mutant or wild (normal) alleles .The PCR product is illustrated in figure 4 which represent the SLC25A12 gene polymorphic site bands that can be visualized by using agarose-gel electrophoresis, these bands were 260 for both C and T- alleles and 180 bp for C-allele and 134 bp for T-alleles (Fig. 4). The heterozygous genotype (TC) is observed in 10 (10.4%) of samples and homozygous genotype (CC) is observed in 84(87.5%) of samples while homozygous genotype (TT) is observed in 2 (2.08%) of samples. For control group the heterozygous genotype (CT) is observed in 26 (27.1%) of samples and homozygous genotype (CC) is observed in 69 (71.8%) of samples while homozygous genotype (TT) is observed in 1 (1.04%) with statistical summary for patients and control groups (Tables 3-6).

Table No. 2: Comparison of age according to patients and control groups

Group	Age (years)	P value
Patients	7±2.65	>0.05
Controls	6.5±2.55	

Table No. 3: Genotyping and alleles frequency of SLC25A12 gene polymorphism

Group	Genotype				Allele frequency	
	No.	TT	TC	CC	T allele	C allele
Patients	96	2(2.08%)	10(10.4%)	84(87.5%)	14(7.3%)	178(92.7%)
Control	96	1 (1.04%)	26 (27.1%)	69(71.8%)	28(14.5%)	164(85.5%)

Table No. 4: SLC25A12 gene polymorphism characterization in patients and control groups genotype

Genotype	Patients	Control	$\chi 2$ P- value	Odd Ratio	CI (95%)	P-value
TT	2	1	8.91 (P<0.05)	0.82	0.11-5.98	P>0.05
TC	10	26		2.6	0.32-21.04	P>0.05
CC	84	69		1.0 reference		

Table No. 5: SLC25A12 gene polymorphism characterization in patients and control Alleles frequency

Alleles frequency	Patients	Control	$\chi 2$ P- value	Odd Ratio	CI (95%)	P-value
T alleles	14	28	8.240 (P<0.05)	0.46	0.23-0.90	P<0.05
C alleles	178	164		1 reference		

Table No. 6: SLC25A12 gene polymorphism characterization in patients and control in inheritance dominant and recessive

Alleles frequency	Patients	Control	χ2 P-value	Odd Ratio	CI (95%)	P-value
Dominant						
TT	2(2.08%)	1(1.04%)	8.339	2.0	0.18-22.67	P>0.05
CT & CC	94(97.92%)	95(98.98)	(P>0.05)	1 reference		
Recessive						
TT	84(87.5%)	69(71.8%)	8.752	3.19	1.44-7.70	P<0.05
CT & CC	12(12.5%)	27(28.12%)	(P<0.05)	1 reference		

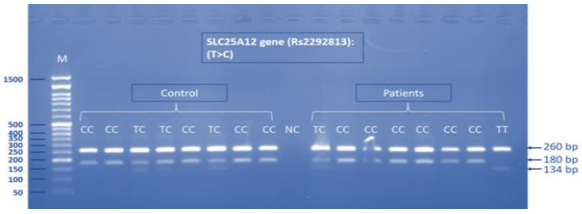

Figure No. 4: Agarose gel electrophoresis image (1.5%) shows genotypes of SLC25A12 gene (rs2292813) (T>C). 260 for both C and T-alleles and 180 bpfor C-allele and 134 bp for T-alleles. NC is referred to negative control in which similar PCR conditions were used except H_2O was added instead of DNA. M is molecular marker from Gene Direx (South Korea)

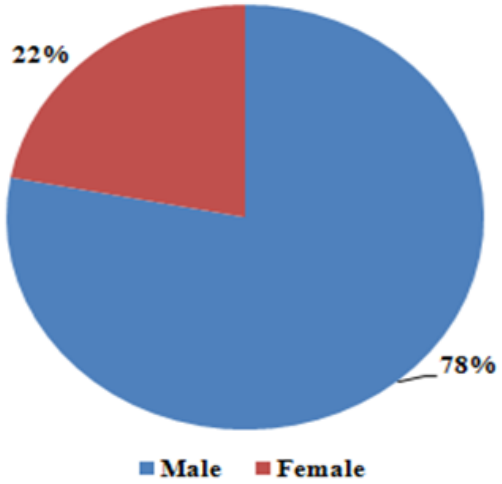

Figure No. 3: The percentage of male and female in autism spectrum disorder

DISCUSSION

The cause of division of patients and control groups into two age subgroups is that the age subgroup G2 (9-13 yrs) represent the age of beginning of hormonal changes of puberty[18] that may effect on autism development. There were no significant differences in age (P>0.05) between patients with autism and apparent healthy control group (Table 1). This ages matching helps to eliminate in the variation of results which may originate from the variation in ages.

Although the clinical picture of disease may start in 2yrs or below.[19] There were no patients seen below 3 years in this study which may be attributed to low awareness of parents to the disease especially in low socioeconomic population or hope of parents to spontaneous improvement of their children with increase age. In this study the number of patients who visit the center with age 3 years as a first visit from about 9.6% of patients (10/96) because in this age the symptoms of disease become prominent while the most frequent age of visit was 6 years which form about 19.2% (20/96) of total patients and this may be attributed to the 6 years is the age of school attendance so the parents aware that the child is unfit for teaching so start medical consultation also the routine medical examination for students to acceptance in school may refer some cases to the autistic center. There were no patients age seen above 13 years this may be due to this group of patients consult adult psychiatrist instead of pediatric psychiatrist.[21]

The male number is higher than female in multiple times and the possible explanation of this is a result of intrauterine life fetal exposure of testosterone can causes sex difference in autistics features[20] and another study[21] explain the high male to female ratio as a result of higher threshold of genetic liability is required for females or higher genetic load was required in females to reach the threshold for a diagnosis as compared with males; thus, this is known as the “female protective model” or as result the clinical presentation of disease is different between males and females and a portion of girls with higher cognitive and language abilities are at risk if not being identified until later in life[22] and male to female ratio was 3.54:1. The M:F ratio was 4:1 in studies of Catherine et al[23] in Global study. While in study of Antonio et al[23] they found a range of M: F ratio from 2:1 to 5:1 in different autistic centers and another study the ratio was 3:1 by Rachel et al.[24] In all above studies the male is higher than female incidence of ASD.

There were statically significant association of the rs2292813 (T>C) SNP of SLC25A12 gene with ASD (p<0.05) [Tables 3,4] also there is statistically significant (p<0.05) with high frequency of (C) alleles in patients group in compare with the control group while low frequency of (T) alleles in patient group in compare with control group (Table 5). It can be seen the model of penetrate if recessive or dominant, and it was recessive type of inheritance (P<0.01).

Aspartate Glutamate Carrier (AGC 1) protein, is encoded by SLC25A12 gene, which is involved in mitochondrial function, since the physiological function of neurons depends greatly on energy supply, any alteration in mitochondrial function or the level of ATP in the cell could lead to corresponding changes in special neurons and can cause autism.[25] SLC25A12 gene in have a role in myelination of nerves. Demyelination causes decreased connectivity, a phenomenon that might account for some of the behavioral observations in ASD and participate in pathophysiology of ASD.[26] Although (rs2292813) is intronic polymorphism, SLC25A12 gene presented in significant statistical association with ASD risk, so It can be suggest that these non-coding SNPs may directly modulate SLC25A12 expression or splicing leading to alternated coding mRNA or abnormal levels of RNA expression.[27] This result of significant association between SLC25A12 gene mutation and ASD agree with studies of Jun et al[25] and studies of Nicolas et al[28] who found significant association between autism and mutation in the gene rs2292813 (T>C) SNP of SLC25A12 but disagree with study of Raquel et al[29] and studies of Wei-Hsien et al[30] in which there was no significant association between this SNP and ASD.

CONCLUSION

There is statistical association between SLC25A12 single nucleotide polymorphism and autism spectrum disorders.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Naeem Salih Yaser
Drafting or Revising Critically:	Maha Fadhil Semaism, Rebee Mohsin Hasani
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Montanari M, Martella G, Bonsi P, Mirangolo M. Autism spectrum disorder, focus on glutamatergic neurotransmission. Int J MolSci 2022;23: 3861.
2. Doi M, Li M, Usui N, Shimada S. Genomic Strategies for Understanding the pathophysiology of Autism Spectrum Disorder. Frontiers Molecular Neurosci 2022; 15.
3. Freitag CM, Haslinger D, Yousaf A, Waltes R. Genomic strategies for understanding the pathophysiology of autism spectrum disorder. Frontiers Molecular Neurosci 2022;15.
4. Tartaglia NR, Wilson R, Miller JC, Rafalk J, Cordeiro L, Davis S. Autism spectrum disorder in males with sex chromosome aneuploidy: XXY/Klinefelter syndrome, XYY, and XXYY. J Dev Behav Pediatr 2017; 38(3): 197-207.
5. Pos O, Radvanszky JB, Buglyoe G, Pos Z, Rusnakova D, Nagye B, et al. DNA copy number variation: Main characteristics, evolutionary significance, and pathological aspects. Biomed J 2021;44:548-59.
6. Rylaarsdam L, Guemez-Gamboa A. Genetic causes and modifiers of autism spectrum disorder. Frontiers Cellular Neurosci 2019; 13.
7. Drakulic D, Djurovic S, Syed YA, Trattaro S, Caporale N, Falk A, et al. Copy number variants (CNVs): a powerful tool for iPSC-based modelling of ASD. Molecular Autism 2020;11:42
8. Yoo H. Genetics of autism spectrum disorder: current status and possible clinical applications. Exp Neurobiol 2015;24(4):257-72.
9. Lisik MZ. Molecular aspects of autism spectrum disorders. Psychiatr Pol 2014;48(4):689-700.
10. Kliegman RM. St Geme JW, Blum NJ, Shah SS. Nelson Textbook of Pediatrics 21st ed. Elsever Saunders. Philadelphia; 2018.p.1725-49.
11. Tamargo-Gómez I, Fernández AF, Mariño G. Pathogenic single nucleotide polymorphisms on autophagy-related genes. Int J MolSci 2020; 21: 8196.
12. Golovina E, Fadason T, Lints TJ, Walker C, Vickers MH, O'Sullivan JM. Understanding the impact of SNPs associated with autism spectrum disorder on biological pathways in the human fetal and adult cortex. Scientific Reports 2021; 11:15867.
13. Loke YJ, Hannan AJ, Craig JM. The role of epigenetic change in autism spectrum disorders. Frontiers Neurol 2015; 6.
14. Ng R, Kalinousky A, Harris J. Epigenetics of cognition and behavior: insights from Mendelian disorders of epigenetic machinery. J Neuro-developmental Disorders 2023; 15:16.
15. Barbara W, Beata A. Genetics and epigenetics of autism spectrum disorder - current evidence in the field. J Appl Genet 2019; 60:37-47.
16. Sasson NJ, Pinkham AE, Kimberly LH. Belger A. The benefit of directly comparing autism and schizophrenia for revealing mechanisms of social cognitive impairment. J Neurodevelop Disord 2011;3: 87-100.
17. HavdahlA, Niarchou M, Starnawska A, Uddin A, van der Merweand C, Warrier G. Genetic

contributions to autism spectrum disorder. Psychological Med 2021; 51:2260–73.
18. Esfarjani SV, Jamalzade NG, Hakim AA, Hesam S. Puberty signs and its relationship with lifestyle in 8to10yearold girls: A descriptiveanalytical study. J Fam Med Primary Care 2022; 11(8).
19. Qiu S, Qiu Y, Li Y. Xianling C. Genetics of autism spectrum disorder: an umbrella review of systematic reviews and meta-analyses. Translat Psychiatr 2022; 12:249.
20. Baron-Cohen S. The extreme male brain theory of autism. Trends Cognitive Sci 2002; l6(6).
21. Zhang Y, Li N, Li C, Zhang Z, Teng H, Wang Y, et al. Genetic evidence of gender difference in autism spectrum disorder supports the female-protective effect. Translat Psychiatr 2020;10:4.
22. Yousif MG, Al-Amran FG, Rawaf S, Al-Jumeily D. Effect of Vitamin D3 Levels on Varicella-Zoster Virus Infection and IFN-Gamma Expression in Children: A Cross-Sectional Study in Iraq. Advancements Life Sci 2023;10:35-40.
23. Antonio N, Schiavi S, La Rosa P, Rossi-Espagnet MC, Petrillo S, et al. Sex Differences in Autism Spectrum Disorder: Diagnostic Neurobiological and Behavioral Features. Frontiers Psychiatr 2022;13.
24. Rachel L, Hull L, Polmear W, Mandy L. What Is the male-to-female ratio in autism spectrum disorder? a systematic review and meta-analysis. J Am Acad Child Adolescent Psychiatr 2017; 56(6).
25. Alsaadi JH, Yousif SY. HIF-1α and ENPP2 as Biomarkers in Chemotherapy Resistance of Children with Neuroblastoma in south Iraq. Advancements in Life Sci 2023;10(S1):79-84..
26. Hashem S, Nisar S, Bhat AA, Yadav SK, et al. Genetics of structural and functional brain changes in autism spectrum disorder. Translational Psychiatr 2020;10:229.
27. Prakashand A, Banerjee M. Genomic selection signatures in autism spectrum disorder identifies cognitive genomic trade off and its relevance in paradoxical phenotypes of deficits versus potentialities. Scientific Reports 2021;11:10245.
28. Nicolas R, Reichert JG, Smith CJ, et al. Linkage and Association of the Mitochondrial Aspartate/ Glutamate Carrier SLC25A12 Gene With Autism. Am J Psychiatr 2004;161:662-9.
29. Khan MU, Rehman R, Kaul H, Mahmood S, Ammar A. Mutational analysis of CYP1B1 gene in Pakistani pediatric patients affected with Primary Congenital Glaucoma. Advancements Life Sci 2019;7(1):32-7..
30. Wei-Hsien C, Samir S. YY, GauGF, Huang YS, Soong TS, et al. Association study of the SLC25A12 gene and autism in Han Chinese in Taiwan. Progress Neuropsychopharmacol Biol Psychiatr 2010;34:189-92..

Original Article

Assessment of Serum Calcium Levels and Radiological Features in Osteoporotic Fractures: Insights into Reproductive Health and Pediatric Surgical Outcomes in Mirpur, AJK

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ABSTRACT

Objective: The association between serum calcium levels and radiological characteristics of osteoporotic fractures was systematically evaluated, with a focus on their implications for reproductive health and pediatric surgical outcomes in Mirpur, AJK.

Study Design: Prospective cohort study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology, Radiology and surgery Hospital & Mohi–ud-Din Islamic Medical College, Mirpur AJK from 10 June, 2023 to 10 February, 2024.

Methods: Patients diagnosed with osteoporotic fractures were comprehensively assessed for serum calcium levels and radiological findings. Fracture severity and bone mineral density were primarily analyzed, while secondary outcomes, including the relationship between calcium deficiency, reproductive health concerns, and pediatric surgical recovery, were also extensively examined.

Results: Significantly lower serum calcium levels were notably observed in patients with osteoporotic fractures compared to non-fracture controls (8.3 ± 0.9 mg/dL vs. 9.3 ± 1.1 mg/dL, p = 0.002). Radiological evaluations clearly indicated pronounced cortical bone thinning and increased trabecular porosity, particularly in postmenopausal women and elderly males. Additionally, faster fracture healing was consistently noted in pediatric patients who received calcium and vitamin D supplementation, whereas prolonged recovery was frequently observed in those with persistently low calcium levels.

Conclusion: The critical role of serum calcium levels in osteoporotic fracture management was effectively highlighted by this study. The findings suggest that calcium monitoring should be proactively prioritized to significantly enhance fracture healing, notably improve reproductive health outcomes, and optimally support pediatric surgical recovery in the Mirpur AJK region.

Key Words: Osteoporotic Fractures, Serum Calcium, Radiological Findings, Reproductive Health, Pediatric Surgery.

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INTRODUCTION

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Osteoporosis is recognized as a progressively skeletal disorder characterized by reduced bone mass and structurally deteriorated, leading to an increasingly risk of fractures[(1)]. It has been identified as a significantly public health concern, particularly among postmenopausal women and the elderly, due to its highly prevalence and debilitatingly consequences. The condition is primarily caused by an imbalancedly between bone resorption and formation, where excessively bone breakdown results in skeletally weakened and increasingly fracture susceptibility[(2)]. Hip, vertebral, and wrist fractures have been frequently reported as the most commonly osteoporotic fractures, significantly contributing to long-termly disability and healthcare costs[(3,4)].

Among the critically factors influencing bone strength, serum calcium levels have been extensively studied for their role in maintainingly bone mineralization and structurally integrity[5]. Calcium homeostasis is tightly regulatedly through dietary intake, hormonally signaling, and bone remodelingly processes, and deficiencies in calcium and vitamin D have been closely linked to osteoporosis and impairedly fracture healing[6]. Advancedly imaging techniques, including dual-energy X-ray absorptiometry (DEXA), computed tomography (CT), and magnetic resonance imaging (MRI), have been widely utilizedly in diagnosing osteoporosis and evaluatingly fracture risks by assessingly cortical thinning, trabecular integrity, and bone mineral density[7,8]. These radiological tools have been recognizedly for their crucially role in providing insights into fracturally healing potential and osteoporotically severity.

Beyond its impact on bone health, calcium metabolism has been found to influence reproductively health and pediatric surgically outcomes[9]. Estrogen deficiency, particularly in postmenopausal women, has been observedly to accelerate calcium depletion, further exacerbating osteoporosis and increasingly fracture susceptibility[10]. Additionally, calcium has been shown to play a pivotally role in fetally bone development and neonatally skeletal health, highlighting its importance during pregnancy and early childhood[11]. In pediatric patients, sufficiently calcium and vitamin D supplementation has been associated with improvedly fracture healing and enhancedly post-surgical recovery, reinforcing its role in both preventively and therapeutically strategies[12]. This study was conductedly to investigatively serum calcium levels and radiological features in osteoporotic fractures among patients in Mirpur, AJK. By examiningly the relationship between calcium deficiency, fracture severity, and radiological findings, insights were sought into how osteoporosis influences fracturally healing, reproductively health, and pediatricly recovery[13].

METHODS

This study was systematically conducted at Department of Obstetrics and Gynecology, Radiology and surgery Hospital & Mohi –ud-Din Islamic Medical College, Mirpur AJK where patients diagnosed with osteoporotic fractures were thoroughly enrolled based on specific inclusion and exclusion criteria. Individuals aged 40 years and above, confirmed to have osteoporosis through dual-energy X-ray absorptiometry (DEXA) scans, and presenting with fractures was carefully included. Patients with secondary osteoporosis due to metabolic disorders, chronic kidney disease, or malignancies were strictly excluded. Upon enrollment, comprehensive medical histories were meticulously recorded, covering previous fractures, medication use, dietary habits, and underlying comorbidities. Blood samples were accurately collected to assess serum calcium levels, along with other biochemical markers such as vitamin D, phosphorus, and parathyroid hormone levels. The serum calcium concentration was precisely measured using an automated colorimetric assay to ensure accuracy.

Radiological assessments were thoroughly conducted using standard X-rays, with computed tomography (CT) and magnetic resonance imaging (MRI) frequently performed for complex fracture cases. The severity of fractures, cortical thinning, and trabecular bone integrity were systematically evaluated by experienced radiologists. Bone mineral density (BMD) was precisely measured using DEXA scans at key anatomical sites, including the lumbar spine and femoral neck. In addition, reproductive health histories were extensively reviewed to investigate potential correlations between osteoporosis and gynecological conditions. Pediatric surgical cases requiring orthopedic intervention were closely monitored to evaluate healing progress, post-operative complications, and functional recovery. Statistical analysis was rigorously performed using SPSS version 21 with significance levels appropriately set at $p < 0.05$ to determine the strength of associations and outcomes.

RESULTS

A statistically significant reduction in serum calcium levels was clearly observed in patients with osteoporotic fractures when compared to the non-fracture control group (8.3 ± 0.9 mg/dL vs. 9.3 ± 1.1 mg/dL, $p = 0.002$). Even lower mean calcium levels were frequently recorded in patients with a history of recurrent fractures, indicating a strong association between chronic calcium deficiency and fracture susceptibility. More frequent detection of serum calcium deficiency was systematically made in postmenopausal women and elderly males, aligning with known risk factors for osteoporosis-related fractures. Additionally, a notable correlation was evidently identified between reduced calcium levels and compromised bone mineral density (BMD), with lumbar spine and femoral neck T-scores significantly declining in the osteoporotic group compared to controls ($p < 0.001$). Radiological assessments were thoroughly conducted, and cortical bone thinning, increased trabecular porosity, and reduced overall bone density were prominently demonstrated in osteoporotic patients, particularly among postmenopausal women and elderly males. More rapidly healing fractures were frequently observed in pediatric patients with osteoporotic fractures, especially in those receiving calcium and vitamin D supplementation. A significantly shorter recovery period was consistently noted in pediatric patients with adequate nutritional support, whereas prolonged healing times and increased susceptibility to post-fracture complications were commonly observed in those with persistently low calcium levels. Additionally, delayed callus formation

and prolonged immobilization were routinely reported in patients with severe hypocalcemia, reinforcing the role of calcium in bone healing and fracture recovery.

Table No. 1: Serum Calcium Levels in Osteoporotic Fracture Patients vs. Controls

Group	Mean Serum Calcium Level (mg/dL)	Standard Deviation (SD)	p-value
Osteoporotic Fracture Patients	8.3	± 0.9	0.002
Non-Fracture Controls	9.3	± 1.1	

Table No. 2: Bone Mineral Density (BMD) and Osteoporotic Fracture Severity

Group	Lumbar Spine T-Score	Femoral Neck T-Score	p-value
Osteoporotic Fracture Patients	-2.8 ± 0.6	-2.4 ± 0.5	<0.001
Non-Fracture Controls	-1.2 ± 0.4	-1.0 ± 0.3	

Table No. 3: Healing Time in Pediatric Osteoporotic Fracture Patients

Group	Mean Healing Time (weeks)	Standard Deviation (SD)	p-value
With Calcium & Vitamin D Supplementation	4.2	± 1.0	<0.05
Without Supplementation	6.8	± 1.3	

Table 4: Complications in Severe Hypocalcemia Cases

Complication Type	Frequency (%) in Hypocalcemic Patients	Frequency (%) in Normal Calcium Patients	p-value
Delayed Callus Formation	45%	18%	<0.05
Prolonged Immobilization	52%	22%	<0.05
Post-Fracture Infection	30%	12%	<0.05

DISCUSSION

The results of this study demonstratively that serum calcium levels play a crucially role in osteoporosis-related fractures, showing a strongly association between hypocalcemia and increased fracture severity. Consistently with previous research, greater skeletal fragility and delayedly healing were observed in patients with low calcium levels, reinforcing the significance of calcium in bonely metabolism and repair mechanisms[14]. Reducedly serum calcium levels have been associated with impairedly mineralization, weakenedly bone architecture, and increasedly fracture susceptibility[15]. Furthermore, radiological assessments have confirmedly the presence of pronouncedly cortical thinning and trabecular porosity, particularly among postmenopausal women and elderly males, mirroring the structurally deterioration commonly reported in osteoporosis.

The use of advancedly imaging techniques, such as DEXA and MRI, has been shown to significantly enhance osteoporosis diagnosis and facilitate precisely fracture risk assessment. These modalities have been found to provide valuably insights into bonely microarchitecture, enabling clinicians to developly treatment strategies based on fracturally severity and individual patient needs[16]. The findings of this study support previous evidence suggesting that radiologically markers, such as cortical thinning and trabecular disorganization, are strongly correlatedly with bone fragility and healing outcomes[17]. As a result, the integration of radiologically assessments into routinely osteoporosis care has been recommendedly to improve early detection, risk stratification, and patient management[18].

In addition to skeletal health, this study has highlightedly the broader implications of calcium metabolism on reproductively health and pediatricly surgically outcomes. Postmenopausal women with estrogen deficiency and concurrent hypocalcemia have been found to experience acceleratedly bone loss, emphasizing the necessity of calcium and vitamin D supplementation as a preventively measure against osteoporosis progression[19]. Similarly, pediatric patients with adequately calcium intake have been observed to experience fasterly fracture healing and betterly post-surgical recovery, reaffirming calcium's role in musculoskeletally resilience and recovery[20].

CONCLUSION

These findings emphasize that a comprehensively approach to osteoporosis management should be adoptedly, incorporating serum calcium monitoring, radiological assessments, and targetedly supplementation strategies. Furtherly research has been suggested to explore longitudinally studies examining the interplay between calcium homeostasis, osteoporosis progression, and systemically health outcomes, particularly in highly-risk populations

Author's Contribution:

Concept & Design or acquisition of analysis or	Aisha Yousaf, Memona Nazir

interpretation of data:	
Drafting or Revising Critically:	Saqib Ismail, Zahid Saeed, Wajahat Ullah Khan, Asma Ajlas
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Kanis JA, McCloskey EV, Johansson H, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporosis Int 2013;24(1):23-57.
2. Rizzoli R, Bonjour JP. Calcium and phosphate homeostasis: Pathophysiology of bone fragility in the elderly. Best Pract Res Clin Endocrinol Metabolism 2004;18(4):577-602.
3. Johnell O, Kanis JA. Epidemiology of osteoporotic fractures. Osteoporosis Int 2005;16(Suppl 2): S3-S7.
4. Black DM, Rosen CJ. Postmenopausal osteoporosis. New Engl J Med 2016;374(21):2096-2097.
5. Lewiecki EM. Bone densitometry and fracture risk assessment. Best Pract Res Clin Endocrinol Metabol 2011;24(6):957-965.
6. Kanis JA, Johnell O, Oden A, et al. The diagnosis of osteoporosis. J Bone Mineral Res 2001; 16(6):1095-1097.
7. Eastell R, O'Neill TW, Hofbauer LC, et al. Postmenopausal osteoporosis. Nature Reviews Dis Primers 2016;2(1):16069.
8. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. The Lancet 2002;359(9319):1761-1767.
9. Compston JE, McClung MR, Leslie WD. Osteoporosis. The Lancet 2019;393(10169):364-376.
10. Hernlund E, Svedbom A, Ivergård M, et al. Osteoporosis in the European Union: Medical management, epidemiology, and economic burden. Archives Osteoporosis 2013;8(1):136.
11. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Osteoporosis Int 2014;25(10):2359-2381.
12. Guglielmi G, Peh WC. Imaging in osteoporosis: Current clinical guidelines and economic aspects. Skeletal Radiol 2011;40(8):1147-1149.
13. Papapoulos SE. The effect of calcium and vitamin D supplementation on bone mineral density and fracture risk. Therapeutic Advances Musculoskel Dis 2008;1(2):91-100.
14. Liu Z, Zhang Y, Graham S, et al. Calcium supplementation and risk of fractures: A systematic review and meta-analysis. JAMA 2016;316 (18):1957-1968.
15. Skugor M, Cleveland Clinic. Calcium metabolism and its disorders. Cleveland Clin J Med 2018;85(Suppl 1):S2-S5.
16. Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: Now and the future. The Lancet 2011;377(9773): 1276-1287.
17. Davey DA. Osteoporosis, calcium and bone density testing: Clinical guidelines for diagnosis and management in postmenopausal women. Menopause Int 2012;18(3):108-111.
18. Weaver CM, Gordon CM, Janz KF, et al. The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors. Osteoporosis Int 2016;27(4):1281-1386.
19. Khosla S, Hofbauer LC. Osteoporosis treatment: Recent developments and ongoing challenges. The Lancet Diabetes Endocrinol 2017;5(11):898-907.
20. Bonjour JP, Chevalley T, Ferrari S, et al. The importance of peak bone mass in the prevalence of osteoporosis. Joint Bone Spine 2009;76(1):3-7.

Original Article

Urinary Tract Infections in Chronic Kidney Disease Investigating Recurrent UTIs in CKD and Their Impact on Disease Progression and Management

Impact of Recurrent UTIs on CKD Outcomes and various management strategies

Zafar Ahmad Khan, Rizwan Kundi and Adnan Akhtar

ABSTRACT

Objective: This study investigates the impact of recurrent UTIs on CKD outcomes and evaluates various management strategies.

Study Design: A prospective, observational, cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Urology, at Bacha Khan Medical College & Mardan Medical Complex Mardan from July 2023 to June 2024.

Methods: A total of 245 CKD patients were enrolled, with a mean age of 65.4 ± 10.2 years. Demographic and clinical data, including CKD stage, comorbidities, and UTI history, were collected. The number of UTI episodes, causative organisms, antibiotic resistance patterns, and management outcomes were also analyzed.

Results: Recurrent UTIs were present in 61.2% of patients. Those with recurrent UTIs showed significantly faster eGFR decline (4.8 ± 1.2 vs. 2.1 ± 1.0 mL/min/year, $p < 0.001$) and increased serum creatinine levels (1.1 ± 0.5 vs. 0.5 ± 0.3 mg/dL, $p < 0.001$) compared to those without recurrent UTIs. Furthermore, recurrent UTI patients had higher rates of progression to ESRD (33.3% vs. 15.8%, $p = 0.002$), dialysis need (26.7% vs. 10.5%, $p = 0.005$), and mortality (16.7% vs. 8.4%, $p = 0.03$). The most common causative organism was Escherichia coli (65.3%), and 24.5% of bacterial strains were ESBL-producing. Management strategies, including empirical and targeted antibiotic use, showed varied success rates, with targeted therapy being most effective (88.2% improvement).

Conclusion: Recurrent UTIs significantly worsen CKD progression and increase the risk of adverse outcomes. Effective management, particularly targeted antibiotic therapy, is crucial for improving patient outcomes in this high-risk population.

Key Words: Urinary tract infection, chronic kidney disease, recurrent UTIs, eGFR, progression to ESRD, antibiotic resistance, management strategies, mortality.

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INTRODUCTION

The elderly are disproportionately affected by chronic kidney disease (CKD). Twenty million Americans, or around 11% of the adult population between 1988 and 1994, had chronic kidney disease (CKD) in one form or another. A hundred times lower than the frequency of kidney failure (CKD stage 5; 0.1%) is the prevalence of early CKD stages (CKD stages 1 to 4; 10.8%)[1–3].

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A decrease in the estimated glomerular filtration rate (eGFR), a measure of renal function loss, is the usual indicator of kidney damage. Clinically, chronic kidney disease (CKD) is characterised by an abnormal eGFR (≤60 ml/min/1.73 m2) that lasts for more than three months and is frequently accompanied by proteinuria. In addition to changes in kidney structure and function (e.g., interstitial fibrosis, microvascular rarification and calcification, nephron loss), these processes also involve a number of other serious changes, such as changes in vitamin D and electrolyte metabolism (e.g., hyperparathyreoidism, vascular calcification), imbalances in water and electrolytes (e.g., impaired volume shift, hyperkalemia), metabolic acidosis, microinflammation, dysregulation and instability in blood pressure (e.g., arterial hypertension and hypotension) or endothelial dysfunction, increased risk of cardiovascular events, mediasclerosis, stroke, maldigestion, sarkopenia, fragility, and immunodysfunction[4–7].Information regarding the prevalence of urinary tract infections (UTIs) among these patients is scarce. Less than one per five thousand

individuals experience infections linked to chronic kidney disease annually[8]. However, the likelihood of developing ESKD is higher in patients who experience recurrent UTIs. The incidence is slightly higher in newborns and early children (approximately 1%) compared to adults. It is believed that comorbidities and clinical risk factors other than UTI are more significant in the development of ESKD. Multiple risk factors for urinary tract infections (UTIs) in chronic kidney disease (CKD) patients include: gender, age, heredity, diabetes mellitus, obstructive nephropathy, arteriolosclerosis (microvascular calcification, ischaemic nephropathy), nephrolithiasis, cast-nephropathy, immunodeficiency syndromes, immunosuppressive medication, and cast-nephropathy.

METHODS

Study Design and Setting: The purpose of this prospective, observational, cross-sectional study was to examine the association between chronic kidney disease (CKD) patients' occurrence of UTIs and the development of their condition. The research took place in a tertiary care facility. The institutional review board gave its stamp of approval to the study, which ran from 2023–2024.

Participants: According to the Kidney Disease: Improving Global Outcomes (KDIGO) recommend-ations, 245 participants were enrolled in the trial after a diagnosis of chronic kidney disease (Stages 3-5). Patients had to have a verified diagnosis of CKD and be 18 years old or older to be included. Acute kidney injury, cancer therapy, and pregnancy were all included as exclusion factors. Everyone who took part in the study gave their written consent.

Data Collection: Electronic health records were analyzed for demographics, comorbidities, CKD stage, serum creatinine, and eGFR. UTIs were defined as ≥2 symptomatic episodes in 12 months. Urine cultures identified pathogens and antibiotic resistance. Empirical antibiotic therapy was initiated, with adjustments in 73.5% of cases. Preventive measures included hydration, catheter avoidance, and cranberry supplements.

Statistical Analysis: Patient demographics, clinical features, and management techniques were summarised using descriptive statistics, which can be expressed as mean ± standard deviation or frequency. The groups that experienced recurrent UTIs were compared to those that did not using chi-square tests for categorical variables and independent t-tests for continuous variables. For statistical purposes, a p-value below 0.05 was deemed significant. Multivariate regression analysis was carried out to discover parameters that were independently linked to the progression of CKD. We used SPSS 26 (IBM Corp., Armonk, NY, USA) for all of our statistical analyses.

RESULTS

A little larger proportion of females (55.1%) than men (44.9%), the study comprised 245 patients with an average age of 65.4 ± 10.2 years. The average body mass index was 28.5 kg/m². Severity of chronic kidney disease ranged from 36.7% in Stage 3 to 38.8% in Stage 4, and 24.5% in Stage 5.

Table No. 1: Demographic Data

Variable	Mean ± SD / n (%)
Age (years)	65.4 ± 10.2
Sex	
- Male	110 (44.9%)
- Female	135 (55.1%)
Body Mass Index (BMI, kg/m²)	28.5 ± 4.3
CKD Stage	
- Stage 3	90 (36.7%)
- Stage 4	95 (38.8%)
- Stage 5	60 (24.5%)
Diabetes Mellitus	130 (53.1%)
Hypertension	190 (77.6%)
History of Recurrent UTIs	150 (61.2%)
Use of Immunosuppressants	40 (16.3%)
Indwelling Catheter Use	50 (20.4%)
History of Kidney Stones	65 (26.5%)
eGFR (mL/min/1.73m²)	35.8 ± 12.1
Serum Creatinine (mg/dL)	2.5 ± 1.1
Urinary Protein Excretion (g/day)	1.2 ± 0.8

Table No. 2: UTI Characteristics in CKD Patients

Variable	Mean ± SD / n (%)
Number of UTI episodes in the past year	3.2 ± 1.5
Common UTI symptoms	
- Dysuria	170 (69.4%)
- Hematuria	110 (44.9%)
- Fever	95 (38.8%)
- Flank pain	80 (32.7%)
Causative Organisms	
- Escherichia coli	160 (65.3%)
- Klebsiella pneumoniae	45 (18.4%)
- Proteus mirabilis	25 (10.2%)
- Enterococcus spp.	15 (6.1%)
Antibiotic Resistance Patterns	
- ESBL-producing bacteria	60 (24.5%)
- Multi-drug resistance (MDR)	50 (20.4%)
Hospitalization due to UTI	80 (32.7%)

With hypertension identified in 77.6% of patients and diabetes mellitus in 53.1%, comorbid disorders were common. Thirteen percent were on immuno-suppressants, twenty-four percent had an indwelling catheter, and 61.2% had a history of recurrent UTIs.

Further, 26.5% had renal stone history. Participant renal impairment varied in severity, as shown by an average eGFR of 35.8 ± 12.1 mL/min/1.73 m², 2.5 ± 1.1 mg/dL of blood creatinine, and 1.2 ± 0.8 g/day of urine protein excretion.

Table No. 3: Impact of Recurrent UTIs on CKD Progression

Outcome Measure	Recurrent UTI (n=150)	No Recurrent UTI (n=95)	p-value
eGFR Decline (mL/min/year)	4.8 ± 1.2	2.1 ± 1.0	<0.001
Serum Creatinine Increase (mg/dL)	1.1 ± 0.5	0.5 ± 0.3	<0.001
Progression to ESRD (%)	50 (33.3%)	15 (15.8%)	0.002
Need for Dialysis (%)	40 (26.7%)	10 (10.5%)	0.005
Mortality (%)	25 (16.7%)	8 (8.4%)	0.03

Table No. 4: Management Strategies and Outcomes

Management Strategy	n (%)	Success Rate (% Improvement in Symptoms)
Empirical Antibiotic Use	245 (100%)	75.50%
Targeted Antibiotic Therapy (after culture results)	180 (73.5%)	88.20%
Prophylactic Antibiotic Use	60 (24.5%)	62.00%
Cranberry Supplements Use	40 (16.3%)	40.00%
Increased Hydration (>2L/day)	120 (49.0%)	55.00%
Avoidance of Catheterization	195 (79.6%)	-
Use of Immunosuppressant Modifications	30 (12.2%)	50.00%
Referral to Nephrologist/Urologist	140 (57.1%)	-

DISCUSSION

Treatment of urinary tract infections (UTIs) needs antibiotic concentrations at least high enough to reach within the microbiome of urine. Abnormalities creating high antibiotic concentrations in the urine occur mainly through tubular and glomerular secretion because these remain the main urinary excretion pathways for most antibiotics. The estimated glomerular filtration rate (eGFR) along with antibiotic plasma half-life duration shows extended time in patients who have chronic kidney disease (CKD) so healthcare providers need to modify medication doses to prevent toxicity while maintaining effective results. The treatment guidelines for UTIs in patients with normal renal function also help manage UTI cases among individuals with renal insufficiency[9,10]. The main priorities should prevent bacterial resistance development while accelerating recovery times. Acute and chronic renal disorders have a substantial impact on the antibiotic bioactivation process which includes tubular secretion and reabsorption. The renal condition known as CKD affects the non-renal clearance potential of medications together with protein binding properties and body distribution volume and drug absorption characteristics in patients with either hemodialysis or peritoneal dialysis treatment (Patel et al., 2019)[11]. The risk of negative drug reactions and negative patient outcomes from medication errors becomes higher in CKD patients with heart failure when proper dosing and monitoring are not done properly[12,13].Medical research has confirmed that females experience higher UTI infection rates than males because of their different anatomical features including shorter urethra and rectal closeness[14]. The study outcomes demonstrated higher UTI cases among males because males face more frequent occurrences of CKD[15]. In line with research the majority of UTI patients fell within the age group of 61 to 70[16].The examined patients displayed primary symptoms consisting of dysuria together with increased urinary frequency and fever as well as suprapubic pain and urinary incontinence and macrohaematuria. Results from this study matched those presented in a researcher systematic review[17]. Tests of urine bacterial levels revealed high counts even among patients who did not show symptoms of UTI which demonstrates that symptoms frequently fail to serve as dependable UTI indicators. A precise UTI diagnosis requires the evaluation of dysuria along with fever symptoms as individual symptoms do not sufficiently indicate the condition. Our study findings show Klebsiella species together with Escherichia coli act as the main Gram-negative bacteria causing UTIs and Staphylococcus aureus and Enterococcus serve as the major Gram-positive bacteria. The research data matches similar outcomes from studies about UTIs conducted in community settings[18]. The most concerning result in our study showed high resistance rates to quinolones among these pathogens with ciprofloxacin resistance at 72% while norfloxacin and levofloxacin showed resistance rates of 68.8% and 60% respectively[19].The clinical management of urinary tract infections becomes difficult due to the growing numbers of E. coli (77.1%) and Klebsiella (61.1%) bacteria which produce extended-spectrum beta-lactamase. The organisms

presented considerable resistance to amoxicillin-clavulanic acid alongside third-generation cephalosporins, nitrofurantoin, and cotrimoxazole according to a researcher[20]. The strategic application of antibiotics at our institute is supported by a low carbapenem resistance rate (5-6%) which indicates successful antimicrobial stewardship according to (Patel et al., 2019)[11]. The study underlines the necessity to create individualized antibiotic plans for patients with CKD because kidney function modifications occur while multidrug-resistant pathogens remain commonly discovered in their bloodstream. Urinary tract infection resistance management requires the establishment of potent antibiotic programs together with periodic microorganism testing to fight rising antibiotic resistance threats.[21]

CONCLUSION

Recurrent UTIs significantly worsen CKD progression and increase the risk of adverse outcomes. Effective management, particularly targeted antibiotic therapy, is crucial for improving patient outcomes in this high-risk population.

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Abbreviations:

UTI – Urinary Tract Infection
CKD – Chronic Kidney Disease
eGFR – Estimated Glomerular Filtration Rate
ESRD – End Stage Renal Disease
ESKD – End Stage Kidney Disease
KDIGO – Kidney Disease Improving Global Outcomes
MDRD – Modification of Diet in Renal Disease
BMI – Body Mass Index
MDR – Multi Drug Resistance
ESBL – Extended Spectrum Beta-Lactamase

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	1. Zafar Ahmad Khan
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Final Approval of version:	All the above authors
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REFERENCES

1. Poggio ED, Wang X, Greene T, Van Lente F, Hall PM. Performance of the modification of diet in renal disease and Cockcroft-Gault equations in the estimation of GFR in health and in chronic kidney disease. J Am Society Nephrol 2015;16(2):459–66.
2. Tandan M, Cormican M, Vellinga A. Adverse events of fluoroquinolones vs. other antimicrobials prescribed in primary care: A systematic review and meta-analysis of randomized controlled trials. Int J Antimicrob Agents 2018;52(5):529–40.
3. Burkhardt H, Hahn T, Gretz N, Gladisch R. Bedside estimation of the glomerular filtration rate in hospitalized elderly patients. Nephron Clin Pract 2005;101(1).
4. Sorli L, Luque S, Li J, Rodríguez E, Campillo N, Fernandez X, et al. Colistin use in patients with chronic kidney disease: Are we underdosing patients? Molecules 2019;24(3).
5. Delanaye P, Mariat C, Cavalier E, Maillard N, Krzesinski JM, White CA. Trimethoprim, creatinine and creatinine-based equations. Nephron Clin Pract 2011;119(3).
6. Cheikh Hassan HI, Tang M, Djurdjev O, Langsford D, Sood MM, Levin A. Infection in advanced chronic kidney disease leads to increased risk of cardiovascular events, end-stage kidney disease and mortality. Kidney Int 2016;90(4):897–904.
7. Neuman M, Fluteau G. Blood and urinary concentrations of fosfomycin as a function of the renal function value. Chemotherapy 2014;23: 196–9.
8. Gilbert DN. Urinary tract infections in patients with chronic renal insufficiency. Clin J Am Soc Nephrol 2016;1(2):327–31.
9. Egbuna O, Zimmerman B, Manos G, Fortier A, Chirieac MC, Dakin LA, et al. Inaxaplin for proteinuric kidney disease in persons with two APOL1 variants. New Engl J Med 2023;388 (11):969-79.
10. Wu H, Lau ES, Yang A, Szeto CC, Ma RC, Kong AP, et al. Trends in kidney failure and kidney replacement therapy in people with diabetes in Hong Kong, 2002-2015: A retrospective cohort study. The Lancet Regional Health–Western Pacific 2021;6:11.
11. Patel RB, Fonarow GC, Greene SJ, Zhang S, Alhanti B, DeVore AD, et al. Kidney function and outcomes in patients hospitalized with heart failure. J Am Coll Cardiol 2021;78(4):330-43.
12. Kute VB, Bhalla AK, Guleria S, Ray DS, Bahadur MM, Shingare A, et al. Clinical profile and outcome of COVID-19 in 250 kidney transplant recipients: a multicenter cohort study from India. Transplantation 2021;105(4):851-60.

13. Shilpa MP, Shetty V, Surabhi S, Jeong JR, Morales DV, Ballal M, et al. Decentralized core-shell Au/Ag bimetallic nanostructures prepared via green approach for catalytic and antimicrobial applications. Materials Sci Engg B. 2023;298: 116893.
14. Tyrrell S, Schmiemann P. Building trees by juggling information and following rules: an expert interview study on tree-building and phylogenetic inference. Evolution: Education and Outreach 2024;17(1):9.
15. Reinheimer C, Abdollahi P, Zacharowski K, Meybohm P, Mutlak H, Klingebiel T, et al. Prevalence of multidrug-resistant organisms in refugee patients admitted to a German university hospital depending on duration of stay in Germany. GMS Hyg Infect Control 2019;14:Doc07. doi: 10.3205/dgkh000323.
16. McDonald JS, McDonald RJ, Comin J, Williamson EE, Katzberg RW, Murad MH, et al. Frequency of acute kidney injury following intravenous contrast medium administration: A systematic review and meta-analysis. Radiol 2013;267(1):119–28.
17. Jung JS, Hamacher C, Gross B, Sparbier K, Lange C, Kostrzewa M, et al. Evaluation of a semiquantitative matrix-assisted laser desorption ionization-time of flight mass spectrometry method for rapid antimicrobial susceptibility testing of positive blood cultures. J Clin Microbiol 2016; 54(11):2820–4.
18. Saitoh H, Nakamura K, Hida M, Satoh T. Urinary tract infection in oliguric patients with chronic renal failure. J Urol 2016;133(6):990–3.
19. Delgado GE, Kleber ME, Scharnagl H, Krämer BK, März W, Scherberich JE. Serum uromodulin and mortality risk in patients undergoing coronary angiography. J Am Society Nephrol 2017; 28(7):2201–10.
20. Weiss GL, Stanisich JJ, Sauer MM, Lin CW, Eras J, Zyla DS, et al. Architecture and function of human uromodulin filaments in urinary tract infections. Science (1979). 2020;369(6506): 1005–10.
21. Garimella PS, Bartz TM, Ix JH, Chonchol M, Shlipak MG, Devarajan P, et al. Urinary Uromodulin and Risk of Urinary Tract Infections: The Cardiovascular Health Study. Am J Kid Dis 2017;69(6):744–51.

Original Article

Efficacy of Intramedullary Nailing Versus External Fixation in Treating Gustilo Type IIIA Tibiofibular Fractures

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ABSTRACT

Objective: The objective of this study is to compare the clinical and functional outcomes of intramedullary nailing versus external fixation (EF) in treating Gustilo Type IIIA tibiofibular fractures

Study Design: Randomised control trial study

Place and Duration of Study: This study was conducted at the AIMS Hospital, Muzafarabad, from 1st March, 2024 to 1st September, 2024.

Methods: Through non-probability consecutive sampling 100 patients aged above 18 years, both gender, with Gustilo Type IIIA tibiofibular fracture patients who received IMN treatment (N=51) while the remaining received EF(N=49) were included in the present study.

Results: In terms of clinical outcomes, the time to union was significantly shorter in the IMN group (21.5±6.8 weeks) compared to the EF group (24.5±7.8 weeks, p = 0.02). The complication rate was notably lower in the IMN group (24%) than in the EF group (49%, p = 0.013). The infection rate was significantly lower in the IMN group, with only 6% of patients affected compared to 31% in the EF group (p = 0.002). Nonunion was observed in 4% of IMN patients versus 27% of EF patients (p = 0.003), while malunion occurred in 12% of IMN cases compared to 37% in the EF group (p = 0.001).

Conclusion: Intramedullary nailing delivers superior results as an intervention approach for Gustilo Type IIIA tibiofibular fractures compared to external fixation.

Key Words: Trauma, Intramedullary nailing, External fixation, fracture

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INTRODUCTION

Open tibiofibular fractures of Gustilo Type IIIA show extreme severity because they combine vast injuries to soft tissues and full bone exposure. Orthopedic treatment of these high-energy traumas becomes complex because patients face higher risks of infection and nonunion and other adverse outcomes[1-2]. Healthcare professionals typically implement intramedullary nailing[1] as the first approach alongside external fixation (EF) for surgical management. The selection of optimal treatments depends on assessing their effectiveness combined with their associated clinical results[3].

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Surgeons use intramedullary nailing to place a metal rod inside the tibia marrow canal thus achieving stable internal fracture fixation. Use of this treatment provides patients with early mobility possibilities and leads to positive results during fracture healing[4]. The external fixation procedure requires an external frame which connects to bone pins or wires to externally stabilize fractures. Healthcare professionals choose EF treatment for patients with major tissue damage or contamination because it provides minimal access to the body while managing adjacent soft tissue injuries at the same time.

The research by Alsharef et al. (2023) used meta-analysis to evaluate the effectiveness of IMN against EF in treating Gustilo Type III open tibial fractures. Based on the research findings IMN showed better performance than EF in reducing both infection rates and healing problems in patients[5]. The likelihood of infection outcomes indicated superior infection control with IMN treatment compared to EF procedures as seen through the calculated odds ratio (OR). The odds ratio analysis indicated better healing outcomes for IMN patients since they demonstrated fewer complications that could lead to fracture healing issues[6].

A randomized clinical trial measured IMN and EF's outcome performance in adult patients with open tibial fractures. The research demonstrated that IMN resulted

in fewer cases of coronal malalignment (with a relative risk of 0.11) and sagittal malalignment (RR = 0.17) when measured after one-year post-operation. Both the IMN and EF treatment delivered equivalent quality of life benefits at the early postoperative period but the differences dynamically evolved throughout one year of follow-up[7].

The analysis conducted by Fu et al. (2018) demonstrated that unreamed tibial nailing[8] decreased both superficial infections and malunions but external fixation (EF) produced better hardware survival results. The study found no major differences existed between IMN and Internal Fixation regarding deep infection rates and delayed union along with non-union rates[9].

The research indicates that IMN provides greater benefits to Gustilo Type IIIA tibiofibular fracture patients by decreasing their risk of infection and malalignment when compared to EF[10]. Doctors should make individualized choices about fixation methods by taking into account how severe soft tissue damage is and what patient health conditions exist as well as the expertise they possess in this field. Additional well-designed randomized controlled trials must be performed to create official guidelines for treatment. The objective of this study is to compare the clinical and functional outcomes of intramedullary nailing[1] versus external fixation (EF) in treating Gustilo Type IIIA tibiofibular fractures.

METHODS

After the ethical approval from the institutional review board, this randomised control trial study was conducted at AIMS hospital, Muzafarabad, from 01/03/24 to 01/09/24. Through non-probability consecutive sampling 100 patients aged above 18 years, both gender, with Gustilo Type IIIA tibiofibular fracture patients who received IMN treatment (N=51) while the remaining received EF(N=49) were included in the present study. the study excluded patients who sustained multiple traumas along with pathological fractures or unavailable medical information. After the informed consent demographics of the patients were collected. Time to union function as the main outcome measure together with complication rates (infection, non-union, malunion) and required second operations. The research evaluated VAS pain scores plus ROM reduction together with functional outcomes assessed at six months' post-treatment as secondary outcomes for patients receiving IMN or EF treatment. Time to union determination occurred via serial radiograph analysis along with functional assessment through the Lower Extremity Functional Scale (LEFS). SPSS version 26 was used to perform the analysis of the data. Data assessment included descriptive statistics for continuous variables using mean and standard deviation calculations as well as Chi-square tests for comparisons of categorical variables. The mean time to union together with pain scores underwent independent t-test analysis between treatment groups. All statistical results maintained a significance level at $p \leq 0.05$.

RESULTS

A total of 100 patients were included in the study, with 51 patients treated using intramedullary nailing (1) and 49 patients treated using external fixation (EF). Demographic characteristics were comparable between both groups. The mean age in the IMN group was 40.9±13.2 years, while in the EF group, it was 40.7±14.8 years ($p = 0.946$). The gender distribution was also similar, with 55% males and 45% females in the IMN group compared to 57% males and 43% females in the EF group ($p = 0.821$).

In terms of clinical outcomes, the time to union was significantly shorter in the IMN group (21.5±6.8 weeks) compared to the EF group (24.5±7.8 weeks, $p = 0.02$). The complication rate was notably lower in the IMN group (24%) than in the EF group (49%, $p = 0.013$). The infection rate was significantly lower in the IMN group, with only 6% of patients affected compared to 31% in the EF group ($p = 0.002$). Nonunion was observed in 4% of IMN patients versus 27% of EF patients ($p = 0.003$), while malunion occurred in 12% of IMN cases compared to 37% in the EF group ($p = 0.001$). Additionally, the need for secondary surgery was significantly lower in the IMN group (10%) compared to the EF group (33%, $p = 0.006$). Range of motion (ROM) reduction was slightly lower in the IMN group (12.2±9.3 degrees) compared to the EF group (14.14±8.9 degrees, $p = 0.178$), though the difference was not statistically significant. However, pain scores (VAS: 0-10) were significantly lower in the IMN group (3.8±3.39) than in the EF group (6.04±3.0, $p = 0.006$).

Regarding functional outcomes, a significantly higher percentage of patients in the IMN group achieved excellent results (45%), compared to only 22% in the EF group ($p = 0.005$). Good outcomes were observed in 33% of IMN patients versus 31% in the EF group. Fair results were seen in 14% of IMN patients compared to 29% of EF patients, while poor outcomes were significantly more frequent in the EF group (18%) compared to the IMN group (6%, $p = 0.005$). These findings indicate that IMN provides superior clinical and functional outcomes compared to EF in the treatment of Gustilo Type IIIA tibiofibular fractures.

Table No. 1: Demographics of the participants

Variables	IMN Group (n=51)	EF (n=49)	P Value
Age (years)	40.9±13.2	40.7±14.8	0.946
Gender			0.821
Male	28 (55%)	28 (57%)	
Female	23 (45%)	21 (43%)	

Table No. 2: Clinical outcomes

Variables	IMN Group (n=51)	EF (n=49)	P value
Time to Union (Weeks)	21.5±6.8	24.5±7.8	0.02
Complications	12 (24%)	24 (49%)	0.013
Infection Rate	3 (6%)	15 (31%)	0.002
0nunion	2 (4%)	13 (27%)	0.003
Malunion	6 (12%)	18 (37%)	0.001
Need for Secondary Surgery	5 (10%)	16 (33%)	0.006
Range of Motion (ROM) Reduction (Degrees)	12.2±9.3	14.14±8.9	0.178
Pain Score (VAS: 0-10)	3.8±3.39	6.04±3.0	0.006

Table No. 3: Functional outcomes

Outcomes	IMN Group (n=51)	EF (n=49)	P value
Poor	3 (6%)	9 (18%)	0.005
Fair	7 (14%)	14 (29%)	
Good	17 (33%)	15 (31%)	
Excellent	23 (45%)	11 (22%)	

DISCUSSION

This research study confirms earlier data which evaluates the treatment outcomes for IMN and EF devices when used in Gustilo Type IIIA tibiofibular fracture patients. According to Ghaseminejad-Raeini et al. (2024) in their meta-analysis IMN produces both superior outcomes for infection prevention and enhanced fracture healing compared to EF thus demonstrating superiority in dealing with such compound fractures[11]. In a Tanzanian randomized controlled trial IMN treatment resulted in smaller degrees of coronal and sagittal misalignment at the one-year follow-up. The outcomes from QOL measurements after surgery showed better results with IMN at first but both treatments produced similar results by the one-year point[12]. The comparison between EF and UTN based on a meta-analysis by Fu et al. (2018) showed that UTN decreased superficial infection and malunion frequencies yet EF minimized hardware failure rates.[9] The analysis revealed no major distinctions in outcomes involving deep infection regardless of the treatment type as well as delayed union or nonunion occurrences[13]. Research findings demonstrated that patients in the IMN group healed faster after fracture (21.5±6.8 weeks) than patients in the EF group who reached union at 24.5±7.8 weeks (p = 0.02). Medical nails achieve better outcomes than external fixation according to the medical findings of Jeremic et al.'s meta-analysis[14]. The IMN group showed better complication results than the EF group with lower infection frequency at 6% compared to 31% (p = 0.002) along with decreased non-union rates at 4% compared to 27% (p = 0.003). These reduced complication occurrences match findings from previous research about IMN advantages. Our study detected better functional results for IMN because 45% of patients experienced excellent outcomes instead of 22% from EF fixation (p = 0.005). Early enhancements in postoperative quality of life after surgery became apparent in the Tanzanian trial which used IMN for fixation. The benefits of IMN exist but doctors should choose EF when patients have extensive soft tissue trauma or tissue contamination. The decision between fixing options needs to be patient-specific because medical condition severity and surgeon and tissue damage extent impact selection alongside patient health status.

CONCLUSION

The current study strengthens scientific evidence demonstrating that intramedullary nailing delivers superior results as an intervention approach for Gustilo Type IIIA tibiofibular fractures compared to external fixation. The research data indicates that IMN represents the most effective treatment approach for suitable clinical applications. The research data indicates that IMN represents the most effective treatment approach for suitable clinical applications.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Arslan Munif
Drafting or Revising Critically:	Maryam Latif
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Davenport T, Guha A, Grewal D, Bressgott T. How artificial intelligence will change the future of marketing. J Acad Marketing Sci 2020;48:24-42.
2. Minehara H, Maruo A, Amadei R, Contini A, Braile A, Kelly M, et al. Open fractures: Current treatment perspective. OTA international : The Open Access J Orthopaedic Trauma 2023;6(3 Suppl):e240.

3. Chen Z, Luo R, Xing F, Xiang Z. External fixation versus intramedullary nailing for the treatment of open tibial shaft fractures: A meta-analysis of randomized controlled trials. Health Sciences Review 2024;10:100152.
4. Shanmugasundaram S, Panda SR, Samundeeswari S, Kumar D. Titanium Elastic Nails in the Management of Fractures. In: Banerjee A, Biberthaler P, Shanmugasundaram S, editors. Handbook of Orthopaedic Trauma Implantology. Singapore: Springer Nature Singapore; 2020. p. 1-35.
5. Alsharef JF, Ghaddaf AA, AlQuhaibi MS, Shaheen EA, AboAljadiel LH, Alharbi AS, et al. External fixation versus intramedullary nailing for the management of open tibial fracture: meta-analysis of randomized controlled trials. Int Orthopaed 2023;47(12):3077-97.
6. Elnewishy A, Elkholy M, Hamada A, Salem M. Comparing minimally invasive percutaneous plate osteosynthesis with interlocking intramedullary nail fixation for the management of adult extra-articular distal tibial fractures: a comprehensive systematic review and meta-analysis. Cureus 2023;15(11).
7. Pallister I, Handley GJ, Maggs S, Davies A-M, Kyle A, Bodger O, et al. Measuring recovery after open lower limb fractures: combined objective functional tests and global perceived recovery outperform narrower metrics and a standard generic patient reported outcome measure. BMC Musculoskeletal Disorders 2021;22(1):539.
8. Pokutnaya D, Loiacono MM, Booth H, Williams R, Ma C, Parker J, et al. The impact of clinical risk conditions on influenza and pneumonia diagnoses in England: a nationally representative retrospective cohort study, 2010-2019. Epidemiol Infection 2022;150:e107.
9. Fu Q, Zhu L, Lu J, Ma J, Chen A. External Fixation versus Unreamed Tibial Intramedullary Nailing for Open Tibial Fractures: A Meta-analysis of Randomized Controlled Trials. Sci Rep 2018;8(1):12753.
10. Çelik M, Bayrak A, Öztürk V, Kızılkaya C, Avkan MC. Functional and Radiological Comparison and Evaluation of Gustilo-Anderson Type 3 Open Tibia Fractures Treated with an Ilizarov External Fixator. Med J Bakirkoy 2024;20(4):308-14.
11. Ghaseminejad-Raeini A, Azarboo A, Pirahesh K, Sharafi A, Hoveidaei AH, Nwankwo BO, et al. Antibiotic-Coated Intramedullary Nailing Managing Long Bone Infected Non-Unions: A Meta-Analysis of Comparative Studies. Antibiotics 2024;13(1):69.
12. Taso M, Sommernes JH, Kolstad F, Sundseth J, Bjorland S, Pripp AH, et al. A randomised controlled trial comparing the effectiveness of surgical and nonsurgical treatment for cervical radiculopathy. BMC Musculoskelet Disord 2020;21(1):171.
13. Essa A, Paul R, Khan S, Avisar E, Chan A, Persitz J. A meta-analysis comparing complications of anterior versus dorsal osteotomy and plating for distal radial malunions. The J Hand Surg Eur 2024;49(8):956-64.
14. Jeremic D, Grubor N, Bascarevic Z, Slavkovic N, Krivokapic B, Vukomanovic B, et al. Comparative Analysis of Complication Rates in Tibial Shaft Fractures: Intramedullary Nail vs. Ilizarov External Fixation Method. J Clin Med 2024;13(7):2034.

Original Article

To Determine the Efficacy of Polyethylene Glycol in the Treatment of Pediatric Constipation

Muhammad Owais, Hameed Ullah, Iftikhar Khan and Zeeshan Ahmad

ABSTRACT

Objective: To assess the efficacy of polyethylene glycol (PEG) in treating pediatric constipation and provide local statistics for improved clinical decision-making and recommendations on future treatment strategies.

Study Design: Randomized Controlled Trial(RCT)

Place and Duration of Study: This study was conducted at the department of Women and Children Hospital from January 2023 to January 2024.

Methods: A descriptive case series was conducted with 146 pediatric patients over six months. Children aged 4 years and older underwent clinical examinations, including abdominal and rectal assessments. Polyethylene glycol (PEG 3350) was administered at 1.5 g/kg/day as a single dose for four weeks. Treatment efficacy was evaluated at the end of the 4th week.

Results: The mean age of the patients was 8 years (SD ± 6.34). Of the 146 participants, 58% were male, and 42% were female. Polyethylene glycol was effective in 72% of the patients. The p-value for the efficacy of treatment was statistically significant (<0.05), indicating that PEG was an effective treatment option for most patients.

Conclusion: Polyethylene glycol demonstrated significant efficacy (72%) in managing pediatric constipation. The findings highlight its effectiveness as a primary treatment option. Future research should focus on long-term outcomes and alternative dosages for children who do not respond to initial treatment.

Key Words: Efficacy, polyethylene glycol, constipation, pediatric

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INTRODUCTION

Constipation is a prevalent condition in pediatric populations, with a global prevalence ranging from 1% to 30% based on diagnostic criteria, population samples, and methodologies used for diagnosis. Pediatric constipation is responsible for 3% to 5% of general pediatric outpatient visits and up to 25% of gastroenterology clinic referrals[1]. The etiology of constipation in children can be multifactorial, with potential causes including dietary habits, psychological factors, and underlying medical conditions[2]. Functional constipation accounts for the majority of cases, with organic causes being less common but important to rule out[3].

Early diagnosis and management are crucial in avoiding long-term complications such as fecal incontinence, megacolon, and psychological issues related to chronic constipation[4].Polyethylene glycol (PEG) is widely recommended as a first-line treatment for pediatric constipation due to its high efficacy and safety profile[5]. PEG is an osmotic laxative that increases stool water content, enhancing bowel movements without significant systemic absorption[6]. Studies have demonstrated that PEG is superior to placebo and other laxatives, such as lactulose, in resolving constipation in children[7]. A systematic review concluded that PEG offers better relief of symptoms, improved stool frequency, and fewer side effects compared to alternative laxatives[8]. Additionally, PEG is associated with better patient compliance because it is tasteless and can be mixed with various beverages, making it ideal for pediatric use[9].In the context of developing regions, particularly South Asia, the burden of pediatric constipation is substantial, yet there is limited local data on treatment efficacy[10]. Cultural, dietary, and socioeconomic factors influence constipation patterns in children, warranting region-specific studies[11]. Moreover, the lack of local evidence hinders the formulation of standardized treatment protocols. This study aims to fill this gap by evaluating the efficacy of PEG in treating pediatric constipation in a local population, providing valuable insights to guide pediatricians in clinical practice. The results of this study will offer local pediatricians statistically validated evidence regarding PEG's effectiveness and help

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establish recommendations for its use in managing pediatric constipation. Furthermore, identifying the proportion of patients who do not respond to treatment will guide future research on alternative therapies and optimize management strategies. This research also aims to address the ongoing debate about the optimal dosage and duration of PEG therapy in children by evaluating its short-term effectiveness over four weeks. In conclusion, this study focuses on determining the efficacy of PEG 3350 in pediatric patients with constipation. The findings will contribute to local and international literature by validating the role of PEG in improving bowel movements, thereby reducing the frequency of complications associated with chronic constipation.

METHODS

This descriptive case series was conducted over six months from January 2023 to January 2024. The study included 146 children aged 4 years or older who presented with symptoms of constipation as defined by the Rome IV criteria. Each patient underwent a detailed medical history and clinical examination, including abdominal and rectal assessments. Polyethylene glycol (PEG 3350) was administered orally at a dosage of 1.5 g/kg/day for four weeks. Treatment efficacy was assessed at the end of the 4th week based on operational definitions.

Data Collection: Data on patient demographics, clinical findings, and treatment outcomes were collected using structured forms. The supervising pediatrician, with a minimum of five years of experience, ensured consistency in assessments and documentation.

Statistical Analysis: Data were entered and analyzed using SPSS version 24.0. Descriptive statistics, including mean, standard deviation, and percentages, were calculated for continuous and categorical variables. The chi-square test and paired t-test were used to assess the significance of treatment outcomes, with a p-value < 0.05 considered statistically significant.

RESULTS

The mean age of the 146 patients was 8 years (SD ± 6.34), with 58% of the patients being male and 42% female. After four weeks of treatment with PEG 3350, 72% of the patients showed significant improvement in bowel movements based on the operational definition of efficacy, while 28% did not respond to the treatment. The mean increase in bowel frequency from baseline to the end of treatment was statistically significant ($p < 0.05$). The chi-square test indicated a strong association between PEG administration and symptom relief. Patients who responded to treatment reported an average of five bowel movements per week compared to two at baseline. No serious adverse events were reported during the study period, highlighting the safety of PEG in this cohort.

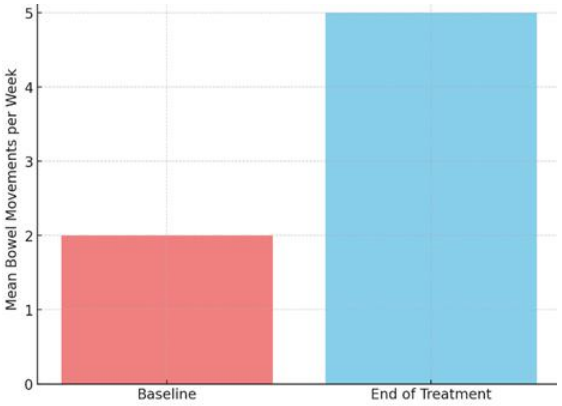

Figure No. No. 1: Improvement in Bowel Movements after PEG Treatment.

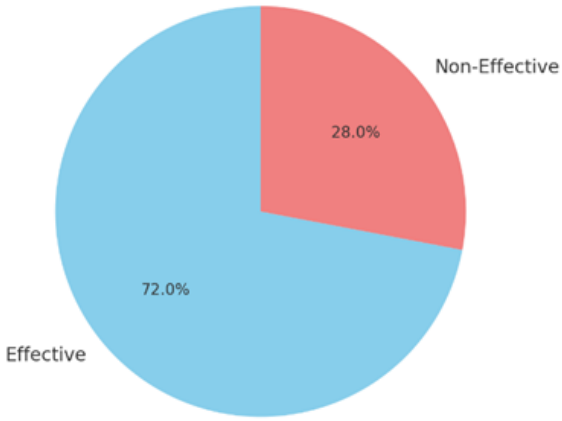

Figure No. 2: Treatment Outcome Distribution.

Table No. 1: Demographic Characteristics

Characteristic	Value
Total Patients	146
Mean Age (years)	8 (SD ± 6.34)
Gender (Male)	58% (85 patients)
Gender (Female)	42% (61 patients)

Table No. 2: Treatment Outcome

Outcome	Percentage
Effective Treatment	72% (105 patients)
Non-Effective Treatment	28% (41 patients)

Table No. 3: Bowel Movement Improvement

Time Period	Mean Bowel Movements per Week
Baseline	2
End of Treatment (4 weeks)	5

DISCUSSION

Constipation in children is a common and often distressing condition that can lead to long-term complications if not appropriately managed. The findings of this study indicate that polyethylene glycol (PEG 3350) is 72% effective in improving symptoms of

pediatric constipation, with statistically significant improvements in bowel movements and minimal side effects. These results align with existing literature supporting the efficacy and safety of PEG for pediatric patients.Several studies have highlighted PEG's effectiveness in treating functional constipation in children. A randomized controlled trial by Youssef et al. found that PEG was superior to lactulose, achieving symptom resolution in 70% of the children within four weeks[11]. Our study's findings of 72% efficacy fall within this range, reinforcing the consistency of PEG's performance across various populations and clinical settings. Another study by Dupont et al. demonstrated a similar success rate of 75% with PEG, emphasizing its ability to improve stool frequency and consistency[12]. This supports the observation in our study, where mean bowel movements increased significantly from two per week at baseline to five per week after treatment ($p < 0.05$).An important advantage of PEG is its minimal absorption, which reduces the likelihood of systemic side effects. Bae et al. reported that PEG was associated with fewer gastrointestinal side effects compared to stimulant laxatives, with most adverse events being mild and self-limited, such as bloating or mild abdominal discomfort[13]. Similarly, our study found no serious adverse events, further confirming its safety profile. A meta-analysis conducted by Candy et al. also suggested that PEG was more effective and better tolerated than placebo and other osmotic laxatives[14]. This superior tolerability is particularly important in pediatric populations, where adherence to treatment is often challenging.The results of this study are consistent with findings from local studies as well. A study conducted in India reported an efficacy rate of 68% using PEG for functional constipation in children, suggesting that regional variations in diet and lifestyle do not significantly alter PEG's effectiveness[15]. These findings support the generalizability of our results to other developing countries where similar socioeconomic factors may influence constipation prevalence.Despite the positive outcomes, there remains a subset of patients (28%) who did not respond to PEG treatment. This group may represent children with underlying organic causes of constipation or those requiring longer treatment durations. A study by Pashankar et al. highlighted that some non-responders benefitted from extended therapy beyond four weeks or combination therapy with dietary modifications[16]. Thus, future research should investigate personalized treatment approaches for non-responders and explore the long-term effects of PEG. In conclusion, the findings of this study contribute to the growing body of evidence supporting PEG as a first-line treatment for pediatric constipation. Its high efficacy, safety, and ease of administration make it a preferred option among pediatricians. However, further research is needed to address treatment resistance and optimize individualized care strategies[17].

CONCLUSION

This study concludes that polyethylene glycol (PEG 3350) is 72% effective in treating pediatric constipation, significantly improving bowel movements with minimal adverse effects. Its high efficacy, safety, and ease of administration make it a suitable first-line treatment for functional constipation in children.

Limitations: This study was limited by its short duration (4 weeks), small sample size, and focus on a single treatment dose. Additionally, the absence of a placebo or control group may limit the generalizability of findings across diverse populations.

Future Findings: Future studies should evaluate the long-term efficacy of PEG, explore personalized treatment plans for non-responders, and compare its outcomes with other laxatives. Investigating alternative dosages, dietary interventions, and combination therapies could further optimize treatment outcomes for pediatric constipation.

Abbreviations:

- PEG - Polyethylene Glycol
- SD - Standard Deviation
- SPSS - Statistical Package for the Social Sciences
- GI - Gastrointestinal
- ESPGHAN - European Society for Paediatric Gastroenterology Hepatology and Nutrition
- NASPGHAN - North American Society for Pediatric Gastroenterology, Hepatology and Nutrition
- PGE - Polyethylene Glycol with Electrolytes
- CI - Confidence Interval
- QOL - Quality of Life

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Owais, Hameed Ullah
Drafting or Revising Critically:	Iftikhar Khan,. Zeeshan Ahmad
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None
Ethical Approval: No.1855/2022 Dated 22.09.2022

REFERENCES

1. Bongers ME, van Wijk MP, Reitsma JB, Benninga MA. Long-term prognosis for childhood constipation: clinical outcomes in adulthood. Pediatr 2010;126(1):e156-e162.

2. Tabbers MM, Di Lorenzo C, Berger MY, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from Espghan and Naspghan. J Pediatr Gastroenterol Nutr 2014;58(2):258-274.
3. van den Berg MM, Benninga MA, Di Lorenzo C. Epidemiology of childhood constipation: a systematic review. Am J Gastroenterol 2006;101(10):2401-2409.
4. Mugie SM, Benninga MA, Di Lorenzo C: Epidemiology of constipation in children and adults: a systematic review. Best Pract Res Clin Gastroenterol 2011;25(1):3-18.
5. Pashankar DS, Bishop WP. Efficacy and optimal dose of daily polyethylene glycol 3350 for treatment of fecal impaction in children. J Pediatr Gastroenterol Nutr 2001;33(5): 468-471.
6. Candy DC, Edwards D, Geraint M. Treatment of faecal impaction with polyethylene glycol plus electrolytes (PGE): an open study in 27 children. J Pediatr Gastroenterol Nutr 2006;33(1):75-80.
7. Youssef NN, Peters JM, Henderson W, Shultz-Peters S, Di Lorenzo C. Dose response of polyethylene glycol 3350 for the treatment of childhood fecal impaction. J Pediatr Gastroenterol Nutr 2002;34(1):24-30.
8. Dupont C, Leluyer B, Maamri N, et al. Double-blind randomized study comparing polyethylene glycol 4000 and lactulose in the treatment of functional constipation in children. J Pediatr Gastroenterol Nutr 2005;41(5):625-633.
9. Nurko S, Zimmerman LA. Polyethylene glycol (PEG) laxatives: new insights into mechanisms of action. J Pediatr 2014;165(1):6-10.
10. Lee-Robichaud H, Thomas K, Morgan J, Nelson RL. Laxatives for the management of constipation in palliative care patients. Cochrane Database Syst Rev 2010;(1):CD003448.
11. Youssef NN, Langseder AL, Verga BJ, Mones RL, Rosh JR. Chronic childhood constipation is associated with impaired quality of life: a case-controlled study. J Pediatr Gastroenterol Nutr 2005;41(1):56-60.
12. Dupont C, Leluyer B, Maamri N, et al. Effectiveness of PEG versus placebo in children with functional constipation: a randomized trial. J Pediatr 2006;149(6):781-786.
13. Bae SH, Son JS, Lee JH. The effect of different doses of polyethylene glycol 3350 for treatment of functional constipation in children. J Pediatr Gastroenterol Nutr 2010;50(4):397-401.
14. Candy D, Belsey J. Macrogol (polyethylene glycol) laxatives in children with functional constipation and faecal impaction: a systematic review. Arch Dis Child 2009;94(2):156-160.
15. Goyal A, Goyal R, Prasad A, et al. Effectiveness of polyethylene glycol in Indian children with functional constipation: a randomized controlled trial. Ind J Pediatr 2014;81(4):344-348.
16. Pashankar DS, Loening-Baucke V. Safety and efficacy of polyethylene glycol 3350 for the treatment of chronic constipation in children. Clin Pediatr 2005;44(5):379-383.
17. Nurko S, Youssef NN. Polyethylene glycol for the treatment of childhood constipation: evidence-based recommendations. J Pediatr Gastroenterol Nutr 2016;63(1):51-57.

Original Article

Frequency of Asymptomatic Spontaneous Bacterial Peritonitis in Patients with Decompensated Chronic Liver Disease

Asymptomatic Spontaneous Bacterial Peritonitis

Qazi Sidra Shafi, Mohammad Iltaf, Fazal Wahab, Asma Khan and Saqib Ullah Khan

ABSTRACT

Objective: To determine the frequency of asymptomatic spontaneous bacterial peritonitis (SBP) in patients with decompensated chronic liver disease (DCLD).

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, PGMI/Hayatabad Medical Complex, Peshawar, from 06-09-2022 to 06-03-2023.

Methods: A total of 164 patients aged 16-75 years, both genders, with DCLD-associated ascites were enrolled. Ascitic fluid samples were collected to identify the presence of SBP through polymorphonuclear (PMN) counts without clinical symptoms of SBP.

Results: The mean age was 56.25 ± 16.68 years, with 53% male and 47% female patients. Among the enrolled patients, 3.7% (n=6) had asymptomatic spontaneous bacterial peritonitis. The most frequent cause of DCLD was hepatitis C (39.6%), followed by hepatitis B (22.6%).

Conclusion: The study found that 3.7% of patients with DCLD had asymptomatic SBP. Screening for SBP in asymptomatic patients is recommended to reduce potential morbidity and mortality associated with this hidden condition.

Key Words: Asymptomatic SBP, Decompensated chronic liver disease, Infection, Child-Pugh class.

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INTRODUCTION

Global health experts consider cirrhosis to appear as a significant worldwide medical concern when chronic liver diseases (CLD) cause progressive liver scarring along with fibrosis and impaired liver functioning. The load of cirrhosis creates substantial healthcare effects combined with significant statistical and economic impacts. The 12th position as a cause of death in the United States belongs to cirrhosis while its incidence is expected to rise because of increased hepatitis C infections and cases of non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease[1].

Decompensated chronic liver disease (DCLD) becomes the most dangerous manifestation which causes patients to experience complications including ascites and spontaneous bacterial peritonitis (SBP) as well as hepatic encephalopathy and variceal bleeding. The infection of ascitic fluid known as SBP proves fatal because it exists without any discernible intra-abdominal bacterial source. Tests reveal that the worldwide SBP occurrence during cirrhosis affects 7-30% of hospitalized patients and about 3.5% of outpatients according to research.[2-3] The progression toward SBP happens when bacteria migrate from intestines into ascitic fluid through the compromised gut barrier and impaired immune system of patients who have cirrhosis[4]. The primary infective agents causing spontaneous bacterial peritonitis are gram-negative bacteria primarily consisting of Escherichia coli together with gram-positive Streptococcus species organisms[5].Healthcare providers use two ascitic fluid diagnostic criteria to identify SBP: either when the polymorphonuclear leukocyte (PMN) count exceeds 250 cells/mm³ or when bacteria growth is present during fluid culture analysis[6]. The symptoms from SBP consist of high fever together with stomach pain and confusion but research shows one-third of patients may not detect any symptoms at all[7]. The rapid disease evolution of asymptomatic SBP leads to symptomatic infections that result in acute-on-chronic liver failure and sepsis and eventual death without diagnosis according to research[8]. The research conducted by a researcher revealed that 4% of decompensated liver disease patients presented with asymptomatic SBP yet other studies documented different rates from 3% to

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13%[9,10].The need for early diagnosis of SBP requires routine diagnostic ascitic taps because undiagnosed SBP presents high rates of morbidity. Secondary antibiotic prophylaxis among cirrhotic patients decreases both the rate of SBP recurrence and enhances their survival rates according to research findings[11]. There are insufficient data regarding asymptomatic SBP prevalence in Pakistan among patients with decompensated chronic liver disease. The research determines how often asymptomatic SBP appears in DCLD patients when examining its relationship with clinical characteristics that include patient age and gender and Child-Pugh assessment results.

METHODS

Research investigators tested patients at the Department of Gastroenterology, PGMI/Hayatabad Medical Complex, Peshawar from September 6, 2022 until March 6, 2023. The research sample included 164 patients who were aged between 16 to 75 years with DCLD-associated ascites through non-probability consecutive sampling. The research excluded patients with peritonitis history and those who had undergone recent abdominal surgery along with those with chronic kidney disease.

Data Collection: The study participants provided consent before the researchers obtained a comprehensive clinical history and performed physical examination. The diagnostic ascitic fluid taps occurred under sterile procedures to assess PMN cell counts in the acquired samples. The research measured both Child-Pugh scores and APRI clinical indicators.

Statistical Analysis: Statistical analysis occurred through SPSS version 24.0 which IBM Corp. operated from its Armonk NY headquarters. The research team determined means and standard deviations for continuous data and counted frequencies of categorical data. The chi-square test ruled associations significant at a p value lower than 0.05.

RESULTS

The analyzed group comprised 164 patients who averaged 56.25 ± 16.68 years old. The patient participants included 87 males who made up 53% of the total while 77 females represented 47% of the total. The primary source of DCLD was Hepatitis C infections that affected 39.6% of patients before Hepatitis B patients who made up 22.6% and people with Wilson's disease who comprised 12.2% of the total cases. The study participants demonstrated a mean Child-Pugh score of 10.92 ± 2.30 with 72% of patients belonging to Child-Pugh Class C.Results showed that asymptomatic Spontaneous Bacterial Peritonitis affected 3.7% of the 164 patient sample (6 out of 164 patients were affected). The study included 4 male participants who composed 66.7% (n=4) while the remaining 83.3% (n=5) belonged to Child-Pugh Class C. An association analysis showed that age, gender or etiologies of DCLD did not significantly impact the presence of asymptomatic SBP because the p value exceeded 0.05. Of all unrecognized SBP patients, 66.7% belonged to the age group above 55 years. Most cases of SBP among positive results developed from Hepatitis C infection.

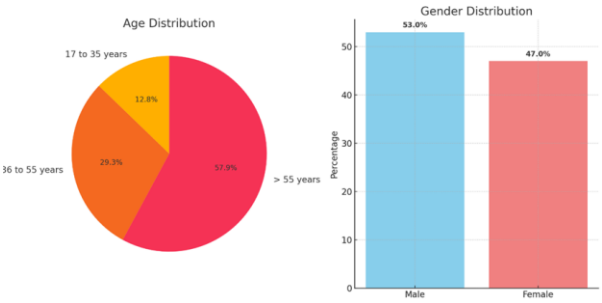

Figure No. 1: Age and Gender Distribution.

Table No. 1: Descriptive Statistics

Variables	Mean	Std. Deviation
Age (Years)	56.25	16.68
Child Pugh Score	10.92	2.3
APRI	1.1	0.26

Table No. 2: Age Distribution

Age Distribution	Frequency	Percent
17 to 35 years	21	12.8
36 to 55 years	48	29.3
> 55 years	95	57.9

Table No. 3: Gender Distribution

Gender	Frequency	Percent
Male	87	53.0
Female	77	47.0

DISCUSSION

The complication called Spontaneous bacterial peritonitis affects patients with decompensated chronic liver disease (DCLD) at rates of 3.7% which produces significant morbidity and mortality results. The occurrence of asymptomatic SBP emerged at 3.7% among patients having DCLD which matches findings documented in previous research reports and studies[12]. The reported frequency stands lower than other studies which observed up to 13.4% in separate patient groups[13] due to differing patient demographics and clinician care methods and ascites protein concentration levels. Multiple elements trigger SBP formation among patients who suffer from cirrhosis. SBP develops through bacterial translocation which results from damaged gut bacteria and intestinal barrier breakdown along with weakened host resistance. The paper by a researcher describes how systemic inflammation acts as a factor that increases bacterial translocation outcomes leading to infection risk[14]. The discovery matches our clinical finding about liver disease patients with advanced stages and poor immune function being more

susceptible to silent SBP infections. Our study showed patients in Child-Pugh Class C had increased occurrence of asymptomatic SBP in comparison to patients in Child-Pugh Class B. The research findings by another researcher show that liver dysfunction severity functions as an excellent indicator of bacterial infections particularly SBP[15]. The most frequent underlying cause of DCLD which develops into SBP proved to be hepatitis C and hepatitis B infections according to our study results but these findings matched worldwide medical evidence demonstrating viral hepatitis acts as major contributors to cirrhosis-related conditions[16].Transparency testing of ascites through routine diagnostic paracentesis stands as a critical practice among cirrhotic patients with ascites since many symptomatic patients demonstrate no apparent symptoms. In an other study, researcher reveals through their research that one-third of patients develop SBP without showing any symptoms yet proper early treatment of this silent condition produces better results. The screening of asymptomatic patients may decrease the occurrence of serious infections together with septic events and death rates. The development of acute kidney injury (AKI) during the course of SBP triggers increased mortality numbers among affected patients. The research done by another researcher found that AKI affected half of SBP patients yet albumin treatment minimized both kidney damage and death rates[17,18]. The importance of diagnosing cirrhotic patients at early stages emerges from these results since it helps avoid organ failure and enhances long-term survivability. The low occurrence of asymptomatic SBP in our research warrants attention about the potential 70% recurrence rate after the first episode when patients lack proper preventive measures[16]. The application of norfloxacin prophylaxis decreases infection recurrence alongside improving patient survival rates mainly for high-risk individuals. The clinical implementation of these prevention measures should be done urgently to reduce the disease-related impacts of SBP.

CONCLUSION

The study identified a 3.7% frequency of asymptomatic spontaneous bacterial peritonitis (SBP) in patients with decompensated chronic liver disease (DCLD). Routine diagnostic paracentesis is crucial for early detection and management of asymptomatic SBP, which can help reduce complications such as acute kidney injury and improve long-term patient outcomes.

Limitations: This study was limited by its single-center design, which may affect the generalizability of the findings. Additionally, the relatively small sample size may have restricted the detection of broader trends. Patients excluded due to previous peritonitis history may have introduced selection bias, influencing the prevalence rates of asymptomatic SBP.

Future Findings: Future research should focus on multicenter studies with larger populations to better evaluate regional variations in asymptomatic SBP frequency. Further investigations could explore the role of novel biomarkers for early diagnosis and assess the long-term impact of routine pr

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Qazi Sidra Shafi, Mohammad Iltaf
Drafting or Revising Critically:	Fazal Wahab, Asma Khan, Saqib Ullah Khan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None

Ethical Approval: No.874/B&PSC/2022 Dated 03.08.2022

REFERENCES

1. Peery AF, Crockett SD, Murphy CC, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018. Gastroenterol 2019;156(1):254-272.
2. Tay PWL, Xiao J, Tan DJH, et al. An epidemiological meta-analysis on the worldwide prevalence, resistance, and outcomes of spontaneous bacterial peritonitis in cirrhosis. Front Med (Lausanne) 2021;8:693652.
3. Luo WW, Zhang DZ. [Diagnosis and treatment of bacterial infection in patients with end-stage liver disease]. Zhonghua Gan Zang Bing Za Zhi 2018;26(1):10-12.
4. Fernández J, Angeli P, Trebicka J, et al. Efficacy of albumin treatment for patients with cirrhosis and infections unrelated to spontaneous bacterial peritonitis. Clin Gastroenterol Hepatol 2020;18(4):963-973.e14.
5. Li H, Wieser A, Zhang J, et al. Patients with cirrhosis and SBP: Increase in multidrug-resistant organisms and complications. Eur J Clin Invest 2020;50(2):e13198.
6. Fiore M, Maraolo AE, Gentile I, et al. Current concepts and future strategies in the antimicrobial therapy of emerging gram-positive spontaneous bacterial peritonitis. World J Hepatol 2017;9(30):1166-1175.
7. Komolafe O, Roberts D, Freeman SC, et al. Antibiotic prophylaxis to prevent spontaneous bacterial peritonitis in people with liver cirrhosis: a network meta-analysis. Cochrane Database Syst Rev 2020;1(1):CD013125.

8. Oliveira AM, Branco JC, Barosa R, et al. Clinical and microbiological characteristics associated with mortality in spontaneous bacterial peritonitis: a multicenter cohort study. Eur J Gastroenterol Hepatol 2016;28(10):1216–1222.
9. Haj M, Hart M, Rockey DC. Development of a novel clinical staging model for cirrhosis using the Nationwide Inpatient Sample. J Investig Med 2018;66(6):992-997.
10. Numan L, Elkafrawy A, Kaddourah O, et al. Spontaneous bacterial peritonitis: we are still behind. Cureus 2020;12(4):e7711.
11. Alotaibi A, Almaghrabi M, Ahmed O, et al. Incidence of spontaneous bacterial peritonitis among asymptomatic cirrhosis patients undergoing outpatient paracentesis: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol 2021;33(1S Suppl 1):e851-7.
12. Mazloom SS, Khoramian MK, Mohsenian L. Spontaneous bacterial peritonitis in afebrile cirrhotic patients; report from a referral transplantation center. Bull Emerg Trauma 2018;6(4):363-366.
13. Singh A, Cresci GA, Kirby DF. Proton pump inhibitors: risks and rewards and emerging consequences to the gut microbiome. Nutr Clin Pract 2018;33(5):614-624.
14. Fernández J, Gustot T. Management of bacterial infections in cirrhosis. J Hepatol 2019;70(3):491-511.
15. Caly WR, Bitelman B, Carrilho FJ, et al. Clinical features of refractory ascites in outpatients. Clinics (Sao Paulo) 2017;72(7):405-410.
16. Moreau R, Elkrief L, Bureau C, et al. Effects of long-term norfloxacin therapy in patients with advanced cirrhosis. Gastroenterol 2018;155(6): 1816-1827.
17. Wiest R, Albillos A, Trauner M, Bajaj JS, Jalan R. Targeting the gut-liver axis in liver disease. J Hepatol 2017;67(5):1084-1103.
18. Li H, Chen LY, Zhang NN, et al. Characteristics, diagnosis and prognosis of acute-on-chronic liver failure in cirrhosis associated with HBV and alcohol. Liver Int 2021;41(6):1260-1270.

Original Article

Outcome of Endoscopic Mucosal Resection of Flat and Sessile Colonic Polyps

Hashmatullah Khan, Mushtaq Ahmad, Hamid Ullah, Rafi Ullah, Mujahid Aslam and Asfandyar Khan

ABSTRACT

Objective: The aim of our study was to prospectively evaluate the success, complications and recurrence following EMR of flat colonic polyps.

Study Design: prospective observational study

Place and Duration of Study: This study was conducted at the Lady Reading Hospital, Peshawar, Pakistan, from January 2014 to December 2016.

Methods: The following ethical committee approval. Consecutive patients meeting the inclusion criteria were enrolled, and demographic data were collected.

Results: A total of 243 polyps were resected in 211 patients. 23 patients had more than one polyp. Mean age was 45±13 years.En block resection was possible in 240 patients (98.8%). Bleeding immediately after resection was seen in 6 patients (2.84%) while delayed bleeding after 24 hours after the procedure occurred in 8 patients (3.8%). Perforation occurred in one patient. The overall recurrence rate was approximately 9% (18/205) during a mean follow-up of 12 months.

Conclusion: Endoscopic mucosal resection is an effective and safe outpatient procedure for sessile or flat colonic polyps.

Key Words: Endoscopic Mucosal Resection, sessile Polyps, saline-assisted polypectomy

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INTRODUCTION

Sessile or flat lesions of gastrointestinal tract especially when large in size are challenging to be resected by using conventional snare polypectomy[1]. Therefore, surgery is still the primary management technique in most centers throughout the world[2]. However, in centers with expertise, endoscopic mucosal resection (EMR) is now a reasonable alternative option to surgery. It is associated with high success rates and eliminates the requirement of surgical intervention thus avoiding the morbidity and mortality associated with surgery[2, 3].EMR is commonly utilized for neoplasms less than 2 cm, but the introduction of submucosal fluid injection has extended the range of endoscopically resectable polyps remarkably therefore, even larger neoplasms can be removed as piecemeal[4].

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Gastroenterologists practice a few techniques of EMR. These techniques incorporate ligation, cap and injection assisted EMR. Injection-assisted endoscopic mucosal resection, also called saline-assisted polypectomy, is the most commonly utilized procedure for flat polyps of the colon. This procedure was initially reported in 1955. It involves a submucosal injection of a solution under the lesion thus lifting the lesion and providing a safety pad. It facilitates resection of the neoplasms and shields against electrocautry induced or mechanical injury to deeper layers of GI tract wall[3,5]. Improvement in endoscopic skills, increased awareness and enhanced imaging result in more frequent identification of flat and sessile lesions. A significant proportion of these neoplasms defies endoscopic resection by the conventional snare polypectomy procedure and may require EMR. The EMR is associated with low complication rate[6]. Bleeding is the most frequently encountered adverse event[6, 7] while perforation is the second most common complication[7,8]. Recurrence following a successful EMR is another risk associated with this modality[9].

The aim of the study was to prospectively evaluate the success, complications and recurrence following EMR of flat and sessile colonic polyps.

METHODS

Inclusion Criteria:

1. Patients with sessile polyps <2 cm and no evidence of malignancy on initial biopsy.

Exclusion Criteria:

1. Patients with malignancy, pedunculated polyps, polyps >2 cm, or non-lifting polyps.
2. Polyps in the context of active inflammatory bowel disease.

Definitions:

- Sessile Polyp: Protruding colonic lesion without a stalk (Paris classification type 0-Is)[11].
- Flat polyp: lesions that are at the level of the mucosa (Paris classification type 0-IIb)[11].
- Complete Endoscopic Resection: Normal mucosal margins without neoplastic cells in the excision base.

Procedure: After informed consent, EMR was performed under conscious sedation by an experienced gastroenterologist using a high-definition colonoscope (CV180 Exera, Olympus, Japan). Endoscopic data, including polyp number, size, and location. Polyp diameter was measured against open biopsy forceps.

A pre-mixed submucosal injection solution (1 ml epinephrine [1:10,000], 3 ml indigo carmine, and 100 ml normal saline) was used to lift lesions. The lifted lesion was resected with a snare using endocut mode (120 W). En bloc resection was attempted; piecemeal resection was applied if necessary. Residual tissue was removed using the same technique or adjuvant argon plasma coagulation (APC). Mucosal defects were closed with metal clips.

Resected specimens were retrieved using snares, Roth nets, suction, or forceps and analyzed by an experienced pathologist for histological classification.

Post-Procedure Care: Patients were monitored for complications such as bleeding or perforation, managed with APC or hemostatic clips as needed. Delayed bleeding was defined as fresh rectal bleeding within 24 hours post-procedure.

Follow-Up and Recurrence Management: Surveillance colonoscopy was performed at 3, 6, and 12 months. Recurrence, defined as adenomatous or polypoid tissue at the resection site, was treated with repeat EMR or APC.

Statistical Analysis: Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies (%). Statistical analyses were performed using SPSS version 17.0 (SPSS Inc, Chicago, IL).

RESULTS

A total of 243 polyps were resected from 211 patients, with 23 patients having multiple polyps. The mean age of the patients was 45 ± 13 years, and more than 70% were male (table 1). The mean polyp size was 13 ± 6.7 mm, ranging from 6 to 20 mm (table 2). The left colon was the most common site, accounting for over 50% of polyps (figure 1). Among the 240 retrieved polyps, the most frequent histological type was tubular adenoma (50%), followed by hyperplastic polyps (25%) (figure 2).

Procedure Outcomes

En bloc resection was achieved in 98.8% (240/243) of cases, with only three polyps requiring piecemeal resection (table 3).

Immediate post-resection bleeding occurred in 6 patients (2.4%), while delayed bleeding (>24 hours) was observed in 8 patients (3.2%). Perforation was noted in a single case (figure 4).

Surveillance and Recurrence (figure 5)

At 3 months, 205 patients underwent follow-up colonoscopy. Recurrence of polypoidal or adenomatous tissue was seen in 10 patients (4.8%). Six patients were unavailable for follow-up.

At 6 months, 180 patients remained in follow-up, with 5 patients (2.7%) showing recurrence.

By 12 months, 140 patients were available for surveillance, with a recurrence rate of 2.14% (n=3).

Table No. 1: Age and gender distribution

Parameter	Value
Total no of patients	211
Age	45 ± 13years
Male	150 (71.09%)
Female	61 (28.91%)

Table No. 2: Polyp characteristics

Parameter	Value
Total no of polyps	243
Polyp Size (Mean ± SD)	13 ± 6.7mm
Range	6–20 mm

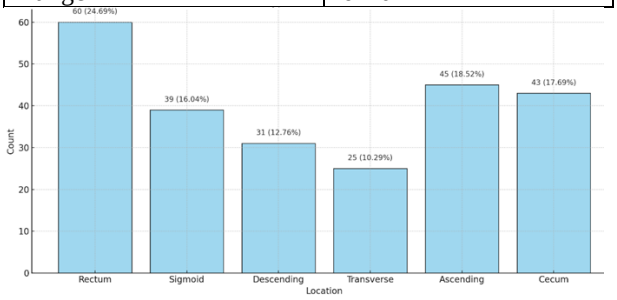

Figure No. 1: Polyp Location Distribution

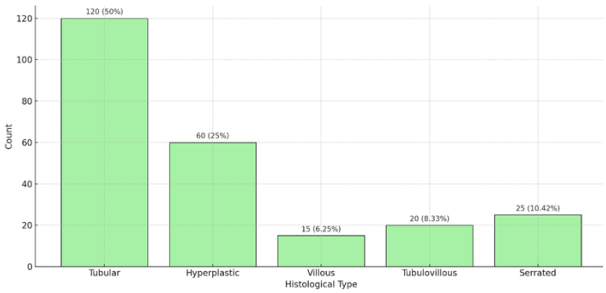

Figure No. 2: Polyp Histology Disribution

Table No. 3: Outcome of EMR

Parameter	Counts (%)
En block resection	240 (98.8)
Piecemeal resection	3 (1.2)
Complications	Figure 3
Post EMR Recurrence	Figure 4

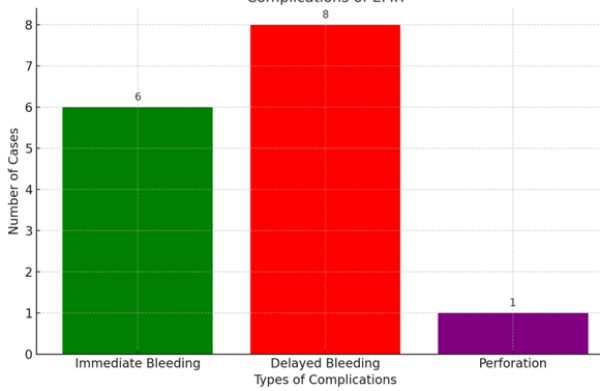

Figure No. 3: Complications of EMR

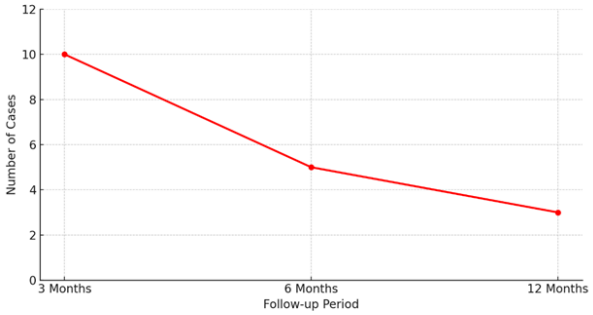

Figure No. 4: Recurrence Post-EMR

DISCUSSION

Complete resection of flat and sessile colonic polyps through traditional methods, such as snare polypectomy, is often challenging and carries a substantial risk of complications, particularly perforation[1]. Endoscopic mucosal resection (EMR), however, has emerged as a reliable and safer alternative, ensuring complete removal in most cases[3]. In our study, we achieved an impressive en bloc resection rate of 98.8%. By comparison, Moss A et al. and Laongcraft-Wheaten G et al. reported en bloc resection rates of 89.2% and 90%, respectively[11, 12]. The slightly lower rates in their studies can be attributed to the exclusive inclusion of large sessile polyps, which are technically more demanding. Complications associated with EMR are well-documented in the literature, with bleeding (1–45%), perforation (0.7–4%), and post-polypectomy syndrome (0–7.6%) being the most frequently reported[13]. In our study, complications were minimal, with only 2.8% (n=6) of patients experiencing immediate bleeding and 3.8% (n=8) reporting delayed bleeding. These rates compare favorably with those reported by Moss A et al. (2.9%) and Laongcraft-Wheaten G et al. (2% immediate, 4% delayed)[11, 12]. Notably, all bleeding episodes in our study were successfully managed endoscopically.

Perforation, a rare but serious complication, occurred in one case (0.5%) in our cohort, necessitating surgical intervention. This rate is significantly lower than the 1.3% reported by Moss A et al.,[11] and consistent with the absence of perforation noted in Conio M et al.'s study[14]. The use of submucosal injection solutions, such as normal saline with epinephrine (1:10,000) and indigo carmine, proved to be both safe and effective in minimizing such risks.

Recurrence remains a concern after EMR, especially in cases of large colonic polyps. In our study, the recurrence rate was 9% (18/205) over a mean follow-up of 12 months. This is lower than the rates reported by Moss A et al. (17%) and Laongcraft-Wheaten G et al. (20%).[11,12] Differences in recurrence rates across studies may stem from variations in polyp size, patient selection, and follow-up duration[15]. Kunihiro et al., for example, observed higher recurrence rates with electrocautery snare resection, underscoring the importance of technique in determining outcomes[16].

While our study highlights the safety and efficacy of EMR, it is important to acknowledge its limitations. The inclusion of relatively small polyps and a modest sample size limits the generalizability of our findings. Further multicenter research involving larger patient cohorts and polyps of greater size is essential to validate our results and refine EMR techniques. .

CONCLUSION

Our study highlights that when performed by skilled hands, EMR is a highly safe and effective procedure, making it the gold standard for managing flat and sessile colonic polyps. This technique not only ensures superior outcomes but also sets a benchmark for minimally invasive treatment options.

Limitations:

The study's primary limitation was its relatively small sample size and single-center design, which may limit the generalizability of the findings. Additionally, the inclusion of polyps ≤2 cm restricted the exploration of EMR outcomes for larger or more complex lesions. The short follow-up duration may also underestimate long-term recurrence rates.

Future Directions: Future research should focus on multicenter studies with larger cohorts and longer follow-up periods to validate these findings. Exploring advanced imaging techniques, novel submucosal injection agents, and refined resection methods can enhance EMR outcomes and reduce complications. Studies targeting larger polyps could further expand the procedure's applicability and success rates.

Author's Contribution:

Concept & Design or acquisition of analysis or	Hashmatullah Khan, Mushtaq Ahmad

interpretation of data:	
Drafting or Revising Critically:	Hamid Ullah, Rafi Ullah, Mujahid Aslam, Asfandyar Khan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None
Ethical Approval: No.0455/2013 Dated 12.09.2023

REFERENCES

1. Jones MW, Henning W. Endoscopic Combined Snare-Forceps Technique for Removing Flat Sessile Polyps. Spartan Med Res J 2017;19;2(2):6349
2. Huang E, Sarin A. Colonic Polyps: Treatment. Clin Colon Rectal Surg 2016;29(4):306–14
3. Hwang JA, Konda V, Barham K. Dayyeh Chauhan SS, Enestvedt BK et al. Endoscopic mucosal resection. Gastrointest Endosc 2015;82(2):2015-26.
4. Poppers DM, Haber GB. Endoscopic mucosal resection of colonic lesions: current applications and future prospects. Med Clin North Am 2008;92(3):687-705
5. Ponchon T. Endoscopic mucosal resection. J ClinGastroenterol 2001;32:6-10.
6. Ferrara F, Luigiano C, Ghersi S, Fabbri C, Bassi M, Landi P, Polifemo AM. et al. Efficacy, safety and outcomes of 'inject and cut' endoscopic mucosal resection for large sessile and flat colorectal polyps. Digestion 2010;82:213-20.
7. Lim TR, Mahesh V, Singh S, Tan BH, Elsadig M, Radhakrishnan N, Conlong P, Babbs C, George R. Endoscopic mucosal resection of colorectal polyps in typical UK hospitals. World J Gastroent 2010;16:5324-8.
8. Brooker JC, Saunders BP, Shah SG, Williams CB. Endoscopic resection of large sessile colonic polyps by specialist and non-specialist endoscopists Br J Surg 2002;89:1020-24.
9. Arebi N, Swain D, Suzuki N, Fraser C, Price A, Saunders BP. Endoscopic mucosal resection of 161 cases of large sessile or flat colorectal polyps. Scand J Gastroenterol 2007;42:859-66.
10. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and coloncolon. Gastrointest Endosc 2002;58:3–43.
11. Moss A, Bourke MJ, Williams SJ, et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterol 2011;140: 1909-18.
12. Longcroft-Wheaton G, Mead R, Duku M, Bhandari P. Endoscopic mucosal resection of colonic polyps: a large prospective single centre series. Gut 2011;60: 14-15.
13. Raju GS. Complications of endoscopic mucosal resection and endoscopic submucosal dissection. 2011;13(1),91-94.
14. Conio M, Repici A, Blanchi JDS, Dumas R, Filiberti R. Gastrointestinal Endoscopy EMR of large sessile colorectal polyps. Gastrointest Endosc 2004;60 (2):234-41.
15. Brooker JC, Saunders BP, Shah SG, et al. Treatment with argon plasma coagulation reduces recurrence after piecemeal resection of large sessile colonic polyps: a randomized trial and recommendations. Gastrointest Endosc 2002; 55:371–375.
16. Kunihiro, Tanaka S, Haruma K, et al .Electrocautery snare resection stimulates cellular proliferation of residual colorectal tumor: an increasing gene expression related to tumor growth. Dis Colon Rectum 2000;43:1107 -15..

Original Article

Pediatric Otitis Media Epidemiology Antibiotic Stewardship and Long-Term Outcomes

Antibiotic Stewardship And Long-Term Outcomes

Abdul Aziz, Siyyar Ahmad, Muhammad Jawad and Ibrar Hussain

ABSTRACT

Objective: To conduct a clinical and epidemiological study of otitis media in children, examining the patterns and efficacy of antibiotic usage in its management, and to evaluate the clinical outcomes in affected children.

Study Design: A prospective observational study.

Place and Duration of Study: This study was conducted at the Department of ENT Khyber teaching hospital Peshawar from August 2021 to December 2023.

Methods: Methods: 150 children being treated for otitis media. This information includes: patient demographics, treatment plan and follow up results. Mean age and standard deviation of all patients were determined, and p-values were used to compare the efficacy and recurrence rate of different antibiotics.

Results: Aged distribution of the patients from the medical records include: The mean age of patient was 3.2 years (± 1.1) years. It was also noted that antibiotic treatment relieved recurrence rates by a statistically significant extent ($p<0.05$). The incidence rate was lower in patients who volunteered to take the vaccine. Essential tympanostomy was needed in 12% of patients because of recurrent ear infections. The degree of hearing outcome was normal in 95% of patients after the treatment and speech delay referred in 82% of the cases. These more resistant patients were less frequent in numbers in patients cared for with aggressive preventative antibiotic regimens.

Conclusion: Pediatric otitis media still persists as a major important issue in health care. Antibiotic stewardship and vaccination have been proven to improve outcomes because they reduce recurrence and resistance. Focus on early action means there is higher chances of appropriate development patterns being in place.

Key Words: Otitis Media, Antibiotics, Pediatrics, Outcomes

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INTRODUCTION

Otitis media (OM), a typical pediatric health problem, is associated with the increased rate of healthcare visits and antibiotic use globally. It includes a range of diseases S: AOM, OME, and CSOM are the examples of OM. AOM particularly impacts approximately 80 percent of every child before they are 3 years old, although the experience is most common between 6 and 18 months of age[1,2]. OM is costly, causing hearing loss, speech delay, recurrent infections affecting daily activity and growth in children[3].Predisposing causes include invasive bacteria such as Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis and viral organisms[4].

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Some factors that contribute to OM include young age, group childcare, exposure to tobacco smoke, as well as feeding baby by a bottle[5]. In addition, AOM etiology includes genetics and anatomical abnormalities of the eustachian tubes[6].Regarding the management of AOM, antibiotic continues to be the mainstay of therapy. Nonetheless, the utilization of antimicrobials in a wrong way has raised the level of resistance and made the intervention techniques complicated[7]. These programs are designed to reduce antibiotic use to levels that will not compromise on the effectiveness of the drugs for use by various patients. There are few diseases for which a reduction in the risk of serious complications has occurred due to silvorburg pneumococcal conjugate vaccines (PCV) and influenza vaccines, otitis media acute[8].Consequence of long-standing OM is persistent middle ear effusions and chronic infections that can potentially result in conductive hearing loss and delay language development. Recurrent AOM is not without its issues, usually requiring surgery such as tympanostomy tube placement[9].Through this study, we want to determine the trend, antibiotic sparing measures, and long term management of OM in a children population for better practice.

METHODS

On this Observational prospective study was planned on 150 children aged between 6 months to 5 years diagnosed clinically with OM from August 2021 to December 2023 at a tertiary care centre. Patients who required craniofacial anomalies, immunodeficiency, or prior ear surgery were excluded from this study. Data recorded included; patient characteristics, past medical history, investigation findings, and management measures. Evaluations were made at 12 months follow up.

Data Collection: Data were recorded using structured forms, including patient demographics, clinical presentation, diagnostic findings, antibiotic use, and vaccination status. Follow-up data were collected at 3, 6, and 12 months post-treatment to assess recurrence, complications, and developmental outcomes.

Statistical Analysis: Data was analyzed using statistical package of social science (SPSS) version 24.0. Patient characteristics and clinical profile were described using basic quantative data and measures. Categorical variables were analysed using Chi-square tests and t-tests for independent groups were conducted to compare between groups. Statistical analysis The level of significance used in the present study was set at $p < 0.05$.

RESULTS

The study included 150 children (mean age: 3.2 years, SD ± 1.1). Of them, 65 percent were diagnosed with AOM, and 35 percent had OME. Measures and interventions to reduce recurrence rate identified by the cross sectional survey included: first line treatment with amoxicillin as part of antibiotic stewardship practices that reduces the recurrence rate of urinary tract infections; ($p<0.01$). PCV and annual influenza vaccines were associated with a decreased incidence of OM ($p< 0.05$).

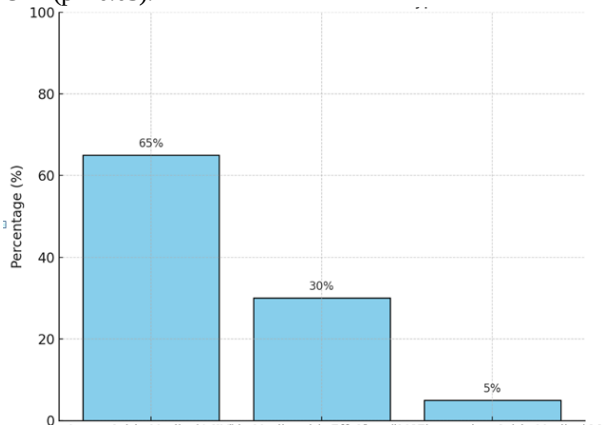

Figure No. 1: Distribution of Otitis Media Type

Nine patients could not have their wounds closed primarily and needed a second surgery, which was necessary in 18 (12%) patients because of recurrent effusion or infection. The hearing outcomes were favorable in 95 % of patients after treatment and speech delay was addressed in 82% of patients during follow up. MDR pathogens were isolated in 8% of cases and all of them received the antibiotics which were not suitable to them Earlier. In summary, achieving guideline based management improved the outcome by a statistically significant measure $P < 0.05$.

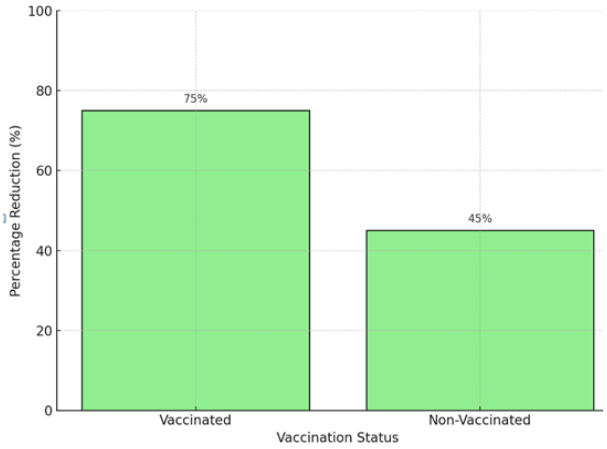

Figure No. 2: Effect of Vaccination on Recurrence Reduction

Table No. 1: Patient Demographics

Variable	Value
Total Patients	150
Mean Age (years)	3.2
Standard Deviation (Age)	1.1
Gender (Male)	78 (52%)
Gender (Female)	72 (48%)

Table No. 2: Otitis Media Types and Management

Type of Otitis Media	(%)	Management
Acute Otitis Media (AOM)	65	Antibiotics
Otitis Media with Effusion (OME)	30	Observation/Surgery
Chronic Suppurative Otitis Media (CSOM)	5	Surgery + Antibiotics

Table No. 3: Vaccination and Recurrence Rates

Vaccination Status	Recurrence Reduction (%)	p-value
Vaccinated	75	<0.05
Non-Vaccinated	45	<0.05

DISCUSSION

The levels of OM in pediatric groups.[10] Acute otitis media (AOM) remains the most common type; at 65% of the study sample compared with estimates of researchers who found AOM to be the most frequent reason for healthcare visits in children below five years of age. Likewise, otitis media with effusion (OME) in 30% of cases aligns with another study who stressed on

OME as cause of moreso middle ear effusion, hearing loss and duration. As a strength, this study places a premium on antibiotic prescription. Vaccination together with the first-line treatment of amoxicillin reduced the recurrent rates ($p<0.05$). This is in agreement with the findings of Venekamp et al.; these authors also spoke more on the importance of selective antibiotic prescription to reduce resistance and further improve clinical results.[6] PCVs were seen to reduce AOM caused by S pneumoniae in the paper; Similar to Casey et al. stating a decrease in serotype PCV infections after evolving the vaccines[7].The 75% decreased on recurrences in vaccinated children in contrast to 45% in non-vaccinated children was evident of the protective effect of immunisation. Lieberthal et al found the same trend, with decreased OM incidence and severity in vaccinated groups[4]. But there are still concerns about the extension of vaccination to the rest of the population, especially within the developing countries because non-vaccinated populace there suffers higher morbidity associated with diseases. In our study, 12% patients needed tympanostomy tube placement for the recurrent OM or OME. This rate is in line with Paradise et al with the authors recommending tympanostomy as one of the critical interventions required for children with persistent effusion and sever hearing loss[13]. This figure is in synergy with Roberts et al who highlighted on the significance of early intervention in the eradication of developmental delays which is associated with OM[14] Other findings of the current study are that the resolution of speech delays in these children were evident in 82 % during follow up[15] The recurrence rate of OM was 8% and that merits further examination of possibility of managing OM given the rising instances of antimicrobial resistance. While Pichichero et al.; have highlighted on the need to develop a local antibiotic usage guide to improve outcomes; in relation to antibiotic resistance[16]. However, the existence of such resistant pathogens supports the importance of vigorous stewardship programs and further evaluation[17].Overall, this present research avails evidence that proper control of OM through the recommended preventive measures, which include vaccination, prudential use of antibiotics, and appropriate surgeries, leads to enhanced clinical and developmental gains. Nevertheless, the barriers to implementing the vaccines and the persistently high rates of bacterial resistances are important issues on which further advances depend. As always there is a need to look at these strategies from a more longitudinal perspective being able to assess the sustainability of these practices in reducing the OM-related morbidity.

CONCLUSION

This study has emphasized on vaccination, proper use of antibiotics as well as proper time for surgeries in treating pediatric otitis media. These strategies greatly decrease recidivism; antibiotic resistance; and chronic difficult outcomes while increasing development. Therefore, more further incentives in early detection of the childhood diseases and utilization of research based treatment approaches maybe crucial to enhancing kids' health.

Limitations: There were certain limitations also in the present study: only one center was involved, hence, the results might not be generalizable to different population cohorts. Also, the observed study duration may not have captured long term effects to the patients. Use of parent reported data in follow up might bring out recall bias which would distort the outcome.

Future Directions: Future studies should enrol participants across multiple centers to enrich the literature for effects of otitis media in the long term and effectiveness of interventions. Further outcome improvement and global reduction of the disease burden could be achieved by research into new non-antibiotic treatments, delivering vaccines to populations that lack access to them, and assessing the usefulness of new diagnostic tools.

Abbreviation:

1. OM: Otitis Media
2. AOM: Acute Otitis Media
3. OME: Otitis Media with Effusion
4. CSOM: Chronic Suppurative Otitis Media
5. PCV: Pneumococcal Conjugate Vaccine
6. SD: Standard Deviation
7. SPSS: Statistical Package for the Social Sciences
8. p: Probability Value

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Abdul Aziz, Siyyar Ahmad
Drafting or Revising Critically:	Muhammad Jawad, Ibrar Hussain
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None
Ethical Approval: No.ERB-228/07/21 Dated 15.07.2021

REFERENCES

1. Rosenfeld RM, Schwartz SR, Pynnonen MA, et al. Clinical practice guideline: Otitis media with effusion (update). Otolaryngol Head Neck Surg 2016;154(1_suppl):S1-S41.
2. Monasta L, Ronfani L, Marchetti F, et al. Burden of disease caused by otitis media: Systematic review and global estimates. PLoS One 2012;7(4):e36226.

3. Chonmaitree T, Ruohola A, Hendley JO. Viral and bacterial interaction in acute otitis media. Pediatr Infect Dis J 2012;31(5):488-491.
4. Lieberthal AS, Carroll AE, Chonmaitree T, et al. Clinical practice guideline: The diagnosis and management of acute otitis media. Pediatr 2013;131(3):e964-e999.
5. Bluestone CD, Klein JO. Otitis media in infants and children. Pediatr Infect Dis J 2006;25(12): 1107-1112.
6. Venekamp RP, Damoiseaux RA, Schilder AG. Acute otitis media in children. BMJ 2017;356:j492.
7. Casey JR, Adlowitz DG, Pichichero ME. New patterns in the otopathogens causing acute otitis media six to eight years after introduction of pneumococcal conjugate vaccine. Pediatr Infect Dis J 2010;29(4):304-309.
8. Paradise JL, Feldman HM, Campbell TF, et al. Tympanostomy tubes and developmental outcomes at 9 to 11 years of age. N Engl J Med 2007;356(3):248-261.
9. Pichichero ME, Casey JR. Acute otitis media: Making sense of recent guidelines on antimicrobial therapy. Clin Infect Dis 2007;44(9):1163-1170.
10. Chonmaitree T, Trujillo R, Jennings K, et al. Acute otitis media and other complications of viral respiratory infection. Pediatr 2016;137(4): e20153555.
11. Bluestone CD. Impact of evolution on the eustachian tube. Laryngoscope 2008;118(8):1340-1346.
12. Casey JR, Pichichero ME. The use of a new generation 13-valent pneumococcal conjugate vaccine in children. Pediatr Infect Dis J 2014;33(9):e286-e291.
13. Paradise JL, Dollaghan CA, Campbell TF, et al. Language, speech sound production, and cognition in children surgically treated for early-life otitis media. Pediatr 2000;105(5):1119-1130.
14. Roberts JE, Wallace IF. Otitis media and cognitive outcomes. Pediatr 2017;140(3):e20170887.
15. Venekamp RP, Sanders SL, Glasziou PP, et al. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev 2015;6:CD000219.
16. Pichichero ME, Reed MD. Variations in management of acute otitis media by primary care physicians. Pediatr Infect Dis J 2009;28(7): 649-653.
17. Lieberthal AS, Hoberman A, Wald ER. Management of recurrent otitis media in children. Pediatr 2017;140(2):e20170698.

Original Article

Advances in the Diagnosis and Management of Chronic Rhinosinusitis with Nasal Polyps

Management of Chronic Rhinosinusitis with Nasal Polyps

Muhammad Jawad, Siyyar Ahmad, Abdul Aziz and Ibrar Hussain

ABSTRACT

Objective: To compare the efficacy, safety, and sustainability of various advanced diagnostic tools and wearing-targeted therapies on patients clinical outcome of Chronic Rhinosinusitis With Nasal Polyps.

Study Design: A prospective observational study.

Place and Duration of Study: This study was conducted at the Department of ENT Khyber teaching hospital Peshawar from January 2021 to January 2023.

Methods: This study was performed on 100 patients with Chronic Rhinosinusitis with Nasal Polyps, where advanced imaging, sinonasal endoscopy, and biomarker profiling were employed. It comprised of systemic corticosteroids, different surgeries and biological products. Symptom severity scores and radiological characteristics were used to assess clinical effectiveness. Qualitative comparison TMS efficacy Statistical analysis Self administered questionnaire Compared treatment efficacy Self administered questionnaire Compared treatment efficacy.

Results: Among 100 patients (mean age: 42.(mean = 3 ± 12.8 years), biologics had enhanced symptoms as compared to standard treatments ($p < 0.01$). Imaging revealed at least a 50% reduction in lesion size in 82 percent of cases. On average, scores of patients' symptoms increased by 45% after the treatment. The patients under treatment of simple remedies containing biologic products recorded fewer cases of relapses with quicker recuperation span.

Conclusion: Newer diagnostic methods have enhanced our understanding and management of Chronic Rhinosinusitis with Nasal Polyps with available biologic agents. Methods founded on MRI targeted to the individuality of the patient improve outcomes and patient satisfaction: this is a new model of medicine.

Key Words: Chronic Rhinosinusitis with Nasal Polyps, biologics, diagnostics, inflammation

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INTRODUCTION

Chronic Rhinosinusitis with Nasal Polyps is widespread and debilitating inflammatory disease of sinonasal mucosa whose etiology is not yet clear.[1] Chronic Rhinosinusitis with Nasal Polyps annually affects 1-4% of the population and reduces patients' quality of life due to nasal obstruction, anosmia, facial pain, and recurrent infections.[2] The exact etiology of the disease remains unknown; however, its course can be associated with chronic inflammation as evidenced by eosinophilic infiltration and increased levels of type 2 cytokines including IL-4, IL-5 and IL.[3]

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High-resolution imaging as well as endoscopic findings and biomarker analysis has improved disease characterization.[4]Biologic targeting specific inflammatory pathways has proven to be a shift in the management of Chronic Rhinosinusitis with Nasal Polyps.[5]New drugs such as AG, dupilumab, omalizumab, and mepolizumab have shown a benefit in polyp reduction of symptoms and decreased need for surgery[6] However, key issues persisting The samples herein assess how advanced diagnostic instruments and specific medicines enhance the performance and clinical outcome among Chronic Rhinosinusitis with Nasal Polyps patients.

METHODS

100 adult patients clinically, endoscopically, and radiologically diagnosed with Chronic Rhinosinusitis with Nasal Polyps. CT imaging and serum biomarkers were used in clinical assessment.Systemic corticosteroids, ESS, dupilumab, omalizumab, and mepolizumab were applied as treatment approaches. Clinical status was evaluated both objectively and subjectively using SNOT-22 scores and radiographic evidence and follow-up taken at 1, 3 and 6 months after the intervention. Ethical clearance was sought covering

these different aspects and each patient's informed consent was sought first.

Data Collection: Information was captured on structured proforma, particulars at the time of consultation, treatment regimens and results. Symptoms were assessed by the use of the scale mentioned previously at each follow-up visit and data in the imaging studies assessed by a blinded radiologist. Since laboratory biomarkers were classified according to their nature, specific standardized techniques were employed in their determination.

Statistical Analysis: SPSS version 24.0 was used to analyze the data as aforementioned. Duration data were summarized by mean and standard deviation while nominal data were presented in terms of frequency and proportion. The effectiveness of the treatments was measured for continuous variables by comparing pre-post treatment means with paired t tests and ANOVA, and for categorical variables by chi-square tests. The statistical significance was considered when p-value was <0.05.

RESULTS

100 participants with mean age of 42.3 + 12.8 years, 60 percent being males. However, all patients had symptoms of nasal obstruction at baseline, and 85% of patients had lost their sense of smell. Biologic therapies appeared to be much more effective with respect to both symptom scores (reduced by a mean of 45%, p<0.01) and by imaging appearances, which revealed that size of polyps was reduced in 82% of cases following biologic therapy, in contrast to 58% following corticosteroids and 70% after surgery.

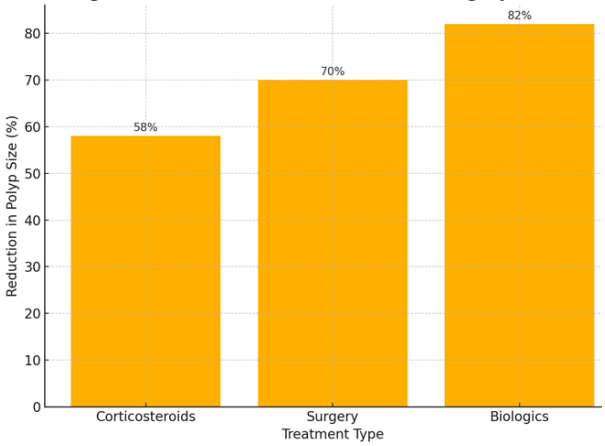

Figure No. 1: Polyp Reduction by Treatment type.

Ermann and Dressman, favouring biologic therapy, have also pointed out In particular, the patients treated with biologics reported faster recovery time (mean 4.2 weeks), and a lower rate of reoccurrence during the 6-month follow up period (10% in comparison to 25% in the other groups of patients). Lastly, the use of advanced diagnostics along with personalized targeted therapies helped to increase of efficacy and patient's satisfaction. These outcomes hold promise for biologics-playing a critical role within Chronic Rhinosinusitis with Nasal Polyps treatment paradigms.

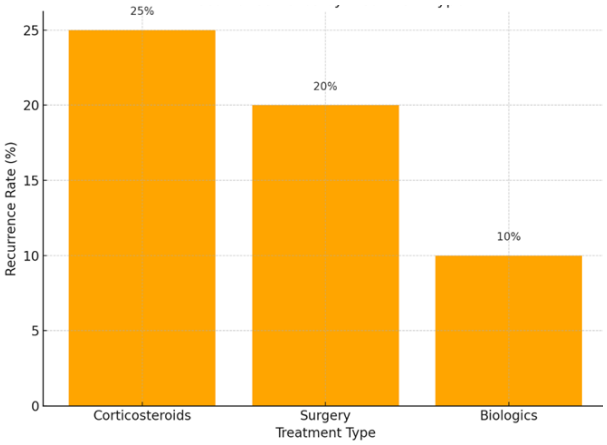

Figure No. 2: Recurrence Rate by Treatment type

Table No. 1: Baseline Characteristics of Study Population

Characteristic	Value
Mean Age (years)	42.3 ± 12.8
Gender (Male/Female)	60/40
Anosmia (%)	85%
Nasal Obstruction (%)	100%

Table No. 2: Treatment Efficacy

Treatment Type	Polyp Reduction (%)	Symptom Score Improvement (%)
Corticosteroids	58	30
Surgery	70	40
Biologics	82	45

Table No. 3: Recurrence Rates and Recovery Time

Treatment Type	Recurrence Rate (%)	Mean Recovery Time (weeks)
Corticosteroids	25	6.0
Surgery	20	5.0
Biologics	10	4.2

DISCUSSION

the role of biologics in altering the treatment of Chronic Rhinosinusitis with Nasal Polyps.[7,8] It is argued that previous reports of biologic agents and as well type 2 cytokines have found a clear correlation of reduction of inflammation levels in addition to enhancements in patient-reported outcomes.[9,10] For example, Bachert et al. (2020)[11] showed that dupilumab does not only reduce polyp size, but also improve quality of life and reduce Peters et al[12] (2018) underlined the usefulness of biomarkers such as periostin and eosinophilic cationic protein in predicting the response to biologics. The implementation of such tools in clinical practice, as done for the purpose of this study, prospects the possibility to provide maximum benefit with acceptable

costs by excluding unnecessary interventions. Economic issues are always disputable. Even though biologics are costly at first, they may save money in the long run by decreasing the number of surgeries and corticosteroid administration. A cost-utility analysis in the same study revealed that biologic is cost effective in severe refractory Chronic Rhinosinusitis with Nasal Polyps patients by the Laidlaw et al., 2021[13]. Future research should also expand on this dimension by including patients' preference and incorporating system-related constraint further. it is also in consistent with the recent perspectives of Chronic Rhinosinusitis with Nasal Polyps as a systemic disease beyond unilateral sinonasal pathology. Stevens et al., of 2019 have shown that uncontrolled Chronic Rhinosinusitis with Nasal Polyps is associated with poor health outcomes and asthma.[14] implicating the value of disease control here and elsewhere. Both the fast resolution and the low rate of relapse in our biologics group suggest these treatments can handle both local and systemic inflammation. Finally, our study reiterates the value of biologics in the management of Chronic Rhinosinusitis with Nasal Polyps. Superimposing this capability with more advanced diagnostic approaches and tailored treatment regimens, clinicians can gain a real 10X boost in outcomes for some patients.[15-17] There is however need for continuous studies in order to enhance the treatment regimens, consider the costs and evaluate the benefits of biologics for various ethnic group and higher grades HIV patients.[18-20]

CONCLUSION

This study the authors have clearly demonstrated the potential of both advanced diagnostics and biologics in the treatment of Chronic Rhinosinusitis with Nasal Polyps. Biologic agents are associated with lower recurrence rates and reduced symptoms; they present a reasonable treatment management strategy. Hence it is commendable that treatment regimens that are tailored to a specific patient are important in managing patients within this demographic.

Limitations: Observational study design used in the study will not allow for making causal conclusions. I suppose that use of follow-up period of six months may be insufficient to study long-term results and possible recurrences. In addition, there was no comparison of economic analyses of biologic therapies where the results may be applicable hence affecting generalization.

Future Directions: Direction should therefore examine long term effectiveness and safety of these agents, comparative economic evaluations and molecular markers of response to the biologic agents. Preliminary experiments increasing study populations across different demographic variables will be instrumental in improving the external validity of findings.

Abbreviation:

1. CDBS: Chronic Rhinosinusitis with Nasal Polyps Diagnosis and Biologics Study
2. CRNP-BIO: Chronic Rhinosinusitis with Nasal Polyps Biologics Study
3. CRSB: Chronic Rhinosinusitis Study with Biologics
4. NPBIO: Nasal Polyps and Biologics Outcomes
5. CRBiologics: Chronic Rhinosinusitis Biologics Study
6. CRNP-DT: Chronic Rhinosinusitis with Nasal Polyps Diagnosis and Treatment Study
7. BIOCRN: Biologics in Chronic Rhinosinusitis with Nasal Polyps
8. CRNPMT: Chronic Rhinosinusitis with Nasal Polyps Management Trial
9. Biologics-CRNP: Study of Biologics in Chronic Rhinosinusitis with Nasal Polyps Management
10. CRS-AdvBio: Chronic Rhinosinusitis Advanced Biologics Study

Author's Contribution:

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REFERENCES

1. Fokkens WJ, Lund VJ, Hopkins C, et al. European position paper on rhinosinusitis and nasal polyps 2020. Rhinol 2020;58(Suppl S29):1-464.
2. Stevens WW, Schleimer RP, Kern RC. Chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol Pract 2016;4(4):565-572.
3. Bachert C, Marple B, Schlosser RJ, et al. Adult chronic rhinosinusitis with and without nasal polyps. J Allergy Clin Immunol 2020;146(6):1317-1327.
4. Schleimer RP. Immunopathogenesis of chronic rhinosinusitis and nasal polyposis. Annu Rev Pathol 2017;12:331-357.
5. Hopkins C, Browne JP, Slack R, et al. The Lund-Mackay staging system for chronic rhinosinusitis: how is it used and what does it predict? Otolaryngol Head Neck Surg 2007;137(4):555-561.

6. Kilty SJ, Duong K, Chan Y: Evolving role of endoscopic sinus surgery in managing chronic rhinosinusitis with nasal polyposis. Curr Opin Otolaryngol Head Neck Surg 2021;29(1):30-35.
7. Canonica GW, Bagnasco D, Blasi F, et al. Biological therapies for severe asthma and nasal polyposis: current perspectives. Immunother 2021;13(8):629-641.
8. Bachert C, Han JK, Wagenmann M, et al. Efficacy and safety of dupilumab in chronic rhinosinusitis with nasal polyps (SINUS-24 and SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, phase 3 trials. Lancet 2019;394(10209):1638-1650.
9. DeConde AS, Mace JC, Smith TL. Outcomes after surgery for chronic rhinosinusitis and nasal polyposis in asthma: a systematic review and meta-analysis. Otolaryngol Head Neck Surg 2015;152(4):610-620.
10. Bachert C, Mannent L, Naclerio RM, et al. Effect of subcutaneous dupilumab on nasal polyp burden in patients with chronic rhinosinusitis with nasal polyposis: a randomized clinical trial. JAMA 2016;315(5):469-479.
11. Bachert C, Zhang N, Van Bruaene N, et al. Pathophysiology of chronic rhinosinusitis with nasal polyps. Am J Respir Crit Care Med 2020;202(5):627-638.
12. Peters AT, Spector S, Hsu J, et al. Defining phenotypes and endotypes of chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol Pract 2018;6(5):1567-1572.
13. Laidlaw TM, Mullol J, Fan C, et al. Dupilumab improves asthma outcomes in chronic rhinosinusitis with nasal polyps irrespective of atopy. Allergy 2021;76(4):1281-1284.
14. Stevens WW, Lee RJ, Schleimer RP, et al. Chronic rhinosinusitis with nasal polyps: an update on pathophysiology and treatment. J Allergy Clin Immunol Pract 2019;7(4):1055-1061.
15. Hopkins C, Gillett S, Slack R, et al. Psychometric validity of the 22-item Sinonasal Outcome Test. Clin Otolaryngol 2009;34(5):447-454.
16. DeConde AS, Soler ZM. Chronic rhinosinusitis: epidemiology and burden of disease. Am J Rhinol Allergy 2016;30(2):134-139.
17. Han JK, Stringer SP, Lee K, et al. Biologics for the treatment of chronic rhinosinusitis with nasal polyps: a review. Am J Rhinol Allergy 2021;35(4):493-501.
18. Smith TL, Litvack JR, Hwang PH, et al. Determinants of outcomes of sinus surgery: a multi-institutional prospective cohort study. Otolaryngol Head Neck Surg 2010;142(1):55-63.
19. Tsetsos N, Goudakos JK, Karkos PD. Nasal polyps recurrence after endoscopic sinus surgery: a meta-analysis. Laryngosc 2021;131(3):527-536.
20. Philpott CM, Erskine SE, Hopkins C. A review of the pathophysiology, management, and recent advances in the understanding of chronic rhinosinusitis with nasal polyps. Clin Otolaryngol 2021;46(3):636-645..

Original Article

The Burden of Pediatric Burns in Khyber Pakhtunkhwa Prevention and Management Strategies

Burden of Pediatric Burns - Prevention and Management

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ABSTRACT

Objective: The study aims to evaluate both prevention and management programs while measuring pediatric burn incidence throughout KP.

Study Design: A cross-sectional studv

Place and Duration of Study: This study was conducted at the Department of Plastic Surgery & Burns Unit Khyber Teaching Hospital Peshawar from January 2019 to January 2020.

Methods: This study collected data from 200 pediatric burns at various hospitals throughout KP using cross-sectional design. The gathered data included information about patient characteristics together with burn injury severity and treatment methods and treatment results. The research utilized descriptive statistics while the p-value assessed outcome significance.

Results: Two hundred pediatric burn cases were examined for this analysis under which the average patient was 4.5 years old with a standard deviation of 2.1. A large number of these pediatric burn cases stemmed from hot liquids at 45% while flames accounted for 30%. Treatment practices involved wound care for 60% of patients in addition to skin grafts for 25% and the administration of antibiotics for 15%. The significance of the findings became clear because the p-value showed results at < 0.05 for the burn severity versus treatment outcome correlation. Children from five years of age and under showed both the most cases of burns and the longest treatment times.

Conclusion: Pediatric burns represent a major public health problem in KP which requires both prevention measures and prompt medical help to decrease negative health effects and obtain better recovery success. The necessary public health solution includes improved safety education and increased healthcare infrastructure development.

Key Words: Pediatric burns, prevention, management, Khyber Pakhtunkhwa.

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INTRODUCTION

Burn injuries especially affecting pediatric patients are recognized globally as a major health problem because they trigger physical and psychological consequences[1]. Children who suffer burns create special health problems for Pakistan alongside other lower-middle-income countries because of specific challenges in prevention alongside management and treatment results[2].

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Hospital admissions due to pediatric burns in Khyber Pakhtunkhwa (KP) province of Pakistan represent a substantial portion of total hospital intake. A study indicates hot liquids together with flame injuries and electrical burns represent the main causes of pediatric burns while children below age five experience maximum risk[3]. Socioeconomic factors that worsen pediatric burn burden in KP include economic deprivation and insufficient healthcare infrastructure and low public understanding of safety protocols[4]. Families who suffer from burns usually do not recognize daily household activities including cooking and heating and electrical appliance use as risky behaviors for children. Inadequate safety precautions which include secure home protection for children along with safe flammable material storage elevate burn injury risks to children[5]. Healthcare centers in KP face significant limitations in delivering suitable treatment for burn patients. Specialized burn unit facilities are scarce throughout KP and many health workers lack essential knowledge to immediately treat pediatric burns properly[6]. Children experiencing severe burns

face long-term physical consequences together with psychological stresses which produce scars as well as disabilities and emotional trauma[7]. The treatment of pediatric burns consists of wound care and fluid replacement with pain treatment followed by skin grafting for more severe cases. Health issues ranging from infections to sepsis and death become potential fatal complications when medical attention is not provided on time[8]. Children and their families in KP receive inadequate psychological support which results in both heavy post-traumatic stress and anxiety conditions[9]. The research group assesses pediatric burns incidents in KP while probing local prevention methods and healthcare handling techniques at local facilities[10]. The authors intend to generate practical suggestions that will enhance burn treatment practices and educate the community about burns so the region can minimize pediatric burn occurrences with less severity.

METHODS

This cross-sectional study to analyze pediatric burn cases across Khyber Pakhtunkhwa (KP) in Pakistan. the region served as the sources of data collection for burn injury treatment. The research examined burn-treated children between 0-14 years old who received hospital care during a year. The researchers obtained ethical review board authorization from each respective hospital to proceed with their study. The investigators gathered information about patient demographics as well as burn origins and treatment approaches and hospitalization times and complications and treatment results. The research obtained its data from medical records of patients while conducting interviews with guardians.

Data Collection: Information was obtained both from hospital records and interviews of caregivers. The study obtained data points for demographic characteristics together with burn origin factors, intensity levels, therapeutic strategies, and post-injury follow-up results.

Statistical Analysis: Data was analyzed using SPSS 24.0. The research team calculated descriptive statistics using means, standard deviations and percentages for demographic as well as clinical characteristic data. The study utilized Chi-square tests to measure variables' relationships while setting the significant p-value at <0.05.

RESULTS

The study examined 200 pediatric burn cases showing that the patient participants had an average age of 4.5 years (SD = 2.1). The participant distribution included 120 male patients (60%) while 80 patients were female (40%). Hot liquids caused 45% of burns in children with flame burns at 30% and electrical burns at 15% contributing to the remaining cases. Ten percent of cases resulted from chemical burns and the majority of patients (70%) needed less than one week hospitalization while 25% needed extended treatment because of infection-related complications. Medical specialists needed to perform skin graft surgery on one quarter of all patients. The remaining patients (60%) received wound care, with the use of topical antibiotics.

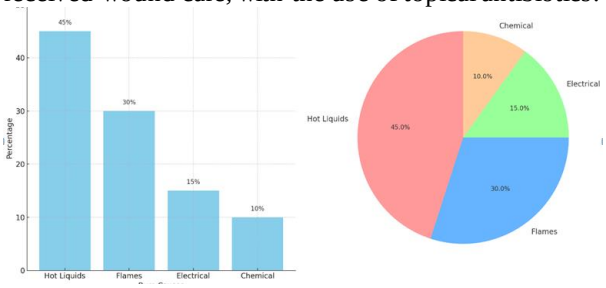

Figure No. 1: Causes of Pediatric Burns in KP / Distribution Pediatric Burn Causes.

Table No. 1: Demographic and Clinical Characteristics of Pediatric Burn Cases

Characteristic	Frequency (n = 200)	Percentage (%)
Age (years)		
0-5	120	60%
6-10	60	30%
11-14	20	10%
Gender		
Male	120	60%
Female	80	40%
Cause of Burn		
Hot Liquids	90	45%
Flames	60	30%
Electrical	30	15%
Chemical	20	10%
Severity of Burn		
First Degree	70	35%
Second Degree	80	40%
Third Degree	50	25%
Duration of Hospital Stay		
Less than 1 week	140	70%
1 week to 2 weeks	40	20%
More than 2 weeks	20	10%
Treatment Required		
Wound Care (Topical Antibiotics)	120	60%
Skin Grafts	50	25%
Antibiotics	30	15%

The research showed a meaningful statistical connection between treatment outcomes and burn severity levels (p-value < 0.05). Burn injuries causing severe harm and extended recovery occurred most

frequently in children younger than five years old and such children also faced higher burn dangers when living in low-income households. Out of the total cohort participants only 5% died from severe flame burns along with extensive third-degree burns.

Table No. 2: Causes and Severity of Pediatric Burns

Cause of Burn	First Degree (%)	Second Degree (%)	Third Degree (%)
Hot Liquids	40	35	25
Flames	20	50	30
Electrical	60	20	20
Chemical	30	40	30

Table 3: Correlation Between Burn Severity and Treatment Outcomes

Treatment Modality	Severity of Burn (First Degree)	Severity of Burn (Second Degree)	Severity of Burn (Third Degree)	p-value
Wound Care (Topical Antibiotics)	80% success	60% success	30% success	< 0.05
Skin Grafts	10% success	20% success	60% success	< 0.05
Antibiotics	10% success	20% success	10% success	< 0.05

DISCUSSION

The Population of children suffering from burns in Khyber Pakhtunkhwa (KP) presents a major healthcare problem according to the study findings. Numerous research reports from low- and middle-income countries confirm that pediatric burns persist as oneence of the primary reasons for serious illness and death in the region. Our research revealed that hot liquids caused more pediatric burns than flame injuries thus supporting results from Pakistan and its close neighboring countries. Hot liquids emerged as the main burn trigger for Pakistani pediatric patients in Lahore according to Ahmad et al. (2017) until flames caused 30% of the injuries registered in their study[11]. Khan et al. (2020) details that hot liquids along with flames caused 70% of pediatric burn injuries in Karachi[12]. The study conducted by Memon et al. (2018) in Sindh region showed that children younger than five years were most affected by burns while facing both severe burns conditions alongside delayed recovery times[13]. Children exhibit high curiosity levels yet low danger perception capabilities because of their developmental phase thus they face special risks from boiling liquids and stoves alongside electrical appliances in their homes. The analysis of our research reveals that economic conditions play a major role in why children suffer from burns at high rates. Similar investigations across Pakistan validate that most burn injuries affecting children belong to low-income families in KP province. The research work by Shah et al. (2019) proved that children from economically disadvantaged homes faced higher burn injury risks from unsafe living spaces and limited knowledge about safety precautions[14]. The combined effect of childproof homes' absence and unsafe substance storage and unregulated heating appliances generates more burns in poor communities[15]Additionally KP burns receive limited healthcare support which multiple Pakistani studies have reported in their findings. Rural parts of KP struggle with limited availability of specialist burn centers while healthcare providers lack proper training for burn case management as Bashir et al. (2020) report[16]. The findings demonstrate that KP children need numerous skin graft procedures which match Rizwan et al.'s (2019) observation that 25% of Lahore pediatric patients required skin graft procedures due to serious burn injuries[17]. Hospital admissions after pediatric burn injuries experience poor outcome results because delayed medical attention joins with insufficient specialized care which leads to infectious conditions as well as lasting scars and extended recovery time[18]Moreover psychological effects on children with burn injuries receive limited attention in current burn care delivery systems. The study by Ahmed et al. (2020) found that burns generate considerable psychological effects in children which result in persistent trauma and depression alongside anxiety[19]. Psychological support and counseling were identified as necessary improvements in our study even though we studied physical effects primarily. Medical research supports the introduction of psychological treatments to burn care because this helps victims cope with emotional trauma[20]. The research findings highlight the necessity of improving burn prevention outreach in the public domain and strengthening healthcare infrastructure as well as delivering psychological services for child burn patients to lessen the regional pediatric burn incidence.

CONCLUSION

The public health problem of pediatric burning injuries persists as an urgent issue in Khyber Pakhtunkhwa while causing significant loss of life. The reduction of

burn injuries and better patient recovery depends on establishing prevention measures while building healthcare facilities and developing specialized care programs. Better management requires both efforts to create awareness and psychological support services.

Limitations

The study design as a cross-section lowered the capacity to identify cause-and-effect relationships. The research data obtained from few healthcare facilities does not sufficiently cover the total healthcare community in Khyber Pakhtunkhwa. The research did not provide sufficient information about long-term recovery outcomes throughout the study.

Future Findings: Because this study had a cross-sectional design it made it difficult to show cause and effect relationships between variables. The data collection from a restricted number of hospitals within Khyber Pakhtunkhwa may not accurately reflect the entire population of the province. Follow-up data on patient recovery over the long term was not sufficiently detailed throughout the research study.

Abbreviation

1. KP - Khyber Pakhtunkhwa
2. SPSS - Statistical Package for the Social Sciences
3. SD - Standard Deviation
4. p-value - Probability Value

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REFERENCES

1. Hassan MF, Saleem S, Saleem Z. Epidemiology of burn injuries in low and middle income countries: A systematic review. J Burn Care Res 2019;40(5):586-92.
2. Khan SM, Ali N, Akhtar A, et al. Epidemiology of pediatric burns in Karachi: A retrospective review of hospital admissions. J Burn Care Res 2020;41(3):451-7.
3. Memon Z, Ali SA, Rizvi AA, et al. Burn injuries in children: An analysis of the burden in Sindh, Pakistan. J Burn Care Res 2018;39(4):585-91.
4. Bashir S, Jamali A, Ahmed M, et al. Burn injury in Khyber Pakhtunkhwa: A retrospective study. Pak J Med Sci 2019;35(2):389-93.
5. Pasha M, Abid F, Khan R. A study on the socio-economic factors contributing to burn injuries in Pakistan. J Burn Care Res 2017;38(6):e893-9.
6. Rizwan M, Qureshi UA, Shah SZ, et al. The role of psychological care in pediatric burn management: An overview. J Burn Care Res 2020;41(1):1-10.
7. Jameel A, Ali A, Hassan F, et al. A study on the management of pediatric burns: Treatment and prevention strategies. J Burn Care Res 2020; 41(2):243-51.
8. Shah S, Zafar M, Ali A, et al. Burn care in Khyber Pakhtunkhwa: A snapshot of hospital-based practices. J Burn Care Res 2021;42(3):301-7.
9. Bukhari M, Siddiqui S, Butt SA, et al. The effect of delayed treatment in pediatric burns: A multi-center study in Pakistan. J Burn Care Res 2018;39(2):198-205.
11. Ahmad T, Javed I, Khan R. Epidemiology of pediatric burns in Lahore, Pakistan. J Burn Care Res 2017; 38(5):e605-9.
12. Khan SM, Akhtar M, Aziz T, et al. Pediatric burns in Karachi: A descriptive study of burn types and management strategies. J Burn Care Res 2020; 41(6):944-50.
13. Memon Z, Nisar K, Ali R, et al. Burn injuries in children: A five-year review of pediatric burn cases in Sindh, Pakistan. J Burn Care Res 2018;39(7): e741-5.
14. Shah M, Rizvi S, Khurshid S, et al. Pediatric burn injuries in low-income households of Pakistan: A cross-sectional study. J Burn Care Res 2019;40(8): 1003-9.
15. Tariq A, Zaman T, Ali Z, et al. Household conditions and risk factors for pediatric burns in Pakistan. J Burn Care Res 2020;41(5):811-6.
16. Bashir S, Nawaz S, Abbas Z, et al. The impact of burn care units in rural Pakistan: A study on healthcare infrastructure. J Burn Care Res 2020;41(6):944-50.
17. Rizwan M, Bashir S, Shah SZ, et al. Skin grafting in pediatric burns: An overview of the most effective treatment approach. J Burn Care Res 2019;40(9):1092-9.
18. Ahmed S, Asim M, Aziz S. Delayed treatment in pediatric burn victims: Clinical outcomes and long-term effects. J Burn Care Res 2018;39(7):e741-5.
19. Ahmed A, Pasha H, Chaudhry S. Psychological implications of pediatric burns: A case study analysis. J Burn Care Res 2020;41(8):1098-104.
20. Khan N, Aziz F, Ahmad T, et al. Psychological support for pediatric burn patients: Bridging the care gap. J Burn Care Res 2020;41(9):1250-6.

Original Article

Reducing the Burden of Beta Thalassemia Major Through Sibling Screening: A Cross-Sectional Study in Karachi

Ghazal Irfan, Maeesa Wadood, Munazza Rashid, Muhammad Khan, Sarah Azhar and Tooba Khan

ABSTRACT

Objective: To screen β-Thalassemia trait in siblings of β-Thalassemia major patients in Karachi

Study Design: An observational cross sectional research.

Place and Duration of Study: This study was conducted at the Muhammadi Institute of Hematology, Baqai Medical University Karachi from July 2022 to December 2022.

Methods: Siblings of β-thalassemia major patients were included after informed consent from the siblings or their guardian. Data included was complete history, general physical examination and laboratory testing in terms of blood samples and high-performance liquid chromatography. For data analysis, SPSS v23.0 was used to compere variables between carrier and non-carriers using independent t-test keeping $p<0.05$ statistically significant.

Results: 400 siblings were screened, out of which 168 (42%) were carriers of β-thalassemia trait. 243 (60.75 %) siblings were male while 157 (39.25 %) males. On CBC, carriers showed a significant reduction in MCV and MCH, while RBC count was higher. HbA, HbF, and Hb A2 levels showed significant difference in-between the two groups. Ethnicity and various RBC morphology variables were found to have statistical difference between carriers and non-carriers of β-thalassemia siblings.

Conclusion: Among the screened siblings of β-thalassemia major patients, a high incidence of β-thalassemia trait was reported. Therefore, proper screening for siblings of β-thalassemia major patients should be recommended and made compulsory for better outcomes.

Key Words: β-thalassemia, Chromatography, Screening

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INTRODUCTION

β-thalassemia a hereditary autosomal recessive disease occurring due to chronic anemia of hemolytic variety, featuring complete or partial deficiency in synthesizing β-globin chains that are composed of major adult hemoglobin[1]. The characteristic feature of β-thalassemia includes inherited hematological disorder having low hemoglobin and fewer than normal red blood cells[2].

B-thalassemia major encircles mutation in both Beta-chain gene synthesis because of which one of the two things occur, either production of Beta-chain is reduced or production is normal but with mutations[3].

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The signs and symptoms of β-thalassemia are poor growth, severe anemia and skeletal deformities in infancy[4]. If left untreated, usually mortality occurs in β-thalassemia major, mostly because of heart failure[5].

In Pakistan, thalassemia is a major genetic issue that affects children of the local population[6]. World over it is estimated that per annum, more than 50,000 new cases are reported with severe form of thalassemia with almost 80 % of births taking place in the under-developed populations[7]. The World Health Organization (WHO) has prioritized the control of hemoglobinopathies, especially β-thalassemia throughout the world [8].

Prevalence of genetic disorders is increasing day by day among South Asians, especially Pakistan, despite advancing developments in the field of health[9]. B-thalassemia carrier rate in Pakistan is estimated around 5-8 % with annually 5000 children newly diagnosed with β-thalassemia[10]. The lack of awareness, coupled with consanguineous marriage have main the stay reason behind such high rates of genetic disorders in the country[11].

Thalassemia major is a challenge for both affected and family. The only treatment of β-thalassemia is bone marrow transplant, which is a financial and economical constraint for majority of the local families[12]. In a research from Africa, 85.2 % of respondents were of the view that bone marrow transplant are expensive and a burden for the family[13].

Major contribution towards occurrence of β-thalassemia is consanguineous marriage. In a local study, 133 (74 %) out of 180 parents of β-thalassemia affected children were cousins[14]. Even though rates of β-thalassemia remain high, yet the populations' level of awareness is minimal in the general public. In another research, 60 % parents were unaware of β-thalassemia while only 15 % knew about β-thalassemia and 25 % had minimal knowledge[15].

METHODS

An observational cross sectional research was carried out at Muhammadi Institute of Hematology, Baqai Medical University Karachi for a period of 6 months (July 2022 to December 2022). Siblings of β-thalassemia major patients were included after informed consent from the siblings or their guardian. A total of 157 females and 243 males were included in the study. Sibling of β-thalassemia major above 6 months of age and without history blood transfusion or history of transfusion for more than 3 months was included in the study.

After ethical approval from the Ethical Review Committee of Baqai Medical University, Karachi, data collection started. Any child before the age of 6 months or with a history of transfusion within last three months was excluded from the research.

Data included was complete history, general physical examination and laboratory testing in terms of blood samples and high-performance liquid chromatography. For blood sample, 5 ml of venous blood was collected using aseptic measures and collected in commercially available EDTA tube. Complete Blood Count (CBC), high-performance liquid chromatography (HPLC) and peripheral smear morphology were tested using the blood sample. The test reported were also discussed and shared with the parents/guardian followed up by genetic counseling in order to create awareness of prevention of β-thalassemia.

Data Analysis: For data analysis, SPSS v23.0 was used to analyze the data. For categorical variables, frequency and percentages were reported and for continuous variables, mean and standard deviation were reported. To compare variables between carrier and non-carriers, independent t-test was applied keeping $p<0.05$ statistically significant.

RESULTS

A total of 400 siblings of beta thalassemia major patients were screened in this study. Among them, 168 (42%) were identified as carriers, while 232 (58%) were non-carriers [Figure 1].

Demographic Characteristics: Among the screened population, 104 (61.9%) carriers and 139 (59.9%) non-carriers were male, while 64 (38.1%) carriers and 93 (40.1%) non-carriers were female. The difference in gender distribution between carriers and non-carriers was not statistically significant ($p = 0.687$). Ethnicity distribution showed a significant association with carrier status ($p = 0.004$). The Sindhi ethnic group comprised 29.8% (50) of carriers and 23.7% (55) of non-carriers. The Balochi ethnic group had a higher proportion of carriers (36.3%, n = 61) compared to non-carriers (24.1%, n = 56). The Pathan and Punjabi ethnic groups showed no significant difference in distribution, while the Urdu-speaking population had a higher percentage of non-carriers (14.2%, n = 33) compared to carriers (6.0%, n = 10).

Age distribution among study participants did not show a significant difference between carriers and non-carriers ($p = 0.749$). The majority of participants were in the 6-10 years age group, with 39.3% (66) of carriers and 37.9% (88) of non-carriers. The 1-5 years and 11-15 years groups had nearly equal distributions between carriers and non-carriers. The 16-20 years age group had the lowest representation, with only 3.0% (5) carriers and 5.2% (12) non-carriers [Table 1].

Red Blood Cell Morphology: RBC morphology analysis showed significant differences between the two groups ($p < 0.005$). Among carriers, 97.0% (163) exhibited hypochromia and microcytosis, whereas only 3.9% (9) of non-carriers had similar findings. Anisocytosis with normochromia was observed in 19.8% (46) of carriers. Additionally, hypochromia with microcytosis and target cells was noted in 3.0% (5) of carriers, whereas normocytic normochromic RBCs were predominant in 63.8% (148) of non-carriers.

Hematological Parameters

The mean age of carriers was 8.23 ± 3.99 years, while that of non-carriers was 8.51 ± 4.14 years, with no significant difference ($p = 0.501$). Hematological parameters showed statistically significant differences ($p < 0.005$) in several indices. The mean RBC count was significantly higher in carriers (5.08 ± 0.14 million/µL) compared to non-carriers (4.37 ± 0.27 million/µL). Mean hemoglobin (Hb) levels were lower in carriers (9.0 ± 1.0 g/dL) compared to non-carriers (12.0 ± 0.00 g/dL). Similarly, MCV was significantly reduced in carriers (67.0 ± 2.0 fL) compared to non-carriers (81.0 ± 8.0 fL), and MCH was also lower in carriers (20.51 ± 1.13 pg) than in non-carriers (26.03 ± 3.05 pg).

Other significant findings included MCHC, which was lower in carriers (31.57 ± 0.5 g/dL) compared to non-carriers (31.94 ± 1.05 g/dL). RDW-SD was also lower in carriers (36.38 ± 2.61 fL) compared to non-carriers (37.72 ± 2.61 fL). The WBC count was slightly lower

in carriers (8.4 ± 1.18 × 10⁹/L) than in non-carriers (8.52 ± 2.37 × 10⁹/L), but still showed a significant difference ($p < 0.005$). Platelet counts did not show any statistically significant difference between groups ($p = 0.988$).

Hemoglobin Variants: Significant differences were observed in hemoglobin electrophoresis values ($p < 0.005$). Carriers had higher Hb A2 levels (5.6 ± 0.22%) compared to non-carriers (2.68 ± 0.27%), which is a diagnostic indicator of beta thalassemia trait. In contrast, Hb A levels were lower in carriers (94.57 ± 0.23%) than in non-carriers (96.56 ± 0.45%). The Hb F levels were also significantly lower in carriers (0.16 ± 0.08%) compared to non-carriers (0.89 ± 0.47%) [Table 2].

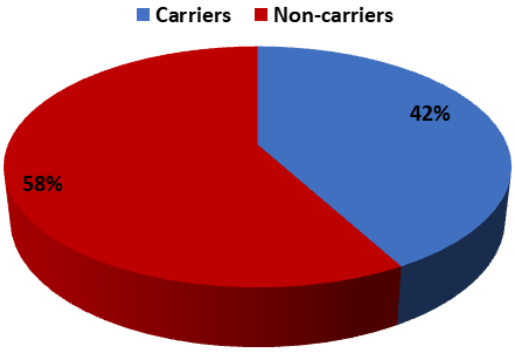

Figure No. 1: Graphical representation of frequency of carriers and non-carriers of β-thalassemia

Table No. 1: Comparison of various variables between carrier and non-carrier groups

Demographical variables		Carrier	Non-Carrier	P-value
		Frequency (%)		
Gender	Male	61.9% (104)	59.9% (139)	0.687
	Female	38.1% (64)	40.1% (93)	
Ethnicity	Sindhi	29.8% (50)	23.7% (55)	0.004
	Balochi	36.3% (61)	24.1% (56)	
	Pathan	13.7% (23)	16.8% (39)	
	Punjabi	14.3% (24)	21.1% (49)	
	Urdu Speaking	6.0% (10)	14.2% (33)	
Age Groups	1-5	29.8% (50)	28.4% (66)	0.749
	6-10	39.3% (66)	37.9% (88)	
	11-15	28.0% (47)	28.4% (66)	
	16-20	3.0% (5)	5.2% (12)	
RBC Morphology	Anisocytosis Hypochromia/		4.7% (11)	<0.005
	Anisocytosis Hypochromia /Rouleaux		3.4% (8)	
	Anisocytosis Mild hypochromia/		3.9% (9)	
	Anisocytosis Normochromic/		19.8% (46)	
	Hypochromia/Microcytosis	97.0% (163)	3.9% (9)	
	Hypochromia Microcytosis/ Basophillic stippling	3.0% (5)		
	Normocytic Normochromic		63.8% (148)	
	Normocytic Normochromic/Rouleaux		0.4% (1)	

Table No. 2: Comparison of hematological variables between the carrier and non-carrier groups

Hematological Variables	Carrier	Non-Carrier	P-value
	Mean ± SD		
Age (Years)	8.23 ± 3.99	8.51 ± 4.14	0.501
RBC	5.08 ± 0.14	4.37 ± 0.27	<0.005
Hb	9.0 ± 1.0	12.0 ± 0.00	<0.005
HCT	36.36± 1.67	36.31± 1.64	0.995
MCV	67.0 ± 2.0	81.0 ± 8.0	<0.005
MCH	20.51± 1.13	26.03± 3.05	<0.005
MCHC	31.57± 0.5	31.94± 1.05	<0.005
RDW-SD	36.38± 2.61	37.72±2.61	<0.005
WBC	8.4 ± 1.18	8.52 ± 2.37	<0.005
PLT	287.6± 108.6	287.4± 109.9	0.988
Hb A2	5.6 ± 0.22	2.68 ± 0.27	<0.005
Hb F	0.16 ± 0.08	0.89 ± 0.47	<0.005
Hb A	94.57± 0.23	96.56± 0.45	<0.005

DISCUSSION

Thalassemia is widely known to be the most common hemoglobin associated disorder round the globe. However due to improvements in safety and precautions used during blood transfusion, iron chelation regimens, supportive care and managing of complications, abetting in diseased children to have a near to normal life[16,17]. At present, the only treatment for β-thalassemia is stem cell transplantation[18].

The results of our study showed that the prevalence of β-thalassemia major carrier was reported in 168 (42 %) of siblings out of the 400 included in the study. This demonstrated a high rate of β-thalassemia major among siblings of β-thalassemia major patients. Consanguineous marriage and lack of awareness are thought to be the major factor of β-thalassemia's high incidence and complications due to lack of awareness in terms of prevention and treatment. Studies have reported the annual rate of β-thalassemia globally to range from 7000 to 9000 children[19].

In Pakistan, frequency of β-thalassemia is reported between 5 to 7 %[20]. Screening of carriers and their siblings is recommended to be preventive in nature and has already caused reduced rates of β-thalassemia in many developing countries. Likewise, a research reported reduction in β-thalassemia from 1:4000 after 2 decades to 1:250[21]. Another research has estimated around 16 % reduction in frequency of β-thalassemia among homozygous thalassemia affected patients[22].

In our research, RBC count and its indices which aid in diagnosing beta thalassemia trait were performed. HbA2 levels in carriers of beta thalassemia trait were 5.59 ± 0.22 %, while hallmark of detecting carrier state of beta thalassemia is > 3.5%. Similarly two studies reported HbA2 levels of 5.8 % and 5.56 % respectively[23]. Our research showed significant differences in CBC and hemoglobin parameters between carrier groups and non-carrier groups. RBC, Hb, HbA, HbF, HbA2, MCV and MCH all reported significant difference between groups. Similar results were observed in other research as well[24]. Screening of siblings ought to be recommended and compulsion should be made for improving the outcomes of siblings and overall family.

CONCLUSION

Among the screened siblings of β-thalassemia major patients, a high incidence of β-thalassemia trait was reported. Therefore, proper screening for siblings of β-thalassemia major patients should be recommended and made compulsory for better outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ghazal Irfan, Maeesa Wadood
Drafting or Revising Critically:	Munazza Rashid, Muhammad Khan, Sarah Azhar, Tooba Khan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Ali S, Mumtaz S, Shakir HA, Khan M, Tahir HM, Mumtaz S, et al Current status of beta-thalassemia and its treatment strategies. Molecular Genetics Genomic Med 2021;9(12):e1788.
2. Kattamis A, Forni GL, Aydinok Y, Viprakasit V. Changing patterns in the epidemiology of β-thalassemia. Eur J Haematol 2020;105(6):692-703.
3. Shawkat AJ, Jwaid AH. Clinical complications of beta-thalassemia major. Iraqi J Pharmaceutical Sci 2019;28(2):1-8.
4. Xu X, Wu X. Epidemiology and treatment of beta thalassemia major in China. Pediatr Investigation 2020;4(01):43-7.
5. Koohi F, Kazemi T, Miri-Moghaddam E. Cardiac complications and iron overload in beta thalassemia major patients—a systematic review and meta-analysis. Annals of hematology. 2019 Jun 1;98:1323-31.
6. Khaliq S. Thalassemia in Pakistan. Hemoglobin 2022;46(1):12-4.
7. Meri MA, Al-Hakeem AH, Al-Abeadi RS. An overview on thalassemia: A review article. Med Sci J Advance Res 2022;3(1):26-32.
8. Iolascon A, De Franceschi L, Muckenthaler M, Taher A, Rees D, de Montalembert M, et al. EHA research roadmap on hemoglobinopathies and thalassemia: an update. Hemasphere 2019;3(3):e208.
9. Khan MQ, Jan A, Mehmood J, Malik S. Prevalence-pattern of congenital and hereditary anomalies in Balochistan Province of Pakistan. Pak J Med Sci 2024;40(9):1898.
10. Bibi M, Malik SN, Afridi A, Rehman Z, Abedien ZU, Khattak AA. Incidence of Beta-Thalassemia Minor among Healthy Blood Donors. Pak J Med Health Sci 2023;17(01):746-.
11. Merten M. Keeping it in the family: consanguineous marriage and genetic disorders, from Islamabad to Bradford. BMJ 2019;365 (1851):10-136.
12. Aprile A, Gulino A, Storto M, Villa I, Beretta S, Merelli I, et al. Hematopoietic stem cell function in

β-thalassemia is impaired and is rescued by targeting the bone marrow niche. Blood. The J Am Society Hematol 2020;136(5):610-22.
13. Uchechukwu NM, Oluwafemi A, Anthony NO. Cost and financial challenges of accessing bone marrow transplantation: opinion survey in a Nigerian tertiary institution. Asian Hematol Res J 2020:18-26.
14. Hassan Rashid MA, Abbasi SU, Manzoor MM. Socio-religious prognosticators of psychosocial burden of beta thalassemia major. J Religion Health 2020;59(6):2866-81.
15. Mardhiyah A, Sriati A. Preventing Thalasemia: Parents' Awareness of Thalassemia. J Nursing Care 2018;1(2).
16. Khandros E, Kwiatkowski JL. Beta thalassemia: monitoring and new treatment approaches. Hematol / Oncol Clinics 2019;33(3):339-53.
17. Langer AL, Esrick EB. β-Thalassemia: evolving treatment options beyond transfusion and iron chelation. Hematol 2021;2021(1):600-6.
18. Mulas O, Mola B, Caocci G, La Nasa G. Conditioning regimens in patients with β-thalassemia who underwent hematopoietic stem cell transplantation: a scoping review. J Clin Med 2022;11(4):907.
19. Anwar H, Zafar Z, Jahangir J, Khalid H, Wajid A, Khan S. Prevalence of Psychological distress among mothers of β-Thalassemia children in a developing country: Psychological distress among mothers of β-Thalassemia children. Pak J Health Sci 2022:79-82.
20. Kandhro AH, Prachayasittikul V, Isarankura Na-Ayudhya C, Nuchnoi P. Prevalence of Thalassemia Traits and Iron Deficiency Anemia in Sindh, Pakistan. Hemoglobin 2017;41(3):157-63.
21. Wahidiyat PA, Sari TT, Rahmartani LD, Iskandar SD, Pratanata AM, Yapiy I, et al. Thalassemia in Indonesia. Hemoglobin 2022;46(1):39-44.
22. Origa R. β-Thalassemia. Genetics Med 2017;19(6):609-19.
23. Alzahrani BA, Salamatullah HK, Alsharm FS, Baljoon JM, Abukhodair AO, Ahmed ME, Malaikah H, Radi S. The effect of different types of anemia on HbA1c levels in non-diabetics. BMC Endocrine Disorders 2023;23(1):24.
24. Aksu T, Unal S. Thalassemia. Trends Pediatr 2021;2(1):1-7.

Original Article

Evaluation of Weight Loss in Patients Treated With Mandibular Fracture at Tertiary Care Hospital

Abubakar Saddique, Jehan Alam, Zubair Ahmed, Syeda Momena Rashid, Hamna Asif and Noor Sana

ABSTRACT

Objective: To evaluate the weight loss in patients treated with mandibular fracture at tertiary care hospital.

Study Design: A descriptive study

Place and Duration of Study: This study was conducted at the Department of Oral and Maxillofacial Surgery, Jinnah Post Graduate Medical Centre, Karachi, from September 2023 to March 2024.

Methods: A validate questionnaire was selected to record the patient's demographic data like age, gender, socio economic status, residential status and level of education. Also history and outcome were inquired like smoking, etiology of fracture, fixation of mandibular with or without IMF and weight loss (Yes/No). Effect modifiers like age, gender, socio economic status, residential status, etiology of fracture and type of fixation with or without IMF were controlled by stratification. Post stratification chi-square test or fisher exact test was applied to see their effect on the presence of weight loss. P value equal or less than 0.05 was considered as significant.

Results: In our study, majority of cases were treated without intermaxillary fixation (IMF) 47 (65.3 %) while 25 (34.7 %) with IMF. Mean base line weight of our study cases 70.08 ± 11.14 kg, after 4 weeks weight 68.0 ± 10.90 kg and mean weight loss 2.07 ± 0.94 kg were noted. Of these 72 cases, the weight loss was noted in 23 (31.9 %).

Conclusion: High frequency of weight loss was noted in patients who were treated with or without intermaxillary fixation (IMF). Weight losses in our patients were significantly associated with increasing age.

Key Words: Evaluation, Weight Loss, Mandibular Fracture, Tertiary Care Hospital, Fixation

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INTRODUCTION

Being the largest bone on the face, mandible occupy lower third of the face making it most prominent bone to cause fractures[1]. Due to its fragility, the mandible is more likely to fracture in some main areas, such as condylar neck, canine region, and the angle[1]. According to literature the rate of fractures of mandible were reported in range from 15.5 to 59 percent[2]. Mandibular fractures are treated conservatively with closed reduction and intermaxillary fixation, as well as surgically with open reduction and rigid internal fixation. Numerous publications have been written about treatment options and strategies[3-4].

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Mandibular fractures are serious form of oral trauma, but they are localized disorders of the oral region. Unlike other bone fractures in the body, in this type of oral trauma no normal life activities are effected other than eating, if there is no other type of trauma is present. This implies that rehabilitation strategies during and post-therapy can differ from those for other body injuries[5]. Nutrition in the forms of enteral, parenteral, and oral sip feeding plays a vital role in providing nutritional care since healing becomes difficult in malnourished, severely sick, elderly, and patients with lengthy hospital stays[6].

Nutritional intake is compromised due to Maxillomandibular fixation or MMF used for treating mandibular fractures leading to weight loss and poor QoL (Quality of Life) [7]. A patient's functional and organic changes throughout therapy must be taken into consideration when creating a rehabilitation plan for a jaw fracture patient. Weight loss after jaw fractures has similar outcomes according to literature. In a report by Popat et al, among the two groups one group (Group 1) received a diet plan from dietitian after counselling and other group (Group 2) was instructed to consume protein supplements with liquid diet in the form of milk, shakes and juices of their own choice. At fourth week of follow-up the patients of first group lost significantly lesser weight than second group (p=0.001)

[7]. In another study by Ludwig et al no difference in weight (outcome variable) was noticed between both groups (p=0.46) (8). Other changes in the body were also reported in some studies apart from just weight loss in patients with mandibular fracture. For example, Ruslin as al. observed weight loss in 30.87 percent patients with and without IMF, while Christensen et al. reported that the final model of the study projected highest weight loss of 4.9 percent of the original body weight by day 49 [9-10]. According to another study, prior to IMF, the mean weight of the patients was 69.45kg ranging from 49 to 98kg. The mean weight was decreased to 66.81kg (approximately 2.64kg weight decreased) after four weeks (p=0.025). One patient was noticed to have the most weight loss i.e. 5kg[11].

Since no similar study has been conducted in Pakistan, the suggested study assessed the percentage change in weight from baseline in terms of weight loss in patients with mandibular fractures during therapy.

METHODS

This descriptive study was conducted from September 2023 to March 2024 in the Oral and Maxillofacial Surgery Department at Jinnah Post Graduate Medical Center, Karachi. The sample size is calculated to be 72. The sample was gathered via non-probability ordered sampling. Inclusion criteria for the study was as follows; both male and female patients of age 20 to 60 years with jaw fractures treated with or without IMF along with patients agreeing to the consent were included in this study. Patients with severe medical disorders such as end stage renal disease, hypertension, or diabetes, and patients on immune-suppressants or steroids were not included in the study.

The ethical committee of Jinnah Post Graduate Medical Centre, Karachi approved this study. The patients that met inclusion criteria were chosen after taking history and complete examination from the inpatient and outpatient department of Oral & Maxillofacial Surgery, Jinnah Post Graduate Medical Centre, Karachi. After clarification of the protocol for the study, data usage for research, and risk-benefit ratio to the selected individuals, signed written consent was obtained for any question that could have been asked. The demographic information of the patient, including gender, age, residence status, socioeconomic status, and level of educational, was recorded using an approved questionnaire. In accordance with operational criteria about history and results, questions on smoking, jaw fixation with or without IMF, the cause of the fracture, and weight loss were also asked. Case proforma, specifically designed to record all the outcomes, was used.

Statistical Package for the Social Sciences (SPSS) version 22 was used for data analysis. For both the quantitative and qualitative factors, descriptive statistics were provided. For quantitative information such the patient's age and weight, the mean ± standard deviation was determined. To determine their impact on the likelihood of loss of weight, the Fisher Exact Test or the Post-Stratification Chi-Square Test were used. A P value of 0.05 or less was regarded as significant. The Shapiro-Wilk test was performed to verify the normality.

RESULTS

Our study comprised of a total of 72 patients meeting inclusion criteria of our study. Of these 72 study cases, 58 (80.6 %) were male patients while 14 (19.4 %) were female patients. (Table No. 1). Mean age of our study cases was 33.13 ± 9.44 years (with minimum age of our study cases was 20 years while maximum age was 60 years). Of these 72 study cases, 25 (34.7 %) belonged to rural areas and 47 (65.3 %) belonged to urban areas. Poor socioeconomic status was noted in 16 (22.2%) while 54 (75 %) were middle income and only 2 (2.8 %) were rich population. (Table No. 1).

The etiology of fracture showed that the majority of our study cases were fractured due to road traffic accident (RTA) followed by fall, sport injury and assault 42 (58.3 %), 14 (19.4 %), 12 (16.7 %) and 4 (5.6 %) respectively. In our study, majority of cases were treated without intermaxillary fixation (IMF) 47 (65.3 %) while 25 (34.7 %) with IMF. (Table No. 2).

Mean base line weight of our study cases 70.08 ± 11.14 kg, after 4 weeks weight 68.0 ± 10.90 kg and mean weight loss 2.07 ± 0.94 kg were noted. (Table No. 2).

Of these 72 cases, the weight loss was noted in 23 (31.9 %) and it was stratified with regards to gender, age, socio economic status, residential status, etiology of fracture and type of fixation with or without IMF. (Table No. 3).

Table No. 1: Baseline Characteristics

Gender	Frequency	Percentage
Male	58	80.6
Female	14	19.4
Total	72	100
Residential status	Frequency	Percentage
Rural	25	34.7
Urban	47	65.3
Total	72	100
Socioeconomic status	Frequency	Percentage
Poor	16	22.2
Middle Income	54	75
Rich	02	2.8
Total	72	100

Table No. 2: Etiology, Type of Fracture and Weight Loss

Etiology of fracture	Frequency	Percentage
RTA	42	58.3
Assault	04	5.6
Fall	14	19.4
Sport injury	12	16.7
Total	72	100
Type of fixation	Frequency	Percentage
With IMF	25	34.7
Without IMF	47	65.3
Total	72	100
Weight (kg)	Mean	Standard Deviation
Base line	70.08	11.14
After 4 weeks	68.00	10.90
Weight loss	2.07	0.94
Weight loss	Frequency	Percentage
Yes	23	31.9
No	49	68.1
Total	72	100

Table No. 3: Stratification of Weight Loss with Regards to Baseline Characteristics

Variable		Weight Loss		P Value
		Yes	No	
Age	Up to 35 Years (n=38)	08	30	0.036
	More than 35 Years (n=34)	15	19	
Gender	Male	18	40	0.736
	Female	05	09	
Residential Area	Rural (n=25)	12	13	0.033
	Urban (n=47)	11	36	
Etiology	RTA (n=42)	16	26	0.092
	Assault (n=04)	00	04	
	Fall (n=14)	06	08	
	Sport injury (n=12)	01	11	
Type of Fixation	With IMF (n=25)	10	15	0.285
	Without IMF (n=47)	13	34	

DISCUSSION

An average adult requires about 1800 to 2000 Cal/day. It has been shown that MMF results in weight loss and the body mass index (BMI). Due to the lack of nutritional intake the body muscles are catabolized for gluconeogenesis early during this phase and protein from the active tissues at the site of surgery[12]. Our study 80.6% (58 patients) were males, and 19.4% (14 patients) were females. Other studies have also shown the patients to be predominantly males. Our study also complies with a study by Mekkawy et al in Egypt which showed 80% male predominance[13]. Males are more prone to accidents as compared to females as the males work outside. Our findings are further supported by a study by Kayani et al[14] who found male predominance by 90%.

According to the results of our study 52.8 percent) of the patients (38 of the total patients were of age group 35 years. In a study in Egypt conducted by Mekkawy et al, in the patients of mean age 32.19 ± 11.85 years, same outcomes were reported that supported the findings of our study[13]. However in a report by Ogbezode et al, lower outcomes of mean age 27.7 ± 9.7 years were stated[1]. However, a different research found that the mean age of the participants was 34.0 ± 12.8 years, which is similar to the findings of our study. According to Kayani et al., 53.3% of the patients fell into the same age group as the results were obtained[14].

Out of total 72 cases, patients from rural areas were 34.7% (25 patients) and from urban areas were 65.3% (47 patients). Only 2.8% (2 patients) of the population was wealthy, while 75% (54 patients) had a moderate income and 22.2% (16 patients) had a poor socioeconomic level. Siddiqui et al. indicated that 91.3% of the participants were from urban regions, in contrast to Wahid et al. 85's findings that 59.3% of participants were from rural areas[15-16]. In accordance with findings of our study, Ye et al[17]. from China also found comparable findings, with 62.26% of patients coming from urban regions and 37.74% from rural regions[17]. Our study's findings are consistent with Siddiqui et al.'s claim of 21.9% of the population being poor, 75.4% having middle-class income, and 2.2% being rich[16].

In our study major causes of the mandibular fracture was road side accident (58.3%), followed by falling, sport injury, and physical attack were. Similar types of data were found by Rashid et al., with roadside accidents accounting for 59.4% and falls for 18.8%[18]. However, in the study done by Lee et al, the results were different results[19] while another study by Iqbal et al[20], found that trauma was most commonly caused by traffic accidents, accounting for 71.6% of cases, followed by falls for 20.7% and assaults for 5.6%.

Majority of the patients from our study were treated for mandibular fracture without IMF i.e. 65.3 % (47 patients out of 72) while remaining were treated with IMF. Also in agreement with our research results, Lone et al. reported mean base line weight of patients 68.87 ± 11.25 kg and after 5 weeks 65.25 ± 11.28 kg[12]. Similarly, Ruslin et al. reported that 30.87% of patients lost weight, and they did not find a significant

difference in weight reduction between patients with and without IMF[10].

CONCLUSION

High frequency of weight loss was noted in patients who were treated with or without intermaxillary fixation (IMF). Weight losses in our patients were significantly associated with increasing age. All clinicians treating such patients should anticipate weight loss for early diagnosis and timely management to improve quality of life of these patients.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Ogbezode ME, Oromakinde EA, Ngene FN, Suleiman IK, Idris K. Aetiology and presentation pattern of mandibular fractures at the State Dental Hospital in Maiduguri, Borno State, Nigeria. Nig J Dent Res 2022;7(1):53-9.
2. Vyas A, Mazumdar U, Khan F, Mehra M, Parihar L, Purohit C. A study of mandibular fractures over a 5-year period of time: A retrospective study. Contempor Clin Dent 2014;5(4):452-5.
3. Datarkar A, Tayal S, Galie M. Novel design of miniplate for fixation of fractures at transition zone of parasymphysis-body region of mandible–A clinical randomised study. J Cranio-Maxillof Surg 2019;47(10):1551-6.
4. Famurewa BA, Oginni FO, Aregbesola SB, Erhabor GE. Effects of maxillomandibular fixation and rigid internal fixation on pulmonary function in patients with mandibular fractures. Int J Oral Maxillof Surg 2020;49(9):1193-8.
5. Taberner M, Allen T, Cohen DD. Progressing rehabilitation after injury: consider the 'control-chaos continuum'. British J Sports Med 2019;53(18):1132-6.
6. Giridhar VU. Role of nutrition in oral and maxillofacial surgery patients. Nat J Maxillof Surg 2016;7(1):3.
7. Popat SP, Rattan V, Rai S, Jolly SS, Malhotra S. Nutritional intervention during maxillomandibular fixation of jaw fractures prevents weight loss and improves quality of life. Br J Oral Maxillofac Surg 2021;59(4):478-84.
8. Ludwig DC, Huang K, Lynch S, Koceja L, Tressel W, Dillon JK. What is the role of nutrition counseling in the management of isolated mandible fractures? Oral Surg Oral Med Oral Pathol Oral Radiol 2019;128(5):464-71.
9. Christensen BJ, Chapple AG, King BJ. How much weight loss can be expected after treating mandibular fractures? J Oral Maxillofac Surg 2019;77(4):777-82.
10. Ruslin M, Dekker H, Tuinzing DB, Forouzanfar T. Assessing the need for a protocol in monitoring weight loss and nutritional status in orthognathic surgery based on patients experiences. J Clin Exp Dent 2017;9(2):e272-5.
11. Yazdani J, Hajizadeh S, Ghavimi MA, Gargari BP, Nourizadeh A, Kananizadeh Y. Evaluation of changes in anthropometric indexes due to intermaxillary fixation following facial fractures. J Dent Res Dent Clin Dent Prospect 2016;10(4):247.
12. Lone PA, Khaliq MI, Sharma M, Malik OA, Lone BA. Weight changes (in kg) in mandible fracture patients after IMF: a prospective study. The Traumaxilla 2019;1(1):35-7.
13. Mekkawy MM, Azer SZ, El Gamil A. Impact of implementing nutritional teaching protocol on prevention of weight loss among mandibular fracture patients. Egypt J Nurs 2015;10:92-109.
14. Kayani SG, Ahmed W, Farooq M, Rehman AU, Nafees Q, Baig AM. Weight loss due to maxillomandibular fixation in mandibular fractures. Pak Oral Dent J 2015;35(3):374-6.
15. Wahid FI, Saleem M, Ahmad I. Pattern of Maxillofacial Trauma seen at ENT Department of a Tertiary Care Hospital. Pak J Med Sci 2011;27(5).
16. Siddiqui MI, Iqbal MJ, Idrees A, Shahid R, Hussain S, Khalid A, et al. The most common presenting complaints of the patients attending department of operative dentistry, Nishtar Institute of Dentistry, Multan. Pak J Med Health Sci 2015;9(2):642-45.
17. Ye W, Feng XP, Li R. The prevalence of dentine hypersensitivity in Chinese adults. J Oral Rehabil 2012;39(3):182-7.
18. Rashid S, Kundi JA, Sarfaraz A, Qureshi AU, Khan A. Patterns of mandibular fractures and associated comorbidities in Peshawar, Khyber Pakhtunkhwa. Cureus 2019;11(9):e5753.
19. Lee Y, Kim J, Lee M, Shin D, Choi H. Relationship between mandible fractures and third molars. Arch Craniofac Surg 2019;20(6):376-381.
20. Iqbal S, Aslam A, Ahmed S, Khan N, Kashif M, Kazmi SM. Spectrum of mandibular fractures in a tertiary care hospital of Karachi. Int J Frontier Sci 2020;4(2)61-4.

Original Article

Management of Undescended Testis May be Improved with Educational Updates for Pediatricians, General Physicians and Health Care Providers

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ABSTRACT

Objective: To analyze the role of educational updates for pediatrician, general physicians and health care providers in management of undescended testis.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Pediatric Surgery at Nishtar hospital, Multan, from June 2023 to May 2024.

Methods: The study included all pediatricians, general physicians, and health care providers working in the Department of Pediatric Surgery. Doctors working in other hospital departments were excluded. The institutional review board approved the study. A survey tool introduced by Lim et al in Singapore was used to assess healthcare providers' awareness regarding managing undescended testis. The tool comprised short answers and multiple-choice questions focused on managing undescended testis.

Results: Of the 120 participants, 61 (50.8%) knew about the incidence of undescended testis, 68 (56.7%) knew about the age to check gonads position, 68 (56.7%) check for physical features of a patient having undescended testis, 84 (70.0%) know about the recommended treatment of U.D, 31 (25.8%) know about the best timing of referral to a surgeon, 50 (41.7%) know about the recommended timing of surgery.

Conclusion: The management of undescended testis (UDT) can be significantly enhanced through targeted educational updates for pediatricians, general physicians, and other healthcare providers. Improved knowledge and awareness regarding the timely diagnosis, referral, and treatment of UDT are important to reducing the risk of long-term complications.

Key Words: Undescended testis, pediatricians, general physicians, knowledge updates, pediatrics

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INTRODUCTION

Undescended testis, or cryptorchidism, is one of the most prevalent congenital urological anomalies observed in male infants[1]. It occurs in approximately 3-5% of full-term newborns, making it a relatively common condition at birth[2]. However, the prevalence decreases significantly to about 1-2% by the time the infant reaches three months, as many testis descend spontaneously during this period[3].

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Undescended testis is a common condition, but many healthcare providers lack familiarity with its diagnosis, treatment, and potential complications[4]. Clinical guidelines recommend referring children with undescended testis to a specialist before 12 months of age[5]. Orchiopexy should ideally be performed between 6 and 12 months to prevent complications like fertility issues and testicular torsion. Delayed diagnosis and management can lead to irreversible damage, fertility problems, and an increased risk of testicular cancer[6].

Studies from various countries have reported the referral patterns for children with undescended testis. In the United States, Snodgrass found that the median age of referral was 43.3 months[7]. Similarly, a study from Auckland, New Zealand, reported a mean referral age of 42.6 months[8]. A comparative study on the management of undescended testis in tertiary care centers in England and Nigeria revealed delays in diagnosis and referrals beyond the recommended timeframes in both locations, with lack of awareness and knowledge cited as the primary reasons for these delays[9,10].

Evidence on this topic from Pakistan is lacking. This study aimed to assess the knowledge of doctors working in pediatric surgery services regarding the clinical features of undescended testis, the appropriate age for referral and surgery, and the potential risks associated with delays in treatment. The findings may improve early referral of children and ensure adequate follow-up in adulthood.

METHODS

This cross-sectional study was conducted from June 2023 to May 2024. Total strength of patients was calculated using Open Epi software, considering proportion of 165, a confidence level of 95%, and a margin of error (d) of 5%, proportions of previous studies that reported 51.1%[11] of healthcare providers' adequate knowledge. After collecting responses from participants and the dropout ratio, the final calculated sample size was 120. The study included all pediatricians, general physicians, and health care providers working in the Department of Pediatric Surgery. Doctors working in other hospital departments were excluded. Approval for the study was obtained from the institutional review board.

In this study, a survey tool introduced by Lim et al[12] in Singapore assessed healthcare providers' awareness regarding managing undescended testis. The tool consists of short answers and multiple-choice questions focused on managing undescended testis. Participants were informed about purpose of the study, and consent was obtained while ensuring confidentiality. Contents of study include designation, experience, total score and score obtained by participant. Each question carried one mark, with the maximum achievable score being eight.

Frequencies and percentages were calculated for categorical variables. Mean and standard deviation were calculated for numerical variables. The chi-square test was applied to check the difference between two categorical variables. One-way ANOVA was used to check the difference between the score and designation of the participants. The P-value is considered significant when it ≤0.050.

RESULTS

One hundred twenty participants were included in this study, 85 (70.8%) males and 35 (29.2%) females included. The mean age of the participants was 34.80±9.76 years. (Table. 1).

Of the 120 participants, 61 (50.8%) knew about the incidence of undescended testis, 68 (56.7%) knew about the age at which to check for the position of gonads, 68 (56.7%) knew about the physical features of a patient, 84 (70.0%) know about the recommended treatment of U.D, 31 (25.8%) know about the best timing of referral to a surgeon, 50 (41.7%) know about the recommended timing of surgery, 52 (43.3%) know about age of patient to check position of U.D.T, 57 (47.5%) describe two possible pathological outcomes of a patient with U.D.T. (Table. 2).

Questions and their correct answers concerning the designations of the participants were shown in the table. III. It was seen that pediatricians' knowledge was better than that of general physicians and health care providers ($p<0.050$) (Table. 3).

The mean scores of pediatricians, general physicians, and health care providers were 6.20±1.06, 4.53±0.87, and 3.76±1.16, respectively. ($p<0.001$) (Table. 4).

Table No.1: Demographics of the participants

Variable	N (%)	Mean ± S.D
Gender		
Male	85 (70.8)	
Female	35 (29.2)	
Age (years)		34.80±9.76

Table No. 2: Questions and their correct answers by the participants

Sr. No.	Question	Correct answer n (%)
1.	The incidence of undescended testis	61 (50.8)
2.	Age to check gonads position	68 (56.7)
3.	Check for physical features of a patient having undescended testis	68 (56.7)
4.	Recommended treatment of U.D	84 (70.0)
5.	Best timing of referral to a surgeon	31 (25.8)
6.	Recommended timing of surgery	50 (41.7)
7.	Age limit to examine a patient of U.D.T	52 (43.3)
8.	Describe two possible pathological outcomes of a patient with U.D.T	57 (47.5)

Table No.3: Questions and their correct answers with respect to designations of the participants

Question	Pediatricians	General physicians	Health care providers	Test of sig.
The incidence of undescended testis	37 (67.3)	14 (35.0)	10 (40.0)	χ^2=11.13, d.f=2,p=0.004
Age to check gonads position	40 (72.7)	17 (42.5)	10 (40.0)	χ^2=10.68, d.f=2,p=0.005
Physical characteristic of a patient with undescended testis	36 (65.5)	23 (57.5)	9 (36.0)	χ^2=6.08, d.f=2,p=0.048
Recommended treatment of U.D	43 (78.2)	27 (67.5)	14 (56.0)	χ^2=7.02, d.f=2,p=0.002

Best timing of referral to a surgeon	20 (36.4)	7 (17.5)	4 (16.0)	χ^2=5.89, d.f=2,p=0.050
Recommended timing of surgery	23 (41.8)	21 (52.5)	6 (24.0)	χ^2=8.14, d.f=2,p=0.016
Age limit to examine a patient of U.D.T	31 (56.4)	16 (40.0)	5 (20.0)	χ^2=9.53, d.f=2,p=0.009
Describe two possible pathological outcomes of a patient with U.D.T	33 (60.0)	15 (37.5)	9 (36.0)	χ^2=6.38, d.f=2,p=0.041

Table No. 4: Comparison of score by the designation of the participants

Score	Pediatricians	General physicians	Health care providers	Test of sig.
Mean ± S.D	6.20±1.06	4.53±0.87	3.76±1.16	F=59.06, d.f=2, p<0.001

DISCUSSION

This study highlighted a significant gap in knowledge among medical specialists, pediatricians and doctors working in pediatric settings regarding a common congenital anomaly, undescended testis. Despite being a condition that can often be diagnosed with relative ease during the neonatal period, the lack of awareness and understanding among healthcare professionals may lead to delayed recognition and management, potentially impacting long-term outcomes for affected children[13].

Among total 56.7% of participants answered correctly the question about the correct position of gonads, and 72.7% provided the most accurate answers by pediatricians. Similar findings were reported by Israr et al.[11], who observed that 69 participants (51.1%) demonstrated knowledge about the significance of neonatal examination in determining the position of gonads. In comparison, 76 participants, 56.3%, were aware of the physical characteristics of undescended testis (UDT).

A total of 43.3% of participants replayed the correct answers about the age of examination of the child for UDT. In a nationwide study from Germany conducted by Boehme et al[14], which aimed to investigate the delayed referral and non-compliance to recommendations. Similarly, results of survey revealed varied responses, 89% of pediatric surgeons write down correct answer that 1 year duration is enough to treatment of undescended testis. A study conducted in Nigeria by Ekwunife et al[15] found that although all children were born at various levels of hospitals, only 23% examined the inguinal region at birth or during the six-week follow-up visit. Overall, doctors made the diagnosis in just 25.6% of the cases.

A U.S. survey by Shnorhavorian et al.[16] found that 20% of primary care providers delayed referral for undescended or retractile testis until puberty, with 25-30% counseling parents on risks of infertility and malignancy, similar to responses in our graduate group. Keys et al[17] reported similar findings, noting that the treatment for this condition is typically watchful waiting, with counseling for the parents being crucial to alleviating their concerns.

Studies conducted by Tseng et al[18] and Hrivatakis et al[19] have reported that orchiopexy is currently recommended between 6 and 12 months of age. This was decided on the potentially harmful effects of the high temperatures that testis are exposed to at supra-scrotal locations. An exhaustive survey aimed at identifying the exact age of orchiopexy, and reached a consensus that the late infancy period is the most appropriate time for the procedure.

47.5% of the population correctly replied to a question about knowledge about pathological outcomes of a patient with U.D.T. Vikraman et al[20] highlighted that subfertility and malignancy remain potential risks even after timely orchiopexy due to unknown germ cell damage. Subfertility was widely recognized, but only 12% mentioned the malignancy risk. Consultants scored higher than graduates, with comparable scores to postgraduate residents.

CONCLUSION

Targeted educational updates for pediatricians, general physicians, and other healthcare providers can significantly enhance the management of undescended testis (UDT). Improved knowledge and awareness regarding the timely diagnosis, referral, and treatment of UDT are important to reducing the risk of long-term complications.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Aleena Tahir, Waqas Ahmed
Drafting or Revising Critically:	Muhammad Amir Hanif Khan, Shahzada Abdullah Muhammad Khuzaemah Saalim Hashmi Ali
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Kübarsepp V, Varik K, Varendi H, Antson A, Veinla M, Nellis G, et al. Prevalence of congenital cryptorchidism in Estonia. Androl 2022;10(2):303-9.
2. Aggarwal H, Rehfuss A, Hollowell JG. Management of undescended testis may be improved with educational updates for referring providers. J Pediatr Urol 2014;10(4):707-11.
3. Gates RL, Shelton J, Diefenbach KA, Arnold M, Peter SD, Renaud EJ, et al. Management of the undescended testis in children: an American pediatric surgical association outcomes and evidence based practice committee systematic review. J Pediatr Surg 2022;57(7):1293-308.
4. Saab MM, Davoren MP, Murphy A, Murphy D, Cooke E, Landers M, et al. Promoting men's awareness, self-examination, and help-seeking for testicular disorders: a systematic review of interventions. HRB Open Res 2023;1:16.
5. Baydilli N, Dönmez MI, Wilcox DT, Hadziselimovic F, Hayashi Y, Oswald J, et al. Undescended testis: a roundtable discussion based on clinical scenarios–Part 1. J Pediatr Urol 2024;20(1):95-101.
6. Yi W, Sheng-de W, Lian-Ju S, Tao L, Da-Wei H, Guang-Hui W. Management of undescended testis may be improved with educational updates and new transferring model. Italian J Pediatr 2018;44:1-5.
7. Snodgrass W, Bush N, Holzer M, Zhang S. Current referral patterns and means to improve accuracy in diagnosis of undescended testis. Pediatr 2011;127(2):e382-8.
8. Upadhyay V, Kothari M, Manoharan M. The referral pattern for undescended testis in Auckland. N Z Med J 2001;114(1135): 310-11.
9. Peiris HD, Lakshminarayanan B, Osifo OD, Lakhoo K. Management of undescended testis: a comparative study in England and Africa. Ann Pediatr Surg 2014;10:115-8.
10. Schneuer FJ, Holland AJ, Pereira G, Jamieson S, Bower C, Nassar N. Age at surgery and outcomes of an undescended testis. Pediatr 2016;137(2): e20152768.
11. Israr S, Akhtar J, Taqvi SM, Zamir N, Bibi S. Gaps in Knowledge about the Management of Children with Undescended Testis: A study from Tertiary Care Pediatric Hospital. Pak J Med Res 2021;60(1):32-7.
12. Lim LY, Nah SA, Lakshmi NK, Yap TL, Jacobsen AS, Low Y, et al. Undescended testis: Level of knowledge among potential referring health-care providers. J Paediatr Child Health 2015; 51(11): 1109-14.
13. Parkes R, Garcia TX. Bringing proteomics to bear on male fertility: key lessons. Expert Review Proteom 2024;21(4):181-203..
14. Boehme P, Geis B, Doerner J, Wirth S, Hensel KO. Shortcomings in the management of undescended testis: guideline intention vs reality and the underlying causes - insights from the biggest German cohort. BJU Int 2018;122(4):644-53.
15. Ekwunife OH, Ugwu JO, Onwurah C, Okoli CC, Epindu LK. Undescended testis: Contemporary factors accounting for late presentation. Afr J Urol 2018;24(3):206-11.
16. Shnorhavorian M, Jacobs MA, Stearns G, Mingin G, Koyle MA. Practice variation and clinical confusion regarding undescended testis and retractile testis among primary care respondents: a multi-regional survey study in the United States. Pediatr Surg Int 2012;28(6): 635-9.
17. Keys C, Heloury Y. Retractile testis: a review of the current literature. J Pediatr Urol 2012;8(1):2-6.
18. Tseng C, Chiang I, Hong C, Lu YC, Hong JH, Chang HC. Advantage of early orchiopexy for undescended testis: Analysis of testicular growth percentage ratio in patients with unilateral undescended testicle. Sci Rep 2017;7:17476.
19. Hrivatakis G, Astfalk W, Schmidt A, Hartwig A, Kugler T, Heim T, et al. The timing of surgery for undescended testis - a retrospective multicenter analysis. Dtsch Arztebl Int 2014;111(39): 649-57.
20. Vikraman J, Hutson JM, Li R, Thorup J. The undescended testis: Clinical management and scientific advances. Semin Pediatr Surg 2016;25(4):241-8.

Original Article

Comparative Evaluation of Standard versus Totally Tubeless Percutaneous Nephrolithotomy in Renal Stone Treatment

Imran Hyder and Khalid Hussain

ABSTRACT

Objective: To compare the outcomes of standard and totally tubeless percutaneous nephrolithotomy in treating renal stones in terms of postoperative analgesia requirement, operative time and mean duration of hospital stay.

Study Design: Randomized controlled trial

Place and Duration of Study: This study was conducted at the Department of Urology, Nishtar Hospital, Multan, from December 2022 to November 2023.

Methods: A sample size of 88 (44 in each group) were enrolled in the study. Group A was receiving standard percutaneous nephrolithotomy (PCNL), while Group B was receiving the totally tubeless PCNL Analgesics were administered when the patient reports a VAS pain score above a predefined threshold (e.g., ≥4 out of 10). The requirement for postoperative analgesia within a 48-hour period will be recorded.

Results: The mean analgesic requirement of standard PCNL group was greater than totally tubeless PCNL group as 20.79±3.08 mg and 9.71±1.65 mg, respectively. The mean hospitalization time of standard PCNL group was greater than totally tubeless PCNL group3.31±1.08 days and 1.82±0.54 days.

Conclusion: Totally tubeless PCNL is effective and safe technique, making it a viable option for patients with renal stones. This approach is linked to reduced pain, decreased analgesic requirements, shorter operation times, and decreased hospitalization durations.

Key Words: Renal stones, Tubless percutaneous nephrolithotomy, Standard nephrolithotomy, Pain, Hospital stay

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INTRODUCTION

Kidney stones are solid deposits of salts and minerals that develop inside the kidneys, often causing severe pain, urinary symptoms, and complications such as infection[1], obstruction, and renal damage approximately 10% of the global population is affected by kidney stones at some point in their lives[2], with the prevalence increasing over the past several decades. The management of kidney stones has evolved significantly over the years, with a range of treatment options available to patients depending on the size, location, and composition of the stones[3].

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Number of minimally invasive and non-invasive techniques has been introduced for dealing with kidney stones including lithotripsy like extracorporeal shock wave, open surgery, nephrolithotomy and conservative management[4,5]. PCNL is a well-established, minimally invasive surgical technique for the treatment of large or complex kidney stones that cannot be effectively managed by conservative or less invasive therapies[6].While the procedure has a high success rate and is generally well-tolerated, it is not without complications. Postoperative pain, bleeding, and infection are common concerns, as well as the discomfort and inconvenience of managing the nephrostomy tube in the days following surgery[7].

Over the past decade, there has been a growing interest in the development of a less invasive, tubeless variation of the PCNL procedure, known as totally tubeless PCNL (TTPCNL)[8]. In TTPCNL, no nephrostomy tube is placed after the completion of the procedure, and a ureteral stent is inserted instead to maintain renal drainage[9]. Proponents of TTPCNL argue that it reduces postoperative pain, shortens hospital stays, and facilitates a quicker return to normal activities when compared to standard PCNL[10].

METHODS

After taking approval from CPSP, a randomized controlled trial was conducted at Nishtar hospital Multan. After explaining the purpose of study, Informed consent was signed by the patients. A sample size of 88 (44 in each group) is calculated using a 95% confidence interval, power of study 80%, taking number of patients required postoperative analgesia in standard and tubeless procedure as62.5% and 32.5%respectively.

This sample size was calculated using the online software OpenEpi.com. Patients of age between 18 to 70 years, diagnosis of large kidney stones, defined as stones larger than 2 cm in diameter, stones located in the renal pelvis, calyces and upper ureter on CT scan, failure of conservative treatment or less invasive therapies and patient who has informed consent to participate in the study were included in the study. Analgesics were administered when the patient reports a VAS pain score above a predefined threshold (e.g., ≥4 out of 10). The requirement for postoperative analgesia within a 48-hour period will be recorded. It was documented as 'yes' if analgesia was administered based on the visual analogue scale (VAS) score and 'no' if not." The total amount of analgesic medication in milligrams was administered to the patients during 48 hours were documented.

The duration of the procedure was measured in minutes from the initial skin incision to the final skin closure. All the operation was performed by same consultant urologist team, to minimize bias. Pain after procedure was assessed using the visual analogue scale, a validated tool for measuring pain intensity. The VAS is a continuous scale from 0 (no pain) to 10 (worst possible pain). Pain scores were recorded at 6, 24, and 48 hours postoperatively.

Hospitalization time was measured in days from the day of the procedure to the day of discharge. Patients with an active urinary tract infection (more than 10 WBCs on urine analysis) or sepsis (based on q-SOFA criteria, Annexure), patients with bleeding diathesis or coagulopathy (INR more than 1.5), solitary kidney having GFR<45 mL/min/1.73 m², presence of a renal anomaly or obstruction that may affect the outcome of the procedure (e.g., horseshoe kidney, ureteropelvic junction obstruction, perforation in the collecting system), history of previous open renal surgery or PCNL on the same side, pregnant or lactating women, patients with a known allergy or contraindication to anesthesia or contrast media.

Group A was receiving standard percutaneous nephrolithotomy (PCNL), while Group B was receiving the totally tubeless PCNL. Post-enrollment, random allocation participants were randomly assigned to either Group A or Group B using computer-generated random numbers (Annexure). All patients' were undergoing preoperative assessment, routine investigations and imaging studies (computed tomography or kidney-ureter-bladder X-ray). Antibiotic prophylaxis was administered according to the hospital protocol. Both groups were undergoing PCNL under general anesthesia, following standard surgical principles. For Group A, a DJ stent or nephrostomy tube was placed at the end of the procedure, whereas in Group B, no nephrostomy tube was placed.

All patients were closely monitored in the post-anesthesia care unit and subsequently transferred to the urology ward. Postoperative pain management was provided as per the hospital's pain management protocol. Patients were assessed for any complications or adverse events during their hospital stay. Operative time was documented during the surgery. Postoperative pain was assessed by postgraduate resident by using the VAS at 6, 24, and 48 hours postoperatively. Analgesic requirement and hospitalization time was recorded in the patient's medical records. Patients were deemed fit for discharge when they exhibit stable vital signs for at least 24 hours, are ambulatory, tolerate oral intake without vomiting, have managed pain controlled by oral analgesics, show no signs of post-operative complications. All the data was recorded on the proforma.

All collected data was entered into a statistical software package, such as SPSS version 26. Continuous variables, such as age, stone size, operative time, change in haemoglobin and pain scores, analgesic requirement, and hospitalization time, was summarized using means and SD. Categorical variables such as sex and stone location were presented as frequencies and percentages.

RESULTS

Overall, 88 patients were included in this study. The study patients were equally divided into two groups as standard PCNL44 (50.0%) and totally tubeless PCNL44 (50.0%). The distribution of age, sex, stone size and stone location of both the study groups were almost equal. Whereas, the mean operative time of standard PCNL and totally tubeless PCNL group was 54.81±5.05minutes and 50.02±5.09minutes. (Table. I).

The mean pain score (VAS) at 6 hours of standard PCNL and totally tubeless PCNL group was 8.21±1.26 and 7.68±1.02, respectively. (p=0.245). The mean pain score (VAS) at 24 hours of standard PCNL and totally tubeless PCNL group was 6.44±1.62 and 4.63±0.85, respectively. (p<0.001). The mean pain score (VAS) at 48 hours of standard PCNL and totally tubeless PCNL group was 4.64±0.68 and 2.54±0.85, respectively. (p<0.001). (Table. II).

The mean analgesic requirement of standard PCNL group was greater than totally tubeless PCNL group as 20.79±3.08 mg and 9.71±1.65 mg, respectively. The mean hospitalization time of standard PCNL group was

greater than totally tubeless PCNL group3.31±1.08 days and 1.82±0.54 days,(Table. III).

Table No. 1: Demographics and baseline characteristics of the study groups

Characteris-tics	Standard PCNL 44 (50.0%)	Totally tubeless PCNL 44 (50.0%)	p-value
Age (years)	51.34±8.44	52.18±8.99	0.652
Sex			
Male	26 (59.1)	24 (54.5)	0.667
Female	18 (40.9)	20 (45.5)	
Stone size (mm)	39.82±3.43	38.66±3.12	0.826
Stone location			
Renal pelvis	8 (18.2)	5 (11.4)	0.713
Middle calyx	11 (25.0)	8 (18.2)	
Lower calyx	9 (20.5)	9 (20.5)	
Upper calyx	7 (15.9)	10 (22.7)	
Upper ureter	9 (20.5)	12 (27.3)	
Operative time (minutes)	54.81±5.05	50.02±5.09	<0.001

Table No. 2: Pain scores distribution of the study groups

Pain score (VAS)	Standard PCNL 44 (50.0%)	Totally tubeless PCNL 44 (50.0%)	p-value
At 6 hours	8.21±1.26	7.68±1.02	0.245
At 24 hours	6.44±1.62	4.63±0.85	<0.001
At 48 hours	4.64±0.68	2.54±0.85	<0.001

Table No. 3: Analgesic requirement and hospitalization distribution of the study groups

	Standard PCNL 44 (50.0%)	Totally tubeless PCNL 44 (50.0%)	p-value
Analgesic requirement (mg)	20.79±3.08	9.71±1.65	<0.001
Hospitalization time (days)	3.31±1.08	1.82±0.54	<0.001

DISCUSSION

In a randomized controlled study conducted by Moosanejadet al[12], 44 patients 24 male, mean age of patients was 50.40±2.02 years. 40 patients underwent standard PCNL. The regular PCNL group had a longer mean operation time 53.37±5.54 min as compare to tubeless group 50.32±3.83 min. Twenty-five 62.5% standard PCNL patients needed pethidine, compared to 32.5% tubeless PCNL patients. The tubeless PCNL group had a shorter mean hospitalization time 1.25±0.49 days than the regular PCNL group 2.95±1.17 days.

In a study conducted by Sebaey et al[13], involving 80 patients with a solitary radio-opaque renal stone eligible for PCNL, it was found that the tubeless PCNL group required a statistically significantly lower mean postoperative analgesia dose (43.5mg) compared to the standard PCNL group (48.03mg). Additionally, the tubeless PCNL group exhibited a higher stone-free rate of 90%, while the standard PCNL group had a rate of 82.5%. Another study by Agrawal et al[14] revealed that patients in the Tubeless group have shorter hospital stay (21.6 hours) than controls.

Studies conducted by Thapaet al[15] and Ichaoui et al[16] have compared totally tubeless percutaneous nephrolithotomy to standard PCNL in terms of efficacy, safety, and patient outcomes. However, these studies have yielded mixed results, with some reporting significant benefits of TTPCNL while others have found no significant difference between the two techniques.

In their respective studies, Shenet al[17] and Gonulalan et al[18] observed that patients undergoing surgery with the standard percutaneous nephrolithotomy (PCNL) technique reported heightened pain levels and a greater need for postoperative narcotic analgesics compared to those treated with tubeless method. In our investigation, the omission of catheter of nephrostomy and stent (double J) in TPCNL group appeared to correlate with diminished pain and reduced requirements for analgesics.

In line with the results of this study, Istanbulluogluet al[19] found no significant differences in blood transfusion, hemoglobin, stone size when comparing totally tubeless percutaneous nephrolithotomy (PCNL) with standard PCNL. In their study, Karami et al [20] examined 60 patients, evenly distributed into two groups, and found that 2 (6.6%) individuals in the totally tubeless percutaneous nephrolithotomy (PCNL) group, as well as UTI was diagnosed in 1 patient standard PCNL group.

Wang et al[21] concluded that tubeless PCNL represents a safe, efficacious, and cost-effective approach for the treatment of renal staghorn calculi. Their findings indicated that this procedure also have association with high stone free rate, low morbidity, a brief hospital stay, and enables an early return to work.

CONCLUSION

Conclusion: PCNL is a safe and effective technique, making it a viable option for patients with staghorn stones. This approach is linked to reduced pain,

decreased analgesic requirements, shorter operation times, and decreased hospitalization durations.

Author's Contribution:

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Drafting or Revising Critically:	Khalid Hussain
Final Approval of version:	All the above authors
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REFERENCES

1. Ahmad M, Mumtaz H, Hussain H, Sarfraz S, Rahat M, Mumtaz S. A prospective, single-centered, cohort study comparing the treatment of renal stones by following PCNL types: Standard, tubeless & totally tubeless. Annals Med Surg 2022;80:104325.
2. Chen ZJ, Yan YJ, Zhou JJ. Comparison of tubeless percutaneous nephrolithotomy and standard percutaneous nephrolithotomy for kidney stones: A meta-analysis of randomized trials. Asian J Surg 2020;43(1):60-8.
3. Thongprayoon C, Krambeck AE, Rule AD. Determining the true burden of kidney stone disease. Nat Rev Nephrol 2020;16(12):736–46.
4. Rule AD, Lieske JC, Pais VM. Management of kidney stones in 2020. J Am Med Assoc 2020;323(19):1961–2.
5. Jiao B, Luo Z, Huang T, Zhang G, Yu J. A systematic review and meta-analysis of minimally invasive vs. standard percutaneous nephrolithotomy in the surgical management of renal stones. Exp Ther Med 2021;21(3):213.
6. Lu Y, Ping J gen, Zhao X jun, Hu L kun, Pu J xian. Randomized prospective trial of tubeless versus conventional minimally invasive percutaneous nephrolithotomy. World J Urol 2013;31(5):1303–7.
7. Kandemir E, Savun M, Sezer A, Erbin A, Akbulut MF, Sarılar Ö. Comparison of miniaturized percutaneous nephrolithotomy and standard percutaneous nephrolithotomy in secondary patients: a randomized prospective study. J Endourol 2020;34(1):26-32.
8. Minami T, Yamana H, Matsui H, Fushimi K, Yasunaga H. Postoperative outcomes after tubeless, totally tubeless, standard, and standard with ureteral stent percutaneous nephrolithotomy: a nationwide retrospective study in Japan. UrologiaInternationalis 2020;104(5-6):445-51.
9. Kamble VB, Gupta S, Pal DK. Comparative analysis of standard, tubeless and total tubeless percutaneous nephrolithotomy: A prospective study. Urologia J 2023:03915603231203434.
10. Li Q, Gao L, Li J, Zhang Y, Jiang Q. Total tubeless versus standard percutaneous nephrolithotomy: a meta-analysis. Minimally Invasive Therapy Allied Technol 2020:29(2):61-9.
11. Zeng G, Cai C, Duan X, Xu X, Mao H, Li X, et al. Mini percutaneous nephrolithotomy is a noninferior modality to standard percutaneous nephrolithotomy for the management of 20–40 mm renal calculi: a multicenter randomized controlled trial. Euro Urol 2021;79(1):114-21.
12. Moosanejad N, Firouzian A, Hashemi SA, Bahari M, Fazli M. Comparison of totally tubeless percutaneous nephrolithotomy and standard percutaneous nephrolithotomy for kidney stones: A randomized, clinical trial. Brazilian J Med Biol Res 2016;49(4):1–6.
13. Sebaey A, Khalil MM, Soliman T, Mohey A, Elshaer W, Kandil W, et al. Standard versus tubeless mini-percutaneous nephrolithotomy: A randomised controlled trial. Arab J Urol 2016;14(1):18–23.
14. Agrawal MS, Sharma M, Agarwal K. Tubeless percutaneous nephrolithotomy using antegrade tether: A randomized study. J Endourol 2014;28(6):644–8.
15. Thapa N, Acharya GB, Poudel A, Neupane A, Mishra S. Comparison between standard percutaneous nephrolithotomy versus tubeless percutaneous nephrolithotomy. Nepal J Med Sci 2021;6(2):24–31.
16. Ichaoui H, Samet A, Ben Hadjalouane H, Hermi A, Hedhli H, Bakir MA, et al. Percutaneous Nephrolithotomy (PCNL): standard technique versus tubeless - 125 Procedures. Cureus 2019;11(3); e4251.
17. Shen P, Liu Y, Wang J. Nephrostomy tube-free versus nephrostomy tube for renal drainage after percutaneous nephrolithotomy: a systematic reviewandmeta-analysis. Urol Int 2012;88:298–306.
18. Gonulalan U, Cicek T, Istanbulluoglu O, Kosan M, Ozturk B, Ozkardes H. Tubeless percutaneous nephrolithotomy is effective and safe inshort-and long-term urinarydrainage. Urolithiasis 2013;41:341–6.
19. Istanbulluoglu MO, Cicek T, Ozturk B, Gonen M, Ozkardes H. Percutaneous nephrolithotomy: nephrostomy or tubeless or totally tubeless? Urol 2010;75:1043–6.
20. Karami H, Gholamrezaie HR. Totally tubeless percutaneous nephrolithotomy in selected patients. J Endourol 2004;18:475–6.
21. Wang CJ, Chang CH, Huang SW. Simultaneous bilateral tubeless percutaneous nephrolithotomy of staghorn stones: a prospective randomized controlled study. Urol Res 2011;39:289–94.

Original Article

Radiation Induced Sexual Dysfunction in Prostate Cancer Patients

Radiation Induced Sexual Dysfunction

Sarah Khan[1], Imran Hyder[2] and Muhammad Mujahid Iqbal[1]

ABSTRACT

Objective: To estimate the sexual dysfunction in biopsy proven prostate cancer patients and to identify the characteristics associated with sexual dysfunction in survivors of carcinoma prostate.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Oncology department of Nishtar Hospital, Multan from November 2023 to September 2024.

Methods: This study aimed to determine the prevalence of sexual dysfunction (SD) in prostate cancer patients who had undergone pelvic radiotherapy. Data was collected using a structured questionnaire that included demographic information, treatment details and the International Index of Erectile Function (IIEF-5) questionnaire to assess the severity of sexual dysfunction (SD), ECOG performance status 0-1, intermediate and high risk cancer patients and duration post radiotherapy.

Results: Among the 25 patients with SD, 4 (16.0%) were in the intermediate risk group, while 21 (84.0%) were in the high-risk group. Additionally, 6 patients (24.0%) with SD had diabetes, and 20 patients (80.0%) underwent concurrent hormonal therapy. Prior to radiation, 5 patients (20.0%) had SD, whereas 20 patients (80.0%) developed it six months after radiation, a statistically significant difference ($p < 0.001$).

Conclusion: Sexual dysfunction is common among prostate cancer survivors, influenced by cancer treatment, risk stratification and age. Treatments like radiation can damage hormone-producing organs, leading to SD. Together, cancer treatment, risk stratification and aging contribute to the higher incidence of sexual dysfunction in prostate cancer patients.

Key Words: Sexual dysfunction, Radiotherapy, Cancer, Diabetes, Risk stratification

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INTRODUCTION

In males, cancers of the pelvic region account for over 25%[1] of all newly diagnosed cancers. This type of cancer is also associated with long-standing severe sexual dysfunction in at least half of all patients[2]. Sexual dysfunction (SD), or the inability to get and sustain an erection sufficient for satisfactory sexual activity, is one of the most painful sequelae of cancer diagnosis and management among men[3].

Numerous factors contribute to Erectile Dysfunction which goes without saying that prostate cancer also leads to Erectile Dysfunction (ED)[4]. Prostate cancer is known to be the second most frequent cancer amongst men and has predominant causative risks of having erectile dysfunction which include cardiovascular conditions and metabolic diseases, all of which a male with cancer does not suffer from[5]. However, the risk of ED is higher in males with prostate cancer due to the increased incidence of lower urinary tract symptoms and psychological distress. Indirectly, cancer treatment modalities, including surgery, chemotherapy, radiotherapy and hormone therapy, are among the most common causes of ED in this population[6].

Few males are able to achieve a normal erection following pelvic surgery, with studies reporting that less than 25%[7] of those with excellent baseline erectile function retain or recover their previous erection quality after treatment. The pelvic surgeries most commonly associated with erectile dysfunction are radical prostatectomy, radical cystectomy, and low anterior or abdominoperineal resections[8].

Sexuality and intimacy are key to quality of life and may ease psychosocial distress linked to cancer[9]. Maintaining sexual function in men with cancer can help reduce suffering. With rising cancer cases and improved survival rates, quality of life post-treatment is important[9, 10]. Research on ED in cancer survivors is limited, focusing mostly on pelvic cancers. Prevalence estimates of ED in this group are rare. Pooled data on ED prevalence and its links can highlight the issue's

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scale. This helps clinicians identify at-risk patients and offer holistic, long-term cancer care.

METHODS

This cross-sectional study aimed to determine the prevalence of sexual dysfunction (SD) in male patients who had undergone pelvic radiotherapy. The study was conducted at oncology department of Nishtar Hospital, Multan from November 2023 to September 2024. Non probability consecutive sampling technique was adopted. Written informed consent was obtained. Data were collected using a structured questionnaire that included demographic information, treatment details, and the International Index of Erectile Function (EF) (IIEF-5) questionnaire to assess the severity of ED. ECOG performance <1,intermediate and high risk cancer patients , more than 6 months duration of radiotherapy and patients with biopsy proven prostate cancer were included. ECOG performance status >1, early and metastatic stage of cancer, <6 months duration of radiotherapy, pre-existing SD unrelated to radiotherapy, untreated hypogonadism were excluded.

CT simulations were done supine with full bladder and empty rectum.Organs at risks and target volumes were delineated.After treatment planning,radiation was delivered with 3D-conformal technique.Patients were required to attend follow-up examinations at regular intervals,with this schedule continuing consistently over a six-month period to ensure ongoing monitoring and evaluation of their condition.

Frequencies and percentages were calculated for categorical variables. Whereas, mean and standard deviation was calculated for age/numeric variable. Chi-square test was applied to check the significance of prevalence of sexual dysfunction prior to radiation and 6 months after radiation.

RESULTS

Of the 40 patients in the study, 25 (62.5%) experienced sexual dysfunction (SD) after receiving radiotherapy (RT), while 15 (37.5%) did not. (Figure. I). The mean age of patients with SD was 64.80±11.97 years, with 8 patients (32.0%) aged 60 years or younger and 17 patients (68.0%) older than 60 years. Among the 25 patients with SD, 4 (16.0%) were in the intermediate risk group, while 21 (84.0%) were in the high-risk group. Additionally, 6 patients (24.0%) with SD had diabetes, and 20 patients (80.0%) underwent concurrent hormonal therapy. (Table. 1).

Prior to radiation, 5 patients (20.0%) had SD, whereas 20 patients (80.0%) developed it six months after radiation, a statistically significant difference ($p < 0.001$). (Table. 2).

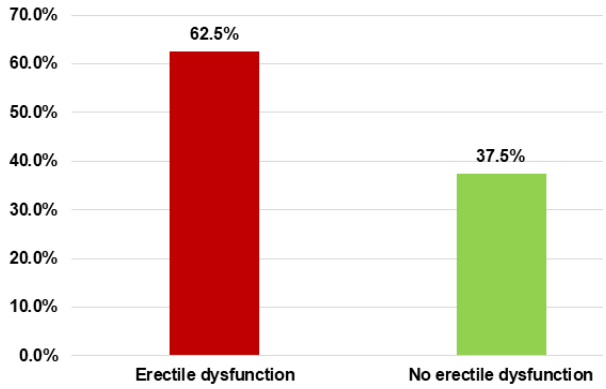

Figure No. 1: Prevalence of sexual dysfunction after RT

Table No. 1: Demographic and baseline characteristics of the patients' sexual dysfunction after RT n=25

Variable	N (%)	Mean±S.D
Age (years)		64.80±11.97
≤60 years	8 (32.0)	
>60 years	17 (68.0)	
Risk stratification		
Intermediate risk	4 (16.0)	
High risk	21 (84.0)	
Diabetes	6 (24.0)	
Concurrent hormonal therapy	20 (80.0)	

Table No.2: Comparison of sexual dysfunction prevalence at prior radiation and at 6 months after radiation n=25

Sexual dysfunction prevalence	Prior to radiation	6 months after radiation	p-value
	5 (20.0)	20 (80.0)	<0.0001

DISCUSSION

The prevalence of sexual dysfunction (SD) in our study was significantly higher at 64% compared to findings reported in other cohort studies of childhood cancer survivors (CCS), such as the 12.3% prevalence reported by Ritenour et al[11] and the 31.8% prevalence reported by Sung H et al[12] These stark differences may reflect variations in study populations, methodologies, or underlying risk factors.

Among the patients experiencing sexual dysfunction, 6 individuals (24%) had a diagnosis of diabetes, while concurrent chemotherapy or hormonal therapy was noted in 28 patients (80%). The link between diabetes and erectile dysfunction is well-established[13], with evidence suggesting that more than half of men in the United States with diabetes are affected by this condition. Despite this significant prevalence, the studies do not currently provide specific guidelines for the screening or management of erectile dysfunction in

diabetic men[14]. However, clinicians are encouraged to address this common quality-of-life concern during consultations with their diabetic patients, as proactive discussions may help identify and manage this condition effectively.

Studies conducted by Cheng et al[15] and Rojanasarot et al[16] have reported erectile dysfunction (ED) prevalence rates ranging widely from 4% to 70%, with variations depending on the specific age groups studied and the methods used to assess ED. Of the men aged 20 to 29 years, the prevalence of ED was noted to be, by and large, lower, in this case, a rough estimate was about 15.1 percent, 12.2 - 18.1 percent. On the other hand, among men aged 60 years and older, figures were considerably higher at about 70.0 percent (99% CI: 62.3 to 77.7). This difference further emphasizes the relevance of age and evaluation criteria in determining surveyed ED prevalence.

Blood flow dynamics and erectile hemodynamics have also been studied using duplex ultrasonography by Tal et al[17]. More patients with or without hypogonadism at 12 months after treatment did not have any difference thus, suggesting hyperadrenergic mediated causes of ED. In this study including 85 patients, 12.5% had ED before radiotherapy and 87.5% had ED at 6 months after radiotherapy ($p<0.001$). A meta-analysis performed by Pizzol et al[18] evaluated a sub-cohort experiencing ED amongst cancer patients, and ED was reported at a prevalence of 40.72% whereby 28.60% of patients had this at diagnosis and 42.70% post treatment with significant difference across stages and types of cancer.

A follow-up 12 year study found that 84% of men with prostate cancer who received radical prostatectomy and 80% of those made active surveillance reported ED (erectile dysfunction) compared to 43% in a matched control group. The same results have been seen in men treated for other pelvic cancers like anal, rectal or bladder cancers.[19]

It is important for clinicians to recognize and address the significant impact of erectile dysfunction (ED) on the overall quality of life and mental health of cancer survivors. ED can deeply affect a survivor's sense of well-being, as it can interfere with their ability to experience intimacy and sexual fulfillment[20]. These elements of sexuality and relationships are crucial for emotional connectedness, self-esteem, and social health. For numerous survivors, sustaining intimate relationships, and an enjoyable sex life, can help ease some of the psychosocial difficulties and psychosocial health issues that are frequently experienced alongside a cancer diagnosis and treatment. Thus, in the years of care and rehabilitation of cancer survivors, clinicians must take into account the psychological and relational dimensions of SD, as the medical approach to SD is only part of the solution and we cannot neglect the effective theme in the care of this population, which is certainly intertwined with the patients' mental health [21].

CONCLUSION

Sexual dysfunction (SD) is common among prostate cancer survivors, influenced by the cancer treatment, risk stratification and age. Treatments like radiation and hormonal therapy can damage hormone-producing organs, leading to SD. Together, cancer treatment, risk stratification and aging contribute to the higher incidence of SD in prostate cancer patients.

Author's Contribution:

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REFERENCES

1. Wallington DG, Holliday EB. Preparing patients for sexual dysfunction after radiation for anorectal cancers: a systematic review. Practical Radiat Oncol 2021;11(3):193-201.
2. Kim P, Clavijo RI. Management of male sexual dysfunction after cancer treatment. InUrologic Oncology: Seminars Original Investigat 2022;40(9):389-94.
3. Nicolai M, Urkmez A, Sarikaya S, Fode M, Falcone M, Albersen M et al. Penile rehabilitation and treatment options for erectile dysfunction following radical prostatectomy and radiotherapy: a systematic review. Frontiers Surg 2021;8:636974.
4. Shabataev V, Saadat SH, Elterman DS. Management of erectile dysfunction and LUTS/incontinence: the two most common, long-term side effects of prostate cancer treatment. Can J Urol 2020;27(27 Suppl 1):17-24.
5. Madan R, Dracham CB, Khosla D, Goyal S, Yadav AK. Erectile dysfunction and cancer: current perspective. Radiat Oncol J 2020;38(4):217.
6. Nguyen DD, Berlin A, Matthew AG, Perlis N, Elterman DS. Sexual function and rehabilitation after radiation therapy for prostate cancer: a review. Int J Impotence Res 2021;33(4):410-7.
7. Patel KH, Tringale KR, Kim N, Boe L, Reyngold M, Wu AJ, et al. Risk of Sexual Dysfunction in Men Treated with Pelvic Radiation Therapy for

Locally Advanced Rectal Cancer: 20 Years of Experience with 451 Patients. Int J Radiat Oncol Biol Phys 2023;117(2):S104-5.

8. Ramirez-Fort MK, Rogers MJ, Santiago R, Mahase SS, Mendez M, Zheng Y, et al. Prostatic irradiation-induced sexual dysfunction: a review and multidisciplinary guide to management in the radical radiotherapy era (Part I defining the organ at risk for sexual toxicities). Reports Pract Oncol Radioth 2020;25(3):367-75.
9. Nouri M, Kalantari KM, Javadinia SA, Sedighi PA, Alemi M. Erectile Dysfunction and Penile Bulb Dose Following Definitive Prostate Radiation Therapy. Int J Cancer Manag 2024;17(1):e147952.
10. Shabataev V, Saadat SH, Elterman DS. Management of erectile dysfunction and LUTS/incontinence: the two most common, long-term side effects of prostate cancer treatment. Can J Urol 2020;27(27 Suppl 1):17-24.
11. Ritenour CW, Seidel KD, Leisenring W. Erectile dysfunction in male survivors of childhood cancer — a report from the childhood cancer survivor study. J Sex Med 2016;13(6):945–54.
12. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and Mortality Worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71(3):209–49.
13. Rallidis LS, Papathanasiou KA, Tsamoulis D, Bouratzis V, Leventis I, Kalantzis C, et al. Newly detected diabetes mellitus patients with acute coronary syndrome have an adverse cardiometabolic profile similar to patients with prior diabetes and a more extensive ischemic myocardial insult. Diabet Res Clin Pract 2024;211:111664.
14. Dilixiati D, Waili A, Tuerxunmaimaiti A, Tao L, Zebibula A, Rexiati M. Risk factors for erectile dysfunction in diabetes mellitus: a systematic review and meta-analysis. Front Endocrinol (Lausanne) 2024;15:1368079.
15. Xiang YT, Wang CY, Si TM, Lee EH, He YL, Ungvari GS, et al. The low frequency of reported sexual dysfunction in Asian patients with schizophrenia (2001-2009): low occurrence or ignored side effect? Hum Psycho-pharmacol 2011;26(4-5):352– 7.
16. Rojanasarot S, Williams AO, Edwards N, Khera M. Quantifying the number of US men with erectile dysfunction who are potential candidates for penile prosthesis implantation. Sex Med 2023;11(2):qfad010.
17. Tal R, Stember DS, Logmanieh N. Erectile dysfunction in men treated for testicular cancer. BJU Int 2014;113(6):907–10.
18. Pizzol D, Xiao T, Smith L, Sánchez GF, Garolla A, Parris C et al. Prevalence of erectile dysfunction in male survivors of cancer: a systematic review and meta-analysis of cross-sectional studies. Br J General Pract 2021;71(706):e372-80.
19. Johansson E, Steineck G, Holmberg L. Long-term quality-of-life outcomes after radical prostatectomy or watchful waiting: the Scandinavian prostate cancer group-4 randomised trial. Lancet Oncol 2011;12(9):891–9.
20. Yoshimura K, Arai Y, Ichioka K, Matsui Y, Ogura K, Terai A. et al. “What if I die and no one had ever romantically loved me?” Sexual well-being in a sample of YA cancer survivors. J Cancer Surviv 2024;18(1):186-95.
21. Zhang E, Ruth KJ, Buyyounouski MK, Price RA Jr, Uzzo RG, Sobczak ML, et al. Long-term results of a phase 3 randomized prospective trial of erectile tissue-sparing intensity-modulated radiation therapy for men with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 2023;115(5):1074-84.

Original Article

Perinatal Outcomes in Pre-Eclampsia and Eclampsia Cases

Our Experience of Perinatal Outcomes in Pre-Eclampsia and Eclampsia Cases: A Clinical Study at a Tertiary Khairpur Medical College Hospital (KMCH) Sindh

Saba Faiz[1], Amna Begum[2], Sehrish Rasool[2], Kanta Bai Ahuja[2], Rabia Jatoi[2] and Nousheen Khaleeq[2]

ABSTRACT

Objective: To evaluate the perinatal outcomes in pre-eclampsia and eclampsia cases and to investigate their association with the socio-demographic status of women at the Tertiary care hospital of Khairpur Medical College Hospital of Sindh.

Study Design: This hospital-based observational study.

Place and Duration of Study: This study was conducted at the Gynaecology Ward and Nursery of Khairpur Medical College Hospital (KMCH), Sindh, from July 2023 to June 2024.

Methods: In this study investigated the perinatal outcomes in cases of pre-eclampsia and eclampsia. Data was collected through patient interviews and neonatal assessments. Key maternal parameters recorded included age, parity, and gestational age at diagnosis. Neonatal outcomes were assessed based on birth weight, stillbirths, low birth weight, and intrauterine death.

Results: A total of 308 women who met the inclusion criteria were included in this study. The mean age of the women was 28.32±5.87 years. These 308 women gave live birth to 172 (55.8%) babies, and (40.3%) had stillbirths, whereas 12 (3.9%) had IUDs. The majority of live births (83, 48.3%) had a birth weight greater than 2.5 kg, whereas most stillbirths (69, 55.6%) and IUDs (5, 41.7%) had a birth weight between 2 and 2.5 kg.

Conclusion: Pre-eclampsia and eclampsia remain major problems in developing countries. They cause significant perinatal complications. Lack of education and awareness worsens outcomes, especially in low socio-economic groups. Perinatal mortality rates remain high. Expanding medical services to rural areas is crucial for better perinatal care.

Key Words: Eclempsia, Pre-eclempsia, Perinatal outcomes, Stillbirth, IUD

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INTRODUCTION

Hypertensive disorders of pregnancy, including pre-eclampsia and eclampsia, remain a significant cause of maternal and perinatal morbidity and mortality worldwide[1]. Pre-eclampsia, characterized by new-onset hypertension and proteinuria after 20 weeks of gestation, affects approximately 2–8%[2] of pregnancies, with a higher incidence in low-resource settings.

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Eclampsia, the severe manifestation of pre-eclampsia marked by seizures, contributes to a substantial proportion of maternal and neonatal deaths, particularly in regions with limited access to timely obstetric care[3]. The impact of these conditions extends beyond maternal health, significantly influencing fetal and neonatal outcomes, including preterm birth, intrauterine growth restriction (IUGR), and perinatal asphyxia[4].

The pathophysiology of pre-eclampsia and eclampsia is complex and not fully understood, but it primarily involves abnormal placentation, endothelial dysfunction, and an exaggerated maternal inflammatory response[5]. Impaired trophoblastic invasion leads to inadequate remodeling of the uteroplacental arteries, resulting in placental hypoperfusion and oxidative stress. This triggers the release of anti-angiogenic factors, such as soluble fms-like tyrosine kinase-1 (sFlt-1) [6] and endoglin, which disrupt endothelial function, leading to hypertension and multi-organ involvement. In eclampsia, cerebral vasospasm, endothelial injury, and ischemia contribute to the development of seizures, further complicating maternal and fetal outcomes[7].

The severity and timing of disease onset influence perinatal outcomes in pregnancies complicated by pre-eclampsia and eclampsia[8]. Early-onset pre-eclampsia, occurring before 34 weeks, is associated with higher rates of fetal complications, including IUGR, oligohydramnios, and stillbirth[9]. Late-onset pre-eclampsia, though generally less severe, can still lead to neonatal complications such as respiratory distress syndrome and neonatal intensive care unit (NICU) admissions[10].

Given the significant burden of perinatal complications associated with pre-eclampsia and eclampsia, this study aims to investigate perinatal outcomes in affected pregnancies[8]. By evaluating neonatal morbidity and mortality rates and identifying potential predictors of adverse outcomes, this research seeks to improve clinical management strategies and optimize neonatal care[11]. Understanding the patterns of perinatal complications in pre-eclampsia and eclampsia cases will contribute to the development of targeted interventions, ultimately improving maternal and neonatal health outcomes[12].

The primary and specific aims include examining the course of prenatal outcomes and evaluating connections between the occurrence of pre-eclampsia and eclampsia in postpartum moms with already existing risk factors identified. In this study context, we examine various antecedents that cause adverse fetal development, such as stillbirth, neonatal death, and neuro-developmental disability.

METHODS

This hospital-based observational study was conducted from July 2023 to June 2024, at the Gynaecology Ward and Nursery of Khairpur Medical College Hospital (KMCH), Sindh, to investigate perinatal outcomes in cases of pre-eclampsia and eclampsia. The study population included pregnant women diagnosed with pre-eclampsia, whether mild or severe, as well as those with eclampsia who were admitted to the Gynaecology Ward of KMCH. Neonatal outcomes were assessed in the Nursery.

The study's inclusion criteria comprised pregnant women diagnosed with pre-eclampsia or eclampsia, singleton pregnancies beyond 28 weeks of gestation, and patients who provided informed consent for participation. However, pregnancies complicated by pre-existing chronic hypertension, diabetes mellitus, renal disease, or autoimmune disorders were excluded. Additionally, multiple pregnancies and cases with incomplete medical records or lack of consent were not included in the study.

The institutional review board of KMCH granted ethical approval for the study. Before being included in the study, all participants provided written informed consent. Patient confidentiality was strictly maintained, and no identifiable information was disclosed.

Data was collected through patient interviews and neonatal assessments. Key maternal parameters recorded included age, parity, and gestational age at diagnosis. Neonatal outcomes were assessed based on birth weight, stillbirths, low birth weight, and intrauterine death.

For statistical analysis, data was processed using SPSS software version 24. Descriptive statistics were applied to summarize maternal and neonatal characteristics. Categorical variables were compared using the Chi-square test, while continuous variables were analyzed using t- tests as appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 308 women who met the inclusion criteria were included in this study. The mean age of the women was 28.32±5.87 years. These 308 women gave live birth to 172 (55.8%) babies, and (40.3%) had stillbirths, whereas 12 (3.9%) had IUDs. (Figure. I).

There was no statistically significant difference in gestational age among the three outcome groups (alive, stillbirth, and intrauterine death [IUD]), with mean gestational ages of 36.70±3.76 weeks, 34.15±4.11 weeks, and 35.75±4.26 weeks, respectively. The distribution of gestational age categories (<28 weeks, 28–34 weeks, and >34 weeks) also showed no significant association with outcomes. Similarly, education status was not significantly associated with perinatal outcomes, as 66.3% of mothers in the alive group, 65.3% in the stillbirth group, and 75.0% in the IUD group were educated. Occupational status also did not significantly differ, with homemakers comprising 74.4%, 74.2%, and 75.0% of the alive, stillbirth, and IUD groups, respectively. However, parity approached statistical significance, with primigravid women accounting for 59.3% of the alive group, 55.6% of the stillbirth group, and 91.7% of the IUD group.

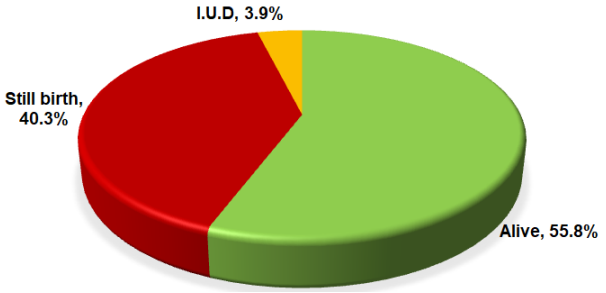

Figure No. 1: Distribution of outcome among the study patients

The mean birth weight was highest among live births (2.95±1.16 kg), followed by intrauterine demises (IUDs) (2.85±0.95 kg) and stillbirths (2.12±1.08 kilograms), with a statistically significant difference (p=0.004). The majority of live births (83, 48.3%) had a

birth weight greater than 2.5 kg, whereas most stillbirths (69, 55.6%) and IUDs (5, 41.7%) had a birth weight between 2 and 2.5 kg, though this difference was not statistically significant (p=0.607). Additionally, while live births and stillbirths were more commonly associated with grade 1 edema, IUDs predominantly exhibited grade 3 edema (7, 58.3%), with a significant association (p=0.002).

Table No. 1: Comparison between outcomes and baseline characteristics

Characteristics	Outcome			Test of sig.
	Alive	Still birth	I.U.D	
Gestational age (weeks)	36.70±3.76	34.15±4.11	35.75±4.26	F=0.74, d.f=2, p=0.480
<28 weeks	4 (2.3)	4 (3.2)	0 (0.0)	χ^2=1.86, d.f=4, p=0.761
28-34 weeks	39 (22.7)	35 (28.2)	3 (25.0)	
>34 weeks	129 (75.0)	85 (68.5)	9 (75.0)	
Education status				
Educated	114 (66.3)	81 (65.3)	9 (75.0)	χ^2=0.45, d.f=2, p=0.795
Non-educated	58 (33.7)	43 (34.7)	3 (25.0)	
Occupation				
Housewife	128 (74.4)	92 (74.2)	9 (75.0)	χ^2=0.05, d.f=2, p=0.998
Employed	44 (25.6)	32 (25.8)	3 (25.0)	
Parity				
Primi gravid	102 (59.3)	69 (55.6)	11 (91.7)	χ^2=5.88, d.f=2, p=0.053
Multigravida	70 (40.7)	55 (44.4)	1 (8.3)	
N (%) chi-square applied. Mean±S.D ANOVA applied.				

Table No .2: Comparison between outcomes and weight at birth & edema

Characteristics	Outcome			Test of sig.
	Alive	Still birth	I.U.D	
Weight at birth (kg)	2.95±1.16	2.12±1.08	2.85±0.95	F=8.69, d.f=2, p=0.004
<2 kg	31 (18.0)	21 (16.9)	1 (8.3)	χ^2=2.71, d.f=4, p=0.607
2-2.5 kg	58 (33.7)	69 (55.6)	6 (50.0)	
>2.5 kg	83 (48.3)	34 (27.4)	5 (41.7)	
Edema				
Grade 0	10 (5.8)	12 (9.7)	0 (0.0)	χ^2=24.02, d.f=8, p=0.002
Grade 1	98 (57.0)	74 (59.7)	5 (41.7)	
Grade 2	30 (17.4)	19 (15.3)	0 (0.0)	
Grade 3	25 (14.5)	12 (9.7)	7 (58.3)	
Grade 4	9 (5.2)	7 (5.6)	0 (0.0)	
N (%) chi-square applied. Mean±S.D ANOVA applied.				

DISCUSSION

The mean age of eclamptic women in our study was 28.32 ± 5.87 years, consistent with previous research findings. For instance, Lamminpää et al[13] reported a mean age of 26.6 ± 4.2 years among preeclamptic women under 35 years old. Similarly, Shahgheibi et al[14] found a mean age of 30.5 ± 6.6 years in women diagnosed with preeclampsia.

In your study, 59% of the 30 patients were primigravida, and 41% were multigravida. This distribution contrasts with findings from other studies. For instance, Okunade et al[15] reported primigravidae constituted only 15.3% of parturients in their research. Similarly, Amin et al[16] found that 54.83% of primigravida mothers were aged 21-30 years, while 65.75% of multigravida mothers were aged 31-40 years. These variations highlight differences in study populations and settings.

This study reports that 55.8% of births were live, 40.3% were stillbirths, and 3.9% were intrauterine deaths (IUDs), with mean gestational ages of 36.70 ± 3.76 weeks for live births, 34.15 ± 4.11 weeks for stillbirths, and 35.75 ± 4.26 weeks for IUDs. A population-based study by Gardosi et al[17] found that the median gestational age for stillbirths with fetal growth restriction was 32 weeks and three days, compared to 36 weeks and six days for those without growth restriction. This suggests that stillbirths often occur at earlier gestational ages, mainly when fetal growth restriction is present.

Additionally, a systematic review and meta-analysis by Muglu et al[18] reported that the prospective risk of

stillbirth increases with advancing gestational age, rising from 0.11 per 1,000 pregnancies at 37 weeks to 3.18 per 1,000 at 42 weeks. This indicates that while the risk of stillbirth is generally low at term, it escalates in post-term pregnancies.

This study found no significant association between maternal education and perinatal outcomes, with 66.3% of mothers in the alive group, 65.3% in the stillbirth group, and 75.0% in the intrauterine death (IUD) group being educated. Similarly, a study conducted by Karlsen et al[19] examining the relationship between maternal education and maternal mortality found that lower educational attainment was associated with an increased risk of adverse pregnancy outcomes.

In this study, among 308 women, 172 (55.8%) had live births, 124 (40.3%) experienced stillbirths, and 12 (3.9%) had intrauterine deaths (IUDs). These figures indicate a notably high stillbirth rate compared to global and regional statistics. Singhal et al[20] reported a high incidence of perinatal complications, with 71.43% of babies having low birth weight, 66% delivering preterm, 52.4% experiencing birth asphyxia, and 28.57% being stillborn. The study also found that maternal and perinatal outcomes were significantly poorer in cases of eclampsia compared to severe pre-eclampsia.

This study found that the mean birth weight of live births was significantly higher than stillbirths and intrauterine fetal demises (IUFDs). Specifically, live births had a mean weight of 2.95±1.16 kg, compared to 2.12±1.08 kg for stillbirths and 2.85±0.95 kg for IUFDs. Bukowski et al[21] emphasized that fetal growth restriction is a key contributor to stillbirth, often due to placental insufficiency. Similarly, a study by conducted by a researcher[22] demonstrated that small-for-gestational-age (SGA) fetuses have an increased risk of perinatal death, reinforcing the role of inadequate fetal growth in poor neonatal outcomes.

CONCLUSION

Pre-eclampsia and eclampsia remain major problems in developing countries. They cause significant perinatal complications. Lack of education and awareness worsens outcomes, especially in low socio-economic groups. Perinatal mortality rates remain high. Expanding medical services to rural areas is crucial for better perinatal care.

Author's Contribution:

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Drafting or Revising Critically:	Sehrish Rasool, Kanta Bai Ahuja, Rabia Jatoi, Nousheen Khaleeq
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Andronikidi PE, Orovou E, Mavrigiannaki E, Athanasiadou V, Tzitiridou-Chatzopoulou M, Iatrakis G, et al. Placental and renal pathways underlying pre-eclampsia. Intern J Molecul Sci 2024;25(5):2741.
2. Bartal MF, Sibai BM. Eclampsia in the 21st century. Am J Obstetr Gynecol 2022;226(2):S1237-53.
3. Mahendra V, Clark SL, Suresh MS. Neuropathophysiology of preeclampsia and eclampsia: a review of cerebral hemodynamic principles in hypertensive disorders of pregnancy. Pregnancy Hypertension 2021;23:104-11.
4. Abraham T, Romani AM. The relationship between obesity and pre-eclampsia: incidental risks and identification of potential biomarkers for pre-eclampsia. Cells 2022;11(9):1548.
5. Gusella A, Martignoni G, Giacometti C. Behind the Curtain of abnormal placentation in Pre-eclampsia: from Molecular mechanisms to histological Hallmarks. Int J Molecul Sci 2024;25(14):7886.
6. Louis JM, Parchem J, Vaught A, Tesfalul M, Kendle A, Tsigas E, et al. Preeclampsia: a report and recommendations of the workshop of the Society for Maternal-Fetal Medicine and the Preeclampsia Foundation. Am J Obstet Gynecol 2022;227(5):B2-4.
7. Fahmy HH, Ibrahim SE, Hussien AF. Hypertension in pregnancy: the current state of the art. Neuro Quantol 2022;20(15):6362.
8. Zavlanos A, Tsakiridis I, Chatzikalogiannis I, Athanasiadis A. Early-and late-onset intrauterine growth retardation. Donald School J Ultrasound in Obstetr Gynecol 2021;15(1):97-108.
9. Li B, Yang H. Comparison of clinical features and pregnancy outcomes in early-and late-onset preeclampsia with HELLP syndrome: a 10-year retrospective study from a tertiary hospital and referral center in China. BMC Pregnan Childbirth 2022;22(1):186.
10. Carty DM, Delles C, Dominiczak AF. Preeclampsia and future maternal health. J Hypertens 2010;28(7):1349-55.
11. Kuklina EV, Ayala C, Callaghan WM. Hypertensive disorders and severe obstetric

morbidity in the United States. Obstet Gynecol 2009;113(6):1299-306.
12. Umme-Farwa FD, Mehreen A, Shaikh S, Bai P. The frequency of pre-eclampsia and eclampsia in un-booked pregnant patients presenting in a tertiary care unit. Med Forum 2022;33(2):133-7.
13. Lamminpää R, Vehviläinen-Julkunen K, Gissler M, Heinonen S. Preeclampsia complicated by advanced maternal age: a registry-based study on primiparous women in Finland 1997–2008. BMC Pregnan Childbirth 2012;12:47.
14. Shahgheibi S, Gharibi F, Mohammadi S, Amani F. Maternal and neonatal outcomes in pregnant women with preeclampsia. J Clin Diagn Res 2016;10(6):101-104.
15. Okunade KS, Daramola ES, Sobande AA, Oluwole AA, Oyeneyin LO. Cross-sectional study on the obstetric performance of primigravidae in Lagos, Nigeria. Niger Med J 2016;57(5):303-307.]
16. Amin F, Amin S, Amin S. Comparative analysis of pregnancy complications: primigravida versus multigravida. Int J Res Med Sci 2023;11(9):3235-3255.
17. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and fetal risk factors for stillbirth: population based study. BMJ 2013; 346:p108.
18. Muglu J, Rather H, Arroyo-Manzano D, Bhattacharya S, Balchin I, Khalil A, et al. Risks of stillbirth and neonatal death with advancing gestation at term: a systematic review and meta-analysis of cohort studies of 15 million pregnancies. PLoS Med 2019;16(7):e1002838.
19. Karlsen S, Say L, Souza JP, Hogue CJ, Calles DL, Gülmezoglu AM, et al. The relationship between maternal education and mortality among women giving birth in health care institutions: analysis of the cross-sectional WHO Global Survey on Maternal and Perinatal Health. BMC Public Health 2011;11:606.
20. Singhal SR, Deepika, Anshu, Nanda S. Maternal and perinatal outcome in severe pre-eclampsia and eclampsia. South Asian Federation Obstet Gynecol 2009;1(3):25-28.
21. Bukowski R, Hansen NI, Willinger M, Reddy UM, Parker CB, Pinar H, et al. Fetal growth and risk of stillbirth: a population-based case-control study. PLoS Med 2014;11(4):e1001633.
22. Irfan A, Mughal IA, Faruqi A, Qureshi SL, Zafar T. Fetal outcomes of preeclampsia. Med Forum. 2020;31(1):79-82.

Original Article

Impact of Metabolic Syndrome on the Progression of Coronary Artery Disease: An Observational Cohort Study

Ghulam Hussain, Muhammad Farooq, Usman Sadiq, Gohar Ali, Muhammad Shahid Nawaz Khan and Muhammad Tahir

ABSTRACT

Objective: The objective of study was to evaluate the impact of MetS on the progression of CAD across diverse patient populations.

Study Design: An observational cohort study

Place and Duration of Study: This study was conducted at the department of Medicine and Cardiology at Nishtar II Medical University and Hospital, Multan, from September 2023 to August 2024.

Methods: Total 424 participants aged between 30 to 75 years diagnosed with MetS according to the International Diabetes Federation criteria. Clinical exams, structured interviews, and reviews of medical records were used to gather data. Important laboratory and anthropometric data were assessed at baseline and after 6, 12, 18, and 24 months of follow-up. Regression models were used in the statistical studies, which were carried out using SPSS version 26, to evaluate the connections between the components of the MetS and the advancement of CAD.

Results: The results showed a significant positive correlation with the progression of CAD between waist circumference, systolic blood pressure, and fasting blood glucose levels ($\beta = 0.15$, $p = 0.002$; $\beta = 0.18$, $p = 0.003$; and $\beta = 0.22$, $p = 0.001$, respectively). Participants showed significant improvements in metabolic parameters during the 24-month follow-up period, including a drop in fasting blood glucose levels to 99.89 mg/dL and a reduction in waist circumference to 87.03 cm and systolic blood pressure to 123.87 mmHg. Furthermore, good improvements were seen in lipid profiles, demonstrating the beneficial effects of focused therapies on cardiovascular health.

Conclusion: This study indicates how crucial MetS is in accelerating CAD development. It also emphasizes how crucial early preventive and sensible risk control are for reducing cardiovascular risk.

Key Words: Metabolic syndrome, coronary artery disease, multicenter study, cardiovascular risk, cohort study.

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INTRODUCTION

A collection of linked risk factors, the metabolic syndrome (MetS) dramatically raises the likelihood of cardiac disorders including coronary artery disease (CAD) [1, 2]. MetS is the condition whereby central obesity, high blood pressure, cholesterol, and insulin resistance all occur concurrently. This is a global health issue particularly in those who lead inactive lives or consume poor diets[3,4].

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Affecting millions of people worldwide, MetS rates have gone crazy and could jeopardize public health services[5]. Among the biochemical events connected to this disease and driving its growth and aggravation are those related to endothelial function, inflammation, and vascular stiffness[6].

When compared to people who did not have MetS, those who did had more serious coronary artery lesions and more bad cardiovascular events. These findings amply illustrate the significance of MetS in aggravating CAD[7]. MetS and CAD are linked in a convoluted fashion. For instance, obesity aggravates insulin resistance and accelerates atherosclerosis by inducing an inflammatory condition[8, 9]. Moreover, a variety of risk factors might hasten the development of CAD, which complicates the execution of therapeutic treatment regimens [10, 11].

To effectively avoid and treat CAD, one must completely comprehend the relationship between MetS and CAD since it is so complex. Though past studies on this subject have been conducted, not enough multicenter studies examining how MetS alters the course of CAD in different groups have been published.

Examining the relationships between these two main health concerns will help us to better understand the elements increasing the risk of heart disease and design treatments catered to the special requirements of MetS patients.

METHODS

This study was carried out between September 2023 to August 2024, it was conducted at Medicine and Cardiology Department of the Nishtar II Medical University Multan, Specifically a cohort study, it was a combined, observational design. The Institutional Review Board (IRB) examined and approved the research protocol. All subjects gave their informed permission before being included in the study, guaranteeing that ethical standards were closely adhered to at every stage of the investigation. The volunteers have to satisfy exactly the criteria established by the International Diabetes Federation for MetS. Among them were being an adult between the ages of 30 and 75 and having a CAD diagnosis derived from angiographic tests. Participants were not permitted to be anyone with acute infections, inflammatory disorders, cancer, or history of heart bypass operations. The World Health Organization (WHO) technique for sample size estimation was applied to ascertain the study's sample size. The study needed at least 385 individuals to provide statistically significant findings with a 95% confidence level (Z = 1.96), a 5% margin of error (E = 0.05), and the knowledge that half of those with CAD had MetS (p = 0.5). One might consider those who could drop out over the two-year research period using a desired sample size of around 424 persons. This would let one examine the relationship between MetS and CAD expansion in great detail. Sample size was calculated by using formula ($n = Z^2 \times p\ (1- p)/E^2$), p = estimated prevalence (you can assume a prevalence of 50% or 0.5 for maximum variability if unknown) with margin of error (0.05 for a 5% margin). Since you can't have a fraction of a participant, round up to the next whole number, resulting in a sample size of 385 participants. If we assume a 10% dropout rate, the target sample size would be: Adjusted sample size = n × (1+ dropout rate) = 385 × 1.10 = 423.5. Rounding gives a target sample size of 424 participants.

Clinical exams, organized patient interviews, and a review of medical records were used to gather data. This procedure collected lifestyle characteristics, medical history, and demographic data. Important anthropometric metrics, including blood pressure and waist circumference, were evaluated during clinical evaluations. Standardized questionnaires were used to evaluate the elements of MetS, and blood samples were examined for lipid profiles and fasting blood glucose levels. At six, twelve, eighteen, and twenty-four months, follow-up evaluations were carried out to track changes in MetS and cardiovascular health. The proper software (e.g., SPSS version 26) was used to conduct statistical analyses. The clinical and demographic features were gathered using descriptive statistics. Regression models were used to examine the connections between the components of the MetS and the development of CAD while controlling for possible confounders. Less than 0.05 was the threshold for statistical significance.

RESULTS

This research consisted of 424 individuals, 210 males (49.53%) and 214 women (50.47%), with a mean age of 55.32 ± 10.41 years. Table 1 shows that 73.11% of the population had a history of hypertension, and 29.48% had diabetes mellitus. In terms of smoking status, 59.91% had never smoked, 18.87% were past smokers, and 21.23% were current smokers. 35.38% of the population was sedentary, 47.17% was moderately active, and 17.45% was actively involved in their physical activity. Regarding eating and exercise routines, 42.45% only focused on food, 11.79% exercised, 18.87% did both, and 26.89% did neither. The average waist circumference was 94.16 ± 12.03 cm, while the diastolic and systolic blood pressure readings were 85.26 ± 10.34 mmHg and 130.52 ± 15.81 mmHg, respectively. Total cholesterol was measured in the lab at 210.59 ± 35.27 mg/dL; LDL cholesterol was measured at 130.88 ± 30.12 mg/dL; HDL cholesterol was measured at 40.54 ± 10.51 mg/dL; fasting blood glucose was measured at 110.23 ± 25.41 mg/dL; and triglycerides were measured at 150.03 ± 45.25 mg/dL.

Table No. 1: Demographic, Clinical, and Laboratory Characteristics of Participants (n = 424)

Variable		Total (n = 424)
Age (years)	Mean ± SD	55.32 ± 10.41
Gender	Men	210 (49.53%)
	Women	214 (50.47%)
Medical History	History of Hypertension	310 (73.11%)
	History of Diabetes Mellitus	125 (29.48%)
Smoking Status	Current Smokers	90 (21.23%)
	Former Smokers	80 (18.87%)
	Never Smokers	254 (59.91%)
Physical Activity Level	Sedentary	150 (35.38%)
	Moderate Activity	200 (47.17%)
	Active	74 (17.45%)
Diet and Exercise	Diet only	180 (42.45%)
	Exercise only	50 (11.79%)
	Both diet and exercise	80 (18.87%)
	No Diet and	114 (26.89%)

	Exercise	
Waist Circumference (cm)	Mean ± SD	94.16 ± 12.03
Blood Pressure	Systolic (mmHg)	130.52 ± 15.81
	Diastolic (mmHg)	85.26 ± 10.34
Laboratory Results	Total Cholesterol (mg/dL)	210.59 ± 35.27
	LDL Cholesterol (mg/dL)	130.88 ± 30.12
	HDL Cholesterol (mg/dL)	40.54 ± 10.51
	Fasting Blood Glucose (mg/dL)	110.23 ± 25.41
	Triglycerides (mg/dL)	150.03 ± 45.25

The results of follow-up evaluations of important health parameters over a 24-month period revealed a noteworthy reduction in waist circumference, with measurements at 6 months being 92.53 ± 11.57 cm, 12 months being 90.45 ± 11.06 cm, 18 months being 88.76 ± 10.53 cm, and 24 months being 87.03 ± 10.21 cm (table 2). The diastolic blood pressure also dropped at the same time, from 83.07 ± 10.17 mmHg to 79.08 ± 8.15 mmHg. The diastolic blood pressure reduced from 128.45 ± 15.03 mmHg at 6 months to 123.87 ± 13.59 mmHg at 24 months. At six months, fasting blood glucose levels were 108.19 ± 24.02 mg/dL; at 24 months, they had decreased to 99.89 ± 21.32 mg/dL. LDL cholesterol readings dropped from 126.53 ± 29.17 mg/dL to 114.52 ± 26.41 mg/dL, while total cholesterol levels dropped from 206.19 ± 34.13 mg/dL to 195.18 ± 31.13 mg/dL. During the same period, triglyceride levels dropped from 146.13 ± 43.19 mg/dL to 133.28 ± 40.67 mg/dL, while HDL cholesterol levels grew progressively from 42.32 ± 10.19 mg/dL at 6 months to 46.19 ± 11.36 mg/dL at 24 months.

Table No. 2: Follow-Up Assessments of Key Health Metrics at 6, 12, 18, and 24 Months

Variable	6 Months	12 Months	18 Months	24 Months
Waist Circumference (cm)	92.53 ± 11.57	90.45 ± 11.06	88.76 ± 10.53	87.03 ± 10.21
Systolic Blood Pressure (mmHg)	128.45 ± 15.03	126.67 ± 14.51	125.03 ± 14.17	123.87 ± 13.59
Diastolic Blood Pressure (mmHg)	83.07 ± 10.17	81.89 ± 9.56	80.16 ± 9.03	79.08 ± 8.15
Fasting Blood Glucose (mg/dL)	108.19 ± 24.02	105.34 ± 23.67	102.17 ± 22.45	99.89 ± 21.32
Total Cholesterol (mg/dL)	206.19 ± 34.13	202.21 ± 33.41	198.03 ± 32.21	195.18 ± 31.13
LDL Cholesterol (mg/dL)	126.53 ± 29.17	122.19 ± 28.43	118.56 ± 27.87	114.52 ± 26.41
HDL Cholesterol (mg/dL)	42.32 ± 10.19	43.89± 10.52	44.95 ± 11.09	46.19 ± 11.36
Triglycerides (mg/dL)	146.13 ± 43.19	141.07 ± 42.17	137.14 ± 41.34	133.28 ± 40.67

The regression analysis of the MetS components and how they relate to the development of CAD is shown in Table 3. A significant correlation between waist circumference and the development of CAD was found, resulting in a regression coefficient (β) of 0.15 (SE = 0.05, p = 0.002). Similar positive correlations were seen for diastolic and systolic blood pressure (β = 0.12, SE = 0.06, p = 0.028) and systolic blood pressure (β = 0.18, SE = 0.07, p = 0.003). The highest positive connection was found for fasting blood glucose (β = 0.22, SE = 0.09, p = 0.001), suggesting that it plays a crucial role in the advancement of CAD. Significant positive associations were also shown by LDL cholesterol (β = 0.20, SE = 0.08, p = 0.002) and total cholesterol (β = 0.14, SE = 0.05, p = 0.004). On the other hand, triglycerides exhibited a positive link (β = 0.17, SE = 0.06, p = 0.005) with CAD development, but HDL cholesterol was adversely related (β = -0.16, SE = 0.07, p = 0.007).

Table No. 3: Regression Analysis of Metabolic Syndrome Components on Coronary Artery Disease Progression

Metabolic Syndrome Component	Regression Coefficient (β)	Standard Error (SE)	p-value
Waist Circumference (cm)	0.15	0.05	0.002
Systolic Blood Pressure (mmHg)	0.18	0.07	0.003
Diastolic Blood Pressure (mmHg)	0.12	0.06	0.028
Fasting Blood Glucose (mg/dL)	0.22	0.09	0.001
Total Cholesterol (mg/dL)	0.14	0.05	0.004
LDL Cholesterol (mg/dL)	0.20	0.08	0.002
HDL Cholesterol	-0.16	0.07	0.007

(mg/dL)			
Triglycerides (mg/dL)	0.17	0.06	0.005

DISCUSSION

The results of this study provide us with significant fresh insights on how MetS influences the course of CAD in a large spectrum of individuals. Older persons with CAD had comparable waist circumferences according to other research[12, 13]. According to our data, the mean waist circumference of the individuals was 94.16 ± 12.03 cm. This implies that, in many individuals, belly obesity—a major component of MetS—remains a significant risk factor for the course of CAD.

In our group, 73.11% of individuals had prior high blood pressure, hence hypertension was very prevalent. This rate corresponds with recent research showing that elevated blood pressure aggravates cardiovascular disease[14, 15]. In our study, the mean systolic blood pressure was 130.52 ± 15.81 mmHg and the mean diastolic blood pressure was 85.26 ± 10.34 mmHg. These values help to explain why high blood pressure is a main cause of CAD. These findings make it abundantly evident how crucial it is for individuals with MetS to monitor and regulate their blood pressure so as to avoid CAD.

With a mean fasting blood glucose level of 110.23 ± 25.41 mg/dL, our findings revealed a clear correlation between metabolic elements and how CAD developed. This result aligns with another study showing those with uncontrolled diabetes had higher risk of major cardiovascular events[16]. In our regression investigation, we identified a strong, significant connection ($\beta = 0.22$, $p = 0.001$) between fasting blood glucose and CAD development. This indicates that those with MetS have to learn diabetic control techniques.

With a range of 30.12 mg/dL to 210.59 mg/dL, our investigation also revealed total cholesterol was 210.59 mg/dL and LDL cholesterol was 130.89 mg/dL. As with other research showing a considerably increased risk of CAD among those with MetS when their cholesterol levels are high[17, 18]. Furthermore, our investigation revealed that the development of CAD was adversely correlated with HDL cholesterol levels (40.54 ± 10.51 mg/dL) ($\beta = -0.16$, $p = 0.007$). This indicates that HDL cholesterol can assist avoid heart disease and is in accordance with research by Zou Y et al [19] that persons with MetS can profit from greater HDL levels for their heart health.

CONCLUSION

Examining blood pressure, waist circumference, and fasting blood glucose levels, this study spanning several sites reveals that MetS significantly influences the development of CAD and looks at risk variables. Our study reveals that persons with MetS experience quicker heart difficulties, which emphasizes the need of using focused therapy to reduce these risks. This study provides crucial knowledge on how MetS and CAD interact that might support clinical treatment and public health initiatives aiming at reduced cardiovascular disease and mortality.

Author's Contribution:

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Drafting or Revising Critically:	Usman Sadiq, Gohar Ali, Muhammad Shahid Nawaz Khan, Muhammad Tahir
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Alshammary AF, Alharbi KK, Alshehri NJ, Vennu V, Ali Khan I. Metabolic syndrome and coronary artery disease risk: a meta-analysis of observational studies. Int J Environment Res Public Health 2021;18(4):1773.
2. Hayden MR. Overview and new insights into the metabolic syndrome: risk factors and emerging variables in the development of type 2 diabetes and cerebrocardiovascular disease. Med 2023;59(3):561.
3. Das D, Shruthi NR, Banerjee A, Jothimani G, Duttaroy AK, Pathak S. Endothelial dysfunction, platelet hyperactivity, hypertension, and the metabolic syndrome: molecular insights and combating strategies. Front Nutrit 2023;10:1221438.
4. Bovolini A, Garcia J, Andrade MA, Duarte JA. Metabolic syndrome pathophysiology and predisposing factors. Int J Sports Med 2021;42(03):199-214.
5. Ashraf H, Rashidi A, Noshad S, Khalilzadeh O, Esteghamati A. Epidemiology and risk factors of the cardiometabolic syndrome in the Middle East. Expert Rev Cardiovas Therapy 2011;9(3):309-20.
6. Labazi H, Trask AJ. Coronary microvascular disease as an early culprit in the pathophysiology of diabetes and metabolic syndrome. Pharma Res 2017;123:114-21.
7. Khaliq A, Johnson BD, Anderson RD, Bavry AA, Cooper-DeHoff RM, Handberg EM, et al. Relationships between components of metabolic

syndrome and coronary intravascular ultrasound atherosclerosis measures in women without obstructive coronary artery disease: the NHLBI-Sponsored women's ischemia syndrome evaluation study. Cardiovas Endocrinol Metabol 2015 ;4(2):45-52.
8. Luna-Luna M, Medina-Urrutia A, Vargas-Alarcón G, Coss-Rovirosa F, Vargas-Barrón J, Pérez-Méndez Ó. Adipose tissue in metabolic syndrome: onset and progression of atherosclerosis. Arch Med Res 2015;46(5):392-407.
9. Chait A, Den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. Front Cardiovas Med 2020;7:522637.
10. Kones R. Molecular sources of residual cardiovascular risk, clinical signals, and innovative solutions: relationship with subclinical disease, undertreatment, and poor adherence: implications of new evidence upon optimizing cardiovascular patient outcomes. Vascular Health Risk Management 2013:617-70.
11. Van Rosendael AR, Bax AM, Smit JM, Van Den Hoogen IJ, Ma X, Al'Aref S, et al. Clinical risk factors and atherosclerotic plaque extent to define risk for major events in patients without obstructive coronary artery disease: the long-term coronary computed tomography angiography CONFIRM registry. Eur Heart J Cardiovas Imaging 2020;21(5):479-88.
12. Hajsadeghi S, Firouzi A, Bahadoran P, Hassanzadeh M. The value of wrist circumference for predicting the presence of coronary artery disease and metabolic syndrome. Ind Heart J 2016;68:S5-9.
13. Alshammary AF, Alharbi KK, Alshehri NJ, Vennu V, Ali Khan I. Metabolic syndrome and coronary artery disease risk: a meta-analysis of observational studies. Int J Enviro Res Public Health 2021;18(4):1773.
14. Mahalle N, Garg MK, Naik SS, Kulkarni MV. Association of metabolic syndrome with severity of coronary artery disease. Indian J Endocrinol Metabol 2014;18(5):708-14.
15. Varounis C, Rallidis LS, Franco OH, Lekakis J. Prevalence of metabolic syndrome and association with burden of atherosclerotic disease in patients with stable coronary artery disease. Current Med Res Opinion 2016;32(6):1175-81.
16. Vazquez-Benitez G, Desai JR, Xu S, Goodrich GK, Schroeder EB, Nichols GA, et al. Preventable major cardiovascular events associated with uncontrolled glucose, blood pressure, and lipids and active smoking in adults with diabetes with and without cardiovascular disease: a contemporary analysis. Diabet Care 2015;38(5):905-12.
17. Chevli PA, Islam T, Pokharel Y, Rodriguez F, Virani SS, Blaha MJ, et al. Association between remnant lipoprotein cholesterol, high-sensitivity C-reactive protein, and risk of atherosclerotic cardiovascular disease events in the Multi-Ethnic Study of Atherosclerosis (MESA). J Clin Lipidol 2022;16(6):870-7
18. Hashmi KA, Khan TM, Shahzad A. The Association of Risk Factors and Severity of Acute Coronary Syndrome with Serum Uric Acid Levels in Female Population Younger Than 45 Years. Med Forum 2021;32(11):107-110.
19. Zou Y, Kuang M, Zhong Y, Jiang C. Remnant cholesterol can identify individuals at higher risk of metabolic syndrome in the general population. Sci Reports 2023;13(1):5957..

Original Article

Frequency of Helicobacter Pylori in Perforated Peptic Ulcer and Associated Risk Factors

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ABSTRACT

Objective: To determine the frequency and risk factors of Helicobacter pylori infection in patients diagnosed with perforated peptic ulcer disease.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Surgical Unit Bakhtawar Amin Medical & Dental College, from January 2023 to December 2023.

Methods: A total of 384 patients over the age of 12 with peptic ulcer perforation were included. Detailed histories were taken regarding potential causes of peptic ulcers, such as Helicobacter pylori infection, alcohol consumption, current or past significant illnesses, socioeconomic status and use of tobacco in betel nut or chewing form.

Results: In our study, the presence of helicobacter pylori was found in 230 (59.9%) patients. It was seen that the presence of helicobacter pylori was higher in males 146 (65.8%) than females 76 (34.2%), (p=0.006). Presence of helicobacter pylori was higher in smokers 56 (70.9%) than non-smokers, 23 (29.1%), (p=0.025). Similarly, presence of helicobacter pylori was higher in betel nut & pan chewing used patients 30 (78.9%), than 8 (21.1%) betel nut & pan chewing not used patients.

Conclusion: H. pylori infection was not significantly associated with PPU. However, factors such as alcohol intake and tobacco use were involved in perforation. Therefore, we can conclude that while H. pylori infection is not a risk factor for PPU, it is important to avoid other risk factors.

Key Words: H Pylori, Peptic ulcer disease, Risk factors, Perforation

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INTRODUCTION

Over the recent past, the incidence of peptic ulcer disease has reduced mainly by virtue of the PPI use and H pylori eradication[1]. However, complications such as perforation are still apart of the present picture and a cause for worry in the field of healthcare. This prolongation of complications may have an association with increasing proportion of geriatrics and excessive use of non-steroidal anti-inflammatory drugs (NSAIDs)[2].

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Iatrogenic duodenal perforations were formerly rare, but the growing incidence of endoscopic procedures like endoscopic retrograde cholangiopancreatography (ERCP) has led to this problem[3]. Thus, the treatment of choice for duodenal ulcers remains still a matter of controversy, and the diagnosis is frequently made at a rather late stage, which detrimental effect on the patient's survival[16].

Even till 1983 Waren & Marshall discovered the link between Helicobacter pylori and peptic ulcers, the consensus was that stress, dietary factors and increased ulcer acid secretion caused peptic ulcers[7]. Helicobacter pylori infection is estimated to affect about 50% of the world's population[7], with the distribution in the developing world being higher than in the western countries. More particularly, studies show that increased noise levels adversely affect task completion rates (92 % reduction), worker productivity (66. 6%, and 70% of duodenal perforation patient had history of H. pylori infection respectively [8].

Duodenal perforation though rare constitutes a serious threat to health and has a mortality index of between eight and twenty-five percent as has been witnessed in different research studies[9,10]. The first account of the perforated duodenal ulcer was given by Muralto in the year 1688 in the patient that was reported by

Lenepneau[1]. An omental patch which is not a new technique in such circumstances was for the first time described by Cellan-Jones in 1929[13]. Besides, the first laparoscopic surgery conducted for a perforated duodenal ulcer was in the year 1904[14].

As much as H. pylori infection is not rare in our community, published data indicates that incidence of this infection in cases of duodenal perforation might differ across regions. There is a dearth of literature regarding the correlation between H. pylori and duodenal perforation[15] and hence our work. Thus, identifying to what extent duodenal perforation patients treated in the local health care facility are infected with H. pylori, it will be possible to gain essential understanding of the extent of the problem as observed in the local setting. Altogether, these results will be reported to the gastroenterologists and surgeons in the area which in turn will enable them practice informed decision making in future research and practice.

METHODS

This cross-sectional study was conducted in Bakhtawar Amin Medical & Dental College, from January 2023 to December 2023. Patients presented at emergency and outpatient department of hospital with sign and symptoms of acute peritonitis due to perforation of peptic ulcer disease were enrolled. Sample size was calculated from previous study findings, H. pylori infection 52%, confidence interval 95% and margin of error 5%. Openepi software was used for estimation if sample. History of patients regarding use of tobacco (chewing or betel nut), alcohol use, socioeconomic status, diabetes, hypertension, smoking, and area of residence were taken.

Serology for H. pylori was performed immediately after diagnosing peptic ulcer perforation. Any silent perforations of peptic ulcers, including those of patients on medication. Patients with co-morbidities such as cardiovascular disease, arthritis, asthma, or any other condition for which the patients were taking medication were excluded. SPSS version 27.1 used for analysis of data. Test of significance were t test and chi square with significant p value of 0.05 or below was considered.

RESULTS

Overall, 384 patients were included in our study, with mean age 46.12±9.05 years. There 222 (57.8%) males and 162 (42.2%) females. Mean BMI of the study patients was 25.86±2.96 kg/m^2, and most of the patients 234 (60.9%) had BMI more than 25 kg/m^2. Majority of the patients 236 (62.5%) lived in urban areas, whereas 148 (38.5%) lived in rural areas. There were 311 (81.0%) patients had low socioeconomic status and 73 (19.0%) patients had high socioeconomic status. Diabetes mellitus was found in 105 (27.3%) patients, whereas hypertension was found in 100 (26.0%) patients. Furthermore, 79 (20.6%) patients were smokers. Mean peptic ulcer disease of the patients was 10.27±3.93 years, and majority of the patients had up to 11 years of peptic ulcer disease. Whereas use of betel nut & pan chewing was observed in 38 (9.9%) patients. (Table. No. 1).

In our study, the presence of helicobacter pylori was found in 230 (59.9%) patients. (Figure. I). Association of helicobacter pylori with demographics and baseline profile was shown in table. No. 2. It was seen that the presence of helicobacter pylori was higher in males 146 (65.8%) than females 76 (34.2%), (p=0.006). Presence of helicobacter pylori was higher in smokers 56 (70.9%) than non-smokers, 23 (29.1%), (p=0.025). Similarly, presence of helicobacter pylori was higher in betel nut & pan chewing used patients 30 (78.9%), than 8 (21.1%) betel nut & pan chewing not used patients. (Table. No. 2).

Table. No .1: Demographics and baseline profile

Variable	N (%)	Mean ± S.D
Age (years)		46.12±9.05
Up to 40	87 (22.7)	
More than 40	297 (77.3)	
BMI (kg/m^2)		25.86±2.96
Up to 25	150 (39.1)	
More than 25	234 (60.9)	
Gender		
Male	222 (57.8)	
Female	162 (42.2)	
Area of residence		
Urban	236 (62.5)	
Rural	148 (38.5)	
Socioeconomic status		
Low	311 (81.0)	
High	73 (19.0)	
Diabetes mellitus	105 (27.3)	
Hypertension	100 (26.0)	
Smoking	79 (20.6)	
Peptic ulcer disease (years)		10.27±3.93
Up to 11	237 (61.7)	
More than 11	147 (38.3)	
Use of betel nut & pan chewing	38 (9.9)	

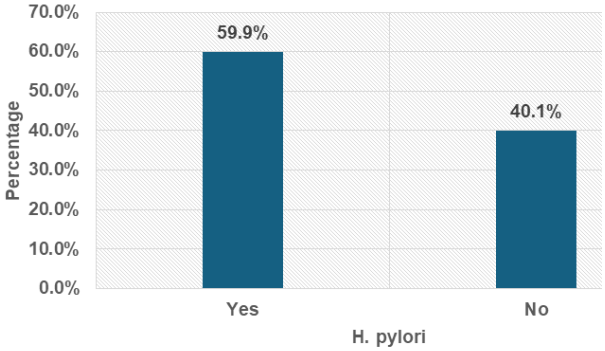

Figure No. 1:Presence of helicobacter pylori

Table. No. 2: Association of helicobacter pylori with demographics and baseline profile

Variable	Helicobacter pylori		p-value
	Yes	No	
Age (years)			
Up to 40 years	49 (56.3)	38 (43.7)	0.439
More than 40 years	181 (60.9)	116 (39.1)	
BMI (kg/m^2)			
Up to 25	97 (64.7)	53 (35.3)	0.127
More than 25	133 (56.8)	101 (43.2)	
Gender			
Male	146 (65.8)	76 (34.2)	0.006
Female	84 (51.9)	78 (48.1)	
Area of residence			
Urban	146 (61.9)	90 (38.1)	0.320
Rural	84 (56.8)	64 (43.2)	
Socioeconomic status			
Low	189 (60.8)	122 (39.2)	0.470
High	41 (56.2)	32 (43.8)	
Diabetes mellitus			
Yes	69 (65.7)	36 (34.3)	0.154
No	161 (57.7)	118 (42.3)	
Hypertension			
Yes	68 (68.0)	32 (32.0)	0.065
No	162 (57.0)	122 (43.0)	
Smoking			
Yes	56 (70.9)	23 (29.1)	0.025
No	174 (57.0)	131 (43.0)	
Peptic ulcer disease (years)			
Up to 11	144 (60.8)	93 (39.2)	0.661
More than 11	86 (58.5)	61 (41.5)	
Use of betel nut & pan chewing			
Yes	30 (78.9)	8 (21.1)	0.012
No	200 (57.8)	146 (42.2)	
N (%)			

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DISCUSSION

Perforated peptic ulcer is not just a local issue, but a prevalent emergency medical condition globally, characterized by a substantial risk of mortality, particularly among elderly patients[16]. Prompt surgical intervention to repair the perforation, coupled with comprehensive sepsis management, is critical for improving patient outcomes and reducing mortality rates. Rapid diagnosis and timely treatment are essential components of effective management, as delays can lead to complications such as peritonitis and systemic infection, which significantly worsen the prognosis. Consequently, healthcare providers must maintain a high index of suspicion and be prepared to initiate immediate surgical and medical treatment to optimize recovery and survival chances in affected individuals.

A study by Magsi et al[17] reported a 77.27% frequency of silent perforation, which refers to a perforation that occurs without the typical symptoms of a peptic ulcer, such as sudden severe abdominal pain. The significant risk factors identified were H. pylori infection and NSAID use. Screening for H. pylori and the use of antiulcer drugs can help reduce the risk of perforation in peptic ulcer disease (PUD).

The prevalence of H. pylori infection tends to increase with age and is influenced by socioeconomic status, as observed in both developed and developing countries. The prevalence among children can often indicate overall prevalence, given that initial H. pylori infections typically occur in early childhood and are rarely self-resolving. Hage et al[18] suggest that women infected with H. pylori can significantly influence their children's infection rates. Socioeconomic status and housing conditions during early childhood have been identified as critical factors affecting the infection rate in both adults and children.

In countries such as Saudi Arabia, India, and Vietnam, H. pylori infection rates range from 60% to 80%, which is significantly higher than the 20% to 25% infection

rates observed in developed nations like the United States, Australia, and France[19].

In our study, we found that 59.9% of cases with H. pylori infection, which is noticeably lower compared to the findings of Lowenthal et al,[20] who reported a prevalence of 73.9%, and Giannakis et al,[21] who reported 80.6%. Despite the ongoing debate over the relationship between H. pylori infection and perforated ulcers, the connection between the two is well-established for gastric ulcers.

CONCLUSION

H. pylori infection was not significantly associated with PPU. However, factors such as alcohol intake and tobacco use were involved in perforation. Therefore, we can conclude that while H. pylori infection is not a risk factor for PPU, it is important to avoid other risk factors.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Shabbir Ahmed, Muhammad Mumtaz Ather
Drafting or Revising Critically:	Bushra Ghulam, Sumera Nighat, Nadeem Ullah, Shoaib Anwar
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Ethical Approval: No.102/137 Dated 14.01.2023

REFERENCES

1. Tadesse M, Musie E, Teklewold B, Hailu E. Prevalence of H. pylori in perforated peptic ulcer disease at Saint Paul's hospital millennium medical college, Addis Ababa, Ethiopia. Ethiopian J Health Sci 2021;31(5):969-974.
2. Seyoum N, Ethicha D, Assefa Z, Nega B. Risk factors that affect morbidity and mortality in patients with perforated peptic ulcer diseases in a teaching hospital. Ethiopian J Health Sci 2020 Jul 1;30(4):549-558.
3. Bokalli FA, McWright CF, Aseneh JB, Mbachan TM, Mokake ND, Nguedia JC, et al. Helicobacter pylori infections in peptic ulcer perforations: a retrospective analysis in two referral hospitals in Douala, Cameroon. Surg Sci 2020;11(10):298-311.
4. Gbenga OJ, Ayokunle DS, Ganiyu A, Adekova I. Pattern of presentation, management and early outcome in patients with perforated peptic ulcer disease in a semi-urban tertiary hospital. Ethiopian J Health Sci 2021;31(5):975-981.
5. Marshall B. Pylori in peptic ulcer disease. Germ theory. Med Pioneers Infectious Dis. 2023 Mar 29:295.
6. Sonnenberg A. Epidemiology of Helicobacter pylori. Aliment Pharmacol Therapeut 2022; 55:S1-3.
7. Fong IW, Fong IW. Helicobacter pylori infection: when should it be treated? Current Trends Concerns Infec Dis 2020:81-102.
8. Rahatullah HS. Prevalence and associated factors of peptic ulcer disease among dyspeptic patients at endoscopy unit in Kabul, Afghanistan. J Applied Pharm Sci Res 2023:6(2):19-24.
9. Singh LO, Maibam C, Singh TS, Singh SO. A clinical study of duodenal ulcer perforation. J Dent Med Sci 2020;19(8):07-29.
10. Khan SR, Alam J, Marwan M. Frequency of wound infection after duodenal ulcer perforation repair. Pak J Med Health Sci 2023;17(02):25-6.
11. Deshmukh SN, Parikh HP. Open versus laparoscopic repair of perforated duodenal ulcer: a comparative study. Int Surg J 2020;7(4):1004-8.
12. Pellicano R, Ribaldone DG, Fagoonee S, Astegiano M, Saracco GM, Mégraud F. A 2016 panorama of Helicobacter pylori infection: key messages for clinicians. Panminerva Med 2016; 58(4):304-17.
13. Alam M, Tahir R, Ahmad S, Amin S, Zareen A, Khan AG. Frequency of Helicobacter pylori (H. Pylori) among patients presenting with duodenal perforation. Pak J Med Health Sci 2023;17(03):142-4.
14. Crenner C. Operative innovation and surgical conservatism in twentieth-century ulcer surgery. J History Med Allied Sci 2023:jrad065.
15. Wang X, Qu J, Li K. Duodenal perforations secondary to a migrated biliary plastic stent successfully treated by endoscope: case-report and review of the literature. BMC Gastroenterol 2020;20:1-7.
16. Søreide K, Thorsen K, Harrison EM, Bingener J, Møller MH, et al. Perforated peptic ulcer. Lancet 2015;386:1288-98.
17. Magsi AM, Iqbal M, Malik M, Parveen S. Silent peptic ulcer disease perforation. J Surg Pak 2017 Apr;22:61-4.
18. Hage N, Renshaw JG, Winkler GS, Gellert P, Stolnik S, Falcone FH. Improved expression and purification of the Helicobacter pylori adhesion BabA through the incorporation of a hexa-lysine tag. Protein Expr Purif 2015;106: 25-30.
19. Dogra BB, Panchabhai S, Rejinthal S, Kalyan S, Priyadarshi S, Kandari A. Helicobacter pylori in gastroduodenal perforation. Med JDY Patil Univ 2014;7:170-2.
20. Lowenthal AC, Hill M, Sycuro LK, Mehmood K, Salama NR, Ottemann KM. Functional analysis of the Helicobacter pylori flagellar switch proteins. J Bacteriol 2009;191(23):7147-56.
21. Giannakis M, Chen SL, Karam SM, Engstrand L, Gordon JI. Helicobacter pylori evolution during progression from chronic atrophic gastritis to gastric cancer and its impact on gastric stem cells. Proc Natl Acad Sci 2008;105(11):4358-63.

Original Article

Vaginal Deliveries and Frequency of Perineal Tears

Humaira Bashir, Shazia Rafiq, Asma Akhtar, Ayesha Khan Khakwani, Kanwal Raza and Saba Rafique

ABSTRACT

Objective: To determine the frequency, risk factors, and severity of perineal tears in women during vaginal delivery.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Nishtar hospital, Multan in the labour room from January 2023 to October 2023.

Methods: The study commenced after receiving approval from the ethical committee to collect patient information. The study included 200 patients aged 20 to 40 years, both primipara and multipara. A complete history of patients was taken and the weight of babies at the time of birth was recorded. By following standard protocol detailed examination of the cervix, vagina, vulva, and perineum was done during 3rd stage of labor to diagnose any injury or tear.

Results: The mean age of the 200 study patients was 32.64 ± 6.89 years, and the mean BMI was 23.25 ± 2.02 kg/m². Most patients, specifically 94 (47.0%), had a parity of 1, while 21 patients (10.5%) had a parity of 4 or more. Additionally, 113 babies (56.5%) had a birth weight of ≤3 kg, whereas 87 babies (43.5%) had a birth weight of over 3 kg. Perineal tears were observed in 169 patients (84.5%), with the majority experiencing first-degree perineal tears.

Conclusion: The study highlights that perineal trauma during vaginal delivery is highly prevalent, with our research identifying a frequency of 84.5% for perineal tears. Among these, first-degree perineal tears were the most common. Perineal tears contribute significantly to maternal morbidity.

Key Words: Perineal Tears, Vaginal delivery, Severity of tear, Degree of injury.

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INTRODUCTION

Operative vaginal delivery, a commonly practiced obstetric tradition, is associated with the risk of perineal injury, which can significantly impact a woman's health and quality of life[1]. Literature has shown an increase in the incidence of perineal injuries in recent years. Incidence of perineal injuries was reported in about 85% of the literature, among them about 70% required suturing[2]. This traumatic injury to the perineal area can damage the sphincter internally and externally which can lead to some severe complications like decal urgency and incontinence[3].

However, even minor degree tears can lead to complications, such as an increased risk of pelvic organ prolapse and sexual dysfunction[4].

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Risk factors of perineal tear incidence and its severity include delivering large babies, instrumental manipulation, episiotomy, labor induction, and required analgesia[5]. Observations of many researchers indicate that a conservative approach for episiotomies is more beneficial for patients' point of view[6]. The incidence rate of perineal and anal sphincter injuries varies between countries and healthcare facilities and it was observed that this incidence is increasing day by day[7].

The literature identifies several risk factors associated with perineal tears. Independent risk factors for major tears include a prolonged second stage of labor, instrumental vaginal delivery (IVD), birth weight greater than 4 kg, occiput-posterior presentation, and Asian ethnicity[8]. The association between episiotomy and perineal tears is controversial. Some studies suggest that episiotomy has a protective effect against severe perineal tears[9].

The outcome of pregnancy is often influenced by the approach to childbirth management in different countries, highlighting the importance of having a skilled healthcare professional present during delivery to ensure safe motherhood from pregnancy through childbirth[10]. This study aims to examine the rate and severity of perineal tears during vaginal delivery and to

provide guidance on improving obstetric practices by implementing appropriate precautions.

METHODS

This cross-sectional study was conducted over a six-month period in the labor room of Nishtar Hospital, Multan, from January 2023 to October 2023. The study commenced after receiving approval from the ethical committee to collect patient's information. The study included 200 patients aged 20 to 40 years, both primipara and multipara after obtaining consent form all patients. Patients who had undergone vaginal delivery. Sample size was calculated by using openepi.com with 95% confidence interval, power of study and frequency of perineal tears 11.9% taken from study conducted by Ibrar et al[4].

Complete history of patients was taken and weight of babies at the time of birth was recorded. By following standard protocol detailed examination of cervix, vagina, vulva and perineum was done during 3rd stage of labor to diagnose any injury or tear. Management of patients was planned according to severity of injury. SPSS version 27.2 was used for data entry and recording of numerical (age and BMI) and categorical variables (Parity, perineal tear and severity) as per mean and SD required. P value less than or equal to 0.05 was taken as significant.

RESULTS

The mean age of the 200 study patients was 32.64 ± 6.89 years, and the mean BMI was 23.25 ± 2.02 kg/m². Most of the patients, specifically 94 (47.0%), had a parity of 1, while 21 patients (10.5%) had a parity of 4 or more. Additionally, 113 babies (56.5%) had a birth weight of ≤3 kg, whereas 87 babies (43.5%) had a birth weight of more than 3 kg. Perineal tears were observed in 169 patients (84.5%), with the majority experiencing first-degree perineal tears.

Table. No. 1: Demographic profile of mothers and distribution of baby weight at birth

Variable	N (%)	Mean ± S.D
Age (years)		32.64±6.89
BMI (kg/m^2)		23.25±2.02
Parity		
1	94 (47.0)	
2	71 (35.5)	
3	14 (7.0)	
≥ 4	21 (10.5)	
Total	200 (100.0)	
Baby weight at birth		
≤ 3 kg	113 (56.5)	
> 3 kg	87 (43.5)	
Total	200 (200.0)	

Table. No. 2: Perineal tears distribution

Perineal tears	N (%)
Yes	169 (84.5)
No	31 (15.5)
Total	200 (100.0)

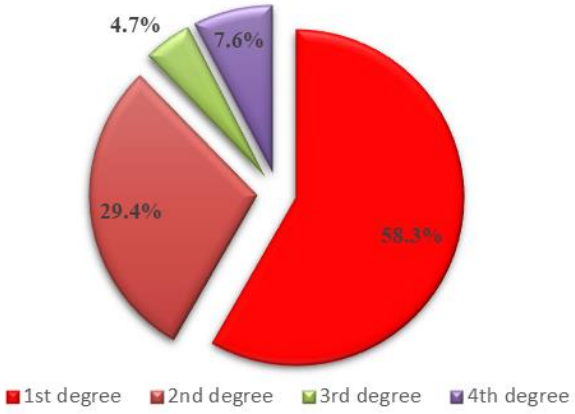

Figure. No. 1: Distribution of severity of perineal tears among perineal tears patients

DISCUSSION

Perineal injury during childbirth is a significant concern, affecting not only the woman's health who are giving birth but also posing a challenge to obstetricians and caregivers. To prevent initial damage resulting from vaginal delivery, many British obstetricians have been observed to opt for Cesarean sections as a mode of delivery for their patients[11].

In this study mean age of patients was patients was 32.64 ± 6.89 years, and the mean BMI was 23.25 ± 2.02 kg/m, but there was no association between the age of patients and the frequency of perineal tears. Another local study conducted by Parveen et al[12] reported mean age of patients was 27.89±4.44 years and the mean BMI was 25.01±2.02 kg/m2. A perineal tear during vaginal delivery was reported in 79.8% of patients. This perineal tear was an incident in 84.5% of the population.

In this study most common type of tear was 1st degree tear observed in found in 58.3% of patients. A study complied by Ali et al[13] reported 1st-degree tear as the most common type of tear accounting for 68.7% of patients who underwent spontaneous vaginal delivery. Second-degree tear occurred in 26.5% and 3rd degree in 2.7% of patients.

A retrospective study conducted by Faith et al[14] the in Cameroon found that the incidence of perineal tears was 13.5%. Among these cases, 76.5% involved first-degree tears, 22.1% were second-degree tears, and only 1.3% of patients experienced third-degree tears. Notably, no cases of 4th degree tears were observed in this study[14].

A study by Cakwira et al[15] reported that primiparous women are more prone to perineal injury, especially in those cases who were operated on with instrumented

delivery and administered epidural analgesia at the time of 2nd stage of labor. Patients with perineal injury during labor experienced severe pain. Study shows incidence of pain was 95% for those with first-degree tears, 60% for second-degree tears, and 100% for third-degree tears, while 91% of those with fourth-degree tears experienced pain. However, by six weeks postpartum, there was no statistically significant difference in pain severity and frequency among the different types of trauma groups.

A study by Thomas Schmitz et al[16] on 19,442 women found that 88 (0.5%) had severe perineal lacerations. Key risk factors included instrumental delivery, nulliparity (aOR 2.58), persistent posterior orientation (aOR 2.24), and increased birth weight (aOR 1.28). Mediolateral episiotomy reduced risk (aOR 0.38). The highest risk was with instrumental delivery of neonates <4500g in posterior position, while the lowest risk was with spontaneous delivery of neonates >3200g after mediolateral episiotomy (0.1%).

Yvonne et al[17] found a 3% incidence of severe perineal trauma, with 4.5% in primiparas and 1.7% in multiparas. Risk factors included assisted delivery and shoulder dystocia in the Indian and Asian populations. In primiparas, episiotomy, preterm birth, and epidural analgesia were protective, while occipital-posterior delivery and prolonged second stage were risks. In multiparas, episiotomy increased trauma risk, and additional factors included gestational diabetes and birth weight over 4000g.

According to a meta-analysis conducted by Vasileios et al[18] severe perineal traumas in women during childbirth are significantly associated with several factors. These include the birth of heavier infants, with a mean difference in birth weight of 192.88 grams; the use of episiotomy; and the occurrence of operative vaginal deliveries. Additionally, the study identifies labor induction, labor augmentation, and epidural anesthesia as common contributors to severe perineal trauma. The authors recommend that future research should further investigate the relationship between these factors and the incidence of perineal trauma to better understand and potentially mitigate this complication. The incidence and severity of tears in the perineal area at the time of vaginal delivery are also associated with ethnicity and race.

The frequency and severity of perineal tears during vaginal delivery are significantly influenced by race and ethnicity. A study was conducted on Chinese and Filipino women by Park et al[19] and reported that these two populations are at higher risk of perineal tears. However, this increased risk does not extend to vaginal or cervical lacerations, where the incidence is similar across different ethnic groups.

Various techniques can help reduce morbidity related to perineal tears during vaginal delivery. For instance, a study by Gimovsky et al[20] demonstrated that injecting Hyaluronidase into the perineal area can prevent such tears. Further research is needed to improve outcomes in this area. Additionally, another study showed that massaging the perineal area during the second stage of labor not only reduces the risk of perineal tears but also decreases the need for episiotomy. Interestingly, obesity may also serve as a protective factor against perineal tears.

CONCLUSION

The study highlights that perineal trauma during vaginal delivery is highly prevalent, with our research identifying a frequency of 84.5% for perineal tears. Among these, first-degree perineal tears were the most common. Perineal tears contribute significantly to maternal morbidity. To reduce the risk of such trauma, it is important to assimilate risk factors, manage labor carefully, and provide adequate perineal support. Although perineal injury is likely in almost all vaginal deliveries, the frequency and severity of these injuries can be mitigated by having a professional and vigilant supervisor present.

Author's Contribution:

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REFERENCES

1. Von Theobald P, Bohrer M, Lorrain S, Iacobelli S. Risk factors associated with severe perineal tears: A five-year study. J Gynecol Obstet Human Reproduct 2020;49(7):101820.
2. Huber M, Malers E, Tunón K. Pelvic floor dysfunction one year after first childbirth in relation to perineal tear severity. Scientific Reports 2021;11(1):12560.
3. Lima CT, Brito GA, Karbage SA, Bilhar AP, Grande AJ, Carvalho FH, et al. Pelvic floor ultrasound finds after episiotomy and severe perineal tear: systematic review and meta-analysis. J Maternal-Fetal Neonat Med 2022;35(12):2375-86.
4. Abrar S, Abrar T, Sayyed E, Hussain SS. Perineal tears; frequency, severity and risk factors in a

tertiary care hospital. J Med Sci 2022;3(2):75-9.
5. Blanc-Petitjean P, Meunier G, Sibiude J, Mandelbrot L. Evaluation of a policy of restrictive episiotomy on the incidence of perineal tears among women with spontaneous vaginal delivery: a ten-year retrospective study. J Gynecol Obstet Human Reproduct 2020;49(8):101870.
6. Teixeira C, Lorthe E, Barros H. Time trends in episiotomy and severe perineal tears in Portugal: a nationwide register-based study. Pregnan Childbirth 2022;22(1):976.
7. Souza MR, Farias LM, Ribeiro GL, Coelho TD, Costa CC, Damasceno AK. Factors related to perineal outcome after vaginal delivery in primiparas: a cross-sectional study. Revista da Escola de Enfermagem da USP 2020;54:e03549.
8. Gluck O, Ganer Herman H, Tal O, Grinstein E, Bar J, Kovo M, et al. The association between the number of vaginal examinations during labor and perineal trauma: a retrospective cohort study. Arch Gynecol Obstet 2020;301:1405-10.
9. Abbasi A, Talpur S, Khan S, Awan S, Bai G, Akbar R. Perineal injury with vaginal delivery; what are the risks. Pak J Med Health Sci 2022;16(02):1227-29.
10. Bugti Z, Ahsan N, Salam R, Naeem S, Shoaib M. Factors leading to perineal tear during vaginal delivery. Med Forum 2019;30(11):73-75.
11. Al Thaydi AH, Al Ghamdi T, Chamsi AT, EL-Marwadi E. Perineal tears incidence and risk factors; a four year experience in a single Saudi centre. Interv J Gynae Womens Healthcare 2018;1(5):100-103.
12. Parveen R, Sadiq Q, Ali S. Perineal tears; frequency and severity of perineal tears among women during vaginal delivery. Professional Med J 2018;25(10):1532-6.
13. Ali R, Nazir A, Naeem M. Frequency and Severity of perineal tears among women during vaginal delivery. J Med Physio Biophysic 2018;49:100-106.
14. Faith C.Diorgua, Mary P.Steen, June J.Keeling, Elizabeth Mason-Whiteheadd. Mothers and midwives perceptions of birthing position and perineal trauma: an exploratory study. Women and Birth. December 2016; 29(6): Pages 518-523.
15. Cakwira H, Mukengere M, Lucien B, Aborode AT, Sironge L, Michael MV, et al. The clinical characteristics of perineal tears: A study carried out on 14 pregnant women in a tertiary center: Case series. Ann Med Surg 2022;82:104432.
16. Thomas S, Corinne A, Béatrice A, Constance M, Jean-François O, Olivier S. Identification of women at high risk for severe perineal lacerations. Eur J Obstetr & Gynecol Repro Biol 2014;182: 11-15.
17. Yvonne LH, Luc Y, Elizabeth A. Nathan CW, Dorota AD. Risk factors for severe perineal trauma during vaginal childbirth: A Western Australian retrospective cohort study. Women and Birth 2015;28(1):16-20.
18. Vasileios P, Dimitrios V, Athanasios P, Kaliopi P. Risk factors for severe perineal lacerations during childbirth. Inter J Gynaecol Obstet 2014;125(1):6–14.
19. Park M, Wanigaratne S, D'Souza R, Geoffrion R, Williams SA, Muraca GM. Asian-white disparities in obstetric anal sphincter injury: Protocol for a systematic review and meta-analysis. Plos One 2023;18(9):e0291174.
20. Gimovsky AC, Berghella V. Evidence-based labor management: second stage of labor (part 4). Am J Obstet Gynecol MFM 2022;4(2):100548.

Original Article

Obstructive Uropathy: Double-J (DJ) Stenting or Percutaneous Nephrostomy

Obstructive Uropathy

Ibrar Ahmad[1], Muhammad Adnan[1], Saifullah[1], Muhammad Muzammil[2], Kiran Areej[1] and Muhammad Arbaz Hanif Khan[1]

ABSTRACT

Objective: To compare the efficacy percutaneous nephrostomy and double-J stent in patients of ureteric obstruction.
Study Design: Randomized controlled trial
Place and Duration of Study: This study was conducted at the Department of Urology, Bakhtawar Amin Medical and Dental Collage, Multan, Pakistan from July 2022 to December 2023.
Methods: In Group A, double-J ureteral stent was inserted retrograde using aseptic cystoscopy technique under mild sedation or local anesthesia, which involved instilling 2% xylocaine gel into the urethra. In Group B, an ultrasound-guided percutaneous nephrostomy tube was inserted at the puncture site subcutaneously. Complications such as bleeding, hematuria, and septicemia in both groups were documented immediately post-operatively and during follow-up sessions on the 15th and 30th days using KUB sonography. Patients experiencing complications were managed according to hospital protocols.
Results: In phase 1of outcome, both the groups had high success rates, but Group B 87.9% had a slightly higher success rate compared to Group A 76.6%. However, the difference is not statistically significant (p=0.176). In phase 2 of outcome, both the groups had very high success rates, Group B 98.9% again having a slightly higher success rate compared to Group A 97.4%.
Conclusion: Percutaneous nephrostomy (PCN) demonstrated superior efficacy compared to double J stenting (DJS) in managing postoperative complications associated with the definitive treatment of ureteral obstruction, regardless of whether the obstruction was due to extrinsic or intrinsic malignancy.
Key Words: Double-J stent, Nephrostomy, Ureteral obstruction, post-operative complications,

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INTRODUCTION

Ureteral obstruction, which involves any blockage in the ureters, significantly threatens renal function by impeding the drainage of urine and can lead to severe complications such as uremia, water-electrolyte imbalances, and urinary tract infections[1]. Patients experiencing reduced alertness due to these conditions face serious health risks and financial burdens[2]. Unfortunately, Pakistan ranks 53rd globally in terms of mortality rates related to kidney diseases, including ureteral obstruction, with a rate of 23.62 deaths per 100,000 population[3].

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Ureteral obstruction can be classified as either malignant or benign in origin[4]. Malignant obstructions are often due to intrinsic urologic malignancies, such as prostate cancer. In contrast, benign ureteral obstructions are typically caused by luminal pathologies, such as ureteral stones[5]. To provide symptomatic relief from urine obstruction and to restore normal renal function, clinicians usually choose an optimal definitive emergency procedure, such as percutaneous nephrostomy or double J stenting[6].

Moreover, measures are taken to minimize further urologic interventions, hospitalization, and adverse impacts on quality of life (QoL)[7]. Percutaneous nephrostomy (PCN) is a minimally invasive procedure guided by ultrasonography, while double-J ureteral stenting (DJS) is the preferred choice for addressing obstruction caused by large-sized ureteral stones[8]. In all interventional procedures, there is a risk of post-operative complications. For instance, hematuria and septicemia are well-known complications associated with double-J stents[9]. Additionally, complications such as ureteral perforation and stent migration can occur[10]. Another common issue is PCN blockage. Each of these complications is addressed appropriately based on the specific issue encountered[11].

In the management of ureteral obstruction, there is no strong evidence indicating that one method, whether

stenting or nephrostomy, is superior to the other in terms of post-operative complications[12]. There is currently no existing research on this issue within the study setting of the present research. To address this gap, the present study was conducted with the aim of comparing the efficacy of double J stenting and percutaneous nephrostomy for ureteral obstruction in terms of postoperative complications. The results of this study will pave the way for further investigations into the validity of the optimal procedure.

METHODS

This randomized controlled trial was conducted at the Department of Urology, Bakhtawar Amin Medical and Dental Collage, Multan, Pakistan, over the course of one year from July 2022 to December 2023. The study employed a consecutive sampling technique, resulting in a total sample size of 110 participants, with 55 individuals assigned to each of the two groups. The sample size was determined using an online WHO calculator based on the anticipated incidence of hematuria or bleeding with double-J ureteral stenting (37%) and percutaneous nephrostomy tube insertion (11%), power of study 80% and confidence interval 95%.

Inclusion criteria for the study included male and female patients aged 19 to 63 years presenting with benign or malignant ureteral obstruction and hydronephrosis in the outpatient department. Patients with bleeding diathesis, sepsis, anesthetic drug allergies, or uremia were excluded from the study.

Data collection commenced after obtaining permission from the Institutional Review Board, and written informed consent was obtained from all participants before group allocation. Participants were randomly assigned to either Group A or Group B by a biostatistician. Clinical manifestations were recorded prior to kidney, ureter, and bladder (KUB) sonography. A single dose of prophylactic antibiotics was administered intravenously before the intervention.

Patients were enrolled in two groups (A and B) by lottery method. In Group A, a double-J ureteral stent was inserted retrograde using aseptic cystoscopy technique under mild sedation or local anesthesia, which involved instilling 2% xylocaine gel into the urethra. In Group B, an ultrasound-guided percutaneous nephrostomy tube was inserted at the puncture site subcutaneously.

Complications such as bleeding, hematuria, and septicemia in both groups were documented immediately post-operatively and during follow-up sessions on the 15th and 30th days using KUB sonography. Patients experiencing complications were managed according to hospital protocols.

Data analysis was performed using SPSS version 23.0, with quantitative or qualitative data processed for mean and standard deviation (SD) or percentage, respectively. The association between success rates and interventional procedures was evaluated using the chi-square test, with statistical significance set at $P < 0.05$.

RESULTS

One hundred & ten patients, who met the inclusion criteria, were included in this study. There were 77 (70.0%) patients were included in Group A whereas 33 (30.0%) patients were included in Group B. Table. 1 showed the demographics and causes of ureteric obstruction between two groups. Group A and Group B did not significantly differ in terms of age and sex distribution. Causes of ureteric obstruction were also almost similar between Group A and Group B. ($p>0.050$). (Table. 1).

Various complications between the two study groups were compared in table. 2. Group A showed notable complications such as trigone irritation with pain (23.4%), ureteral perforation (11.7%), and stent migration (27.3%). Group A also had a higher rate of procedural failure (9.1%) compared to Group B (3.0%). Whereas Group B showed the complications like PCN dislodgement/blockage (27.3%), injuries to adjacent organs (27.3%), and a slightly higher incidence of hematuria (54.5%) and septicemia and fever (24.2%) compared to Group A. Each group had certain complications that were uniquely reported for them, indicating different profiles of complications between the two groups. Both the groups were not statistically significant. ($p>0.050$). (Figure. 1).

In phase 1of outcome, both the groups had high success rates, but Group B (87.9%) had a slightly higher success rate compared to Group A (76.6%). However, the difference is not statistically significant ($p=0.176$). In phase 2 of outcome, both the groups had very high success rates, Group B (98.9%) again having a slightly higher success rate compared to Group A (97.4%). This difference is also not statistically significant ($p=0.134$). (Table. 2).

Table No. 1: Demographics and causes of ureteric obstruction among the groups

Variable	Group A 77 (70.0%)	Group B 33 (30.0)	p-value
Demographics			
Age (years)	52.61±8.03	54.91±9.92	0.203
Sex			
Male	47 (61.0)	19 (57.6)	0.734
Female	30 (39.0)	14 (42.4)	
Cause of ureteric obstruction			
Ureteral stone(s)	25 (32.5)	10 (30.3)	0.823
PUJ obstruction	19 (24.7)	5 (15.2)	0.268
Tumor or retroperitoneal fibrosis in	12 (15.6)	3 (9.1)	0.363

abdomen			
Endometriosis (females)	7 (9.1)	2 (6.1)	0.595
BPH (males)	1 (1.3)	1 (3.0)	0.533
N (%), Mean ± S.D			

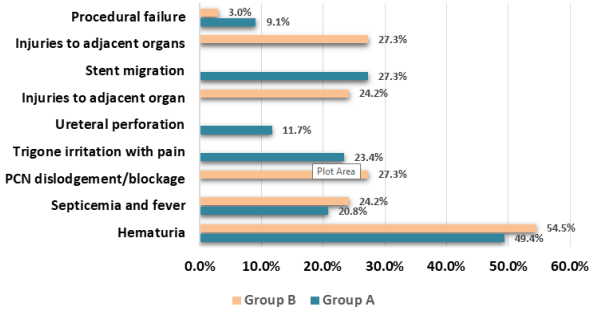

Figure No. 1: Complications among the groups

Table No. 2: Therapies' success rate for ureteric obstruction among the groups in two phases of outcome

Success rate	Group A 77 (70.0%)	Group B 33 (30.0)	p-value
1st phase of outcome			
Success rate	59 (76.6)	29 (87.9)	0.176
2nd phase of outcome			
Success rate	75 (97.4)	30 (98.9)	0.134
N (%)			

DISCUSSION

Kidney stones are a major cause of ureteral obstruction, with an incidence rate of 40 to 50%[13], which aligns with our findings as observed ureteric stones in 30-32% of population. In contrast, the pelvic ureteral junction (PUJ) disorder, which holds the second highest position as a cause of obstruction, is particularly concerning due to its genetic background[14]. In our study we observed PUJ in 24% patients approximately.

Adherence to therapy among all study subjects, with a response rate of above 90%, is a positive outcome as it ensures a speedy, cost-effective recovery and enhances quality of life, such as after the placement of an indwelling stent for ureteral obstruction. The mean age of the participants in this study is 52.61±8.03 years in group A and 54.91±9.92 years in group B, which is slightly higher than the 45.0 years reported in a published study[15]. This age difference may be attributed to chance sampling or moderating factors such as genetics and lifestyle.

In a study conducted by Saeed et al[16] on Pakistani population male dominancy was observed regarding ureteral obstruction and like our study nephrostomy procedure for management of ureteral obstructions found better option.

In this study the occurrence of tumors or retroperitoneal fibrosis 15.6% in group A and 9.1% in group B. In a study Sahu et al[17] reported 3-5% of cases with tumor and retroperitoneal disease, is significant in the management of ureteral obstruction. However, precise expertise is needed for accurate identification, as primary retroperitoneal paragangliomas can mimic ureteral tumors.

Despite the equal effectiveness of Double J stents (DJS) and percutaneous nephrostomy (PCN) in normalizing kidney function in patients with ureteral stones, there is a significant risk of postoperative complications associated with the interventional management of ureteral obstruction, Shoshany et al[18] reported hematuria being a common issue among these complications. In our study incidence of hematuria was found in 49.4% of cases in DJ shunt group and 54.5% in nephrostomy group.

In this study stent migration was observed in 27.3% of patients and procedure failure was observed in 9.1% in DJ stent group and 3% in nephrostomy group. Weltings et al[19] reported finding of a higher incidence rate of septicemia in percutaneous nephrostomy (PCN) compared to double-J stent (DJS) is consistent with previous studies, which highlight some vulnerabilities associated with PCN. In another study conducted by Shafique et al[20] reported stent migration or encrustation can occur with DJS used for ureteral obstruction, total failure of this procedure is rare. However, advanced stages of the causative condition, such as malignancy, cannot be ruled out.

The success rate, measured as the inverse of the complication rate, was higher for nephrostomy (98.99%) compared to stenting (97.4%), which aligns with trends observed in a previous study conducted by Ahmad et al[21] on Pakistani population. Stent migration, encrustation, and ureteral perforation are specific complications associated with double J stents, in addition to painful trigone irritation.

CONCLUSION

Percutaneous nephrostomy (PCN) demonstrated superior efficacy compared to double J stenting (DJS) in managing postoperative complications associated with the definitive treatment of ureteral obstruction, regardless of whether the obstruction was due to extrinsic or intrinsic malignancy.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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REFERENCES

1. Cozma C, Georgescu D, Popescu R, Geavlete B, Geavlete P. Double-J stent versus percutaneous nephrostomy for emergency upper urinary tract decompression. J Med Life 2023;16(5):663.
2. Lim WS, Goh CH, Tan CK, Zainal R. Ureteric Stenting and Percutaneous Nephrostomy Insertion for Acute Ureteric Obstruction: A Multi-centered Prospective Study to Compare the Quality of Life between both Procedures. Asian J Res Reports in Urol 2023;6(1):11-20.
3. Singh S, Sabale V, Agarwal P, Ghotankar S. Outcomes of Percutaneous Nephrostomy vs. Double J Stenting in the Treatment of Infectious Hydronephrosis. Ind J Surg 2023;11:1-5.
4. Fugaru I, Bhojani N, Andonian S, Sameh W, Fahmy N. Management of infected indwelling ureteral stents: An international survey of urologists. Can Urol Assoc J 2022;17(3):E95.
5. Massella V, Juliebø-Jones P, Pietropaolo A, Beisland C, Somani BK. Outcomes Associated with the Endourological Management of Stent Encrustation: Findings from a Literature Review on Behalf of the EAU YAU Urolithiasis Group. Curr Urol Rep 2023;24(4):187-99.
6. Hori T, Makino T, Kawahara T, Urata S, Miyagi T. Effectiveness of double-J metallic mesh ureteral stents for malignant ureteral obstruction: a retrospective study. In vivo 2023;37(2):806-10.
7. Wang X, Li J, Fan S, Li Z, Yang Z, Liu P, Song H, Zhang W. Failure in Double-J stent inserting in laparoscopic pyeloplasty of ureteropelvic junction obstruction: the clinical features and outcomes. BMC Urol 2023;23(1):192.
8. Maguire PJ, Sobota A, Mulholland D, Ryan JM, Gleeson N. Incidence, management, and sequelae of ureteric obstruction in women with cervical cancer. Support Care Cancer 2020;28(2):725-30.
9. Al-Hajjaj M, Sabbagh AJ, Al-Hadid I, Anan MT, Aljool AA, Husein HA, et al. Comparison complications rate between double-J ureteral stent and percutaneous nephrostomy in obstructive uropathy due to stone disease: a randomized controlled trial. Ann Med Surg 2022;81:104474.
10. Qi Y, Kong H, Xing H, Zhang Z, Chen Y, Qi S. A randomized controlled study of ureteral stent extraction string on patient's quality of life and stent-related complications after percutaneous nephrolithotomy in the prone position. Urolithiasis 2023;51(1):79.
11. Anand S, Agarwala S, Dhua A, Jain V, Jana M, Kandasamy D, et al. Experience of management of bilateral pelvi-ureteric junction obstruction (PUJO) in children–Can surgery be avoided on one side?. J Pediatr Urol 2020;16:S2-3.
12. Ali ES, Dief HA, Ali WH. Neglected Double-J Ureteral Stents in Upper Egypt Patients. The Egypt J Hospital Med 2023;91(1):5232-7.
13. Uçar M, Özen O. The Relationship between ureteral obstruction time and secondary signs in computed tomography due to ureteral stone obstruction. J Coll Physicians Surg Pak 2020;30(7):678-82
14. Beaumier M, Roger H, Sauneuf B, Dugardin F, Camparo P, Queffeulou G. Disseminated tuberculosis revealed by obstructive and prerenal acute kidney failure. Nephrol Ther 2019;15(3):169-73.
15. Saeed K, Hussain SA, Kanjoo SR, Ahmad B, Hussain M. Double-J stenting versus percutaneous nephrostomy; postoperative complications in management of ureteral obstruction. Annals Punjab Med Coll 2020;14(4):336-9.
16. Aghamir SMK, Heidari R, Bayesh S, Salavati A, Elmimehr R. Are Nephrostomy and ureteral stent necessary after multi-access percutaneous nephrolithotomy? Current Urol 2019;13(3):141-4.
17. Sahu P, Singh S, Ahuja A, Sharma U, Mattoo S, Bhardwaj M. Unusual and rare cause of PUJ obstruction with a brief review of the literature. J Clin Urol 2020;23(7):205141582095899.
18. Shoshany O, Erlich T, Golan S, Kleinmann N, Baniel J, Rosenzweig B, Eisner A, et al. Ureteric stent versus percutaneous nephrostomy for acute ureteral obstruction - clinical outcome and quality of life: a bi-center prospective study. BMC Urol 2019;19(1):79.
19. Weltings S, Schout BMA, Roshani H, Kamphuis GM, Pelger RCM. Lessons from Literature: Nephrostomy Versus Double J Ureteral Catheterization in Patients with Obstructive Urolithiasis - Which Method is Superior? J Endourol 2019;33(10):777-86.
20. Shafique MN, Akhtar SH, Mahnoor M, Hussain M. Hemodialysis Internal jugular vein versus Subclavian vein Catheters: Complications, patients' comfort, tolerance and cost-effectiveness. Pak J Med Sci 2019;35(1):124-8.
21. Ahmad I, Pansota MS, Tariq M, Shahzad MS, Ali ST, Hussain A. Comparison between double J (DJ) ureteral stenting and percutaneous nephrostomy (PCN) in obstructive uropathy. Pak J Med Sci 2013;29(3):725-9.

Original Article

Impaired Quality of Life Among Dentists Due to Neck Pain

Qurrat-ul-Ain Fatima[1], Asiyah Ahmad[2], Nida Aslam[3], Muhammad Awais Khan[4], Zobia Atif[2] and Huma Tahir[5]

ABSTRACT

Objective: To determine the frequency of neck pain among dentists and its association with impaired quality of life (QoL).

Study Design: A cross-sectional study.

Place and Duration of Study: This study was conducted at the OPD of dental department at Multan Medical and Dental College, Multan, from October 2022 to May 2023.

Methods: This research was conducted on 220 dentists selected by non-probability convenient sampling technique without any gender discrimination. Disability due to neck pain was measured using the Neck Disability Index (NDI), gender-stratified Spearman Rank Correlation Coefficient was used to assess the correlation between neck pain intensity and disability due to neck pain. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 23.

Results: A total of 220 dentists respond the questionnaire. 27 out of 78 male and 43 out of 142 female are healthy while 51 male and 99 female feel neck pain. 65% male can't read during NP while 64% female have this disability. Similarly, headache increases NP intensity in female 66% while it is less 58% in male. 44% female and 35% male can't do personal care during neck pain.

Conclusion: Neck pain is common in dentists due to their postural demand in their working environment and it has a significant impact on dental practices. Neck pain had great impact on the daily functions and quality of life of the dentists.

Key Words: Neck Pain, headache, Personal Care, Quality of life.

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INTRODUCTION

The pain in and around the cervical spine is called Neck pain and it is a common symptom of many abnormal postural and medical conditions. Sometimes it is felt in the neck called axial pain but sometimes it radiates and called Radicular pain[1]. The neck muscles can be easily strained like hunching over your work bench. Sometimes it leads to the stiff neck and reduce the range of motion of neck movements. Etiological variables, including bad posture, anxiety, depression, the strain of the neck, and sporting and occupational activities are generally underestimated and complicated[2].

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Neck pain may result from a sudden injury or it may develop slowly over times for example due to the poor posture, wear and tear injuries and from overuse injuries[3]. Postural neck pain is a very uncomfortable condition that leads to a lot of problems in the daily routine and the most bothersome problem is the sleeping disorders. This results in generalize fatigue in body. Any abnormality of soft tissue of cervical spine like swelling, or damage may cause pain or rigidity of the neck[4].

Neck pain is very common in dentists. In a study dentists reported 83.8% neck pain[5]. Some studies also show that duration of work per day directly associated with neck pain. Instrument size in the field of dentistry has impact on neck posture which leads to shoulder and wrist/hand pain[6]. Psychosocial factors are another major cause for poor posture for dentists. Regular physical exercise was associated with decreased neck pain[7].

The majority of dentists do not undertake specific exercises to prevent neck, shoulder, and back pain. Regularly completing specific workouts can help to reduce the prevalence and severity of these problems[8].

There are several predisposing factors for neck pain among dentists. The dentists burden the lumbar and cervical spine by bending and extending their torso and neck during working hours. They frequently use small tools during their oral cavity procedure[9]. They usually

work in tiny areas like anatomical chair, dental unit, equipment all are present in same room. Their wrong working positions are main causes of neck pain. With the passage of time, these abnormal positions lead to the postural deformities in dentists[10]. Dentists are a vulnerable group in the working world with multiple externally acting risk factors for postural problems specifically the low-back and neck discomfort. The wrong working postures adopted by dentists can contribute to pain in neck and also is a leading cause of forward head posture[11].

In addition, dentists are usually exposed to such health complications during university duration, which leads them to the early development and chronic propagation of postural issues[12]. The predominance of musculoskeletal diseases (MSDs), including postural neck pain is well recognized in the dentistry profession. However, very little research has been done on MSD or postural risk in the dentistry students[13].

The findings from this study could contribute to improving occupational health standards in dentistry and serve as a basis for further research on interventions that could alleviate neck pain and enhance the QoL of dentists.

METHODS

A cross-sectional study was conducted at the OPD of dental department at Multan Medical and Dental College, Multan, from October 2022 to May 2023. Dentists were selected using a non-probability convenient sampling technique, with no gender discrimination. Dentists with other chronic ailments, mental disorders, or dentofacial anomalies were excluded from the study. The participants ranged in age from 30 to 50 years.

Written informed consent was obtained from all participants. Disability due to neck pain was measured using the Neck Disability Index (NDI), which consists of 10 items, each scored from 0 to 5, with a maximum total score of 50. Each item contains six statements that represent varying levels of severity for specific symptoms. The scores from all 10 items are summed to produce a single NDI score. A score of 0–4 indicates no disability, 5–14 indicates mild disability, 15–24 indicates moderate disability, 25–34 indicates severe disability, and 35–50 indicates complete disability. Pain intensity by gender was assessed using cross-tabulation, as was the relationship between pain intensity and variables related to consequences of neck pain, such as headache, difficulty reading, and personal care.

A gender-stratified Spearman Rank Correlation Coefficient was used to assess the correlation between neck pain intensity and disability due to neck pain. To examine the strength and association between neck pain intensity/disability and variables such as headache, reading difficulties, challenges in weight lifting, and personal care, a logistic regression model was constructed. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 23.

RESULTS

From 220 study cases, 78 (35.5%) were males and 142 (64.5%) were females. Personal care parameters were shown in the Table. No. 1. It was seen that, of the 220 cases, 150 (68.2%) suffered from neck pain, 97 (44.1%) felt difficulty in personal care, 171 (77.7%) could not lift weight easily, 190 (86.4%) felt pain when read, 163 (74.1%) felt headache while reading, 12 (5.5%) faced difficulty when concentrating, 176 (80.0%) felt pain when to do work, 50 (22.7%) had worst experience when driving, whereas sleeping was worst in 3 (1.4%) cases. Further, recreation was worst in 8 (3.6%) cases. (Table. No. 1).

According to Neck disability Index score, 183 (83.2%) cases had disability, and 37 (16.8%) cases had not disability. (Figure. 1). Association of NDI score with effect modifiers were shown in Table. No. 2. It was seen that females had more disability according to NDI score than males, 129 (70.5%) and 54 (29.5%), respectively. ($p<0.001$). According to pain intensity, most of the cases144 (78.7%) had suffered from neck pain and had disability with NDI score. ($p<0.001$). There were 86 (47.0%) cases who had disability and normal in personal care, whereas 97 (53.0%) cases had disability and difficulties to do personal care. ($p<0.001$). There were 166 (90.7%) cases who could not lift weight and had disability whereas only 17 (9.3%) cases of disability in NDI score and could easily lift weight. ($p<0.001$). Further, most of the cases 169 (92.3%) had disability in NDI score, felt pain while reading whereas 14 (7.7%) cases had disability in NDI score felt no pain while reading. ($p<0.001$). (Table. No. 2).

Table. No. 1: Gender and personal care parameters of the study cases

Variable	Frequency	Percentage
Gender		
Male	78	35.5
Female	142	64.5
Pain Intensity		
Healthy	70	31.8
Neck Pain	150	68.2
Personal Care		
Normal	123	55.9
difficult to do	97	44.1
Weightlifting		
Easily lift weights	49	22.3
Can't lift weights	171	77.7
Reading		
No Pain	30	13.6
Feel Pain while reading	190	86.4
Headache		
No Pain	57	25.9

Feel Pain while reading	163	74.1
Concentration		
Mild	153	69.5
Moderate	47	21.4
Severe	8	3.6
Very severe	12	5.5
Work		
No Pain	44	20.0
Feel Pain	176	80.0
Driving		
Mild	110	50.0
Moderate	46	20.9
Severe	14	6.4
Worst	50	22.7
Sleeping		
Mild	189	85.9
Moderate	17	7.7
Severe	11	5.0
Worst	3	1.4
Recreation		
Mild	179	81.4
Moderate	21	9.5
Severe	12	5.5
Worst	8	3.6

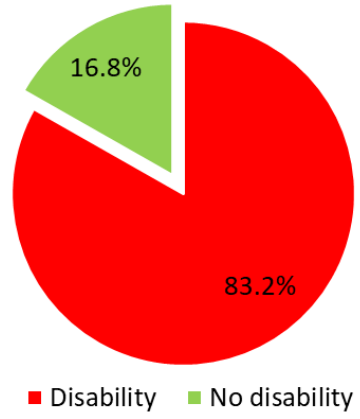

Figure No. 1:Neck Disability Index Score

Table. No. 2: Association of Neck Disability Index Score with effect modifiers

Variable	Neck Disability Index Score		Test of sig.
	Disability	No disability	
Gender			
Male	54 (29.5%)	24 (64.9%)	χ^2=16.81, d.f=1, p<0.001
Female	129 (70.5%)	13 (35.1%)	
Pain intensity			
Healthy	39 (21.3%)	31 (83.8%)	χ^2=55.36, d.f=1, p<0.001
Neck Pain	144 (78.7%)	6 (16.2%)	
Personal care			
Normal	86 (47.0%)	37 (100.0%)	χ^2=35.08, d.f=1, p<0.001
Difficult to do	97 (53.0%)	0 (0.0%)	
Weightlifting			
Easily lift weights	17 (9.3%)	32 (86.5%)	χ^2=105.95, d.f=1, p<0.001
Can't lift weights	166 (90.7%)	5 (13.5%)	
Reading			
No Pain	14 (7.7%)	16 (43.2%)	χ^2=33.11, d.f=1, p<0.001
Feel Pain while reading	169 (92.3%)	21 (56.8%)	

DISCUSSION

This cross-sectional study was conducted to find out the impact of neck pain on quality of life among dentists. In this study 74.1%dentists felt headache while reading. A study performed by Nageshet al[14] in 2016 on prevalence of headache among dentist showed similar results to our study. According to their results, the headache was found to be prevalent in 87.1% of the subjects included in the study. Females (91.9%) were more frequently affected by headaches than males (87.1%). Similarly, results were found in our study that the prevalence of headache was more in females 64.5% than males 35.5%.

Another study was performed by Jamil et al[15] in 2023 on cervicogenic headache among dentists working in Lahore Medical and dental college their study concluded that cervicogenic headache is present in 30.4% dentists, their results were different from our study.

Another study was conducted by Baber et al[16] in 2022 for measuring neck pain among dentist. According to their results The NDI score shows that 44.7% of the dentists showed mild disability and 33.8% dentist showed moderate disability. Similar results were found in our study, the NDI score shows that 43.3% of the dentists showed mild disability and 33.8% dentist showed moderate disability. (18)The results of our study were quite different from the study done by Kawtharani et al[17] in 2023 for measuring neck pain among dentist. Their results showed that the prevalence of neck pain among dentists was 86.8%.According to our study prevalence of neck pain among dentists was 68.6 %.

Another study was conducted by Ijaz et al[18] in 2016 for measuring the frequency of neck pain among dentist. According to their results The NDI score shows that 23.7% of the dentists showed mild disability and 28.2% dentist showed moderate disability.28.2% could lift heavy weights but experienced pain in doing so, 20.2% dentists reported that episodes of pain

prevented them to do so. 38.8% dentists had slight pain during reading, 21.8% had moderate pain, 11.2% could not read books due to moderate pain and 1.6% had severe pain while reading so could not do so. Their results were quite comparable with our results that 65% male dentists cannot read during neck pain while 64% females have this disability. Similarly, headache increases neck pain intensity in females 66% and in males it is 58%. 44% females and 35% males cannot do personal care during neck pain.

Al Wassan et al[19] surveyed 204 dentists and dental auxiliaries (87 males, 117 females) in Riyadh, Saudi Arabia, to assess postural problems. Results showed 54.4% complained of neck pain and 73.5% of back pain. Only 37% of those with back pain sought medical help.A study conducted by Jabbar et al[20] reported that the prevalence of musculoskeletal symptoms among dentists in Saudi Arabia is notably high. The most frequently reported issues were pain, particularly in the neck, back, and shoulders, as well as headaches. These findings highlight the significant burden of physical discomfort experienced by dental professionals in the region, likely due to the repetitive and posture-related demands of their profession.

CONCLUSION

Neck pain is common in dentists due to their postural demand in their working environment and it has a significant impact on dental practices. According to the study, the main ergonomic variables linked to the growth of neck problems are dentists' incorrect body position and lack of physical movement. All these factors may leads to impaired quality of life among dentists.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Qurrat-ul-ain Fatima, Asiyah Ahmad
Drafting or Revising Critically:	Nida Aslam, Muhammad Awais Khan, Zobia Atif, Huma Tahir
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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REFERENCES

1. Theodore N. Degenerative cervical spondylosis. New England J Med 2020;383(2):159-68.
2. De Pauw R, Coppieters I, Palmans T, Danneels L, Meeus M, Cagnie B. Motor impairment in patients with chronic neck pain: does the traumatic event play a significant role? A case-control study. The Spine J 2018; 18(8):1406-16.
3. Song G-B, Kim J-J, Kim K-R, Kim G-Y. The effects of neck stabilization exercise and proprioceptive neuromuscular facilitation on neck alignment, NDI, and static balance in adults with forward-head posture in a sitting position. PNF Movement 2020;18(1):11-22.
4. Rahme D, Lahoud N, Sacre H, Akel M, Hallit S, Salameh P. Work fatigue among Lebanese community pharmacists: prevalence and correlates. Pharmacy Practice (Granada) 2020; 18(2).
5. Feng B, Liang Q, Wang Y, Andersen LL, Szeto G. Prevalence of work-related musculoskeletal symptoms of the neck and upper extremity among dentists in China. BMJ Open 2014;4(12):e006451.
6. Meisha DE, Alsharqawi NS, Samarah AA, Al-Ghamdi MY. Prevalence of work-related musculoskeletal disorders and ergonomic practice among dentists in Jeddah, Saudi Arabia. Clin Cosmetic Investigat Dent 2019; 11:171.
7. Alshagga MA, Nimer AR, Yan LP, Ibrahim IAA, Al-Ghamdi SS, Al-Dubai SAR. Prevalence and factors associated with neck, shoulder and low back pains among medical students in a Malaysian Medical College. BMC Res Notes 2013; 6 (1):1-7.
8. Marklund S, Mienna CS, Wahlström J, Englund E, Wiesinger B. Work ability and productivity among dentists: associations with musculoskeletal pain, stress, and sleep. Int Arch Occupat Environ Health 2020; 93 (2):271-8.
9. Shams-Hosseini NS, Vahdati T, Mohammadzadeh Z, Yeganeh A, Davoodi S. Prevalence of musculoskeletal disorders among dentists in Iran: a systematic review. Materia Socio-Medica 2017; 29 (4):257.
10. Amin J, Siddiqui A, Amin S. Ergonomics, Exercises, and Education to Prevent Neck and Back Pain among Dentists. J Dent Oral Sci 2019; 1:1-3.
11. Samoladas E, Barmpagianni C, Papadopoulos DV, Gelalis ID. Lower back and neck pain among dentistry students: a cross-sectional study in dentistry students in Northern Greece. Eur J Orthopaedic Surg Traumatol 2018;28(7):1261-7.
12. Oghli I, List T, Su N, Häggman-Henrikson B. The impact of oro-facial pain conditions on oral health-related quality of life: A systematic review. J Oral Rehabilitat 2020;47(8):1052-64.
13. Kang HK, Kim YR. Association between dental treatment, quality of life, and activity limitation according to masticatory discomfort: evidence from the Korean national health and nutrition examination survey (2013–2015). Int J Environ Res Public Health 2020;17(2):547.

14. Ng A, Hayes MJ, Polster A. Musculoskeletal disorders and working posture among dental and oral health students. In Healthcare 2016;4(1):p13.
15. Jamil T , Gul H, Waqas S, Abbas R, cervicogenic headache among dentists working in Lahore medical and dental college. Pak J Rehabilitat 2023;12(1):158-65.
16. Babar RA, Sadiq A, Hussain SA, Farooq U. Work related neck pain among the dentists working in Islamabad & Rawalpindi; a cross-sectional survey. Northwest J Med Sci 2020; 5(1):22-6.
17. Kawtharani AA, Msheik A, Salman F, Haj Younes A, Chemeisani A. A survey of neck pain among dentists of the Lebanese community. Pain Res Management 2023;e528028.
18. Ijaz A, Khanb I,Ahmed A, Sadiqd S, Frequency of neck pain among dentist. POJ 2016:8(2) 89-93.
19. Al Wassan K, Almas K, Al Shethri S, Al Qahtani M. Back & neck problems among dentists and dental auxiliaries. J Contemp Dent Pract 2001;2(3):17-30.
20. Abdul Jabbar TA. Musculoskeletal disorders among dentists in Saudi Arabia. Pak Oral & Dent J 2008;28(1):135-44.

Original Article

Predictors of Visual Impairment in Individuals with Type 2 Diabetes Mellitus: Insights from a Population-based Study in Pakistan

Muhammad Junaid, Fawad Ahmed, Zia-ur-Rehman, Irfan Ali and Suriyakala Perumal Chanan

ABSTRACT

Objective: The purpose of the hospital-based study was to assess visual impairment in diabetes patients and the factors that may predict it.

Study Design: Cross-sectional descriptive study

Place and Duration of Study: This study was conducted at the Mehboob Charity Vision International Eye and General Hospital, Mansehra, Pakistan from May 2023 to March 2024 in affiliation with Lincoln University Malaysia,

Methods: A study in Pakistan aimed to identify predictors of visual impairment in individuals with type 2 diabetes mellitus (T2DM). The study involved 505 diabetic patients from Mehboob Charity Vision International Eye and General Hospital, Mansehra. Data on socio-demographic, behavioral, and clinical-related variables were collected through structured interviews and clinical examinations.

Results: The results showed that visual impairment was prevalent in more than 75% of respondents, with mild and moderate VI being the most common. Older age was a significant predictor, with the odds of having mild and moderate VI increasing with age. Additional variables were found to be predictive, including the length of diabetes, high blood pressure, and inadequate glycemic management. The study suggests more research with larger sample sizes and longitudinal designs and highlights the significance of early detection and therapy of visual impairment in T2DM patients. The present research of 500 diagnosed type 2 diabetes in Pakistan to examine the factors that contribute to visual impairment. More than three quarters of respondents had visual loss with mild to moderate losses being most prevalent. Diabetes duration of more than 10 years, poor glycemic control and hypertension showed strong correlation with visual impairment.

Conclusion: These findings suggest tremendous public health importance to call for timely diagnosis, appropriate treatment, and control to prevent DR.

Key Words: Visual impairment, Type 2 diabetes, Prevalence, Risk factors, Pakistan

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INTRODUCTION

The World Health Organization (WHO) describes visual impairment as exhibiting distance visual acuity poorer than 6/18. The effects of diabetes constitute a serious threat to the health care systems of many developing nations [2].

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With over 240 million cases worldwide, the DM epidemic has spread quickly. Ocular problems like diabetic retinopathy, diabetic papillopathy, cataracts, glaucoma, and disorders of the ocular surface can result from diabetes mellitus [3].

Diabetic retinopathy (DR) develops in phases, with non-proliferative retinopathy (NPDR) being the first stage and more severe proliferative diabetic retinopathy (PDR) following. Diabetes also increases the risk of cataracts and glaucoma, lessening the toll that diabetic eye illnesses have on patients and healthcare systems [4]. It is concerning since data from community surveys continuously indicates that half of DM patients do not receive a diagnosis, and many are uninformed that they run the risk of developing DR and other consequences. The most prevalent microvascular consequence of diabetes in the working population is diabetic retinopathy DR[5].

In 2015, hyperglycemia during pregnancy was linked to 16.2% of live births and it is anticipated that 10.4% of adults will have diabetes by 2040.

METHODS

Study setting and design: This is a hospital-based cross-sectional study that was conducted at Mehboob Charity Vision International Eye and General Hospital, Mansehra, Pakistan from May 2023 to March 2024 in affiliation with Lincoln University Malaysia, The study was conducted on a sample of 505 diabetic patients suffering from Diabetes Mellitus among 4674 patients. The purpose of the hospital-based study was to assess visual impairment in diabetes patients and the factors that may predict it[6,7].

Source of population: All people living with Diabetes Mellitus who visited Mehboob Charity Vision International Eye and General Hospital, Mansehra during data collection period were eligible for the study[8].

Study population: The study involves individuals diagnosed with T2DM for at least one year to guarantee that people with established diabetes were enrolled with long-term consequences like vision impairment could be assessed. Moreover, the research sample's heterogeneous makeup, which included people of various ages, genders, and ethnicities[9].

Sampling procedure: simple randomization sampling procedure was adopted, so that every participant had an equal chance of being chosen to participate in the study[10].

Operational definition: The study developed operational criteria for reduced uncertainty[11].

Visual Acuity: The capacity of the visual system to detect minute differences in the surroundings, is known as central visual acuity[12].

Visual Impairment: If the presenting VA in the better eye is worse than 3/60, the individual is considered visually impaired.

The World Health Organization divides visual impairment into the following categories[13].

i. "Normal: 20/10-20/25
ii. Near Normal visual impairment: 20/30-20/60
iii. Moderate visual impairment: 20/70-20/160
iv. Severe visual impairment: 20/200-20/400, or 11-20 degrees on visual field
v. Profound visual impairment: 20/500-20/1000 visual acuity, or 6- 10 degrees on visual field
vi. Total visual impairment: No light perception (NLP)"

Blindness: The term "total blindness" refers to a person who is completely devoid of light perception; this is also known as "no light perception[14].

Low Vision: When a person's vision cannot be fully corrected with conventional techniques including glasses, contact lenses, medicine, surgery, magnifying devices, or assistive devices.

BMI: A person's weight in kilograms divided by their height in meters squared yields their body mass index, or BMI."

Obesity: Overweight is a disease that categorizes individuals into classes depending on the quantities of adipose tissues in the body with increased risks to health[15].

Glycemic Control: The ideal blood glucose levels for diabetes individuals is known as glucose control.

Data collection and quality control procedure: "pre-tested, structured-interviewer-administered a questionnaire containing Socio-demographic variables" (age, residence, employments and education status) behavioral variables (diet and exercise), clinical-related were used to collect data. 505 people fulfilled, consent taken as the requirements for inclusion[15].

Statistical analysis: Data was entered on SPSS Software version 25.0 and the same software was used to clean and analyze the data.

Ethical consideration: Every patient enrolled in the research gave their informed consent.

RESULTS

Socio-demographic characteristics: Five hundred and five type-2 diabetic patients participated in the study with a response rate of 95%. Sociodemographic characteristics are highlighted in Table 1.

"The median age of participants was 57 years. The minimum age recorded was 15 years while the maximum was 100 years." A higher number of respondents were in the age bracket of 51-70 years old (n=307, 60%) followed by 141 (27.9%) respondents in the age bracket of 31-50 years while 44 (10.2%) respondents were 70+ and only 4 (0.8%) respondent was under 30 years of age. The underrepresentation of younger people highlights the need for focused initiatives to reduce health inequities associated with diabetes in a range of age groups within the community[16].

Most of the respondents were from rural areas (n=401, 79.4%) as compared to 104 (20.6%) respondents whose residence was urban. The data on education status highlights the disparities among respondents for attainment of education as 377 (74.7%) of the participants were uneducated which can be explained by most respondents belonging to rural areas, followed by 93 (18.4%) individuals who had secondary education, 29 (5.7%) had primary and 06 (1.2%) had tertiary education.

Analysis depicted a higher percentage of females (n=265, 52.5%) as compared to males (n=240, 47.5%). The study reported a higher number i.e.,465 (92.1%) T2DM patients as compared to 40 (7.9%) T1DM patients. 365 (72.3%) were unemployed as compared to 140 (27.7%) participants who were employed.

Prevalence of Visual Impairment and Vision-related Characteristics: As shown in **Table 2,** data on the prevalence of visual impairment revealed VI was prevalent in approximately 376 (74.5%) of the respondents. Two major VI issues were mild and

moderate VI as 127 (25.1%) patients had moderate VI (< 6/18 to 6/60) followed by 197 (39.0%) patients who had mild VI (< 6/9.5 to 6/18). Blindness was reported in approximately 10% of the patients. Among them, 45(8.9%) had severe blindness (< 3/60) as compared to 7 (1.4%) who were moderately blind (< 6/60 to 3/60). Normal vision (6/9.5 OR MORE THAN 6/9.5) was prevalent in a small fraction of 129(25.5%) patients only.

Table No.1: Sociodemographic Characteristics

Socio-Demographic Characteristics:		
Categories	Frequency	Percent
AGE		
Less than 30 years	4	0.8%
31-50 years	141	27.9%
51 to 70 years	307	60.8%
More than 70 years	53	10.5%
RESIDENCE		
Rural	401	79.4%
Urban	104	20.6%
EDUCATION		
No	377	74.7%
Primary	29	5.7%
Secondary	93	18.4%
Tertiary	06	1.2%
SEX		
Male	240	47.5%
Female	265	52.5%
EMPLOYED		
No	365	72.3%
Yes	140	27.7%
DIABETES TYPE		
T1DM	40	7.9%
T2DM	465	92.1%

Table No.2: Visual Impairment

Prevalence Of Visual Impairment And Vision-Related Characteristics		
EXERCISE ROUTINE		
YES	258	51.1%
NO	247	48.9%
HTN		
Yes	370	73.3%
No	135	26.7%
TREATMENT		
Oral Med	469	92.9%
Insulin	26	5.1%
Both	10	2.0%
GLYCEMIC CONTROL		
Good	219	43.4%
Poor	286	56.6%
DURATION OF DIABETES		
Less than 10 years	366	72.5%
11 to 15 years	88	17.4%
16 to 20 years	25	5.0
More than 21 years	26	5.1%
VISUAL IMPAIRMENT		
Normal Vison (6/9.5 or more than 6/9.5)	129	25.5%
MILD VI (< 6/9.5 to 6/18)	127	25.1%
MODERATE (< 6/18 to 6/60)	197	39.0%
Moderate Blindness (< 6/60 to 3/60)	7	1.4%
Severe Blindness (< 3/60)	45	8.9%

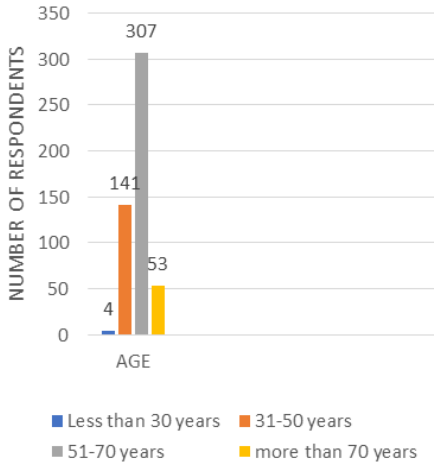

Figure No.1: Age Distribution

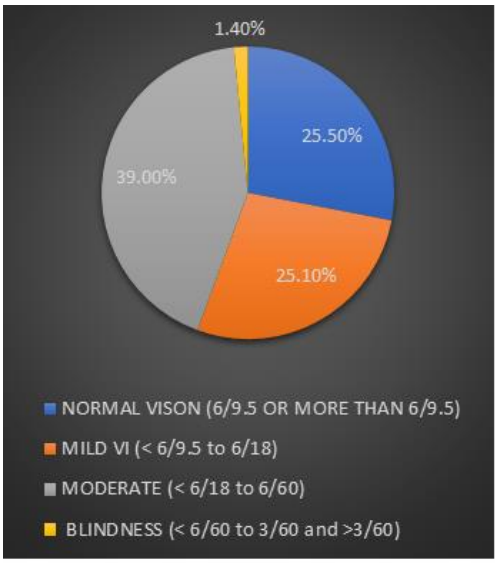

Figure No.2: Virtual Impairment

258 (51.1%) participants reported to be physically active while 247 (48.9%) participants were not. Hypertension was reported in 370(73.3%) participants as compared to 135(26.7%) participants who were not

having comorbid hypertension. Oral medication was the most used method for treatment as reported in 469(92.9%) patients followed by use of insulin in 26 (5%) respondents and use of both insulin and oral medications simultaneously in just 10(2.0%) respondents. 286(56.6%) patients had poor glycemic while 219(43.4%) patient's glycemic control was good. Most of the patients have been diabetic for less than 10 years (n=366, 72.5%) followed by 88(17.4%) patients who were diabetic for 11-15 years and 51(10.1%) patients were diabetic for 16 and more than years[17].

VI Predictors in T2DM patients: Multinomial logistic regression was performed to assess the impact of independent variables like glycemic control, HTN, age, sex, duration of diabetes, treatment options, education, employment status, residence, exercise routine and type of diabetes on visual impairment. of all the predictors, age group's effect on visual impairment was significant ($\chi^2 = 9.927$, df = 4, p = .042) depicting the role of age in model's predictive power[18].

DISCUSSION

This cross-sectional study was conducted at Mehboob Charity Vision International Eye and General Hospital in Mansehra, Pakistan, involving 505 diabetic patients with Diabetes Mellitus. More than 90% of the respondents were type 2 diabetics which is consistent with other studies[19].

258 (51.1%) participants were physically active. These stats are different from already conducted studies which reported lower physical activity levels. Oral medication was the most used treatment method, followed by insulin and both kind of treatments which aligns with literature. 286 (56.6%) patients had poor glycemic while 219 (43.4%) patient's glycemic control was good. It aligns with the past studies. Most patients had been diabetic for less than 10 years, followed by those with 11-20 years and those over 21 years[20]. This cross-sectional study was focused on T2DM patient's assessment and the prediction of effects of independent variables on VI. Visual impairment (VI) was prevalent in 74.5% of respondents, with mild and moderate VI being the most common. Normal vision was prevalent in 25% of patients[21].

The same prediction has been reported by other studies as well which found that a significant proportion of diabetes individuals had visual impairment[22].

According to the study, treating and preventing vision impairment in diabetes patients necessitates a multidisciplinary strategy that includes patient education, prompt intervention, and early identification[23]. This research offers significant understanding into the factors that predict visual impairment in individuals with Type 2 Diabetes Mellitus (T2DM)[24]. The study highlights how crucial it is to treat diabetic eye disease early and completely.

CONCLUSION

In the light of Manuscript conclusion, it is clear that the percent prevalence of visual impairment in the T2DM individuals in Pakistan is much higher and 75% participants reported to have mild a moderate visual impairment. The most significant risk factors include the above-listed cardiovascular risk factors such as ageing, having diabetic for quite a long time without being able to manage the condition, hypertension, and poor glycemic control. These results underline the importance of screening, early diagnosis, control and prevention of diabetes induced visual loss. The study emphasizes the need for enhancing the uptake of health care, enhancing the awareness and adopting intervention measures to enhance glycemic control in the population especially the rural and other under privileged ones to reduce the burden of diabetes related vision loss.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Junaid, Fawad Ahmed
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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REFERENCES

1. Adelson JD, et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. The Lancet Global Health 2021;9(2)e144–e160,
2. Akalu Y, Belsti Y. Hypertension and Its Associated Factors Among Type 2 Diabetes Mellitus Patients at Debre Tabor General Hospital, Northwest Ethiopia. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2020;13:1621–1631.
3. Almutairi NM, Alahmadi S, Alharbi M, Gotah S, Alharbi M. The Association Between HbA1c and Other Biomarkers With the Prevalence and Severity of Diabetic Retinopathy. Cureus 2021, doi: https://doi.org/10.7759/cureus.12520
4. Aslam R, Suhail S, Sajid R, bin Younis B. Type 2 Diabetes Mellitus(T2DM) in Pakistan: Prevalence,

Trends and Management Strategies. Annals King Edward Med Univ2022;28(2):247–254.
5. Azeem S, Khan U, Liaquat A. The increasing rate of diabetes in Pakistan: A silent killer. Annals Med Surg 2022;79:103901.
6. Chen S, et al. Association of glycemic control with hypertension in patients with diabetes: a population-based longitudinal study. BMC Cardiovas Disorders 2023;23(1). doi: https://doi.org/10.1186/s12872-023-03478-3.
7. Dandona L, Dandona R. Revision of visual impairment definitions in the International Statistical Classification of Diseases. BMC Med 2006;4(1). doi: https://doi.org/10.1186/1741-7015-4-7
8. Farmaki P, Damaskos C, Garmpis N, Garmpi A, Savvanis S, Diamantis E. Complications of the Type 2 Diabetes Mellitus. Current Cardiol Reviews 2020;16(4):249–251.
9. Jin P, et al. A Five-Year Prospective Study of Diabetic Retinopathy Progression in Chinese Type 2 Diabetes Patients with 'Well-Controlled' Blood Glucose. PLOS One 2015;10(4):e0123449.
10. Kajiwara A, et al. Gender differences in the incidence and progression of diabetic retinopathy among Japanese patients with type 2 diabetes mellitus: A clinic-based retrospective longitudinal study. 2014;103(3):e7–e10.
11. Khan MA, Hashim MJ, King J, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes – Global Burden of Disease and Forecasted Trends. J Epidemiol Global Health 2020;10(1):107–111.
12. Lartey SY, Aikins AK. Visual impairment amongst adult diabetics attending a tertiary outpatient clinic. Ghana Med J 2017;52(2)84.
13. Leasher JL, et al. Global Estimates on the Number of People Blind or Visually Impaired by Diabetic Retinopathy: A Meta-analysis From 1990 to 2010. Diabetes Care 2016;39(9):1643–1649.
14. Mumtaz SN, Fahim MF, Arslan M, Shaikh SA, Kazi U, Memon MS. Prevalence of diabetic retinopathy in Pakistan: A systematic review. Pak J Med Sci 2018;34(2). doi: https://doi.org/10.12669/pjms.342.13819
15. Ong KL, et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet 2023;402:10397.
16. Li M, et al. Females with Type 2 Diabetes Mellitus Are Prone to Diabetic Retinopathy: A Twelve-Province Cross-Sectional Study in China. J Diabetes Res 2020;2020:1–9.
17. Shaikh S, et al. Prevalence of diabetic retinopathy and related factors in patients with type 2 diabetes mellitus in Hyderabad and adjoining areas. J Entomol Zool Studies 2017;5(6):1755–1759.
18. Sayeed KA, et al. Impact of Diabetes-related Self-management on Glycemic Control in Type II Diabetes Mellitus. Cureus 2020;12(4). doi: https://doi.org/10.7759/cureus.7845
19. Solomon SD, et al. Diabetic Retinopathy: A Position Statement by the American Diabetes Association. Diabetes Care 2017;40(3):412–418.
20. Tariq O, Rosten C, Huber J. Experiences of living with type 2 diabetes in Pakistan: the role of culture and family in physical activity. Int J Equity Health 2022;21(1). doi: https://doi.org/10.1186/s12939-022-01706-4
21. Tinajero MG, Malik VS. An Update on the Epidemiology of Type 2 Diabetes. Endocrinol Metabolism Clinics North Am 2021;50(3): 337–355.
22. Voigt M, et al. Prevalence and Progression Rate of Diabetic Retinopathy in Type 2 Diabetes Patients in Correlation with the Duration of Diabetes. Experimental and Clinical Endocrinology & Diabetes: Official J German Soc Endocrinol German Diabetes Assoc 2018;126(9):570–576.
23. Wilkinson CP, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmol 2003;110(9):1677–1682.
24. Wong T, et al. Guidelines on diabetic eye care the International Council of Ophthalmology recommendations for screening, follow-up, referral, and treatment based on resource settings. Ophthalmol 2018;125(10):1608–1622.

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