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Editorial

Booster Dose Benefits against Omicron

Mohsin Masud Jan
Editor

There was still little evidence that additional doses were needed to protect against developing severe Covid disease, many vulnerable people and health workers in poorer nations have yet to receive a single dose and remain at great risk.

Global supply is again going to revert to high-income countries hoarding vaccine to protect their populations. WHO vaccines Chief Kate O'Brien pointed out that the world had only just begun addressing the dangerous inequity in vaccine access in the past two months, with more donated doses and large shipments going to underserved countries.

She said the WHO was examining the data, and that it may turn out that "additional doses have benefit to provide added protection against Omicron", but stressed it was still "very early days".

She said "where transmission continues ... is where the variants are going to come from," she warned, urging "a much more rational global perspective from countries about what's actually going to shut down this pandemic."

Meanwhile, two doses of the BioNTech and Pfizer coronavirus vaccine may not be enough to protect against the Omicron strain, said the experts, but they stressed it was "still effective" after a third jab.

The first independent data from labs around the world emerged, suggesting that the new variant is better at evading vaccine-trained immunity than those before it by the experts.

In preliminary results published by Pfizer and BioNTech said their vaccine "is still effective in preventing Covid-19, also against Omicron, if it has been administered three times". But they warned that "the Omicron variant is probably not sufficiently neutralised after two doses."

According to early laboratory research using blood serum from vaccinated people, a booster third dose generated around the same level of antibodies against Omicron as is seen after a second dose with the initial strain.

But they added that another part of the immune response -- from T cells -- were probably still effective against the variant, adding that "vaccinated individuals may still be protected against severe forms of the disease".

"Boosters will definitely be helpful in keeping the rate of Omicron breakthrough slower". WHO chief Tedros Adhanom Ghebreyesus summarized what is so far known about Omicron -- it poses higher infection risks to people who have already had the virus or been vaccinated than previous variants, and there is a preliminary indication it could cause milder disease.

But even if confirmed to be less severe, the variant is likely even more transmissible than Delta, meaning it could reach and thus sicken more people.

The United Kingdom has begun giving booster shots to individuals at least three months after their second dose, while the delay to receive an additional shot is longer elsewhere.

The UN health agency's experts also said over-60s fully immunised with China's Sinovac and Sinopharm vaccines should be offered an additional third Covid-19 vaccine dose. The Strategic Advisory Group of Experts on Immunisation (SAGE) stressed it was not recommending an additional booster dose for the population at large, which is already being rolled out in some countries.

Researchers compared 11.3 million vaccinated over-50s with the same number of unvaccinated from the same age group between 27 December 2020, when vaccinations began in France, and 20 July this year.

They found "a reduction in the risk of hospitalisation superior to 90%" from the 14th day after the second dose and a similar reduction in the number of deaths from Covid-19.

No doubt omicron variant is spreading rapidly but not fatal. Booster dose also started at mass level in the whole Pakistan from the protection of new variant omicron.

Prevalence of Tongue (Diseases/ Disorders/Lesions) among Adult Population Visiting Out-Patient Clinic in Central Punjab

Muhammad Osman Masood[1], Muhammad Adeel[2], Sana Zafar[3], Danish Javed[4], Hira Shafique[5] and Fatima Masood[6]

ABSTRACT

Objective: To find the prevalence of various commonly occurring tongue anomalies like geographic tongue, median rhomboid glossitis, hairy tongue and fissured tongue in the patients visiting out-patient clinic in central Punjab.
Study Design: Prospective Observational Study.
Place and Duration of Study: This study was conducted at the Diagnostics and Oral Medicine Department of Islam dental college, Sialkot from October 2020 to July 2021 for a period of 12 months to measure the relative frequency of various tongue anomalies in adult population of central Punjab.
Materials and Methods: 600 patients were examined in this study with an age range of 25-35 years. The examination was conducted in a quiet, comfortable and relaxed environment with the help of mouth mirror, natural light and gauze. The result was analyzed by using chi-square test in SPSS.
Results: The prevalence of all tongue anomalies was 24.3% (4.8% geographic tongue, 1.75% median rhomboid glossitis, 0.8% hairy tongue, 11.8% Fissured tongue).
Conclusion: The results of this study are near to some previous studies while contradict to some other studies as well. This study has shown the tongue anomalies are slightly more in males although the statistical difference is not significant. Moreover, it has also showed that age is not related to tongue anomalies.

Key Words: Tongue, Median rhomboid glossitis, Fissured Tongue, Geographic tongue, hairy tongue

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INTRODUCTION

Tongue is one of the most important organs present inside the oral cavity performing different functions like speech, mastication, taste sensation, breathing etc. It is continuously exposed to various physical, chemical or mechanical insults making it vulnerable to various pathological conditions. Moreover, it may be involved in various abnormalities that some are developmental, genetic and environmental[1, 2].
Many conditions are included under the term of tongue anomalies. Some of these conditions have little clinical significance and considered as morphological variations in the tongue while others have some serious clinical manifestations and are found to be developmental or congenital[3]. Tongue anomalies are also accompanied with various clinical syndromes affecting oro-facial region of the body e.g, Melkerson-Rosentheal Syndrome, Orofacial granulomatosis etc.[4, 5] Local and systemic disorders also produce distress in the tongue causing various pathological conditions like coated tongue, crenated tongue, bald tongue etc.[6,7] The purpose of this study is to found the prevalence of various commonly occurring tongue anomalies like geographic tongue, median rhomboid glossitis, hairy tongue and fissured tongue in the patients visiting out-patient clinic in central Punjab.

Median Rhomboid glossitis: It is characterized by rhomboidal shape depapillated patch on the dorsum of the tongue in the midline[8]. The affected area is devoid of filliform or other papillae. It is found associated with Candida albicans infection and it is a matter of debate as well with significant studies favoring the association with fungal infection[9,10].

Geographic Tongue: It is also known as benign migratory glossitis or erythema migrans. It is an asymptomatic condition clinically characterized by patch depappilation on the dorsum of the tongue

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surrounded by papillated areas in a map like fashion, hence causing the name as geographic tongue[11,12].

Fissured Tongue: It is also known as plicated or scrotal tongue and characterized by increase in number, size and depth of fissured located on the dorsum of the tongue[13]. It normally affects generally less than 10% of the population and has genetic predisposition[14].The frequency of tongue fissuring has been found more in mentally retarded children, a fact that favor its prevalence more in children with Trisomy 21[15].

Hairy Tongue: Among all the four types of papillae the maximum is shared by filliform papillae. The keratinized surfaces of filliform papillae undergo con/tinuous desquamation as of friction of tongue with food, palate and teeth and replaced by new cells[16]. But if the mobility of the tongue got reduced due to any reason, it will make filliform papillae to grow uncontrolled producing hair like appearance on the tongue causing hairy tongue. These elongated filliform papillae also gather various stains of food, tobacco etc leaving discoloration in the midline regions giving esthetic concerns to the patient[17].

MATERIALS AND METHODS

600 patients were selected with randomized sampling having an age range of 25-35 years. Among them 300 were males and 300 were females .Patients with an age up to 29 year were placed in one group and 30 to 35 years were placed in another group. Examination was carried out in a comfortable environment using mouth mirror, light and gauze. The results were analyzed with chi-square test in SPSS.

Inclusion Criteria: Patients otherwise healthy having no other oral diseases or lesions, with an age range of 25-35 years of either gender, no signs of any malignancy and haven't received any other treatment before were included in the study.

Exclusion Criteria: Patients having age less than 25 years, having any systemic illness, malignancy, mental retardation and have got any previous therapies were excluded from the studies.

RESULTS

The total prevalence of tongue anomalies in 600 patients (300 males and 300 females) was 24.3% (146). In our study population the tongue anomalies were more prevalent in females (23.3%) as compared to males (22.6%) though the statistical difference was not significant as shown in Table 1.

Tongue anomalies were found more in patients group having age range of 30 to 35 years with prevalence of 55.47% (81) as compared to the other group having an age range of 25 to 29 years i.e., 44.52% (65) as shown in figure 1.

Among tongue lesions, geographic tongue was observed 7.4% among our subjects with a slight predilection toward female but the statistical difference is non-significant.

Fissured tongue was found 12.4% of our subjects and was equally distributed in males as well as females. Median rhomboid glossitis was found only in 2.6% of our population.

Hairy tongue was found in 1.8% in our subjects and was equally distributed among males and females.

Table No.1: Prevalence of tongue anomalies according to gender

Anomalies	Gender	
	Male (n%)	Female (n%)
Geographic Tongue	22 (7.3)	23 (7.6)
Median Rhomboid glossitis	8 (2.6)	8 (2.6)
Fissured Tongue	37 (12.4)	37 (12.4)
Hairy Tongue	5 (1.8)	5 (1.8)

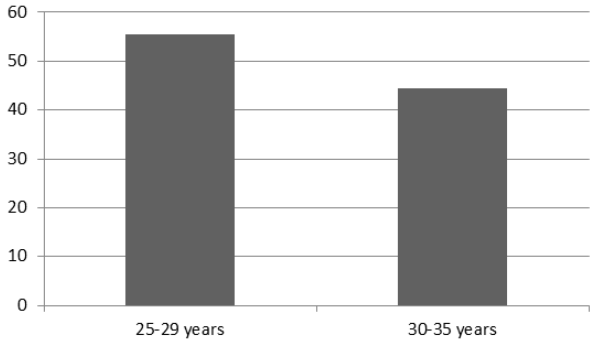

Figure No.1: Prevalence of tongue anomalies according to age distribution

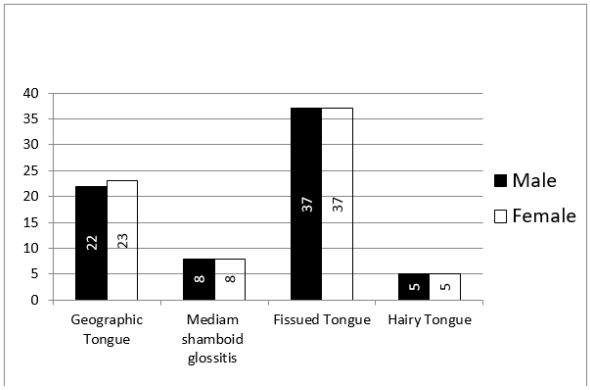

Figure No.2: Prevalence of tongue anomalies according to age distribution

DISCUSSION

The prevalence of geographic tongue in our population was 7.4% which has slight more predilections in the female gender that is in correspondence with the

studied of Voros et al[11]. The etiology of geographic tongue has still remained a matter of debate as similar lesions are also found in various skin disorders that are immunological in nature[19]. An immunological reaction is considered to be responsible for producing that inflammatory infiltrate. Similar cellular infiltrates are also found in allergic type as well. No genetic predisposition has been observed in this condition.

In our study, fissured tongue was found to be 12.4% of the population which is in conjunction to the findings of Rabii et al[12]. The prevalence of tongue fissuring has been found increasing with age and that may be associated with advancing age, salivary hyposalivation, drug usage, Vit. B deficiency and Candida infection according to Feil et al.[20]

The prevelance of median rhomboid glossitis in our population was 2.6% which was near to the prevalence found in American population as published in Barket's oral medicine[23]. But this is significantly higher than what found by Rabii et al. (0.4%).

Hairy tongue was found 1.8% in our population which was found near to the prevalence in Gurvits et al[15].

A lot of data have been gathered and analyzed by various investigators throughout the world with varying prevalence rates of various morphological variations of tongue. The published data vary considerably may be due to different diagnostic criteria used in different races and different age groups.[21-23]

CONCLUSION

Dentist and other oral healthcare workers need to know about the prevalence and management of various tongue disorders, anomalies and lesions of both developmental and acquired origin. As most of these conditions which are affecting the tongue is benign requiring no specific treatment. Patients should be educated about these tongue conditions and advised to brush there tongue along with teeth for better oral hygiene. Very few studies have been carried out in Pakistan regarding the prevalence of tongue disorders, lesions and diseases and hence further studies with larger population should be carried out to determine the prevalence of tongue disorders and factors responsible for producing these conditions.

Author's Contribution:

Concept & Design of Study:	Muhammad Adeel
Drafting:	Muhammad Osman Masood, Sana Zafar
Data Analysis:	Hira Shafique, Danish Javed, Fatima Masood
Revisiting Critically:	Muhammad Adeel, Muhammad Osman Masood
Final Approval of version:	Muhammad Adeel

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REFERENCES

1. Unur M, Bektas Kayhan K, Altop MS, Boy Metin Z, Keskin Y. The prevalence of oral mucosal lesions in children: a single center study. J Istanb Univ Fac Dent 2015;49(3):29-38.
2. Borgnakke WS, Genco RJ, Eke PI, Taylor GW. Oral Health and Diabetes. In: Cowie CC, et al, editors. Diabetes in America. 3rd ed. National Institute of Diabetes and Digestive and Kidney Diseases (US) 2018.
3. Greenberg MS, Glick M, editors. Burket's Oral Medicine. Diagnosis and Treatment. 10th ed. Philadelphia: BC Decker Inc; 2003.p.116,117,135.
4. Patil S, Kaswan S, Rahman F, Doni B. Prevalence of tongue lesions in the Indian population. J Clin Exp Dent 2013;5(3):e128-32.
5. Musaad AH, Abuaffan AH, Khier E. Prevalence of Fissured and Geographic Tongue Abnormalities among University Students in Khartoum State, Sudan. Enz Eng 2015;5:137.
6. Yarom N, Cantony U, Gorsky M. Prevalence of fissured tongue, geographic tongue and median rhomboid glossitis among Israeli adults of different ethnic origins. Dermatology (Basel, Switzerland) 2004;209(2):88–94.
7. Goregen M, Miloglu O, Buyukkurt MC, Caglayan F, Aktas AE. Median rhomboid glossitis: a clinical and microbiological study. Eur J Dentist 2011;5(4):367–372.
8. Ghabanchi J, Andisheh Tadbir A, Darafshi R, Sadegholvad M. The Prevalence of Median Rhomboid Glossitis in Diabetic Patients: A Case-Control Study. Iranian Red Crescent Med J 2011;13:503-506.
9. Daud M, Ghazal R, Zubair A. Median rhomboid glossitis: A peculiar tongue pathology, report of a case and review of literature. Int J Pharm Biological Sci 2016;6:51-53.
10. Al-Maweri SA, Tarakji B, Al-Sufyani GA, Al-Shamiri HM, Gazal G. Lip and oral lesions in children with Down syndrome. A controlled study. J Clinical Experimental Dentistry 2015;7(2):e284–e288.
11. Vörös-Balog T, Vincze N, Bánóczy J. Prevalence of tongue lesions in Hungarian children. Oral diseases 2003;9(2):84–87.
12. Rabii M, MoHtasham Z, Masoudi Rad H, Niazy M. The prevalence of tongue abnormalities among primary school children in Lahijan. Dent J Gilan Univ Med Sci 2003;4:45-49.

13. Swarup N, Gupta S, Sagolsem C, Chowdhary Z, Gupta S, Sinha N. Atrophic Glossitis: Burning Agony of Nutritional Deficiency Anemia. World J Anemia 2017;1(2):48-50.
14. Sudarshan R, Sree Vijayabala G, Samata Y, Ravikiran A. Newer Classification System for Fissured Tongue: An Epidemiological Approach. J Trop Med 2015;2015:262079.
15. Gurvits GE, Tan A. Black hairy tongue syndrome. World J Gastroenterol 2014;20(31).
16. Gonzaga HF, Oliveira LR, Picciani BLS, et al. Investigation of the psychological factors associated with fissured tongue. Revista Gaúcha De Odontologia 2019;67:e20190017.
17. Porter S, Mercadente V, Fedele S. Oral manifestations of systemic disease. BDJ Team 2018;5(1):18012.
18. Dafar A, Çevik-aras H, Robledo-Sierra J, Mattsson U, Jontell M. Factors associated with geographic tongue and fissured tongue. Acta Odontol Scand 2016;74(3):210–216.
19. Mohsin SF, Ahmed SA, Fawwad A, Basit A. Prevalence of oral mucosal alterations in type 2 diabetes mellitus patients attending a diabetic center. Pak J Med Sci 2014;30(4):716.
20. Feil ND, Filippi A. Frequency of fissured tongue (lingua plicata) as a function of age. Swiss Dental J 2016;126(10), 886–897.
21. Poulopoulos AK, Antoniades DZ, Epivatianos A, Grivea IN, Syrogiannopoulos GA. Black hairy tongue in a 2-month-old infant. J Paediatr Child Health 2008;44:377–379.
22. Nisa L, Giger R. Black hairy tongue. Am J Med 2011;124:816–817.
23. Pigatto PD, Spadari F, Meroni L, Guzzi G. Black hairy tongue associated with long-term oral erythromycin use. J Eur Acad Dermatol Venereol 2008;22:1269–1270.

Association of Diabetes Mellitus in Patients with Oral Lichen Planus. A Cross-Sectional Study

Muhammad Adeel[1], Fatima Masood[2], Danish Javed[3], Muhammad Osman Masood[4], Sana Zafar[5] and Rubab Waseem[5]

ABSTRACT

Objective: To find out the incidence of oral lichen planus in patients having diabetes mellitus.
Study Design: Cross-sectional Study.
Place and Duration of Study: This study was conducted at the Oral Medicine out –patient clinic in Islam Dental College, Sialkot over a span of eleven months from October 2020 to September 2021.
Materials and Methods: 500 diabetic patients with an age range of 45-65 years were examined clinically for the features of oral lichen planus using mouth mirror and explorer in the dental clinical settings. Patients having no pain with white striations on mucosa were considered for reticular lichen planus while patients having burning and pain were considered for ulcerative lichen planus.
Results: Among 500 diabetic patients, 18 patients (3.6%) were found with Oral lichen planus and these patients were having type II diabetes.
Conclusion: It was found that the prevelance of oral lichen planus in Diabetic patients was only 3.6% percent which is significant. But alone elevated sugar levels can't be the entire reason as other factors likes stress, anxiety etc to which these diabetic patients might have been exposed can also play role in causing this oral condition.

Key Words: Oral lichen planus, Diabetes mellitus, Grinspan's syndrome, White lesion

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INTRODUCTION

Oral lichen planus is a chronic muco-cutaneous disease targeting both the skin as well as oral mucous membrane. Oral lichen planus was first described in 1869 by Erasmus Wilson[1,2]. It was considered to be the combination of two words "lichien" and "planus" meaning flat moss depending upon its clinical appearance. This condition has been classified into seven different clinical variants i.e, reticular, erosive, ulcerative, bullous, plaque like, popular and desquamative gingivitis[3,4]. Among these seven clinical variants, reticular is considered to be the most commonly occurring with white striations on the oral mucosa called Wickham' striae[5].
Out of these seven variants, reticular, plaque like and popular are considered to be asymptomatic while the others exhibit clinical features including widespread ulceration with burning and pain[6].
No exact etiology of the disease in known but it has various pre-disposing factors that can lead to or has clinical association with this oral pathology. Among various studied pre-disposing factors, one is considered to be diabetes mellitus[7,8].
Diabetes mellitus is a metabolic condition characterized by hyperglycemia due to absolute or relative deficiency of insulin along with polyurea, polyphagia and polydipsia[9,10]. Insulin has role in breaking sugar in the cells into energy and water. Absolute deficinency of insulin leads to type I diabetes mellitus while relative deficiency leads to type II diabetes mellitus[11].
It has been reported that diabetes mellitus is associated with oral lichen planus. In some of the patients, oral lichen planus, diabetes and hypertension co-exist leading to the condition called Grinspan's Syndrome[12]. Diabetes is treated with oral hypoglycemic drugs and some of these can produce lichenoid drug eruptions which are clinically and histologicaly similar to oral lichen planus[13].

MATERIALS AND METHODS

The study was conducted at out-patient clinic of oral medicine department at Islam dental college, Sialkot and 500 patients with an age range of 45-65 years were

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enrolled in the study. These patients are positive for diabetes mellitus and their blood glucose levels were measured and confirmed by tests. It was taken into care while including the patients in the study that they did not have any other systemic condition other than diabetes or diabetes related conditions. Dental mirror, dental unit, tweezer, explorer and gauze were used to examine the oral cavity of diabetic patients.

All the patients were clinically examined under the light using mouth mirror and oral lichen planus was diagnosed on clinical appearances along with features. No pain or burning with whickham's striae was made criteria for diagnosing reticular pattern of oral lichen planus while burning, pain and ulceration with white striations was made for ulcerative lichen planus.

Inclusion Criteria: Patients having diabetes mellitus, no signs of malignancy or any other systemic illness and no mental illness were included in the study.

Exclusion Criteria: Patients having no diabetes, any other associated systemic condition, signs of malignancy, any other oral pathological lesion were excluded from the study.

RESULTS

Out of 500 patients, 170 (34%) were males and 330 (66%) were females. Among these diabetic patients 67 (13.4%) patients were having IDDM with 21 (31.34%) males and 46 (68.65%) females. Also, out of these patients, 433 (86.6%) had NIDDM with 102 (23.55%) males and 331 (76.44%) females (Table 1)

Table No.1: No of male and female patients according to type of diabetes

Gender	No. of diabetic patients	No. of patients with Type I DM	No. of patients with Type II DM
Male	170 (34%)	21 (31.34%)	102 (23.55%)
Female	330 (66%)	46 (68.65%)	331 (76.44%)
Total	500	67 (13.4%)	433 (86.6%)

Table No.2: No of male and female patients according to prevalence of oral lichen planus

Gender	No. of diabetic patients	Patients with Lichen planus
Male	170 (34%)	4 (22.22%)
Female	330 (66%)	14(77.77%)
Total	500	18 (3.6%)

In the present study, out of 500 diabetic patients, 18 (3.6%) had oral lichen planus and all of these had non-insulin dependent diabetes. Out of these 18 (3.6%) patients, 4 (22.22%) were males while 14 (77.77%) were females showing more female predilection (Table 2). Among these 4(22.22%) diabetic males with lichen planus, 1 patient was in age range of 45-55yr , 2 were in age range of 55-60yr and 1 was >60yr. Similarly, among females 2 were in age range of 45-55 yr, 4 were in 55-60yr and 8 were >60 year (Table 3).

Table No.3: No. of male and female oral lichen planus patients according to age

Age Range	Patients with Lichen planus	
	Male	Female
45-55 year	1	2
55-60 year	2	4
> 60year	1	8
Total	4	14

DISCUSSION

Various studies reported the prevelance of oral lichen planus in patients with diabetes mellitus with different percentages.

Bastos et al. study showed that many of the oral lichen planus patients had diabetes mellitus for more than five years[14]. Ara SA et al. and Bastos et al. also favored age as risk factor for oral lichen planus and in their studies they found this pathology as more prevalent in age of more than 50years[15].

The disease has most often targetted middle and old aged group with more of female predilection.[16] According to a study conducted by Maweri et al. the patient with healthy habits and positive for diabetes, the prevalence rate of oral lichen planus was found to be 0.5%.[17] Similarly, Ahmed et al. showed that this prevalence rate in patients without smoking history was 9.3%[18].

According to Bytzer P et al, this prevalence of oral lichen planus in diabetic patients was found to be more due to slow healing power of mucosa in metabolic conditions like diabetes as they found that a lesion normally takes a month to be get properly healed in control group takes two months to heal in patients with diabetes.[19]

With poor metabolic control the patient can have various diabetic complications that lead to tissue damage increasing the permeability of mucous membrane to various irritants leading to these pathological conditions.

A study was conducted by Grinspan in 1963, where he found 23 patients having oral lichen planus with diabetes and out of these seven patients were also having hypertension. Ha later on named the triad of diabetes, hypertension and oral lichen planus as Grinspan Syndrome.[20]

Chalkoo et al. also conducted a study showing correlation of diabetes with oral lichen planus[21].

Another study by Vivek Narayan et al. also showed prevalence of diabetes in patients with oral lichen planus. In this study, out of 2000 diabetic patients they found 15 patients having oral lichen planus.[22]

In a meta-analysis study by Hamid Raz et al. they found the prevalence rate of oral lichen planus In diabetic patients was 0.5 to 9.3%.[23]

CONCLUSION

This study showed the association between oral lichen planus with diabetes mellitus while there are studies where significant association may not be found probably due to varying age, gender, smoking or other systemic conditions. Moreover, not only the elevated blood glucose levels are associated with this oral condition but certain psychological factors like stress or anxiety should also be considered as these factors also increase blood glucose predisposing to oral lichen planus without diabetes. So emphasis should be made to inspect the oral cavity of diabetic patients to find these oral lesions.

Author's Contribution:

Concept & Design of Study:	Muhammad Adeel
Drafting:	Fatima Masood, Danish Javed
Data Analysis:	Muhammad Osman Masood, Sana Zafar, Rubab Waseem
Revisiting Critically:	Muhammad Adeel, Fatima Masood
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Villa, Tomás G, et al. Oral lichen planus: a microbiologist point of view. International microbiology : the official journal of the Spanish Society for Microb 2021;24(3):275-289.
2. Baek K, Choi Y. The microbiology of oral lichen planus: is microbial infection the cause of oral lichen planus? Mol Oral Microbiol 2018;33:22–28.
3. Nosratzehi, Tahereh. Oral Lichen Planus: an Overview of Potential Risk Factors, Biomarkers and Treatments. Asian Pacific J Cancer Prevention : APJCP 2018;19(5):1161-1167.
4. Ansar A, Farshchian M, Ghasemzadeh SM. Comparison of the frequency of diabetes mellitus in the patientswith lichen planus and normal controls: A case-control study. J Cosmet Dermatol 2011a;2:78–84.
5. Ara SA, Mamatha GP, Rao BB. Incidence of diabetes mellitus in patients with lichenplanus. Int J Dent Clin 2011;3:147–52
6. Rabiei M, Sadegh Kanjani M, Kazemnezhad Leili E, et al. The comparison between anxiety, level of salivary cortisol and SIgAIn oral lichen planus. Res Dent Sci 2012;9:125–31.
7. Bagewadi A, Bhoweer AK. Oral lichen planus and its association with diabetes mellitus and hypertension. Indian Acad Oral Med Radiol 2011; 23:300.
8. Chen HM, Wang YP, Chang JY, et al. Significant association of deficiencies of hemoglobin, iron, folic acid, and vitamin B12 and high homocysteine level with oral lichen planus. J Formos Med Assoc 2015;114:124–9.
9. Murray, Cliodhna E, and Cynthia M Coleman. Impact of Diabetes Mellitus on Bone Health. Int J Molecular Sci 2019;20(19):4873.
10. Verhul ST, Martijn JL, et al. Evaluating All Potential Oral Complications of Diabetes Mellitus. Frontiers Endocrinol 2019;10(56):18.
11. D'Aiuto F, Gable D, Syed Z, Allen Y, Wanyonyi KL, White S, Gallagher JE. Evidence summary: The relationship between oral diseases and diabetes. Bri Dental J 2017;222(12):944–948.
12. Grinspan D, Diaz J, Villapol LO, et al. Liquen rogo plano erosive de lar mucosa buccal see association can diabetes. Actes finals del V Congress ibero Latino Americano de Dermatologica1963;1243
13. Lavanya N, Jayanthi P, Rao UK, et al. Oral lichen planus: An update on pathogenesis and treatment. J Oral Maxillofac Pathol 2011;15:127–32.
14. Bastos AS, Leite AR, Spin-Neto R, Nassar PO, Massucato EM, Orrico SR. Diabetes mellitus and oral mucosa alterations: prevalence and risk factors. Diabetes Res Clin Pract 2011;92(1):100–5.
15. Ara SA, Mamatha GP, Rao B. Incidence of diabetes mellitus in patients with diabetes mellitus. J Dental Clin 2011;3(1):29–33.
16. Sonia G, Jawanda MK. Oral Lichen Planus: An Update on Etiology, Pathogenesis, Clinical Presentation, Diagnosis and Management. Ind J Dermatol 2015;60(3):222-9.
17. Al-Maweri SA, Ismail NM, Ismail AR, Al-Ghashm A. Prevalence of oral mucosal lesions in patients with type 2 diabetes attending hospital universiti sains malaysia. Malays J Med Sci 2013;20(4): 39–46.
18. Ahmed SA, Mohsin SF, Fawwad A, Basit A. Prevalence of oral mucosal alterations in type 2. diabetes mellitus patients attending a diabetic center. Pak J Med Sci 2014;30(4):716–9.
19. Bytzer P, Talley NJ, Hammer J, Young LJ, Jones MP, Horowitz M. GI symptoms in diabetes mellitus are associated with both poor glycemic control and diabetic complications. Am J Gastroenterol 2002;97(3):604–11.
20. Seema M, Srinivasan S. Grinspan Syndrome: The triad. Int J Med Sci Diagnosis Res 2020;4(10).
21. Chalkoo AH. Oral lichen planus: relation with transaminase levels and diabetes. J Ind Acad Oral Med Radiol 2010;22(1):1-3.
22. Vivek N, Gnanasundaram N, Arvind M. Prevalence of Oral Lichen Planus in Patients with Diabetes Mellitus. J Ind Acad Oral Med Radiol 2013;2525. 261-264.
23. Mozaffari, Reza H, et al. Prevalence of Oral Lichen Planus in Diabetes Mellitus: a Meta-Analysis Study. Acta informatica medica : AIM : journal of the Society for Medical Informatics of Bosnia & Herzegovina : casopis Drustva za medicinsku informatiku BiH vol 2016;24(6):390-393.

Correlation of Vitamin D and Uric Acid among General Population of Sindh

Correlation of Vitamin D and Uric Acid among Population of Sindh

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ABSTRACT

Objective: To study and correlate vitamin D and uric acid among general population of Sindh.
Study Design: Cross sectional study
Place and Duration of Study: This study was conducted at the Suleman Roshan Medical College, Tando Adam, Sindh from January 2020 to August 2021.
Materials and Methods: A sample of 700 normal healthy subjects of both genders was selected according to pre – determined criteria. Volunteers, age (40 – 60 years), both genders were inclusion criteria. Physical examination was performed, and blood samples were collected to estimate the vitamin D and serum uric acid. Data was analyzed using student t – test for continuous variables and Chi – square test for categorical variables. Pearson`s correlation was used to determine correlation of vitamin D and uric acid. SPSS ver. 20 analyzed data variables at 95% confidence interval (P≤0.05).
Results: Vitamin D was found very low 27.05±14.4 ng/dl in male and 15.7±8.51 ng/dl in female (P=0.0001). High uric acid was noted in both male and female subjects; 7.60±1.38 and 6.47±2.36 mg/dl respectively (P=0.0001). Vitamin D deficiency and sufficiency was noted in 75.4% (14.4186±5.1 ng/dl) and 24.5% (42.7±4.1 ng/dl) (P=0.0001). Serum uric acid normal and high levels were found in 173 (24.7%) and 527 (75.2%) respectively (P=0.0001). Vitamin D shows significantly strong negative correlation with serum uric acid (r=-0.852, p=0.0001). Negative correlation of vitamin D and uric acid in male was (r=-0.706, p=0.0001) and in female (r=-0.892, p=0.0001).
Conclusion: The present study observed strong negative correlation of vitamin D and serum uric acid in normal adult healthy subjects.

Key Words: Vitamin D, Uric acid, Correlation, Sindh

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INTRODUCTION

Vitamin D deficiency and high serum uric acid have been linked with a number of metabolic disorders such as the diabetes mellitus (DM), metabolic syndrome, hyperlipidemia and hypercholesterolemia, and coronary artery disease. Hyperlipidemia and hypercholesterolemia are one of the major risk factors of cardiac diseases.[1-3]

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Currently, vitamin D deficiency and high serum uric acid levels in general population have been reported from different parts of the country.[2,3] High blood uric acid levels causes depositions of uric acid crystals in soft tissues organs and joints such as kidneys leading to the development of urate – nephropathy and gout.[4,5] High plasma uric acid leads to the urate crystals formation in different tissues and organs for example in joints causing pain and arthritis. Gout, nephrolithiasis, urolithiasis, and nephropathy lead to joint – immobility, renal damage and systemic hypertension, urinary problems and metabolic syndrome.[4,5] Besides increasing prevalence of high serum uric acid, the vitamin D deficiency has taken the epidemic shape that has resulted in various osseous and extra-osseous disorders. Vitamin D deficiency is considered an independent risk factor in different chronic metabolic and non - metabolic disorders.[3] Globally, the vitamin D deficiency has become a public health problem of concern because of chronic diseases.[5] Nowadays, the vitamin D deficiency is observed in sunny areas and countries with much exposure to sunlight beside cold weather countries.[6] Similarly, the prevalence of high

uric acid has been reported from countries all over the World.[7] Casual correlation of vitamin D deficiency and high uric acid levels have been narrated in medical literature.[5] Adverse effect of vitamin D deficiency on uric acid metabolism has been found in different genetic studies.[1,8] Link of vitamin D and high uric acid has been found at the level of 1 α-hydroxylase enzyme. Increased uric acid levels in circulation suppress the 1 α-hydroxylase enzyme thus interferes with the vitamin D hydroxylation.[5] Genomic studies have suggested link of high uric acid with vitamin D metabolism through gene stimulation.[9] Uric acid lowering agent allopurinol therapy increased the plasma vitamin D hydroxylation has been suggested.[1,3] Globally, the vitamin D insufficiency and deficiency has become a major public health concern in these days.[6,9] The present study was conducted to analyze the vitamin D and serum uric acid levels in general population of Sindh and their casual association with each other to reach to a proper conclusion as the data is lacking at national level in our country. Therefore, it is important to explore the vitamin D and uric acid in general population of Sindh and their association with each other to make future planning to overcome the related public health problem.

MATERIALS AND METHODS

The present cross – sectional study analyze and correlate vitamin D and serum uric acid in general healthy adult population of Sindh. The study collected sample from different cities of Sindh. The data pool was gathered at the Suleman Roshan Medical College Hospital for final analysis and correlation of research variables. We recruited a sample of 700 normal healthy subjects of both genders of equal number. Data was collected according to pre – determined criteria; volunteers, age (40 – 60 years), healthy adults of both genders were inclusion criteria. Multi vitamin supplementation, pregnancy and breast feeding mothers were strictly excluded. Patients taking anti – hypertensive drug therapy such as angiotensin inhibitors and thiazide diuretics and anti – epileptic drugs were excluded. Any person taking uric acid lowering pill was also exclusion criteria. Of major exclusion criteria were unhealthy adult subjects. Permission was sought from the research ethics committee approved the institute. Volunteers were negotiated of the purpose of study, data and blood sampling. All volunteers thorough clinical history and physical examination. Volunteers were informed of no monetary harm or benefit to them and no expenses of laboratory investigations. Volunteers have been informed that they can leave at any time if they are concerned or indicate the reason. Blood samples were collected to estimate the vitamin D and serum uric acid. Blood was centrifuged to get sera at 3000 rpm (15 minutes) and kept in pre – labeled tubes. Sera were stored at -20 °C until analysis of vitamin D and uric acid. Immunofluorescence assay (VIDAS-Biomerieux-diagnostics) was employed for vitamin D detection. While serum uric acid was detected by uricase enzymatic method. Samples were run on Roche Cobas auto-analyzer. Vitamin D <29.9 ng/dl was defined as deficiency and >30.0 ng/dl as sufficiency.[10] High serum uric acid was defined as >7.0 mg/dl for male and >5.8 mg/dl for female.[11] Data was analyzed using student t – test for continuous variables and Chi – square test for categorical variables. Pearson`s correlation was used to determine correlation of vitamin D and uric acid. Scatter plots were generated on Microsoft Excel Sheet. SPSS ver. 20 analyzed data variables at 95% confidence interval (P≤0.05).

RESULTS

Age of male and female study sample was 52.15±7.7 and 53.47±5.8 years (P=0.91). Findings are shown in table – 1. Vitamin D was found very low approximately 27.05±14.4 ng/dl in male and 15.7±8.51 ng/dl in female (P=0.0001). High uric acid was noted in both male and female subjects; 7.60±1.38 and 6.47±2.36 mg/dl respectively (P=0.0001). Vitamin D deficiency and sufficiency was noted in 75.4% (14.4186±5.1 ng/dl) and 24.5% (42.7±4.1 ng/dl) of total sample size (P=0.0001) (table - 2).

Table No.1: Findings in study groups

	Male	Female	P-value
Age (years)	52.15±7.7	53.47±5.8	0.91
Body weight (Kg)	76.2±11.3	76.7±11.1	0.56
Systolic BP (mmHg)	121.2±6.7	120.8±5.3	0.78
Diastolic BP (mmHg)	79.7±15.2	78.9±0.18	0.45
S. Creatinine (mg)	0.91±0.11	0.95±0.21	0.007
Vitamin D (ng/dl)	27.05±14.4	15.7±8.51	0.0001
Uric acid (mg/dl)	7.60±1.38	6.47±2.36	0.0001

Table No.2: Vitamin D status of study sample

Vitamin D (ng/dl)	N (%)	Mean	Std. Dev.	P-value
Deficiency	528 (75.4%)	14.4186	5.15573	0.0001
Sufficiency	172 (%24.5)	42.7442	4.12151	

Table No.3: Vitamin D status of subjects with normal & high serum uric acid

Uric acid	Vitamin D (ng/dl)			
	N (%)	Mean	Std. Dev.	P-value
Normal	173 (24.7%)	42.2601	5.63280	0.0001
High	527 (75.2%)	14.5237	5.40234	

Subjects with high serum uric acid level (75.2%) showed severe vitamin D deficiency (14.52±5.4 ng/dl) and sufficient vitamin D in those with normal serum uric acid (42.26±5.63 ng/dl) (P=0.0001) (table - 3). Vitamin D shows strong negative correlation with serum uric acid (r=-0.852, p=0.0001) in total study sample. Negative correlation of vitamin D and uric acid in male was (r=-0.706, p=0.0001) and in female (r=-0.892, p=0.0001) (table - 4).

Table No.4: Pearson`s correlation output

	Uric acid		
Vitamin D	**r-value**	**N**	**P**
Female	-0.706**	350	0.0001
Male	-0.892**	350	0.0001
Total sample	-0.852**	700	0.0001

**. Correlation is significant at the 0.01 level (2-tailed)

DISCUSSION

The present cross sectional study was conducted at a Suleman Roshan Medical College Hospital Tando Adam. Data was also collected from other medical hospitals and centers located in different cities of Sindh. Age of male and female study sample was 52.15±7.7 and 53.47±5.8 years (P=0.91). Study sample of present study comprised older age subjects; however, the findings are in agreement with previous studies.[1,2,5,8] Vitamin D was found very low approximately 27.05±14.4 ng/dl in male and 15.7±8.51 ng/dl in female (P=0.0001). High uric acid was noted in both male and female subjects; 7.60±1.38 and 6.47±2.36 mg/dl respectively (P=0.0001). The findings are supported by previous studies.[1,2,5] Vitamin D is an essential micronutrient that plays vital role in bone and body health, and boosts the immune reactions and prevents the chronic metabolic diseases. Vitamin D deficiency has become a public health problem throughout the World and its occurrence is observed in normal health persons as well as those with systemic diseases. Vitamin D deficiency is observed in studies from tropical countries with sunlight exposure, reason remains unknown.[12] Vitamin D deficiency and sufficiency was noted in 75.4% (14.4186±5.1 ng/dl) and 24.5% (42.7±4.1 ng/dl) of total sample size (P=0.0001). Subjects with high serum uric acid level (75.2%) showed severe vitamin D deficiency (14.52±5.4 ng/dl) and sufficient vitamin D in those with normal serum uric acid (42.26±5.63 ng/dl) (P=0.0001). High serum uric acid is highly prevalent in normal populations of developed and developing countries.[13] High uric acid damages joints by forming urate crystals and becomes deposited in the microvasculature, leading to nephropathy, tophi and hypertension.[3] Vitamin D deficiency with high serum uric acid is potential health risk factors and this has been observed in the present study. High serum uric acid has been observed in the general populations of developed and developing countries.[1,14] Negative correlation of vitamin D and uric acid in male was (r=-0.706, p=0.0001) and in female (r=-0.892, p=0.0001). In present study, the vitamin D deficiency was noted in 75.4% and high serum uric acid level in 75.2% that proved vitamin D deficient. The findings are in keeping with previous studies.[1,15] Vitamin D sufficiency was found in 24.5% (42.7±4.1 ng/dl) of total sample size (P=0.0001) that is in line with a recent study by Najeeb et al[1] that found sufficient vitamin D in 20% of sample subjects in their study. The findings are supported by above study. Subjects with sufficient vitamin D have had normal serum uric acid and vice versa. In present study, we observed vitamin D shows strong negative correlation with serum uric acid (r=-0.852, p=0.0001) in our study sample. The findigns are supported by previou studies.[1,15,16] Vitamin D deficiency has been linked with a number of communicable and non – communicable diseases and likelihood of its deficiency with high serum uric acid is reported by a previous study.[18] Vitamin D supplementation reduced serum uric acid levels, has been demonstrated by a previous study.[19] Some of studies had reported genomic link of vitamin D deficiency and uric acid levels.[20,21] Pearson`s correlation of vitamin D and uric acid showed strongly negative correlation (table – 4) indicating a causal relationship that needs further research with large sample size using genomic methods. Inverse correlation of vitamin D and uric acid is consistent with previous studies.[5,13]

CONCLUSION

Normal vitamin D is essential for healthy bone and body. We found, vitamin D deficiency in 75.4% of sample size. High serum uric acid level was found in 75.2% with severe vitamin D deficiency. Significantly negative correlation was found between vitamin D deficiency and serum uric acid. Further studies are demanding to involve large sample size in indigenous population to investigate the correlation to make strategies for the preventable cause of morbidity and mortality.

Author's Contribution:

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REFERENCES

1. Najeeb HA, Rajeb AT, Ali AF. Relationship between plasma vitamin D3 and serum Uric acid levels in adults, Duhok city: a cross-sectional study. Al-Kufa Univ J Biol 2021;13(2):1-7.
2. Peng H, Li H, Li C, Chao X, Zhang Q, Zhang Y. Association between Vitamin D Insufficiency and Elevated Serum Uric Acid among Middle-Aged and Elderly Chinese Han Women. PLoS One 2013; 8(4): e61159.
3. Ragab G, Elshahaly M, Bardin T. Gout: An old disease in new perspective – A review. J Adv Res 2017; 8(5):495–511.
4. Grayson PC, Young Kim S, Lavalley M, Choi HK. Hyperuricemia and incident hypertension: A systematic review and meta-analysis. Arthritis Care Res 2011;63(1):102-10.
5. Thakkinstian A, Anothaisintawee T, Chailurkit L, Ratanachaiwong W, Yamwong S, Sritara P, et al. Potential causal associations between Vitamin D and uric acid: Bidirectional mediation analysis. Sci Rep 2015;29(5):14528.
6. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? J. Steroid Biochem Mol Biol 2014;144 Pt A:138-45.
7. Liu H, Zhang XM, Wang YL, Liu BC. Prevalence of hyperuricemia among Chinese adults: a national cross-sectional survey using multistage, stratified sampling. J Nephrol 2014;27(6):653-8.
8. Bener A, Al-Hamaq AOAA, Öztürk M, Tewfik I. Vitamin D and elevated serum uric acid as novel predictors and prognostic markers for type 2 diabetes mellitus. J Pharm Bioallied Sci 2019; 11(2):127 – 132.
9. Arguelles LM, Langman CB, Ariza AJ, Ali FN, Dilley K, Price H, et al. Heritability and environmental factors affecting vitamin D status in rural Chinese adolescent twins. J Clin Endocrinol Metab 2009;94 (9):3273 – 81.
10. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Kostenberger M, Berisha AT, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. Eur J Clin Nutr 2020;74(11):1498-1513.
11. HK Khoharo, AA Shah, F Qureshi, SA Almani. Hyperuricemia in Systemic Hypertension and its correlation with systolic and diastolic blood pressure. The Professional Med J 2020; 27 (01): 89-93.
12. Hussain T, Eimal Latif A, Malik S, Saeed T, Zahid AS, Nazary K, et al. Vitamin D Deficiency and Associated Risk Factors in Muslim Housewives of Quetta, Pakistan: A Cross-Sectional Study. Cureus 2021;13(9):e17643.
13. Mustafa A, Shekhar C. Concentration levels of serum 25-Hydroxyvitamin-D and vitamin D deficiency among children and adolescents of India: a descriptive cross-sectional study. BMC Pediatr 2021; 21(1):334.
14. Shah SSH, Iqbal U, Ahmad E. Frequency of hyperuricemia in hypertensive patients and its association with age of patients. Pak Armed Forces Med J 2021;71(1):304-08.
15. Rahmadhani R, Zaharan NL, Mohamed Z, Moy FM, Jalaludin MY. The associations between VDR BsmI polymorphisms and risk of vitamin D deficiency, obesity and insulin resistance in adolescents residing in a tropical country. PLoS One 2017;12(6): e0178695.
16. Zhang YY, Qiu HB, Tian JW. Association between Vitamin D and Hyperuricemia among Adults in the United States. Front Nutr 2020;7:592777.
17. Takir M, Solak Y, Erek A, Kostek O, Oral A, Elcioglu OC, et al. Association between Elevated Serum Uric Acid and Vitamin D Insufficiency among the Middle-Aged and Elderly Population. Turk Neph Dial Transpl 2016;25(2):182-186.
18. Nimitphong H, Saetung S, Chailurkit L, Chanprasertyothin S, Ongphiphadhanakul B. Vitamin D supplementation is associated with serum uric acid concentration in patients with prediabetes and hyperuricemia. J Clin Transl Endocrinol 2021;24:100255.
19. Bener A, Al-Hamaq AOAA, Öztürk, M, Tewfik I. Vitamin D and elevated serum uric acid as novel predictors and prognostic markers for type 2 diabetes mellitus. J Pharm Bioallied Sci 2019;11(2):127-132.
20. Reginato AM, Mount DB, Yang I, Choi HK. The genetics of hyperuricemia and gout. Nat Rev Rheumatol 2012;8(10):610-21.

Polypharmacy and Prescription Patterns of General Practitioners in Major Cities of Sindh

Polypharmacy and Prescription Patterns of General Practitioners in Sindh

Majid Ali Hingoro[1], Jawad Mumtaz Sodhar[2], Muhammad Atif Ata[3], Samreen Ali[4], Asim Mehmood[5] and Rasheed Ahmed Soomro[6]

ABSTRACT

Objective: To analyze polypharmacy and prescription patterns of general practitioners in major cities of Sindh.
Study Design: Descriptive cross sectional study
Place and Duration of Study: This study was conducted at the Major cities (Karachi, Sukkur, Tando Muhammad Khan and Tando Adam) of Sindh from January 2021 to June 2021 for a period of six months.
Materials and Methods: An online database system was developed for simultaneous data entry by the authors from different cities of Sindh. Total 7590 prescriptions were collected within six months. Polypharmacy (PP) was defined as use of 5–8 drugs, excessive polypharmacy (EPP) use of > 8 drugs and non –polypharmacy (NP) ≤ 4 drugs concomitantly. The data was analyzed SPSS for Windows ver. 22 (Chicago, IL, USA). Data was presented as frequency and % for categorical variables. The Microsoft Excel sheet was employed for graphing. Chi – square testing was used for categorical variables. Level of significance was taken at ≤0.05.
Results: Polypharmacy and Excessive polypharmacy and Non –polypharmacy were observed in 4653 (61.3%), 1978 (26.1%) and 959 (12.6%) respectively (P=0.0001). Proton pump inhibitors were most frequently prescribed drugs 7103 (93.5%), followed by calcium and vitamin D supplements 6987 (92.1%), steroids 6705 (88.3%), multivitamin and multi-mineral pills 6619 (87.01%).
Conclusion: The present study reports the polypharmacy and excessive polypharmacy are prevalent in the country and highlight the need to revise medical practice and drug dispensing policy in the country.

Key Words: Polypharmacy, Prescription, Drugs, Sindh

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INTRODUCTION

Polypharmacy term was coined about one – and a half century back that refers to poly pill drug consumption with associated risk and complications. It encompasses "unnecessary drug use" and medicaments use without indication. It has been used under different meanings according to the different clinical conditions. In one opinion, use of five or more drugs in a single prescription may be called as Polypharmacy.[1,2]

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It is very difficult to define Polypharmacy as the consensus is lacking because of mild to severe clinical disease status. The WHO suggests the numerical definition may not be reliable, but emphasis should be on the evidence based adverse drug reactions and main goal should least drug number at the maximum. WHO defines Polypharmacy as the administration of multiple numbers of drugs at the same time.[3] Simple defined Polypharmacy is defined as taking 5 or more drugs concomitantly.[4] Polypharmacy may also be defined as the drug prescription and consumption without evidenced clinical indication.[2,5] Excessive drug prescription has been linked with the risk of adverse drug outcome. Polypharmacy has been associated with disability, adverse drug interactions, frailty, falls, and fragility and in extreme conditions even death may occur.[1] Polypharmacy is of public health concern because of toxic drug reactions.[2,6] In certain complicated clinical conditions, the multiple drug numbers may be appropriate to eradicate the disease and saves life of patients. While in other situations, the drugs may exceed the severity of disease status; this may be taken as biased favoring the pharmaceutical industry. Hence it is difficult to decide whether Polypharmacy is appropriate or inappropriate. Polypharmacy is a known risk factor in older age

persons as they are vulnerable to toxic drugs reactions. Polypharmacy increases the risk of adverse drug outcome due to drug – drug interactions, side effects and low adherence and compliance to drug therapy. Polypharmacy increases the chances of drug reactions and causes needless health expenditures. Redundant drug sale and high cost create burden to the general public.[6] Polypharmacy begins form physician to pharmacist and the patients. Patients also promote polypharmacy through self – medication as the drugs are sold without prescription. Patients usually don't follow the instructions of physicians or often the prescriptions are completely lacking the instructions of drug use. The present descriptive cross sectional survey analyzed the polypharmacy and prescription patterns of general practitioners in major cities of Sindh.

MATERIALS AND METHODS

The present descriptive cross sectional survey took place at the major cities of Sindh (Karachi, Sukkur, Tando Muhammad Khan and Tando Adam) from January 2021 to June 2021. An online database system was developed for simultaneous data entry by the authors. The present study is a descriptive cross sectional survey - questionnaire-based. The questionnaire was designed by the authors of research team members. Prescription papers of general practitioners were collected from main pharmacies of major cities of Sindh as mentioned above. Questionnaire included four parts for each prescription. Prescription was checked first for – doctor name, qualification, registration number and date and second – name of patient, age, demographic features, physical examination findings and diagnosis, and third – drugs prescribed, drug dose, instructions of drug intake and fourth – legibility of prescription. Inclusion of prescription was based on the resident of cities as mentioned, doctors practicing in the resident cities and pharmacies of resident cities. Prescriptions were photocopied and data was entered in online database system that was accessed by all authors simultaneously. Prescription data was collected through probability convenient sampling method. Total 7590 prescriptions were collected within six months and data was saved in the questionnaire online. Polypharmacy was defined as use of 5–8 drugs, Excessive Polypharmacy (EPP) use of > 8 drugs and non –polypharmacy (NP) ≤ 4 drugs concomitantly.[8] Counted medications included; antibiotics, anti-hypertensive, anti-diabetic, herbs, minerals, vitamins, sleeping pills, pain killers, steroids, OTC medications, etc. Questionnaires were checked by authors and data was entered online database system that was shared with corresponding author. The data was analyzed SPSS for Windows ver. 22 (Chicago, IL, USA). Data was presented as frequency and % for categorical variables. The Microsoft Excel sheet was employed for graphing. Chi – square testing was used for categorical variables. Level of significance was taken at ≤0.05.

RESULTS

A sample of total 7590 prescriptions was analyzed and checked for the data variables. Prescription letter pad was observed in 5199 (68.4%) while 2391 (31.5%) were written on plain papers. Name of doctor, qualification, registration number were mentioned in 4987 (65.7%), 3561 (46.9%) and 171 (2.25%) respectively. Legibility was observed in 2190 (28.9%) prescriptions. Date and signature were observed in 14.7% and 2.62% respectively (table – 1). Table – 2 shows the details of patients data. Drug indications, diagnosis and laboratory investigations were noted in 109 (1.4%), 119 (1.5%) and 217 (2.8%) prescriptions only. Polypharmacy (5–8 drugs), Excessive Polypharmacy (> 8 drugs) and Non –polypharmacy (≤ 4 drugs) were observed in 4653 (61.3%), 1978 (26.1%) and 959 (12.6%) respectively (P=0.0001) (table – 3 & graph – 1). Proton pump inhibitors were most frequently prescribed drugs 7103 (93.5%), followed by calcium + vitamin D supplements 6987 (92.1%), steroids 6705 (88.3%), multivitamin and multi-mineral pills 6619 (87.01%) (Table – 4). Frequently prescribed drugs are shown in Graph – 2.

Table No.1: Details of prescription paper (n=7590)

	n	%
Plain prescription paper	2391	31.5
Prescription letter pad	5199	68.4
Name of Doctor	4987	65.7
Qualification	3561	46.9
Registration No.	171	2.25
Legibility	2199	28.9
Date	1120	14.7
Signature	199	2.62

Table No.2: Details of patients data (n=7590)

	n	%
Name of patients	6789	89.4
Age	231	0.31
Pulse	89	0.11
BP	913	12
Physical findigns	0	0
Drug indications	109	1.4
Diagnosis	119	1.5
Laboratory investigations	217	2.8

Table No.3: Prescription patterns (n=7590)

	n	%	P
Polypharmacy (5–8 drugs)	4653	61.3	0.0001
Excessive Polypharmacy (> 8 drugs)	1978	26.1	
Non –polypharmacy	959	12.6	

(≤ 4 drugs)			

Table No.4: Drugs prescribed (n=7590)

	n	%
PPI	7103	93.5
Steroids	6705	88.3
Benzodiazepines	3459	45.5
Antibiotics	4671	61.5
Multi vitamin	2312	30.4
Multivitamin + Multimineral	4307	56.7
Calcium + Vitamin D supplements	6987	92.1
NSAIDS	3101	40.8
Anti - hypertensive	319	4.2
Anti - diabetics	1130	14.8
Herbal agents,	2310	30.4
Major tranquilizers	139	1.8

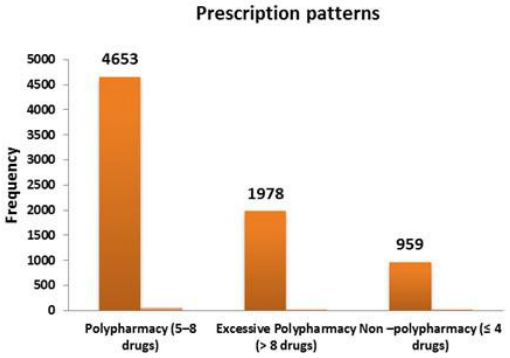

Figure No.1: Prescription patterns – polypharmacy, excessive pharmacy and non – pharmacy

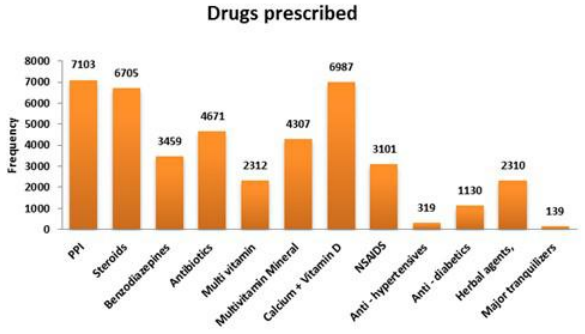

Figure No.2: Frequency of drugs prescribed

DISCUSSION

The present descriptive cross – sectional survey observed high frequency of Polypharmacy (PP) (5–8 drugs) and Excessive Polypharmacy (EPP) (> 8 drugs) found in 4653 (61.3%) and 1978 (26.1%) respectively (P=0.0001). Non –polypharmacy (≤ 4 drugs) were observed in 959 (12.6%). An ideal upper drug limit of 2.0 has been recommended by the World Health Organization.[8,9] but this has never been appreciated by the doctors. A previous study by Raza et al[8] also reported PP is prevalent in the country but authorities have failed to control it. Reports from other countries have also reported PP is prevalent in different areas of the World.[10,11] Bangladesh and Yemen have controlled the PP through successful implementation of drug policy.[12,13] PP carries high risk of adverse reactions through drug – drug interactions and complications in addition to high cost.[8] In present study, majority of prescriptions were not found as per standard of medical practitioners. The findings are supported by previous studies.[1,2,5] Previous studies from Sweden[14] and China[15] has reported high prevalence of polypharmacy that supports the present study. A Korean study[16] reported prevalence of 86.4% that is too much high compared to present and other previous studies.[2,9] A previous study[2] reported PP and EPP of 292 (58.4%) and 51 (10.2%) respectively and is consistent to the present study. In present study, the proper prescription letter pad was observed in 5199 (68.4%) while 2391 (31.5%) were written on plain papers. Plain paper prescriptions were most probably written by quacks. In present study, the name of doctor, qualification and registration number were mentioned in 4987 (65.7%), 3561 (46.9%) and 171 (2.25%) respectively. In present study, the legibility of prescription was 2190 (28.9%) this indicates poor compliance on part of medical practitioners. Poor legibility often results in inadvertent drug substitutions.[17] Finding of poor legibility is consistent with previous studies.[18,19] In present study, the drug indications, diagnosis and laboratory investigations were noted in 109 (1.4%), 119 (1.5%) and 217 (2.8%) prescriptions only. In present study, the proton pump inhibitors (PPI) were most frequently prescribed drugs 7103 (93.5%), followed by calcium and vitamin D supplements 6987 (92.1%), steroids 6705 (88.3%), multivitamin and mineral pills 6619 (87.01%). In present study, the PPI were mostly prescribed drugs that are an alarming situation and has been notified previously.[20,21] Despite increasing awareness of PPI related adverse reactions, its use is very common and moreover it is being used as self-medication. Overuse of PPI adversely affects the patients' quality of life (QoL) and drug costs.[22] Limitations of present study are short duration of study and short number of prescriptions collected from different cities may not be representative of country. It needs similar studies conducted at national level to control the polypharmacy and improve drug prescriptions.

CONCLUSION

The present study reports the polypharmacy and excessive polypharmacy are on rise in the country. Findings of present study highlight the need to revise medical practice and drug dispensing policy in the country. Prescriptions of general practitioners need improvement on urgent basis to stop quackery. Proton pump inhibitors, calcium, vitamin D supplements,

steroids, multivitamin and mineral pills are commonly prescribed drugs without proper clinical diagnosis and indication that needs to be controlled. Establishing innovative clinical strategies of drug prescription is advised to control polypharmacy and self-medication.

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Author's Contribution:

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Data Analysis:	Samreen Ali, Asim Mehmood, Rasheed Ahmed Soomro
Revisiting Critically:	Majid Ali Hingoro, Jawad Mumtaz Sodhar
Final Approval of version:	Majid Ali Hingoro

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

REFERENCES

1. Hosseini SR, Zabihi A, Jafarian Amiri SR, Bijani A. Polypharmacy among the Elderly. J Midlife Health 2018;9(2):97-103.
2. Badawy NA, Labeeb SA, Alsamdan MF, Alazemi BF. Prevalence and Risk of Polypharmacy among Community-Dwelling, Elderly Kuwaiti Patients. Med Princ Pract 2020;29:166–173.
3. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMCGeriatr 2017;17:230.
4. Hovstadius B, Petersson G. Factors leading to excessive polypharmacy. Clin Geriatr Med 2012;28(2): 159–72.
5. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf 2014;13(1):57–65.
6. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. J Am Geriatr Soc 2014; 62(12): 2261–72.
7. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf 2014;13(1):57–65.
8. Raza UA, Khursheed T, Irfan M, Abbas M, Irfan UM. Prescription patterns of general practitioners in Peshawar, Pakistan. Pak J Med Sci 2014; 30(3):303- 31.
9. World Health Organization. Comparative Analysis of National Drug Policies. [Internet]. 2021. Available from: http://apps.who.int/ medicinedocs/ en/d/Jwhozip46e/12.html
10. Ghosh R, Neogi JN, Srivastava BS, Sen P. Prescribing trends in a teaching hospital in Nepal. J Nepal Med Assoc 2003;42:346-349.
11. Sharif SI, Al-Shaqra M, Hajjar H, Shamout A, Wess L. Patterns of drug prescribing in a Hospital in Dubai, United Arab Emirates. Libyan J Med 2007;3(1):10–12.
12. Soerensen A L, Nielsen LP, Poulsen BK, Lisby M, Mainz J. Potentially inappropriate prescriptions in patients admitted to a psychiatric hospital. Nord J Psychiatr 2016;70(5):365–73.
13. Sciarra T, Ciccotti M, Aiello P, Minosi P, Munzi D, Buccolieri C, et al. Polypharmacy and Nutraceuticals in Veterans: Pros and Cons. Front Pharmacol 2019; 10:994.
14. Hovstadius B, Hovstadius K, Astrand B, Petersson G. Increasing polypharmacy - an individual- based study of the Swedish population 2005-2008. BMC Clin Pharmacol 2010;10(1):16.
15. Dong L, Yan H, Wang D. Polypharmacy and its correlates in village health clinics across 10 provinces of Western China. J Epidemiol Comm Health 2010;64(6):549–53.
16. Kim HA, Shin JY, Kim MH, Park BJ. Prevalence and predictors of polypharmacy among Korean elderly. PLoS One 2014;9(6):e98043.
17. Nazir MU, Tanoli SK, Khan R, Saeed S, Muhammad A, Rahim QS. Prescribing Pattern of Vitamins and Supplements in a Tertiary Care Hospital in Abbottabad. Merit Res J Med Med Sci 2020;8(12):772-9.
18. Rafi S, Rasheed H, Usman M, Nawaz HA, Anjum SM, Chaudhry M, et al. Availability of essential medicines in Pakistan—A comprehensive document analysis. PLoS One 2021;16(7): e0253880.
19. Chattha IR, Zaffar S, Tariq S, Siddiqui WA, Zaman K, Kamran R, et al. Prevalence of Self-medication for Acid Peptic Disease amongst People of Manawa, Lahore. Cureus 2020; 12(1):e6817.
20. Afshan A. Rationale use of proton pump inhibitors: Observational study of hospital based prescriptions and role of clinical pharmacist. Pak J Pharm Sci 2018;31(4):1217-27.
21. Hassan GU, Haque IU, Hameed AM, Javed F, Mehmood A, Shafiq M, et al. Practices of proton pump inhibitor use in medical wards. Pak Arm Forces Med J 2017;67(4):524-28.
22. Payne RA, Avery AJ, Duerden M, Saunders CL, Simpson CR, Abel GA. Prevalence of polypharmacy in a Scottish primary care population. Eur J Clin Pharmacol 2014;70(5): 575–81.

Effect of Pumpkin Seed Oil against High Fat Diet Induced Hyperlipidemia in Wistar Albino Rats

Asim Mehmood[1], Samreen Ali[2], Rasheed Ahmed Soomro[3], Majid Ali Hingoro[5], Umair Ali Soomro[6] and Muhammad Atif Ata[4]

ABSTRACT

Objective: To study and analyze the lipid lowering and anti – obesity effect of Pumpkin seed oil (PSO) against high fat diet induced hyperlipidemia in Wistar Albino male rats.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Suleman Roshan Medical College, Tando Adam and Animal House of the Sindh Agriculture University, Tando Jam from April 2021 to September 2021 for a period of six months.

Materials and Methods: Sixty male Wistar albino rats were included in experiment according to the inclusion criteria. Rats were kept in animal house as per standard protocol of animal handling in Laboratory (NIH), USA guidelines. HFD was prepared as described previously. Rats were divided into four groups (A to D), each group comprised 15 rats. Pumpkin seed oil (PSO) was purchased from market. After the experiment, blood samples were collected for blood lipids biochemical analysis. Data was analyzed on SPSS 21.0 ver. (IBM, Incorporation, USA) using 1– way ANOVA, descriptive and Post – Hoc LSD at 95% confidence interval ($P<0.05$).

Results: Six weeks PSO therapy decreased the body weight and exerted lipid lowering potential. Serum triglycerides (TAGs), total cholesterol (TC), serum LDL cholesterol (LDLc) and serum HDL cholesterol (HDLc) shows significant reduction compared to positive control group B ($P<0.05$).

Conclusion: The present study concludes the pumpkin seed oil shows lipid lowering and anti – obesity potential hence it may be used for clinical purpose of treating hyperlipidemia

Key Words: Pumpkin seed oil, Hyperlipidemia, Lipid lowering, Rats

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INTRODUCTION

Hyperlipidemia is a part of metabolic syndrome characterized by high circulating levels of various lipid fractions (VLDL, Chylomicron, LDL and HDL) in the blood circulation.[1] Hyperlipidemia increases the levels of free fatty acids (FFA) in blood that often evoke an inflammatory reaction causing release of cytokines resulting neutral fat deposition in liver parenchyma and arteries. This is the beginning lesion of atherosclerosis. Fatty liver indicates insulin resistance and development of future diabetes mellitus. Blood lipid (VLDL, Chylomicron, LDL and HDL) fractions are often disturbed in obese patients. Hence, the hyperlipidemia is a fore runner of fatty liver, insulin resistance, diabetes mellitus, atherogenesis, ischemic arterial disorders, etc.[1] Currently; many herbs are being evaluated of their lipid lowering potential to overcome above morbid conditions. Many natural herbs had been used in Ayurveda, Chinese traditional medicine (CTM), Western countries and other oldest traditional systems.[2] Pumpkin (Curcurbita maxima L) is one of herbs that is cultivated at high altitudes and near sea levels. Seeds of pumpkin are edible and contain essential oils. Seeds are protein rich and low neutral fats.[3,4] Pumpkin fruit is rich in β-carotene, minerals, poly unsaturated essential fatty acids (PUFA), carbohydrates, vitamins, etc. Pumpkin is rich source of oleic acid.[3-5] Pumpkin is enriched with fixed oils, PUFA, essential amino acids, peptides, Lutein, zeaxanthin, para-amino benzoic acid (PABA), lutein and g-amino butyric acid (GABA), etc. Chromium, manganese, copper, magnesium, selenium,

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zinc, and molybdenum are also found in pumpkins. Some lipid lowering, insulin secretagogue and insulin sensitizing activity has been identified. Anti – fungal and anti – microbial peptides have been identified in pumpkin. This proves the pumpkin is of medicinal value. It has been used in traditional medicine since centuries back. Pumpkin seed oil (PSO) is also enriched in carotene, carotenoids, vitamins, phenolic compounds, riboflavin, thiamine, folic acid, proteins, fibers, poly unsaturated fatty acids (PUFA), α-tocopherol, γ-tocopherol, selenium, zinc (Zn), molybdenum, manganese (Mn), copper, magnesium, chromium, etc. PSO protects against cardiac and prostate diseases, cancers and inflammatory effect.[5,6] Currently, the hyperlipidemia is increasing in the individuals of urban society due to over eating, sedentary life style and obesity[7] hence it is needed to analyze simple herbs of their lipid lowering potential. PSO is easily available herbal essential oil; hence, the research protocol was designed of its hypolipidemic effects. Aim of research was to compare preventive and curative lipid lowering effects of PSO in a high fat fed induced hyperlipidemia animal model of Wistar Albino rats.

MATERIALS AND METHODS

The present experimental study was conducted at the Department of Anatomy, Pathology and Pharmacology, Suleman Roshan Medical College, Tando Adam, Sindh. Written permission of conducting experiment according to animal ethics was taken from the institute. The animals were housed and experiment was performed at the Animal House of the Sindh Agriculture University, Tando Jam. Study was conducted over six months from April 2021 to September 2021. Sixty male Wistar albino rats were included in experiment according to the inclusion criteria of; normal health moving and eating male rats, body weight 120 – 180 grams with successful induction of hyperlipidemia in experimental groups. Rats of other gender, inactive and not feeding well, non – successful induction of hyperlipidemia, and moribund rats. Rats were kept in animal house as per standard protocol of animal handling in Laboratory (NIH), USA guidelines in stainless cages, normal and high fat diet (HFD). HFD was prepared as cited previously.[8,9] Water and food was used for drinking and eating available free (ad libitum). Sixty rats were divided into four groups, each group comprised 15 rats. Negative control (Group – A) were given normal diet (70% Carbs, 20% proteins and 10% fats),[8] Positive controls (Group – B) were given HFD (60% fats, 20% proteins and 20% carbs),[9] Experimental Preventive (Group C –) HFD + Pumpkin seed oil (PSO) in dose of 100 mg/Kg (bwt) for three months (concomitantly),[8,9] and Experimental Curative (Group D) was induced hyperlipidemia with HFD followed by PSO in dose of 100 mg/Kg bwt for three months.[8,9] Hyperlipidemia was induced by feeding HFD for six weeks in the curative group D.[10] Pumpkin seed oil (PSO) was purchased from market. After the experiment, body weight was measured on electronic weigh scale and the blood samples were collected from the retro – orbital venous plexus using a capillary tube inserted behind the eye ball carefully. Blood samples were stored at -20^{0}C for later biochemical analysis. Total cholesterol (TC), TAGs, LDL and HDL were detected by standard methods. Data was analyzed on SPSS 21.0 ver. (IBM, Incorporation, USA). One – way analysis of variance, descriptive and Post – Hoc LSD estimated the continuous variables of blood lipids levels in control and experimental rats. Lipid fractions were tabulated as mean+/- SD. 95% confidence interval ($P<0.05$) was taken statistically significant.

RESULTS

Table – 1 shows the baseline and post – experiment body weight of study rat groups. Results of body weight show the Pumpkin seed oil (PSO) decreases the body weight and possess lipid lowering potential as shown in table – 2. Serum triglycerides (TAGs), total cholesterol (TC), serum LDL cholesterol (LDLc) and serum HDL cholesterol (HDLc) shows significant reduction compared to positive control group B ($P<0.05$).

Table No.1: Body weight in study rat groups

Groups	Body weight (grams)	
	Baseline	After Experiment
Group A. -ve control	181.5±7.5	237.0±10.5
Group B. +ve control	135.1±10.3	287.3±11.2
Group C. Preventive group	131.3±3.3	201.2±9.6
Group D. Curative group	130.2±5.5	219.69±6.17
P-value	0.0001	0.0003

Table No.2: Blood lipids in study rat groups

Groups	TAGs	Cholesterol	LDLc	HDLc
Group A. -ve control	134.7±8.03	111.3±7.3	97.3±8.2	40.3±3.5
Group B. +ve control	312.3±10.5	289.5±9.1	189.3±7.3	25.7±2.1
Group C. Preventive group	230.3±9.7	267.1±9.7	150.1±5.1	37.1±3.2
Group D. Curative group	239.5±7.8	259.3±8.5	147.5±9.3	38.1±5.9
P-value	0.0001	0.0003	0.0009	0.0005

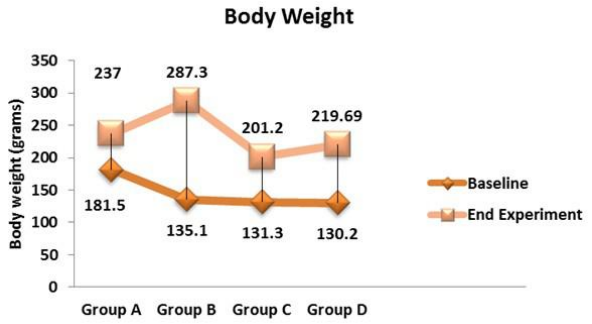

Figure No.1: Body weight in study rat groups (Baseline and end experiment period)

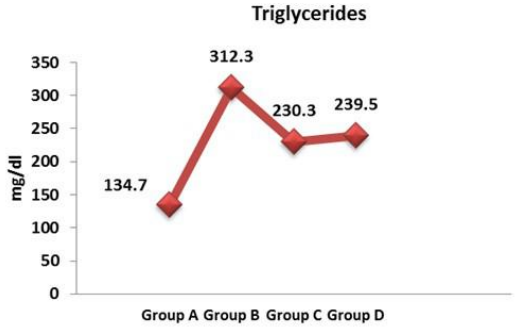

Figure No.2: Serum triglycerides (mg/dl) in study rat groups

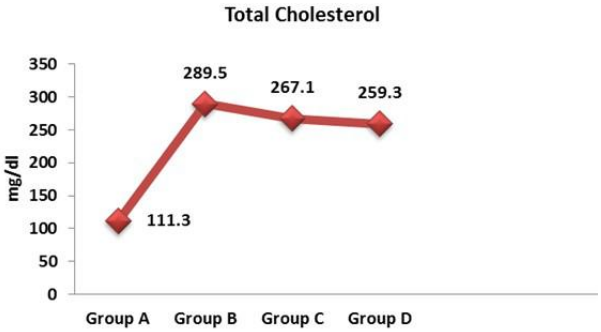

Figure No.3: Serum cholesterol in study rat groups

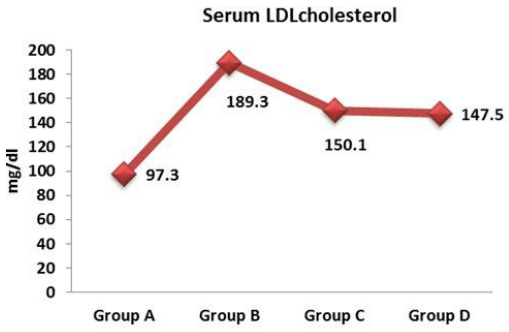

Figure No.4: Serum Low Density Lipoproteins (LDLc) in study rat groups

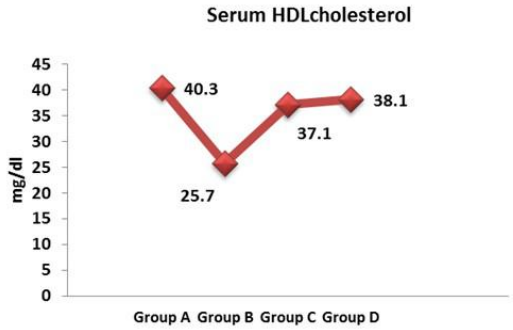

Figure No.5: Serum High Density Lipoproteins levels (HDLc) in study rat groups

DISCUSSION

Present is the first experimental study conducted to study and analyze the lipid lowering and anti – obesity potential of pumpkin seed oil (PSO) in high fat diet induced hyperlipidemia rat model. PSO shows significantly lipid lowering effects with concomitant reduction in body weight. TAGs, LDLc, and TC were decreased with increase in HDLc (P=0.0001). The findings are in agreement with previous studies.[11,12] In present study, hyperlipidemia was ameliorated and increasing body weight was decreased by PSO. This is supported by previous studies.[13,14] The present study observed decrease in body weight that is new finding not observed in a previous study.[15] However, the lipid lowering finding of PSO is consistent with above studies. PSO lipid lowering potential may b may be exploited clinically for treating body weight and hyperlipidemia in community as both disorders are inclining due to over eating habits particularly in urban populace. It is reported the overeating has increased due to economic prosperity particularly in the children of urban areas and are at risk of hyperlipidemia and obesity and related co – morbidities in the future.[15-17] The present WHO based data reveals 58.1% are overweight and 43.9% are obese, both leading to hyperlipidemia hence the future will be worse and a preplanned herbs research is demanding for preparedness of handling the co – morbidities. Data of Asian countries shows 72.3% Pakistani`s are overweight and 58.1% are obese.[18,19] Previous studies[18,19] from Pakistan indicate 17.3% population shows hypercholesterolemia and 17.3% dyslipidemia and 41.0% are suffering from systemic hypertension. This indicates higher future risk of hyperlipidemias and metabolic disorders in near future in the country. The PSO proves significantly effective in improving hyperlipidemia and body weight in present study; this may be further researched in clinical trials for the future. We found an increase in serum HDL cholesterol that is very important clinical finding for prevention of atherosclerotic arterial disease. PSO are enriched in PUFA, α-tocopherol (vitamin E), B vitamins, micro

minerals that may be used for overcoming the hyperlipidemia and obesity.[15,17] The findings of present study are supported by other previous studies.[20,21] A previous study[21] has reported similar lipid lowering effects of PSO in experimental rats. Other previous studies[16,17,22] concluded the hypolipidemic effect of PSO are due to the PUFA, vitamins, carotenoids and tocopherol, etc. PUFA lowers blood lipids and protects against the coronary atherosclerotic disease.[22,23] The findings of present study proves the lipid lowering potential of PSO that may be used as add – on herbal therapy with least adverse effects. Pumpkin seed oil (PSO) is herbal oil hence safe for clinical use. PSO is easily available, inexpensive and cost effective hence it may be used for treating hyperlipidemia but this needs further research studies.

CONCLUSION

The present study shows the pumpkin seed oil (PSO) exerts lipid lowering and anti – obesity potential. Cholesterol, TAGs and LDLc were decreased with a concomitant rise in HDLc. It is concluded PSO may be used treating hyperlipidemia and may be used as add – on therapy in urban community. However, Clinical trials are recommended to validate the lipid lowering potential making it convenient for clinical use.

Author's Contribution:

Concept & Design of Study:	Asim Mehmood
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Haile K, Haile A, Timerga A. Predictors of Lipid Profile Abnormalities among Patients with Metabolic Syndrome in Southwest Ethiopia: A Cross-Sectional Study. Vasc Health Risk Manag 2021;17:461-469.
2. Balgoon MJ, Al-Zahrani MH, Jaouni SA, Ayuob N. Combined Oral and Topical Application of Pumpkin (Cucurbita pepo L.) Alleviates Contact Dermatitis Associated with Depression through Down regulation Pro- Inflammatory Cytokines. Front Pharmacol 2021;12:663417.
3. Amin MZ, Islam TM, Uddin RM, Uddin JM, Rahman MM, Abdus Satter M. Comparative study on nutrient contents in the different parts of indigenous and hybrid varieties of pumpkin (Cucurbita maxima Linn). Heliyon 2019;5(9): e02462.
4. Wang S, Lu L, Zhang M, Shen M, Xu T, Zhan W, et al. Extraction and purification of pumpkin polysaccharides and their hypoglycemic effect. Int J Biol Macromol 2017;(98):182-7.
5. Montesano D, Blasi F, Simonetti MS, Santini A, Cossignani L. Chemical and Nutritional Characterization of Seed Oil from Cucurbita maxima L. (var. Berrettina) Pumpkin. Foods 2018;7:30.
6. Roy S, Datta S. A comprehensive review of the versatile pumpkin seeds (Cucurbita maxima) as a valuable natural medicine". Int J Curr Res 2015;7(8):19355-61.
7. Asif M, Aslam M, Altaf S, Atif S, Majid A. Prevalence and Sociodemographic Factors of Overweight and Obesity among Pakistani Adults. J Obes Metab Syndr 2020;29(1):58–66.
8. Calligaris SD, Lecanda M, Solis F, Ezquer M, Gutiérrez J, Brandan E, et al. Mice Long-Term High-Fat Diet Feeding Recapitulates Human Cardiovascular Alterations: An Animal Model to Study the Early Phases of Diabetic Cardiomyopathy. PLoS One 2013;8(4):60931.
9. Evans CC, Le Pard KJ, Kwak JW, Stancukas MC, Laskowski S, Dougherty J, et al. Exercise Prevents Weight Gain and Alters the Gut Microbiota in a Mouse Model of High Fat Diet-Induced Obesity. PLoS One 2014;9(3):92193.
10. Alsanea S, Gao M, Liu D. Phloretin prevent high fat diet induced obesity and improve metabolic syndrome. The Am Assoc Pharm Sci J 2017; 19(3):797-805.
11. Patel S. Pumkin (Cucurbitasp) seeds as nutraceutic: A review on status quo and scope. Mediter J Nutr Metabol 2013;6(3):183-9.
12. Yadav M, Jain S, Tomar R, Prasad GBKS, Yadav H. Medicinal and biological potential of pumpkin: an updated review. Nutr Res Rev 2010;23: 184–190.
13. Jayachitra J, Shobana S. Anti-Obesity and Antioxidant Activity of Cucurbita maxima Duchesne (L) Albino Wistar Rats. World J Pharm Pharm Sci 2015;4(05):799-807
14. Aboelnaga SMH. Effect of Pumpkin (Cucurbita Sp) Seeds and Husk Tomato (Tomatillo) on Obese Rats Suffering from Diabetes. Intl J Sic Res 2015;6(1):78,96.
15. Ramadan MF, Zayed R, Abozid M, Akser MMS. Apricot and pumpkin oils reduce plasma cholesterol and Triacylglycerol concentrations in rats fed a high-fat diet. Grasas Y Aceites 2011;62(4):443-452.
16. Yadav M, Jain S, Tomar R, Prasad GBKS, Yadav H. Medicinal and biological potential of pumpkin:

an updated review. Nutr Res Rev 2010;23: 184–190.
17. Ramadan BK, Mohammad SA, Mahmoud ES. Ouda EA. Role of Pumpkin seed oil on some cardiovascular and renal aspects in adult male albino rats. Al-Azhar Med J 2016;45(4):931-55.
18. Sayahi M, Shirali S. Study of Cucurbita extract effect on changes of AGEs, lipid and glycemic profile and CRP in type 1 diabetic rats. Bangladesh J Med Sci 2018;17(1):84-7.
19. Bhatti N, Ayaz S, Rehman RU, Ahmad H, Ullah Q, Khan AH, et al. Effect of Flaxseed and Pumpkin Seeds Mixture on Hypercholesterolemia. Pak J Med Biol Sci 2017;1(2):34-39.
20. Stevenson DG, Eller FJ, Wang L, Jane JL, Wang T, George E, et al. Oil and tocopherol content and composition of pumpkin seed oil in 12 cultivars. J Agric Food Chem 2007;55:4005-4013.
21. Amutha M, Geetha A. A biochemical study on the hypolipidemic effect of Curcurbita pepo L seed extract in rats fed with high fat diet. J Bas App Res Intl 2015;11(2):121-130.
22. Gabal AMS. Ameliorative Activity of Pumpkin (Cucurbita maxima) Fruit and Seeds Powders on Diabetic, Oxidative and Pancreatic Status in Rats. Intl J Biochem Res Rev 2019;26(2):1-9.
23. Song H, Sun Z. Hypolipidaemic and hypoglycaemic properties of pumpkin polysaccharides. Biotech 2017;7(3):159.

Pulmonary Fibrosis on High resolution Computed Tomography (HRCT) in Post Covid Patients

Rafia Irum[1], Aneeza Qayyum[1] and Aisha Asghar[2]

ABSTRACT

Objective: To detect people who may develop lung fibrosis early, allowing for the early administration of anti-fibrotic medications, which will not only benefit the infected patients with timely effective disease management, but will also ensure appropriate use of medical resources for this purpose.

Study Design: Descriptive case series study

Place and Duration of Study: This study was conducted at the Department of Radiology, Sharif Medical City Hospital, Lahore for one year from September 2020 to August 2021.

Materials and Methods: This study was conducted after the approval of the ethical review board. Cases of Covid-19 were included as per inclusion criteria using non-probability, consecutive sampling.

Results: Among the patients included in the study, 171 (45.6%) were male and 204 (54.4%) were females. Majority of the patients were of age group more than 50 years. The frequency of pulmonary fibrosis in our study population was 27.5% (103) with degree of pulmonary involvement: mild in 21 (20%), moderate in 39 patients (37.9%) and severe involvement in 43 of 103 patients (41.7%). Data was stratified for various effect modifiers including age (p=0.19), gender (p=0.01), socioeconomic status (p=0.002), BMI (p=0.11), history of chronic illness (p<0.00001), degree of pulmonary involvement (p=0.01) and history of steroid use (p<0.00001).

Conclusion: The aim of this study was to detect people who may develop lung fibrosis early, allowing for the early administration of anti-fibrotic medications. Along with determination of disease severity using HRCT severity scoring, which will not only benefit the infected patients with timely effective disease management, but will also ensure appropriate use of medical resources for this purpose. Side by side our study will guide the medical and government authorities to take suitable steps for the local population depending upon the lethality of disease in the second wave. This study will also able to identify the population at risk of developing fibrosis.

Key Words: Covid-19, HRCT, Pulmonary fibrosis

Citation of article: Irum R, Qayyum A, Asghar A. Pulmonary Fibrosis on High resolution Computed Tomography (HRCT) in Post Covid Patients. Med Forum 2022;33(1):22-25.

INTRODUCTION

Covid-19 has been labeled a worldwide medical emergency, impacting practically the whole world, including Pakistan. In March 2020, WHO declared it a pandemic.[1]

Although Covid-19 can affect any of the body organs, pulmonary involvement has been identified as a main cause of morbidity and mortality in effected individuals.[2] HRCT Chest CT plays a key role in the diagnosis of pulmonary disease in infected patients and also helps in determining the disease severity based on the proportion of pulmonary involvement.[3] Radiological Society of North America Consensus statement has described ground-glass opacities with or without consolidation in a peripheral, posterior, and diffuse or lower lung zone distribution as typical CT finding of Covid-19 Pneumonia.[4]

COVID-19 pulmonary pneumonia can result in progressive fibrotic lung disease. The long-term lung alterations caused by post COVID-19 infection are yet unknown and should be investigated further.

The goal of this study was to detect people who may develop lung fibrosis early, allowing for the early administration of anti-fibrotic medications. Along with determination of disease severity using HRCT severity scoring, which will not only benefit the infected patients with timely effective disease management, but will also ensure appropriate use of medical resources for this purpose. Side by side our study will guide the medical and government authorities to take suitable steps for the local population depending upon the lethality of disease in the second wave.

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MATERIALS AND METHODS

This study conducted at the Department of Radiology, Sharif Medical City Hospital, Lahore during September

2020 to August 2021 after the approval from ethical review board. Sampling was done using non-probability, consecutive sampling. Primary Objective of the study was to determine the frequency of pulmonary fibrosis among the patients with history of COVID-19. Secondary objective was to determine the degree of pulmonary involvement in suspected and diagnosed cases of COVID-19 patients during the second wave of pandemic by using HRCT.

All patients, regardless of gender or age group, who had positive CT chest findings of COVID-19 verified by PCR test were enrolled in the research and were monitored for 4 weeks following discharge. Following the negative PCR result, a follow-up HRCT chest was performed to examine the degree of healing and remaining fibrotic changes. All pregnant women, patients with significant respiratory motion abnormalities on CT images, and patients with a history of chronic interstitial lung disease were excluded from the research.

Sample size of **375** was calculated using WHO sample size calculator, and taking expected pulmonary fibrosis among the patients with history of COVID-19: P 31.2%[7] with confidence level of 95% and absolute precision of 5%.

HRCT – High resolution CT scan of the chest was done to determine the presence of disease and its complications like pulmonary fibrosis. HRCT is a sampling tool that combines 1 to 2mm thin slices with high spatial frequency algorithm to generate exquisite lung details. Severity of the pulmonary involvement was accessed using the 25-point CT severity scoring for COVID 19 using HRCT. (Table no. 1)

After approval from Institutional Review Board, all the patients fulfilling the inclusion criteria who presented to the Radiology department of Sharif Medical City Hospital for HRCT Chest were selected.

The study included all patients of either gender or age group who had positive CT chest findings of COVID-19 verified by a PCR test. The COVID severity score was generated using a 25-point CT grading system, and patients were classified as having mild, moderate or severe illness. Patients were monitored for four weeks following discharge. Following a negative PCR result, a follow-up HRCT chest was performed to examine the degree of healing and remaining pulmonary fibrosis. HRCT was performed using Toshiba Aquilion 16 slicer CT with the patient in prone position. HRCT images were collected and assessed by two experienced radiologist for the presence or absence of pulmonary fibrosis.

Collected data was analyzed by using SPSS 24.0. Data was stratified in age groups, gender and socioeconomic status. Mean and standard deviation was calculated for age. Frequency and percentage was calculated for gender, history of chronic illness, CT severity score category i.e. mild, moderate and severe, and presence of pulmonary fibrosis on follow-up. Chi square test was used to compare the CT severity score with age, gender, socioeconomic status and presence or absence of chronic illness in patients. Student T- test was used to compare CT severity score among the different age groups and gender. $P < 0.05$ to be statistically significant.

RESULTS

In this study the primary objective was to determine the frequency of pulmonary fibrosis among the patients with history of COVID-19. Secondary objective was to determine the degree of pulmonary involvement in suspected and diagnosed cases of COVID-19 patients.

Among the patients included in the study, 171 (45.6%) were male and 204 (54.4%) were females. Majority of the patients were of age group > 50 years. Details of the patients in various age groups are shown in the table 2. Other demographic details of the patients including socioeconomic status, BMI and history of various chronic co-morbidities are also shown in the table 2. The frequency of pulmonary fibrosis among the COVID 19 affected patients in our study population was 27.5% (103) with degree of pulmonary involvement: mild in 21 (20%), moderate in 39 patients (37.9%) and severe involvement in 43 of 103 patients (41.7%).

Data was stratified for various effect modifiers including age, gender, socioeconomic status, BMI, history of chronic illness, degree of pulmonary involvement and history of steroid use. The difference of incidence of pulmonary fibrosis was significant for gender, socioeconomic status, history of chronic illness and history of steroid use. Post stratification chi square p-value was significant. (Table no. 2)

Table No.1: Table showing 25-Point CT severity scoring for COVID 19 using HRCT

25-Point CT severity Score:	
Objective visual assessment by two observers of each lung lobe for the degree of involvement and classified as:	
0 or <5% involvement-score of 0	0
5–25%	1
26–50%	2
51–75%	3
>76% score	4
Total severity score will be then calculated by summing scores of all five lobes scores ranging from 0–25	
Total score:	Severity
7 or less	Mild
8-17	Moderate
18 or more	Severe

Table 1: showing the details of various outcome variables of the COVID - 19 patients

Variables		Pulmonary fibrosis		P value
		Yes	No	
Age	Upto 30 yrs	21	39	0.19
	30-50 years	36	86	
	>50 years	46	147	
Gender	Male	57	114	0.01
	Female	46	158	
Socioeconomic status	Poor class	35	67	0.002
	Middle Class	39	75	
	Upper Class	29	130	
BMI	Underweight	19	53	0.11
	Normal weight	22	74	
	Over weight	39	69	
	Obese	23	76	
History of chronic illness	DM	67	184	<0.00001
	HTN	84	160	
	IHD	95	27	
	CLD	88	36	
	CKD	97	30	
Degree of pulmonary involvement	Mild	21	89	0.01
	Moderate	39	107	
	Severe	43	76	
History of steroid use	Yes	24	233	<0.00001
	No	79	39	

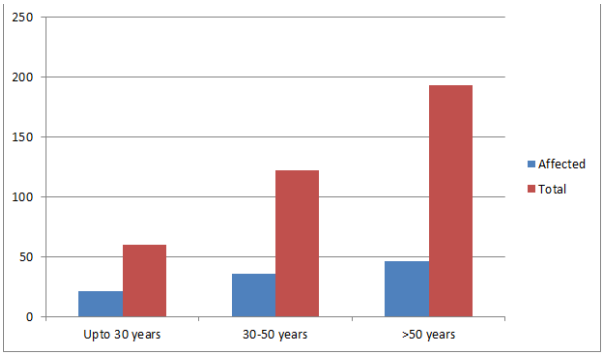

Figure No.1: incidence of pulmonary fibrosis in COVID patients with respect to age

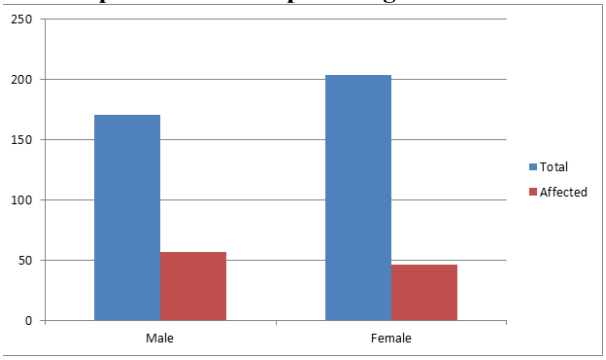

Figure No.2: Comparing the pulmonary fibrosis among males and females COVID patients

DISCUSSION

According to a report of WHO, around 80% of COVID-19 patients had mild infection, 14% had severe, while only 6% died. Acute respiratory distress syndrome patients can develop pulmonary fibrosis after few weeks of recovery.[5]

The occurrence of pulmonary fibrosis is determined by the intensity of COVID infection. Many theories have been offered as probable causes of post-COVID pulmonary fibrosis, including cytokine storm, which is caused by an abnormal immune system and contributes to the development of pulmonary fibrosis. The presence of residual pulmonary fibrosis in COVID-19 survivors after discharge is determined by a variety of parameters, including the patient's age, CT severity, consolidation/crazy-paving scores, and ICU stay.[6]

We investigated the progression of lung parenchymal alterations including lung fibrosis in this work. A total of 375 individuals were enrolled and observed for three months after recovering from COVID-19 pneumonia. As previously stated, almost one-fourth of the overall patients displayed indications of fibrotic abnormalities, with 41 percent having severe fibrosis. The current study was to the best of our knowledge, the first report of post-COVID-19 pulmonary fibrosis in our region. Various studies have referenced to COVID-19 symptoms over time; however, only a small number of studies have focused on lung fibrosis as the primary outcome.

In our study, pulmonary fibrosis after COVID-19 was strongly linked to patients aged 50 to 75, with a somewhat greater frequency in the middle age group. Post-pulmonary fibrosis was found to be substantially more common in patients with a history of co-morbid illnesses. According to Wong et al., elderly persons are more likely to acquire pulmonary fibrosis.[7]

A study reported that in the mild group of disease only 7 of 38 patients (18.4%) developed fibrosis whereas in the severe group pulmonary fibrosis was seen in 18 of 42 patients (42.8%), with overall incidence of pulmonary fibrosis of 25 in 80 patients (31.2%) Ali RMM, et al.[7] Yasin R, et al reported that out of 210 patients enrolled and followed, 101 patients (48.1%) showed pulmonary fibrosis on follow-up CT.[8] Evidence of pulmonary fibrosis was seen in 90 individuals after a 3-month CT scan (52.0 percent). Consolidation, severe illness, and a higher CT severity score at admission were all linked to a greater probability of fibrotic abnormalities seen on a 3-month CT scan. After a 6-month follow-up, 41 patients (66.1%) exhibited no significant changes in their fibrotic results, whereas the remaining 21 patients (33.9%) showed considerably decreased lung fibrosis.[9]

In the research by Han et al,[10] after 6 months of follow-up, fibrotic abnormalities were found in 35% of the patients, which was lower than our results.

Furthermore, following a 3-month follow-up, Ali et al. observed a rate of 32 percent for pulmonary fibrosis in COVID-19 patients, which was lower than what we discovered in our experiment. Changes in the research population, paraclinical measures and monitoring by technicians and clinicians might all explain the differences.

George PM, et al was of the opinion that there is currently no agreement on the use of anti-fibrotic medications in the prevention and treatment of COVID-19 survivors' lung fibrosis. These medicines, which are already used for interstitial lung disorders, can reduce pulmonary damage in high-risk individuals. Given that lung fibrosis is recognized as a significant adverse event in COVID-19 survivors, it is advised that a consensus be reached on including anti-fibrotic medications into the COVID-19 treatment recommendations, particularly for high-risk patients.

According to Ali et al., older age, cigarette smoking, greater CT severity score, and long-term mechanical ventilation were all connected to an increased risk of lung fibrosis.

Han X, et al reported after six-month follow-up, that 6% patients had dry cough, 10% sputum production 14% slight shortness of breath on exertion. Patients with pulmonary fibrosis more commonly experienced dry cough ($p < 0.05$). In this study, 35% patients of severe COVID-19 pneumonia developed pulmonary fibrosis within 6 months follow-up. Among these 40 of 114 patients with severe COVID-19 pneumonia, fibrosis in the lungs was seen in 55% (22/40) patients within 6 months follow-up.

Early detection of cases of post-COVID-19 pulmonary fibrosis may enable for the prevention or at least reduction of this debilitating complication.[11]

CONCLUSION

About 1/4 of the survivors had post-COVID-19 pulmonary fibrosis. Patients with severe COVID-19 pneumonia were also at a greater risk of developing pulmonary fibrosis. Furthermore, co-morbid conditions like old age and history of Covid treatment without steroids were linked to an elevated risk of post-COVID pulmonary fibrosis. Further follow-up of the patients should be done.

Author's Contribution:

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Final Approval of version:	Rafia Irum

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

REFERENCES

1. Lotfi M, Sefidbakht S, Moghadami M et al. Introduction of a Radiologic Severity Index for the 2019 Novel Corona Virus (COVID-19). Research Square 2020; 23633/v1
2. Jain U. Effect of COVID-19 on the Organs. Cureus 2020; 12(8): e9540.
3. Khaliq M, Raja R, Khan N, et al. An Analysis of High-Resolution Computed Tomography Chest Manifestations of COVID-19 Patients in Pakistan. Cureus 2020;12(7): e9373.
4. Simpson S, Kay FU, Abbara S et al. Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. Radiology: Cardiothoracic Imaging 2020;2:2 e200152
5. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol 2020;30(8):4381–4389.
6. Yasin R, Gomaa AAK, Ghazy T, Hassanein SA, Ibrahem RAL, Khalifa MH. Predicting lung fibrosis in post-COVID-19 patients after discharge with follow-up chest CT findings. Egyptian J Radiol Nuclear Med 2021;52(1):118.
7. Wong K, Antonio GA, Hui DS, et al. Severe acute respiratory syndrome: thin-section computed tomography features, temporal changes, and clinicoradiologic correlation during the convalescent period. J Comput Assisted Tomogr 2002;28(6):790–795.
8. Yasin R, Gomaa AAK, Ghazy T, et al. Predicting lung fibrosis in post-COVID-19 patients after discharge with follow-up chest CT findings. Egypt J Radiol Nucl Med 2021;52:118.
9. Nabahati M, Ebrahimpour S, Khaleghnejad Tabari R, Mehraeen R. Post-COVID-19 pulmonary fibrosis and its predictive factors: a prospective study. Egyptian J Radiol Nuclear Med 2021; 52(1):248.
10. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, et al. Six-month follow-up chest CT findings after severe COVID-19 pneumonia. Radiol 2021; 299(1):E177–E186.
11. Ademola S, Simon A, Oyeronke T, et al. Pulmonary fibrosis in COVID-19 survivors: predictive factors and risk reduction strategies. Pulmon Med 2020;5:1–10.

Frequency of Hyperhomocysteinaemia in Ischemic Stroke Patients

Muhammad Tahir[1], Talha Rasheeq[3], Nadeem Ullah[3], Kanwal Khan[4], Meer Wasiq[2] and Waqas Noor Chughtai[5]

ABSTRACT

Objective: To determine the frequency of hyperhomocysteinaemia in ischemic stroke patients and its association with other risk factors.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the department of general medicine Nishtar Hospital, Multan, from November 2020 to November 2021 for a period of one-year,

Materials and Methods: A total of 120 patients were enrolled from outpatients and emergency department of hospital. After clinical examination and 8 hours fasting venous blood sample was taken aseptically for ethylene diamine tetra acetate analysis. Main variables of study were age, gender, diabetes, hypertension and homocysteine level. SPSS version 23 was used for data analysis. Mean and SD was calculated for numerical data and frequency percentages for categorical data.

Results: Majority of the patients were (68.3%) between age group 40-60 years. Hypertension and diabetes mellitus was observed as (47.5%) and (31.7%), respectively. Among total 67.5% patients had hyperhomocysteinaemia, >15mmol/L. It was seen that the differences were not statistically significant.

Conclusion: Hyperhomocysteinaemia is a strong risk factor that is responsible for number of ischemic stroke incidents in Pakistani population. Preventive measures of hyperhomocysteinaemia will lessen the incidence of ischemic stroke.

Key Words: Ischemic stroke, Hyperhomocysteinaemia, Frequency

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INTRODUCTION

A stroke eventuates when blood flow to a part of brain is disturbed, averting oxygen and nutrients supply to the brain tissues. Starved brain cells begin to die within minutes. It is a medical emergency which requires immediate treatment is vital. It is one of the major causes of deaths in the world.[1] About 15 million people suffer a stroke annually, from which five million die and another five million incapacitated because of it creating further problems.[2] Ischemic stroke is serious concern for health care system though it is not fatal, but is a major source of morbidity in stroke patients.[3]

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One of the most paralyzing neurological disorders which is very demanding financially and mentally. There are dozens of risk factors out which some are constant, like age, gender and positive family history, while others are manageable, like diabetes, hypertension, hyperlipidaemia and hyper-homocysteinaemia. According to available data 70% of stroke cases are caused by known risk factors.[4,5] Early diagnosis of manageable risk factors of stroke helps in preventing the incidents of this disease. One of such factors is homocysteine level in blood, it can be easily managed as it is simple and efficient with minimum economic burden and safe to do. Therefore it is of utmost importance to observe the rate of hyper-homocysteinaemia amid patients with ischemic stroke.[6] Homocysteine is a Sulphur-containing amino acid derived from the metabolic demethylation of dietary methionine.5-12mmol/L is a normal amount of homocysteine in blood. More than normal range of homocysteine is responsible for oxidative damage to vascular endothelium with propagation of vascular smooth muscle and creates prothrombotic state as it affects thrombin, platelets and fibrin.[7] there is also a relation between high levels of homocysteine and atherosclerotic vascular disease.[8] Majority of studies also confirmed an association between higher homocysteine levels and stroke[9]. It is also observed that stroke patients with hyperhomocysteinaemia have a

higher chance of developing cerebral micro-angiopathy and multiple infarctions than others with normal homocysteine levels.[10]

It is evident from the above discussion that homocysteine levels have significant impact on human health. As most of the studies are on western population there is considerably few studies which have been done in Pakistani population; self-evidently eating habits, genetic profiles and life style of Pakistani populace is different therefore there is need of more local studies in this regard. The fore most drive of this study was to find out the rate of occurrence of hyperhomocysteinaemia in Pakistani patients suffering from ischemic stroke and its connection with other risk factors, as it is manageable factor, further studies may help in devising approaches in reducing stroke incidence and other complications related to it.

MATERIALS AND METHODS

The cross-sectional study was performed by means of convenience at the Nishtar Hospital, Multan, from Nov 2020 to Nov 2021. For this study ethical approval was taken from hospital ethical board. Patients suffering from Ischemic stroke were carefully chosen from the OPD and ED of the hospital. Informed consent from each patient was taken from each patient. The sample size was calculated using Open Epi, taking p-value as 0.5 with 95% CI.

Ischemic stroke was considered as neurological discrepancy lasting more than 24hours with diagnosed by a CT scan of brain or through indication of necrosis on CT scan of brain performed within 7 days of the episode.

All the patients with known previous history of ischemic strokes, ischemic heart disease, hypothyroidism, peripheral vascular disease, epilepsy as well as pregnant females and patients using medications which can alter homocysteine and also patients taking niacin, multivitamins, methotrexate, anticonvulsants, tamoxifen, bile acid sequestrants, nitrous oxide anesthesia were excluded.

4ml venous blood sample was taken in ethylene di-ammine tetra acetate EDTA vial from all patients after eight hours of fasting and sent to laboratory for analysis. Collected data was entered on predesigned performa. Data analysis was done by using SPSS version 23. Categorical data like gender, diabetes, and hypertension was presented as frequency and percentages(%). Numerical data like age and homocysteine values was presented as mean ± standard deviation. Test of significance student t-test (for numerical) and chi square test (for categorical) was applied to see association among study variables. P value below or equal to 0.05 was taken as significant.

RESULTS

One hundred and twenty patients were included in this study in which male (59.2%) and female (49%). The mean age of the patients was 55.65±9.75 years. Majority of the patients were (68.3%) between age group 40-60 years. Hypertension and diabetes mellitus was observed as (47.5%) and (31.7%), respectively (Table. I).

Overall, (67.5%) patients had hyperhomocysteinaemia, >15mmol/L. (Table. II). The mean homocysteine levels of the patients against the independent variable were shown in table. III. It was seen that the differences were not statistically significant. (Table. 3).

Table No.1: Demographic and baseline among the patients

Variable	N (%)
Gender	
Male	71 (59.2)
Female	49 (40.8)
Age distribution (years)	
40-60	80 (68.3)
61-75	38 (31.7)
Hypertension	57 (47.5)
Diabetes mellitus	38 (31.7)

Table No.2: Presence of hyper-homocysteinaemia among the patients

Homocysteine level	N (%)
≤15mmol/L	39 (32.5)
>15mmol/L	81 (67.5)

TableNo.3: Mean homocysteine levels of stroke patients against the variables

Variable	Category	N (%)	Homocysteine Mean±S.D	P-value
Gender	Male	71 (59.2)	16.25±1.49	0.254
	Female	49 (40.8)	15.95±1.18	
Age (years)	40-60	82 (68.3)	16.05±1.45	0.328
	61-75	38 (31.7)	16.31±1.21	
Hypertension	Yes	57 (47.5)	16.03±1.21	0.462
	No	63 (52.5)	16.22±1.52	
Diabetes mellitus	Yes	38 (31.7)	16.07±1.45	0.771
	No	82 (68.3)	16.15±1.35	

DISCUSSION

Hyperhomocysteinemia was observed to have a significant association with ischemic stroke in the study. Hyperhomocysteinemia was observed in 67.5% of our ischemic stroke patients (Table 2). Similar results observed by Niazi F et al. and Pezeshgi, P et al.[11,12] where they found Hyperhomocysteinemia in 50% and 64% of the patients. Some studies, however, have been unable to find a relationship between hyper-homocysteinaemia and stroke.[13] Males showed greater homocysteine levels than females in our research. Which is consistent with results by Malati Murmu KM et al. and Hao L et al.[14,15]

There was no significant link between homocysteine levels and age in our investigation. Similar results were observed by Huang S et al. and Narang AP et al.[16,17] Homocysteine levels have also been reported to rise with age in a few studies.[15] This conclusion may be explained in terms of nutritional status and vitamin consumption, which is expected to decline as people become older.

Homocysteine levels were not different in hypertensive ischaemic stroke in our research. The evidence on the link between homocysteine and hypertension has been mixed. Sharabi Yet al.[18]found no link between hypertension and homocysteine levels whereas, Narang AP et al.[16] found a link between hypertension and homocysteine levels. Hyperhomocysteinemia is thought to cause an elastolytic process in the artery wall by increasing serine elastase production and release. The lack of elastin can cause the artery wall to harden, leading to hypertension. Although other concurrent variables may also present, this might be one of the ways Hyperhomocysteinemia contributes as a risk factor for stroke.[19]

Similarly, homocysteine levels were not different in diabetic stroke patients. Similarly Narang AP et al. observed ischemic stroke are independent of diabetes mellitus.[16] Other research has shown mixed outcomes when it comes to the link between homocysteine levels and diabetes mellitus.[20] Further research on the relationship between homocysteine levels and diabetic stroke patients is needed.

This research provided a lot of good points. One of them was that the exclusion criteria included all conceivable confounders of homocysteine levels, and patients were rigorously eliminated from the trial if they had any confounders of homocysteine levels. Second, it measured homocysteine levels in fasting blood samples, as non-fasting blood samples in earlier investigations had shown elevated homocysteine levels.[18] Our study's sample size, on the other hand, was rather modest. As a result, more research should be conducted in various sections of the country. Hyperhomocysteinemia is a preventable risk factor linked to a high proportion of ischemic stroke patients in Pakistan's population. Hyperhomocysteinemia prevention would lower the incidence of stroke and, as a result, the prevalence of ischemic stroke in Pakistan.

CONCLUSION

Hyperhomocysteinaemia is a strong risk factor that is responsible for number of ischemic stroke incidents in Pakistani population. Preventive measures of hyperhomocysteinaemia will lessen the incidence of ischemic stroke.

Author's Contribution:

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REFERENCES

1. Katan M, Luft A. Global Burden of Stroke. Semin Neurol 2018;38(2):208-211.
2. Venketasubramanian N, Yoon BW, Pandian J, Navarro JC. Stroke Epidemiology in South, East, and South-East Asia: A Review. J Stroke 2017;19(3):286-294. doi: 10.5853/jos.2017.00234. Epub 2017 Sep 29. Erratum in: J Stroke 2018;20(1):142.
3. Avan A, Digaleh H, Di Napoli M, Stranges S, Behrouz R, Shojaeianbabaei G, et al. Socioeconomic status and stroke incidence, prevalence, mortality, and worldwide burden: an ecological analysis from the Global Burden of Disease Study 2017. BMC Med 2019;17(1):1-30. https://doi.org/10.1186/s12916-019-1397-3.
4. Long DL, Howard G, Long DM, Judd S, Manly JJ, McClure LA, et al. An Investigation of Selection Bias in Estimating Racial Disparity in Stroke Risk Factors: The regards Study. Am J Epidemiol 2019;188(3):587–597, https://doi.org/10.1093/aje/kwy253.
5. Arina CA, Amir D, Siregar Y, Sembiring RJ. Correlation between homocysteine and dyslipidemia in ischaemic stroke patients with and without hypertension. InIOP Conference Series: Earth and Environmental Sci 2018;130(1):012005. IOP Publishing.https://iopscience.iop.org/article/10.1088/1755-1315/130/1/012005/meta
6. Zhang T, Jiang Y, Zhang S, Tie T, Cheng Y, Su X, et al. The association between homocysteine and ischemic stroke subtypes in Chinese: A meta-

analysis. Medicine (Baltimore) 2020;99(12):e19467.
7. Memtsas VP, Arachchillage DRJ, Gorog DA. Role, Laboratory Assessment and Clinical Relevance of Fibrin, Factor XIII and Endogenous Fibrinolysis in Arterial and Venous Thrombosis. Int J Molecular Sci 2021;22(3):1472. http://dx.doi.org/10.3390/ijms22031472
8. Esse R, Barroso M, Tavares de Almeida I, Castro R. The Contribution of Homocysteine Metabolism Disruption to Endothelial Dysfunction: State-of-the-Art. Int J Molecular Sci 2019;20(4):867.
9. Kloppenborg RP, Nederkoorn PJ, van der Graaf Y, Geerlings MI. Homocysteine and cerebral small vessel disease in patients with symptomatic atherosclerotic disease. The SMART-MR study. Atherosclerosis 2011;216(2):461-6.
10. Piao X, Wu G, Yang P, Shen J, De A, Wu J, Qu Q. Association between homocysteine and cerebral small vessel disease: a meta-analysis. J Stroke Cerebrovascular Diseases 2018;27(9):2423-30. https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.04.035
11. Niazi F, Aslam A, Khattak S, Waheed S. Frequency of Homocysteinemia in Young Ischemic Stroke Patients and Its Relationship with the Early Outcome of a Stroke. Cureus 2019;11(9):e5625.
12. Pezeshgi P, Zali A, Safari S, Akhlaghdoust M, Sharghi A. Marandi. Homocysteine Levels and Ischemic Stroke: A Systematic Review. J Cellular Molecular Anesthesia 2021;6(3):269-75.
13. Verhoef P, Hennekens CH, Malinow MR, Kok FJ, Willett WC, Stampfer MJ. A prospective study of plasma homocyst(e)ine and risk of ischemic stroke. Stroke 1994;25(10):1924-30.
14. MalatiMurmu KM, Dash S, Singh LK, Kar A, Mishra PK. Study of serum homocysteine level in cases of non-diabetic ischemic stroke. Int J Res Med Sci 2018;6(5):1611.
15. Hao L, Ma J, Zhu J, Stampfer MJ, Tian Y, Willett WC, Li Z. High prevalence of hyperhomocysteinemia in Chinese adults is associated with low folate, vitamin B-12, and vitamin B-6 status. J Nutr 2007;137(2):407-13.
16. Narang AP, Verma I, Kaur S, Narang A, Gupta S, Avasthi G. Homocysteine--risk factor for ischemic stroke? Ind J Physiol Pharmacol 2009;53(1):34-8. https://pubmed.ncbi.nlm.nih.gov/19810574/
17. Huang S, Cai J, Tian Y. The Prognostic Value of Homocysteine in Acute Ischemic Stroke Patients: A Systematic Review and Meta-Analysis. Front Syst Neurosci 2021;14:600582.
18. Sharabi Y, Doolman R, Rosenthal T, Grossman E, Rachima-Maoz C, Nussinovitch N, et al. Homocysteine levels in hypertensive patients with a history of cardiac or cerebral atherothrombotic events. Am J Hypertens 1999;12(8 Pt 1):766-71.
19. Perry IJ, Refsum H, Morris RW, Ebrahim SB, Ueland PM, Shaper AG. Prospective study of serum total homocysteine concentration and risk of stroke in middle-aged British men. Lancet 1995;346(8987):1395-8.
20. Adunsky A, Weitzman A, Fleissig Y, Levenkrohn L, Arad M, Doolman R, et al. The relation of plasma total homocysteine levels to prevalent cardiovascular disease in older patients with ischemic stroke. Aging (Milano) 2000;12(1):48-52.

Understanding the Gap: Evaluation of General Practitioner's Awareness and Expertise in Managing Substance Use and Addiction in South Punjab, Pakistan

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ABSTRACT

Objective: To determine General practitioner's (GPs) awareness and expertise in management of substance use disorders in southern Punjab, Pakistan.

Study Design: Descriptive Cross-sectional study

Place and Duration of Study: This study was conducted at the department of Psychiatry, Multan Medical and Dental College, Multan, from May 2020 to April 2021.

Materials and Methods: One hundred and three general physicians/ practitioners practicing in public and private setups in South Punjab were interviewed for the study. A self-formulated questionnaire was filled by health care professionals. Data analysis was done by using SPSS version 23. Mean and frequency were calculated and also chi square test was applied. P value ≤0.05 was taken as significance.

Results: The mean age 34.86±9.16and mean experience of PGs were7.93±6.89years. Almost all participants agreed that substance use is a serious issue. However nearly 1/3rd to ½ of the respondents could not correctly identify the classical withdrawals of opioid or disadvantages of long term use of benzodiazepines. One-third of the group was unaware that Delirium Tremens is a serious life threatening complication of Alcohol withdrawal. 71% admitted that they don't feel confident in managing addiction related cases and more than 90% showed willingness to attend workshops and CMEs related to management of substance use disorders. There was no statistically significant difference in groups divided on the base of age or experience of respondents.

Conclusion: In southern Punjab, Pakistan, while most GPs agree about the seriousness of substance abuse disorders, majority are not well trained in tackling it and don't feel confident in managing patients related to addiction. There is a dire need for revision courses, lectures and workshops related to this topic for our general practitioners and family physicians on both private and public fronts.

Key Words: General practitioner, Substance use, Addiction and South Punjab

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INTRODUCTION

Substance abuse or addiction is a serious dilemma affecting many globally across all countries and culture. This issue is a growing concern as it leads to compromised functionality and productivity on an individual basis as well as of the family unit and society at large. Illicit drugs are drugs for which non-medical use has been banned by international drug control treaties because they cause risks of addiction to users and various physical and psychological adverse effects[1]. UNODC estimated that 149–271 million people aged 15–64 years (3·3–6·1%) had used an illicit drug at least once in 2009[2]. There is also a higher risk of mental health issues as well as infectious diseases transmitted by blood in these individuals[3].

Pakistan is one of the ten most populous country in the world (population: 197 million) and holds a very significant position in south Asia in terms of drug trafficking and usage. In the past several years, the rate of drug use has gone up all across the country. A collaborative study done by the Government of Pakistan's Ministry of Interior and Narcotics Control

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reports that nearly 6.7 million people had used any controlled substance including misuse of prescribed drugs. Cannabis was the most commonly used drug with a prevalence of 3.6 per cent among individuals with age ranged from 15 to 64 years. About 860,000 individuals are regular heroin users and 320,000 are opium users that are about 0.8 and 0.3 per cent of the population respectively[4].

Globally, primary care physicians and general practitioners form the first line of defense in identifying and managing addiction related issues even in the western countries. Saitz et al from US emphasizes that there is a dire need to enable and encourage general physician in addiction management across USA[5]. The same argument is followed in an article by Tedeschi et al from New Mexico who opines that "in the face of one of the country's most pressing and fastest-growing public health crises, few primary care doctors treat substance abuse disorders, even though they are uniquely positioned to recognize problems and help patients before it's too late" [6]. There is also a growing concern that the general physicians themselves may be playing an unconscious role in adding to the addiction burden by unsafe prescription practices especially of tranquilizers and opioid analgesics[7]. Several studies argue that the possible causes of sub-optimal management of addiction-related issues by general practitioners may include little or no training, lack of confidence in self-competence, lack of support by the government health care structure and limited availability of time and resources[8-9].

Considering the burden of substance abuse and drug dependence, Pakistan is not fully equipped in term of expertise in managing drug detoxification and substance use disorders. There are approximately around 500-800 fully qualified psychiatrists in Pakistan which amounts to roughly one psychiatrist for half million population[10].

There is no formally trained addiction specialist in the entire country. The onus of treatment ultimately falls on the general practitioners and family physicians running private or government-based setups. They are the first line of contact for most Pakistanis. In the absence of any CME programs or GP-training forums, it is speculated that the general practitioners in Pakistan may not be very well-versed in identifying and/or managing substance abuse and addiction.

This is especially true for south Punjab where the burden is huge and expertise is low. However, to our knowledge, no such study has been conducted in Pakistan till date to validate or invalidate this assumption. This study aims to explore the current knowledge, perception and management expertise of general practitioners in managing substance use related issues in South Punjab, Pakistan. It is hoped that it will shine light on the expertise vacuum [if any] and pave way for robust educational and training measures for our GPs in terms of addiction management.

MATERIALS AND METHODS

Study was conducted at department of Psychiatry, Multan Medical and Dental College, Multan, from May 2020 to April 2021. Total 103general physicians/ practitioners practicing in public and private setups in South Punjab were interviewed for the study. After taking informed written consent from the participants and approval from the institutions, a self-formulated questionnaire will be filled by health care professionals. This questionnaire includes various parts including the demographic details of the participants, their knowledge about the identification of symptoms and withdrawal effects of various common drugs of abuse as well as their current management protocols in contrast or in keeping with the current NICE guidelines [each question will either have four options, [one being the correct one] or a true/false statement question]. Participants were ensured confidentiality and ethical approval from relevant institution were taken.

Data was entered in Statistical package for social sciences (SPSS) and analyzed. Mean and standard deviation were calculated for numerical data like age, experience in years and frequency, percentages were calculated for categorical data like gender, questions regarding expertise and awareness etc. Chi-square test was applied for categorical variables. P value ≤ 0.05 was taken as significant.

RESULTS

One hundred and three GPs were interviewed in this study, the mean age 34.86±9.16and mean experience of GPs were7.93±6.89years. Majority of the participant were male, age upto 35 years, experience up-to 5 years followed by 6-10 years and working in public sector [78 (75.7%), 74 (71.8%), 52 (50.5%), 32 (31.1%) and 93 (93.2%) respectively]. (Table. I).

According to our study results regarding knowledge and awareness 102 (99%) GPs agreed that drug addiction is a common worldwide problem. According to all participants knowledge (in terms of answering) pattern showed that 61% of the GPs could correctly identify body aches/lacrimation 66 (64.1%) as the classical withdrawals of opioid addiction whereas the remaining chose wrong options (confusion/ psychological craving (19.4%), agitation/psychosis (12.6%) and fever/tachycardia (3.9%). 63 % of the participants correctly guessed delirium tremens as the serious life threatening complication of Alcohol withdrawals. [Remaining chose respiratory depression 28 (27.2%), alcoholic hallucinosis 9 (8.7%) and dementia 1 (1.0%)].

Only 20% of the GPs could correctly guess that long term use of Benzodiazepines can cause dementia

whereas roughly more than half incorrectly chose the option of seizures 56 (54.4%). Only 38% rightly identified nicotine as the substance with most psychological craving related withdrawals. Buprenorphine was correctly chosen as an option used globally for opioid detoxification by 82 GPs (79.6%). About half of the respondents correctly identified Methamphetamine 54 (52.4%) as a stimulant drug whereas rest chose LSD 40 (38.8%), Marijuana 6 (5.8%) and alcohol 3 (2.9%) as answers. Nearly 62% of the respondents were rightly aware that Ice is the new stimulating drugs commonly used among university/college students.

In this study, majority of General practitioners 74 (71.8%) reported having no confident and competent in managing addiction related issues and 52 (50.5%) admitted that they do not prescribe with clear justification. 93 (90.3%) of the respondents agreed that workshop and training will benefit them and 94 (91.3%) GPs showed willingness to attend. General practitioners narrated different factors which are involved in lack of management regarding addiction-related cases i. e. due to lack of knowledge on recent management guidelines, lack of time in patient interaction, lack of resources/medicine availability and stigma/fear about handling such patients 34 (33%), 30 (29.1%), 26 (25.2%) and 13 (12.6) respectively. When asked about how frequently do they see addiction related cases in their clinics, 67 (65%) reported at least more than once a month. There was no significant difference in answers between groups divided on basis of age of GPs and/or their years of experience (Table-2).

Table No.1: Demographic detail of participants in the study

Variables	Mean & SD	Mean & SD
Age (years)		34.86±9.16
Upto 35 years	74 (71.8)	
More than 35 years	29 (28.2)	
Gender		
Male	78 (75.7)	
Female	25 (24.3)	
Experience(years)		7.93±6.89
Upto 5 years	52 (50.5)	
6-10 years	32 (31.1)	
More than 10 years	19 (18.4)	
Working place		
Public sector	93 (93.2)	
Private sector	5 (4.9)	
Both sectors	2 (1.9)	

Table No.2: Expertise in management of addiction related issues with age & experiences

Expertise and management skills		Age groups (years)		P-value	Experience (years)			P-value
		Upto 35 n - (%)	> 35 n - (%)		Upto 5 n - (%)	6-10 n - (%)	> 10 n - (%)	
Confident & competency level	Yes	(21.4)22	(6.7)07	0.634	(14.6)15	(6.8)07	(6.8)07	0.510
	No	(50.5)52	(21.4)22		(35.9)37	(24.3)25	(11.6)12	
Benefit from training	Yes	(66.9)69	(23.3)24	0.140	(46.6)48	(28.2)29	(15.6)16	0.593
	No	(4.9)05	(4.9)05		(3.8)04	(2.9)03	(2.9)03	
Prescribe with justification	Yes	(36.9)38	(12.6)13	0.662	(22.3)23	(15.6)16	(11.6)12	0.368
	No	(34.9)36	(15.6)16		(28.1)29	(15.6)16	(6.8)07	
Workshops on safe description guidelines	Yes	(68.0)70	(23.3)24	0.113	(48.6)50	(27.2)28	(15.6)16	0.191
	No	(3.8)04	(4.9)05		(1.9)02	(3.8)04	(2.9)03	
Factors manage addiction due to lack of time, medicine, knowledge & stigma or fear	Time	(18.4)19	(10.7)11	0.479	(13.6)14	(10.7)11	(4.9)05	0.888
	Medicine	(19.4)20	(5.8)06		(12.6)13	(6.8)07	(5.8)06	
	Knowledge	(23.4)24	(9.7)10		(17.5)18	(8.7)09	(6.8)07	
	Stigma/ fear	(10.7)11	(1.9)02		(6.8)07	(4.9)05	(0.9)01	

DISCUSSION

Early services can be provided through different settings like primary care offices and school clinics. Provision of management facility at mild substance disorders can provide better management[11]. Purpose of early intervention is to reduce the disadvantages of substance misuse that may lead to serious injury. But for achievement of goals with use of this intervention needs training of practitioners[12].

In our study mean age of practitioners was 34.86±9.16 years and mostly were upto 35 years of age. We observed statistically insignificant correlations between age of participant and their attitude towards substance use. A study conducted by Barral et al[13] who reported contrast findings to our study. He reported statistically significant correlation between age and attitude after training of practitioners.

In our study, it was noteworthy that almost all participants agreed that substance use is a serious issue. However nearly 1/3rd to ½ of the respondents could not correctly identify the classical withdrawals of opioid or disadvantages of long term use of benzodiazepines. One-third of the group was unaware that Delirium Tremens is a serious life threatening complication of Alcohol withdrawal. 71% admitted that they don't feel confident in managing addiction related cases. This reflects on the concerning gaps in the knowledge base of our family physicians and general practitioners and makes a strong case for need of workshops, CMEs and revision courses as more than 90% showed willingness to attend such sessions.

A study was conducted by Gomes et al[14] in 2003 and reported a significant gap between skills/expertise of physicians regarding diagnosis of alcohol related health problems. About 1/4th of general practitioners were unaware of drinking symptoms among men and women. Roche et al[15] reported that experience of GPs regarding patients using alcohol or alcohol products are varies according to their role and perception of practice. Prochaska et al[16] conducted a study on training of physicians to treat substance use and concluded that training and education of physicians gained too much attention and training guidelines have been developed to improve substance abuse education in practitioners. Geller et al[17] hypothesized that development of curriculum to manage end stage substance abuse is necessary and lack of expertise in this field contribute to negative attitude.

In a survey conducted by National center of substance abuse at Columbia University and 648 physicians were recruited. Survey reported that only 510 subjects receiving substance use treatment. About 50% of patients visiting these clinics described that their physician didn't considered substance abuse[18]. Similarly Chappel and Veach[19] concluded that course of substance use should be included in curriculum of medical education. A minimum 28 hours lecture briefing is sufficient for improvement in attitude of medical professionals towards substance use.

Strang et al[20] conducted a study on this topic and reported that in England half of GPs are prescribing medications for control of drug abuse and 32% of GPs were involved in treatment of substance use at primary care level. Primary care organizations need to plan

different programs and refresher courses on substance use and control of its harmful effects.

CONCLUSION

Southern Punjab belt in Pakistan is often ignored in terms of health care facilities. Substance abuse disorder is a huge issue in this region and the quality of treatment centers as well as expertise of physicians treating is sub-optimal. General practitioners and family physicians are usually the first point of contact for majority of the patients and as per our study findings, our GPs are currently not well-equipped in handling these cases in terms of expertise and knowledge. The heartening news is that they are willing to learn and update their knowledge according to the new guidelines.

The authors propose conducting similar studies in other regions of Pakistan and developing a uniform educational tool and platform to train our GPs in managing and identifying substance use disorders. These educational activities should be time-conscious and more practical and hand-on for optimal utilization. Both public and private health sector needs to hold hands to achieve this much needed milestone together.

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REFERENCES

1. Babor TF, Caulkins J, Edwards G, et al. Drug policy and the public good. Oxford: Oxford University Press; 2010.
2. Degenhardt L, Hall W. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. Lancet 2012;379 (9810):55-70.
3. Lehman AF, Dixon L. Double jeopardy: Chronic mental illness and substance use disorders. Routledge 2016;12:320. https://doi.org/10. 4324/9781315534770
4. Drug use in Pakistan. Narcotics Control Division, Government of Pakistan; 2013. (Accessed on 22nd May 2019) Available from URL:https:// www.unodc. org/do.
5. Saitz R, Daaleman TP. Now is the time to address substance use disorders in primary care. An Family Med 2017;15(4):306.
6. Tedeschi B. Watching the ship sink: why primary care doctors have stayed out of the fight against opioids. https://www.statnews. com/2016/10/19/ primary-care-doctors-opioid-treatment. Published Oct 19, 2016. Accessed Jun 10, 2017.
7. Prathivadi P, Barton C, Mazza D. Qualitative insights into the opioid prescribing practices of Australian GP. Family Pract 2020;37(3):412-7.
8. Desveaux L, Saragosa M, Kithulegoda N, Ivers NM. Family Physician Perceptions of Their Role in Managing the Opioid Crisis. An Family Med 2019;17(4):345-51.
9. Levy S, Seale JP, Alford DP. Medicine, with a focus on physicians: Addressing substance use in the 21st century. Substance Abuse 2019;40(4):396-404.
10. Javed A, Khan MN, Nasar A, Rasheed A. Mental healthcare in Pakistan. Taiwan J Psychiatr 2020;34:6-14.
11. Agerwala SM, McCance-Katz EF. Integrating screening, brief intervention, and referral to treatment (SBIRT) into clinical practice settings: A brief review. J Psychoactive Drugs 2012; 44(4):307–17.
12. Manuel JK, Satre DD, Tsoh J, Moreno-John G, Ramos JS, McCance-Katz EF, et al. Adapting screening, brief intervention, and referral to treatment for alcohol and drugs to culturally diverse clinical populations. J Addiction Med 2015;9(5):343–51.
13. Barral C, Eiroa-Orosa FJ, Navarro-Marfisis MC, Roncero C, Casas M. Assessing knowledge and attitudes towards addictions in medical residents of a general hospital. Drugs: Education, Prevention and Policy 2015;22(6):457–62.
14. Gomes B, Murnion B, Haber P, Fucito L. General practitioners' diagnostic skills and referral practices in managing patients with drug and alcohol-related health problems: implications for medical training and education programs. Drug and Alcohol Rev 2003;22(4):417–24.
15. Roche AM, Parle MD, Stubbs JM, Hall W, Saunders JB. Management and treatment efficacy of drug and alcohol problems: what do doctors believe? Addiction 1995;90:1357–66.
16. Prochaska JJ, Fromont SC, Louie AK, Jacobs MH, Hall SM. Training in tobacco treatments in psychiatry: a national survey of psychiatry residency training directors. Acad Psychiatr 2006; 30:372–378.
17. Geller G, Levine DM, Mamon JA, Moore RD, Bone LR, Stokes EJ. Knowledge, attitudes, and reported practices of medical students and house

staff regarding the diagnosis and treatment of alcoholism. JAMA 1989;261:3115–20.

18. CASA. The National Center on Substance Abuse at Columbia University. *Missed opportunity: national* survey of primary care physicians and patients on substance abuse. National Center on Substance Abuse at Columbia University: New York; 2000.
19. Chappel JN, Veach TL. Effect of a course on students' attitudes toward substance abuse and its treatment. J Med Educ 1987;62:394–400.
20. Strang J, Sheridan J, Hunt C. The prescribing of methadone and other opioids to addicts: national survey of GPs in England and Wales. Bri J Gen Pract 2005;55:444–51.

Development of Islamic Work Ethics Measurement Tool in Health Professional Education in Pakistan

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ABSTRACT

Objective: To develop a data collection instrument that can measure the observance of Islamic Work Ethics in health professional academicians, because lack of such a questionnaire was observed in the academic literature.
Study Design: A mixed-methods exploratory study
Place and Duration of Study: This study was conducted at the Riphah International University and HITEC-IMS, Taxila during a period of 6 months from April to September 2021.
Materials and Methods: A tentative questionnaire was designed by combining the qualitative data from focus group discussions with literature. The tentative questionnaire was then refined during the subsequent stages of a modified Delphi study, conducting cognitive pre-testing interviews and pilot testing of the novel instrument.
Results: The tentative questionnaire developed via Delphi study was then refined by conducting cognitive pre-testing interviews to ensure the prospective respondents easily and clearly understood the questionnaire items in the same manner as the primary researcher designed them. Pilot testing of the novel instrument was then performed to establish its reliability.
Conclusion: A data collection instrument was developed following the guidelines as put forth in the academic literature. The instrument developed is reliable and fit for purpose. The instrument can be utilised to measure the observance of Islamic work ethics in health professional academics, and necessary actions can be taken to reinforce ethical behaviours and remedy unethical behaviours.

Key Words: Islamic work ethics, measurement tool, medical education.

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INTRODUCTION

The rising incidence of ethical misconduct in the medical profession has provoked a global response in stressing the need for ethics education and inculcation of ethical behaviours[1,2]. A study in India reported that the observance of professional ethics is even lower among dental professionals than their medical counterparts[3]. It is the need of the hour to remediate the rising unethical behaviours and practices, especially in the face of increasing social accountability.

In developing countries like Pakistan, there has been a growing rift & miscommunication between doctors and patients, leading to increased dissatisfaction in patients. Some of it can be attributed to the lack of resources and facilities in our healthcare setup, but the doctors are not blameless in this matter. The mindset of health professionals has increasingly become materialistic, and the moral and ethical standards have been on a gradual decline over time. A study investigated the level of awareness of medical ethics among the health professional staff of a tertiary care hospital in Lahore. The study reported a general lack of awareness regarding medical ethics in all respondents ranging from house officers to consultants[4]. In addition, the physicians had poor knowledge about patient autonomy and patient rights; a result echoed in another study which proposed that patient's wishes may not be respected by health professional staff at all times[5].

The studies regarding the work ethic mainly come from the USA and Europe, relatively few studies are conducted in developing countries, and thus further research is needed. In addition to the insufficient work ethic studies in developing countries, research regarding Islamic work ethic (IWE) and its implications in the workplace are limited[6].

The field of measuring Islamic work ethics is relatively nascent compared to that of Protestant work ethics, and hence relatively minor work has been done in the field. The most cited work is that of Mr. Ali[7].

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However, most of the studies use Mr. Ali's questionnaire as such, without any further exploration. Moreover, there were additional deficiencies in Mr. Ali's questionnaire, namely that it was under the heavy influence of both Marx Weber's work on Protestant work ethics and Arabic culture. Hence, a study sought to construct a questionnaire free from protestant religious and Arabic cultural biases[8]. However, this new questionnaire was developed in Indonesia. Moreover, the pilot study used for quantitative data analysis was done in the banking sector with respondents being employees of Islamic banks, so its generalize-ability to the milieu of cultural and organisational settings of Pakistan's medical sector is questionable.

MATERIALS AND METHODS

The study is of a mixed-method, exploratory design that is typically utilised for questionnaire development. The research project follows the guidelines and 9 step process laid down in AMEE guide regarding development of questionnaires[17] as shown in Figure 2. The research methodology consisted of the following sequential steps, following the guidelines of the literature, starting from a comprehensive literature review that informed and guided the focus group discussions, which led to creating a tentative questionnaire upon which expert consensus was achieved during a modified Delphi study. Next, the questionnaire was refined by conducting cognitive interviews. Lastly, the reliability of the questionnaire and correlation among Islamic ethical constructs was established through the pilot study.

Place & Duration of Study: A multi-centre study was conducted at Riphah International University and HITEC - Institute of Medical Sciences, Taxila. The study duration was six months from April to September 2021.

Sampling: Purposive sampling, homogenous sampling subtype was performed technique was chosen to include knowledgeable experts regarding Islamic ethics, medical education, and questionnaire construction.

Declared population was health professional academicians of PMC recognised private and public sector medical & dental teaching institutions.

Inclusion Criteria:

1. Educational leadership, as defined as principal, vice principal and dean of medical institutions.
2. Educational experts as defined as members of DME departments of medical institutions.

Exclusion Criteria: Early career positions in academia, as defined as demonstrators and registrars.

Sequence of Mixed Methods: An alternating sequence of qualitative and quantitative data collection and data analysis processes were performed. Both qualitative and quantitative processes had equal importance, and the results of one process guided and informed the next step in the research process.

Literature Review & Formation of Qualitative Questionnaire For Focus Group Discussions

Islamic ethical constructs of Unisation/Tawheed, Itqan/Ihsan, Amanah/Adl, Consultation/Shura and Dignity were identified from the literature The databases of Google Scholar, PubMed, Research Gate, ERIC and Pakmedinet were utilised, Pakmedinet is a database that indexes all the research work performed in the local context of Pakistan. The keywords utilised were 'Islamic Work Ethics', 'Islamic Work Ethics Measurement', 'Islamic Professionalism', 'Islamic Medical Ethics', 'Snowball search method', 'Snowball literature review'. The search queries were carried out using keywords and phrases using the Boolean operators (i.e., 'AND' and 'OR') in various combinations. Wherever possible advanced search options were utilised to search in publication title and abstract preferably.

Focus Group Discussions: Focus group discussions were conducted because they allow for an in-deep exploration of a wide range of views and knowledge; they also allow for a healthy discussion among the participants, which results in multiple perspectives on a topic being presented and explored[9–11].

Modified Delphi Study: A modified Delphi study was conducted to achieve consensus amongst the expert panel on the inclusion of tentative questionnaire items in the questionnaire. Delphi study consensus achievement is defined as 80% agreement of respondents on questionnaire items after a maximum of three rounds.

Conduction of Cognitive Pretesting Interviews: Cognitive pre-testing is performed to collect evidence for response process validation. The process assesses how the prospective respondents understand and interpret the questionnaire and response items. The objective of the cognitive pre-testing process is to ensure that respondents understanding of questionnaire items is the same as the questionnaire developer's and that there are no misinterpretations or confusion in the respondents regarding the questionnaire and response items[12].

Pilot Testing of Newly Developed Questionnaire: Pilot testing was performed to establish the reliability & internal consistency of the newly developed instrument via measurement of Cronbach α and to observe the correlations such Item-Total corelation and Pearson's corelation between the various Islamic ethical constructs present in the instrument. Measures of dispersion were also calculated from the data collected. The statistical analysis was performed on SPSS version 26.

RESULTS

Development of Preliminary Questionnaire through Literature Review and Focus Group Discussions: Two focus group discussions with six members each were conducted to further elaborate upon the Islamic ethical constructs identified in the literature review phase. First, the expert panel described the possible sub-themes of constructs identified from the literature. Second, the ethical behaviours described by the expert panel underwent qualitative analysis; during the first cycle of coding, 80 codes were identified, which subsequently condensed and merged into 30 codes in the second cycle of coding. Finally, tentative questionnaire items were synthesised from a combination of qualitative data from focus groups and literature.

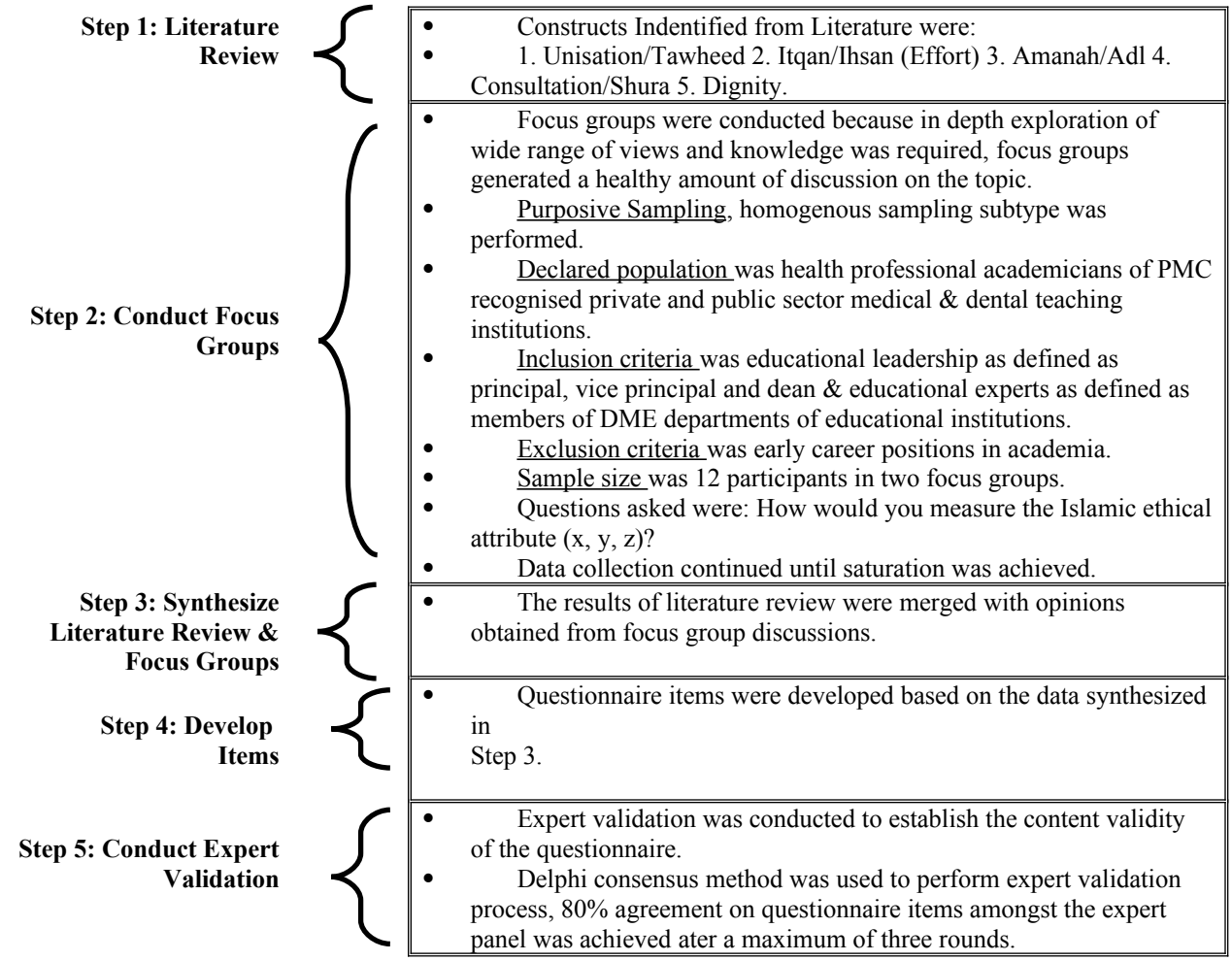
Cognitive Pretesting Interviews: The panel consisting of five faculty members gave feedback that 51 questionnaire items were clearly worded and easily understandable, while 15 questionnaire items were rephrased to make their meaning clearer and more evident.

Table No.1: Modified Delphi Study Results

No. of Items Achieving Consensus	No. of Items Not Achieving Consensus	Response Rate
1st Round		
63	5	62% (33 out of 53)
2nd Round		
3	2	84% (28 out of 33)

Table No.2: Statistical Analysis

Statistical Analysis	Value
Reliability	
Cronbach α	0.9
Item Total Correlation	0.2-0.7
Pearson's Correlation	
Correlation of Unisation/Tawheed with Itqan/Ihsan; Amanah/Adl	.603; .569
Correlation of Itqan/Ihsan with Amanah/Adl; Consultation/Shura; and Unisation/Tawheed	.557; .555; .603



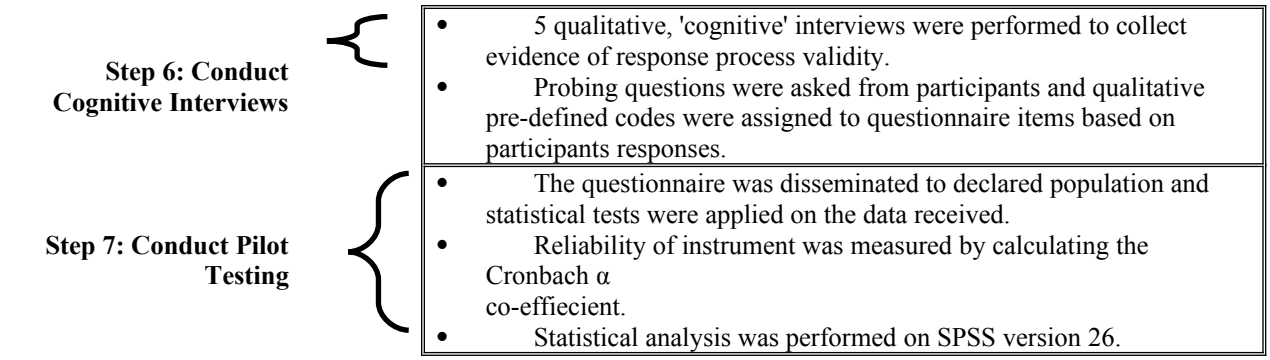


Figure No.1: Research Methodology, adapted according to AMEE Guide No. 87.[8–12, 20-22]

Pilot Study: The newly developed instrument was field-tested at both research sites, namely Riphah International University and HITEC-IMS, Taxila. The sample size was thirty-four respondents, with guidance from literature[13,14] and valuable feedback from Riphah's faculty members. The reliability of the instrument was established via the measurement of Cronbach α in SPSS version 26. In addition, means of dispersion, Item-Total correlation and Pearson's correlation amongst the Islamic ethical constructs was also measured as shown in Table 2.

DISCUSSION

The Delphi study is an iterative approach for achieving content validity for a new questionnaire. First, evidence for the instrument's content validity was gathered in the form of feedback from a panel of five medical education experts as part of a modified Delphi study under the guidance of literature[15,16]. The validated questionnaire was then sent to a panel of fifty-two experts during the first round of modified Delphi study to achieve consensus on the inclusion of questionnaire items in the questionnaire. Results were obtained from the modified Delphi study on a 5-point Likert scale.

Cognitive pre-testing interviews were also conducted to establish the response process validity of the instrument by ensuring that none of the questionnaire items were ambiguous or hard to understand for the prospective respondents.

Item-Total correlation is a test of reliability and internal consistency. The values range from 0.2 to 0.7, which is within acceptable limits and indicates a good relationship of items with constructs and subconstructs[17].

There is a strong correlation between Islamic ethical constructs of Unisation/Tawheed and Itqan/Ihsan; Amanah/Adl because Pearson's correlation value is 0.5 or more[18]. The strong correlation signifies those respondents who believe in Tawheed also tend to be more hardworking and facilitatory to other people and are just and fair in their dealings.

Practical Applications of Instrument / Strength of Study

The data obtained from the instrument's administration will help recognise the ethical and unethical behaviours being performed. Subsequently, an ethics course may be designed to reinforce ethical behaviours and perform remedial actions for unethical behaviours identified in a given population.

An example of such an Islamic bioethics course is "The Fiqh of Medicine" online course conducted by Al Balagh academy in the UK. The course discusses the relationship of medical fiqh with Islamic bioethics and incudes the topics within Islamic theology, Usul Al-fiqh, epistemology and fiqh of modern-day medicine and exemplified by practical application of these topics on contemporary medical cases.[19]

Recommendations: It is recommended for future researchers to apply the novel questionnaire in different contextual settings and adapt the questionnaire for its applications on clinicians to broaden its scope.

CONCLUSION

The final questionnaire developed comprises sixty-six questionnaire items measuring five Islamic ethical constructs on a 5-point Likert scale, and it is meant to measure the observance of Islamic ethical values in health professional academicians. The instrument has good content validity, and it has high reliability to serve its function. Moreover, the data obtained from the administration of the instrument can highlight the deficiencies in the ethical environment of our workplaces and the daily practices performed in it, and efforts can be made to address the deficiencies identified.

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Author's Contribution:

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Data Analysis:	Rahila Yasmeen
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Final Approval of version: Faizan Munir Khan

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

REFERENCES

1. Shaikh A, Humayun N. Medical Ethics in Undergraduate Medical Education in Pakistan: Towards a Curricular Change. Contemporary Issues in Bioethics. InTech ; 2012.
2. Yasmin S. Development of Professional Dental Ethics Course with Additional Islamic Perspective and Dental Students' Feedback. Pak Oral Dental J 2016;36(2):270–6.
3. Janakiram C, Gardens SJ. Knowledge, attitudes and practices related to healthcare ethics among medical and dental postgraduate students in south India. Ind J Med Ethics 2014;11(2):99–104.
4. Tahira QA, Lodhi S, Tasneem Haider S, Abaidullah S. The Study of Knowledge, Attitude and Practice of Medical Law and Ethics among Doctors in a Tertiary Care Hospital. Annals 2013; 19(1):55–60.
5. Hariharan S, Jonnalagadda R, Gora J. Knowledge, attitudes and practices of healthcare personnel towards Care-Ethics: A perspective from the Caribbean. Internet J Law, Healthcare Ethics 2007; 5(1).
6. Yesil Salih OD. An Investigation into the Implications of Islamic Work Ethic (IWE) in the Workplace. J Economics Behavioral Studies 2012; 4(11):612–24.
7. Ali A. Scaling an Islamic Work Ethic. J Social Psychol 1988;128(5):575–83.
8. Ibrahim A, Kamri N 'Azzah. Measuring the Islamic Work Ethics: An Alternative Approach. International Convention on Islamic Management 2013 [cited 2020 Aug 7];135–63. Available from: http://ssrn.com/abstract=2429393
9. Baral S, Uprety S, Lamichhane B. Focus Group Discussions How-to Guide [Internet]. 2016 [cited 2020 Dec 7]. Available from: https://www.herd.org.np/uploads/frontend/Publications/PublicationsAttachments1/1485497050-Focus Group Discussion_0.pdf
10. O.Nyumba T, Wilson K, Derrick CJ, Mukherjee N. The use of focus group discussion methodology: Insights from two decades of application in conservation. Geneletti D, editor. Methods in Ecology and Evolution [Internet]. 2018 Jan 11 [cited 2020 Dec 7];9(1):20–32. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/2041-210X.12860.
11. Prasad M. How to Conduct a Successful Focus Group Discussion - Atlan | Humans of Data [Internet]. 2017 [cited 2020 Dec 7]. Available from: https://humansofdata.atlan.com/2017/09/conduct-successful-focus-group-discussion/
12. Artino AR, la Rochelle JS, Dezee KJ, Gehlbach H. Developing questionnaires for educational research: AMEE Guide No. 87. Medical Teacher [Internet] 2014 Jun 24;36(6):463–74. Available from: http://www.tandfonline.com/doi/full/10.3109/0142159X.2014.889814
13. Chaudhary AK, Israel GD. The savvy survey # 8 : Pilot testing and pretesting questionnaires. Agricultural Education and Communication Department, UF/IFAS Extension [Internet]. 2014 [cited 2021 Jul 5];December(AEC402):1–6. Available from: https://edis.ifas.ufl.edu/pdf/PD/PD07200.pdf
14. Johanson GA, Brooks GP. Initial Scale Development: Sample Size for Pilot Studies. Educational and Psychological Measurement 2010 Jun 18 [cited 2021 Jul 5];70(3): 394–400. Available from: http://journals.sagepub.com/doi/10.1177/0013164409355692
15. Fernández-Gómez E, Martín-Salvador A, Luque-Vara T, Sánchez-Ojeda MA, Navarro-Prado S, Enrique-Mirón C. Content Validation through Expert Judgement of an Instrument on the Nutritional Knowledge, Beliefs, and Habits of Pregnant Women. Nutrients 2020 [cited 2021 Aug 12];12(4):1136.
16. Kubai E. Reliability and Validity of Research Instruments. UNICAF University - Zambia 2019; 1–9. Available from: https://www.researchgate.net/publication/335827941_Reliability_and_Validity_of_Research_Instruments_Correspondence_to_kubaiedwinyahoocom
17. Steyn NP, Labadarios D, Nel JH, Heidi-Lee R. Development and validation of a questionnaire to test knowledge and practices of dietitians regarding dietary supplements. Nutrition 2005;21(1):51–8.
18. Lani J. Pearson's Correlation Coefficient - Statistics Solutions [Internet]. Statistics Solutions. 2018 [cited 2021 Sep 13]. Available from: https://www.statisticssolutions.com/free-resources/directory-of-statistical-analyses/pearsons-correlation-coefficient.
19. The Fiqh of Medicine Level-1 - Al Balagh Academy [Internet]. 2021 [cited 2021 Aug 24]. Available from: https://www.albalaghacademy.org/course/fiqh-of-medicine-level1-online-course/
20. Master of Arts in Applied Islamic Ethics | HBKU [Internet]. [cited 2021 Aug 24]. Available from: https://www.hbku.edu.qa/en/cis/ma-applied-islamic-ethics.
21. Rubio DM, Berg-Weger M, Tebb SS, Lee ES, Rauch S. Objectifying content validity: Conducting a content validity study in social work research. Social Work Research [Internet]. 2003 Jun 1 [cited 2020 Dec 7];27(2):94–104. Available from: https://academic.oup.com/swr/article-lookup/doi/10.1093/swr/27.2.94
22. Willis GB, Artino AR. What Do Our Respondents Think We're Asking? Using Cognitive Interviewing to Improve Medical Education Surveys. J Graduate Med Educ 2013 [cited 2020 Dec 7];5(3):353–6. Available from: https://meridian.allenpress.com/jgme/article/5/3/353/34006/What-Do-Our-Respondents-Think-Were-Asking-Using.

Role of Diacerein in Primary Osteoarthritis Knee: A Cross Sectional Study Conducted in a Tertiary Care Hospital

Subhan Shahid, Muhammad Abubakar, Azeem Iqbal, Tasawar Abbas, Muhammad Zain-ul-Abidin

ABSTRACT

Objective: To determine role of diacerein among the patient with primary osteoarthritis knee.
Study Design: cross sectional study
Place and Duration of Study: This study was conducted at the department of orthopedic surgery Sir Ram Hospital Lahore. Study was completed in six months duration from July, 2021 to December, 2021 for a period of six months.
Materials and Methods: Patients presenting to the out-patient department with primary osteoarthritis knee having age >50 years were included in this study. Patients were evaluated according to WOMAC (Western Ontario and McMaster Universities Arthritis Index) and VAS (visual analogue Scale). Patients were given diacerein 100mg twice daily for 06 months duration. WOMAC and VAS were recorded of study patients initially and after six months and results were compared to see improvement in the patients.
Results: There were 110 cases in this study including 60(54.5%) male and 50(45.5%) female cases. All patients were having age >50 years with mean age of 59.28 ± 4.64 years. Before and after treatment mean WOMAC score was 46.34 ± 5.72 and 35.92 ± 16.4 respectively ($p<0.05$) while mean VAS was 6.43 ± 2.50 and 4.4 ± 1.22 respectively ($p<0.05$). 30% improvement was seen in 45% cases. Efficacy of the drug was labelled as yes in 45% cases. Only two patients suffered from diarrhea while one patient had deranged LFTs after treatment.
Conclusion: Patients showed significant improvement in the mean WOMAC and VAS scores after six months therapy of diacerein. This drug can be considered as an alternative therapy among those patient who don't respond to conventional analgesics therapy.

Key Words: Diacerein, improvement, Osteoarthritis Knee, VAS, WOMAC

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INTRODUCTION

Osteoarthritis is a degenerative joint disease which gradually progress with age.[1] It causes destruction of joint articular cartilage. Initially there is softening, sclerosis, subchondral cysts and ultimately osteophytes formation in the joint.[2] Usual presenting symptoms are joint pain, effusion and stiffness. A Pakistani study has shown that 25% of our rural population is suffering from primary osteoarthritis of knee.[3]
Knee osteoarthritis incidence in the western countries is 18-25% among males and 24-40% among females above 50 years of age.[4] All compartments of knee can be affected but mostly medial compartment is involved because during walking repeatedly varus movements causes increased stress on medial compartment causing degenerative changes in arthritis patients. Main aims of the treatment are to relieve pain, limit the progression of disease and to minimize functional disability of the patient.[5] Anti-inflammatory drugs and analgesics are very important in treating these patients. Previous researches have shown that interluki-1-beta (IL-1B) plays main role in the joint cartilage destruction, chondrocyte apoptosis, subchondral bone remodeling and joint inflammation. Cytokines produce nitric oxide which also contribute in joint destruction.[6] Previously many drugs were studied for its treatment like nimesulide and glucosamine sulphate, but diacerein is an anthraquinone derivative which inhibit IL-1B.[7] It relives symptoms and decreases progression of the disease. Primary osteoarthritis is a very common disease causing disability among old age population.

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There is no gold standard treatment for this disease so far.[8] Usually structure modifying or disease modifying agents are used in its treatment. According to some studies diacerein is a structure modifying agent.[9,10] This study has been conducted to evaluate the role of diacerine in reducing pain and inflammation among the old age patients with knee osteoarthritis.

MATERIALS AND METHODS

This is a cross sectional study, conducted in the department of orthopedic surgery Sir Ram Hospital Lahore. Study was completed in six months duration from July to December 2021. Study sample was calculated using WHO sample size calculator. Patients were collected using consecutive sampling technique. Patients presenting to the out-patient door with primary osteoarthritis knee having age >50 years were included in this study. Patients diagnosed with knee osteoarthritis according to ACR criteria having grade II,III and IV disease were included in this study. Those with secondary osteoarthritis knee, using heavy dose of steroids for more than one year, those who took intra-articular steroid injection in last three months, or with history of trauma to involved knee joint in recent six months were excluded from the study. Patients were evaluated according to WOMAC (Western Ontario and McMaster Universities Arthritis Index) and VAS (visual analogue Scale). Patients were given diacerein 100mg twice daily for 06 months duration. WOMAC and VAS were recorded of study patients initially and after six months and results were compared to see improvement in the patients. Informed consent was taken from all the patients in study group. Approval was taken from the institutional ethical review board. Statistical analysis was done using SPSS (version-20) software.

RESULTS

Total 110 cases were included in this study including 60(54.5%) male and 50(45.5%) female cases. Mostly patients (45.5%) were having age between 50-60 years. All patients were having age >50 years with mean age of 59.28 ± 4.64 years (Table-I). Mean BMI of the patients was 29.83 ± 4.32 kg/m^2. There were 03(2.70%) cases with diabetes mellitus and 12(10.90%) cases with hypertension.

Table No.1: Distribution of patients according to age and gender

Age (years)	Gender		Total
	Male	Female	
50-60	30 (27.3%)	20 (18.2%)	50 (45.5%)
60-70	11 (10%)	17 (15.5%)	28 (25.5%)
>70	09 (8.2%)	13 (11.8%)	22 (20%)
Total	60 (54.5%)	50 (45.5%)	110 (100%)

Before and after treatment mean WOMAC score was 46.34 ± 5.72 and 35.92 ± 16.4 respectively ($p<0.05$) while mean VAS was 6.43 ± 2.50 and 4.4 ± 1.22 respectively ($p<0.05$). 30% improvement was seen in 45% cases (Table-II). Only two patients suffered from diarrhea while one patient had deranged LFTs after treatment.

Table No.2: Distribution of patients according to WOMAC score and VAS at presentation and after six months follow up

	WOMAC score (Mean ± SD)	VAS (Mean ± SD)
Baseline	46.34 ± 5.72	6.43 ± 2.50
After 06 months	35.92 ± 16.40	4.40 ± 1.22
p-value	0.001	0.001

There was no patient with grade-I osteoarthritis, while 35(31.8%) cases were having grade-II, 55(50%) grade-III and 20(18.2%) were having grade-IV osteoarthritis knee (Table-III). Overall 40% improvement was seen in 45% cases so efficacy of the drug was labeled as yes in 45% cases.

Table No.3: Patients distribution according to severity of osteoarthritis knee

Grade of osteoarthritis Knee	Number of patients	Patients showing improvement
Grade-I	00	00
Grade-II	35	27 (77.1%)
Grade-III	55	15 (27.3%)
Grade-IV	20	03 (15%)

DISCUSSION

Diacerein as a structure modifying agent is under practice since many years. There is little data available about its efficacy.[11] This study was conducted to know efficacy of diacerin in primary osteoarthritis knee and improvement in symptoms of patients over the period of six months. Our results were in favor of diacerein with the improvement in mean WOMAC score and VAS after six months therapy. In our study efficacy of the drug was reported as 45%, that is much attractive. Diacerein is an inhibitor of IL-1B production. Previous literature has shown its role as disease modifying agent.[12,13] Previously a study conducted by Pelletier et al reported significant improvement in osteoarthritis knee after use of diacerein. Their outcomes parameters were radiographic evaluation of the joint.[14] In another study by Sharapova et al reported that diacerein showed good outcomes in improving pain and functional disability among patients.[15] Karateev et al conducted study on 100 cases with primary knee osteoarthritis and divided patients in two groups, one group was given conventional treatment and second group given diacerein plus conventional treatment. They concluded

that 60% cases receiving diacerein plus conventional treatment showed good outcomes as compared to 20% cases receiving just conventional treatment.16

In our study 45 cases showed significant improvement in symptoms and functional disability after six months therapy with diacerein. We used WOMAC score VAS comprising on a question to evaluate functional outcomes in patients. Other scales like OMERACT-6 and Lequesne Functional Severity Index have also been used in literature. However VAS and WOMAC are simple, reliable and easy to use.[17] Hailer et al in their study reported that diacerein 50mg given two times a day showed very good improvement in VAS and WOMAC score in their patients.[18]

In our study we observed that most of the patients showed improvement in WOMAC score less than 30% and no patient showed improvement more than 50%. 77% cases with grade-II osteoarthritis, 27.3% with grade-III and 15% with grade-IV showed significant improvement. These results show that %age improvement depends on the severity of osteoarthritis. In our study two patients had diarrhea while one patient showed deranged LFTs after six months therapy. According to a study conducted by Chaudhari et al diarrhea was noted as most common side effect of diacerein, reported in 46% cases in diacerein group as compared to 12% cases in placebo group.[19] Usually diarrhea is mild in severity according to previous studies. Other less common side effects include abnormal LFTs and discoloration of urine.[20,21]

CONCLUSION

Diacerein provides significant improvement in pain and function in patients with primary osteoarthritis of knee joint. This is safe and effective drug with minimum side effects. It is much effective in patients resistant to conventional analgesics therapy with mild to moderate severity of the disease.

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REFERENCES

1. Guerrero EM, Bullock GS, Helmkamp JK, Madrid A, Ledbetter L, Richard MJ, et al. The clinical impact of arthroscopic vs. open osteocapsular debridement for primary osteoarthritis of the elbow: a systematic review. J Shoulder Elbow Surg 2020;29(4):689-98. https://doi.org/10.1016/j.jse.2019.12.003
2. Hellevik AI, Johnsen MB, Langhammer A, Baste V, Furnes O, Storheim K et al. Metabolic syndrome as a risk factor for total hip or knee replacement due to primary osteoarthritis: a prospective cohort study (the HUNT study and the Norwegian Arthroplasty Register). Clin Epidemiol 2018;10:83. https://dx.doi.org/10.2147%2FCLEP.S145823
3. Fatima S, Arslan SA, Sharif F, Ahmad A, Gillani SA, Zaheer A. Translation, cross-cultural adaptation and psychometric properties of the Urdu version of knee injury and osteoarthritis outcome score questionnaire for Pakistani population. BMC Musculoskeletal Disorders 2021;22(1):1-7. https://doi.org/10.1186/s12891-021-04477-1
4. Ackerman IN, Bohensky MA, Zomer E, Tacey M, Gorelik A, Brand CA et al. The projected burden of primary total knee and hip replacement for osteoarthritis in Australia to the year 2030. BMC musculoskeletal disorders. 2019 Dec;20(1):1-0. https://doi.org/10.1186/s12891-019-2411-9
5. Ojemolon PE, Shaka H, Edigin E, Gomez TM, Eseaton P, Bello J, et al. Impact of diabetes mellitus on outcomes of patients with knee osteoarthritis who underwent knee arthroplasty: an analysis of the nationwide inpatient sample. Cureus 2020;12(6). https://dx.doi.org/10.7759%2Fcureus.8902
6. Mahmoud GA, Moghazy A, Fathy S, Niazy MH. Osteoarthritis knee hip quality of life questionnaire assessment in Egyptian primary knee osteoarthritis patients: relation to clinical and radiographic parameters. The Egyptian Rheumatologist 2019;41(1):65-9. https://doi.org/10.1016/j.ejr.2018.05.001
7. Almezgagi M, Zhang Y, Hezam K, Shamsan E, Gamah M, Al-Shaebi F et al. Diacerein: Recent insight into pharmacological activities and molecular pathways. Biomed Pharmacotherap 2020;131:110594. https://doi.org/10.1016/j.biopha.2020.110594
8. de Oliveira PG, Termini L, Durigon EL, Lepique AP, Sposito AC, Boccardo E. Diacerein: A potential multi-target therapeutic drug for COVID-19. Med Hypotheses 2020;144:109920. https://doi.org/10.1016/j.mehy.2020.109920
9. Pelletier JP, Raynauld JP, Dorais M, Bessette L, Dokoupilova E, Morin F, et al. DISSCO Trial Investigator Group. An international, multicentre, double-blind, randomized study (DISSCO): effect of diacerein vs celecoxib on symptoms in knee osteoarthritis. Rheumatol 2020;59(12):3858-68. https://doi.org/10.1093/rheumatology/keaa072

10. Wang F, Shi WX, Chen J, He K, Fang W. Clinical therapeutic effects of combined diacerein and glucosamine in the treatment of osteoarthritis: A protocol for systematic review and meta-analysis. Medicine 2021;100(47).
11. Shakya Shrestha S, Tamrakar S, Shrestha R, Shrestha R, Basi A, Malla M. Comparative Efficacy and Safety of Diacerein in Patients with Knee Osteoarthritis: A Pilot Study. Kathmandu Univ Med J 2021;74(2):260-4.
12. Sharma S, Rijal KP, Prasai T, Khanal H. Comparative Study of Efficacy and Safety of Diacerein versus Acelofenac in Patient with Knee Osteoarthritis. Nepal J Med Sci 2021;6(1):26-33. https://doi.org/10.3126/njms.v6i1.36729
13. Abdel-Aziz MA, Ahmed HM, El-Nekeety AA, Sharaf HA, Abdel-Aziem SH, Abdel-Wahhab MA. Biosynthesis of gold nanoparticles for the treatment of osteoarthritis alone or in combination with Diacerein® in a rat model. Inflammopharmacol 2021:1-5. https://doi.org/10. 1007/ s10787-021-00833-8
14. Pelletier JP, Martel-Pelletier J. Diacerein-containing products: same risk of diarrhoea? Aging Clin Exp Res 2018;30(4):411-2. https://doi.org/10.14412/1996-7012-2018-4-54-58
15. Sharapova EP, Alekseeva LI, Lila AM. Diacerein in the treatment of osteoarthritis in patients with comorbidity. Modern Rheumatol J 2018;12(4):54-8. https://doi.org/10.1007/s40520-018-0911-3
16. Karateev AE, Alekseeva LI, Pogozheva EY, Amirdzhanova VN, Filatova ES, Nesterenko VA, et al. Efficacy of combined use of glycosaminoglycan peptide complex for intramuscular administration and oral diacerein in osteoarthritis: evaluation according to an observational multicenter clinical trial. Terapevticheskii Arkhiv 2021;93(5):587-93. https://doi.org/10.26442/00403660.2021.05.200791
17. Ahmad IW, Rahmawati LD, Wardhana TH. Demographic profile, clinical and analysis of osteoarthritis patients in Surabaya. Biomolecular Health Sci J 2018;1(1):34-9.
18. Hailer NP, Kuja-Halkola R, Brüggemann A, Pedersen NL, Michaëlsson K. Body Mass Index Differentially Moderates Heritability of Total Joint Replacement Due to Hip and Knee Osteoarthritis: A Cohort Study of 29,893 Swedish Twin Pairs. JBJS 2021;6:10-2106.
19. Chaudhari N, Rathwa D, Parmar A, Mali A, Darji P. Observational study to evaluate functional out-come of total knee replacement in primary osteoarthritis of knee joint. Int J Orthopaedics 2021;7(3):42-5. https://doi.org/10.22271/ortho.2021.v7.i3a.2726
20. Murphy BP, Dowsey MM, Choong PF. The impact of advanced age on the outcomes of primary total hip and knee arthroplasty for osteoarthritis: a systematic review. JBJS reviews 2018;6(2):e6.
21. Sun X, Zhen X, Hu X, Li Y, Gu S, Gu Y, et al. Osteoarthritis in the middle-aged and elderly in China: prevalence and influencing factors. Int J Environmental Res Public Health 2019; 16(23): 4701.

Comparison of Efficacy of Cervical Cerclage and Vaginal Progesterone in the Prevention of Preterm Labour

Sara Fayyaz, Joveria Sadaf, Sana Hafeez, Sana Aara, Aisha Ajmal and Aslam Mehmood Malik

ABSTRACT

Objective: To compare the efficacy of prophylactic vaginal progesterone with cervical cerclage in women with previous history of preterm birth.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Shahida Islam Medical and Dental College (SIMDC), Lodhran from April, 2020 to April, 2021 for a period of one year.

Materials and Methods: 120 women at 14-20 weeks of gestation, who had previous history of preterm birth were included in the study. Women who had rupture of membranes, multiple pregnancy, antepartum hemorrhage and severe intra-uterine growth retardation were excluded. Progesterone pessary 200mg was given vaginally once daily at night till delivery in the Group A and McDonald's stitch using prolene 1-0 was applied by the researchers themselves in the Group B. Effectiveness (yes/no) of both methods were noted by the researchers.

Results: The mean age of women in group A was 29.97 ± 5.43 and in group B was 28.63 ± 5.12 years. Majority 68 (56.67%) were between 18 to 30 years of age. Gestational age was from 14 to 20 weeks with mean gestational age of 17.19 ± 1.97 weeks. The mean gestational age in group A was 17.13 ± 1.98 weeks and in group B was 17.23 ± 1.97 weeks. Mean parity was 2.43 ± 0.79. Mean BMI was 29.81 ± 3.11 kg/m^2. Efficacy [no preterm birth (<37 weeks)] was 38 (63.33%) in group A (vaginal progesterone) and 56 (93.33%) in group B (cervical cerclage) with p-value of 0.0001.

Conclusion: Conclusion was that prophylactic cervical cerclage is more efficacious than prophylactic vaginal progesterone in women with previous history of preterm birth.

Key Words: preterm birth, progesterone, cervical cerclage

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INTRODUCTION

One of global obstetrical problem is the preterm delivery of the foetus, around 15 million annually leading to approximately 1 million neonatal deaths[1]. Preterm birth leads to high neonatal mortality as well as short and long term adverse effects[2] like respiratory illnesses, cerebral palsy, sensory deficits and learning disabilities[3].

As far as it's long term effects are concerned these individuals are at increased risk of hypertension, diabetes mellitus, metabolic syndrome and other chronic illnesses[4] . United States reported a rise in preterm birth of 9.63 % in 2015 to 9.8 5% in 2016[5].

Treatment of preterm birth is based mainly on detection of increased uterine contractions, cervical ripening and membrane decidual activation to identify patients at increased risk of preterm birth[4,5].

Women who are at increased risk of preterm labour have been subjected to progestrone, cervical pessaries and cervical cerclage[5]. Mode of administration of progestrone can be intramuscular per oral or per vaginal[7] leading to decrease in neonatal morbidity and mortality[6,7]. Patients with history of preterm birth and having shortened cervical length have been benefited by cervical cerclage application[8]. Abd Elaal NK et al[9] found 40.50% decrease in preterm birth in Progestrone group and 11.60% in cercalage group. A systemic review and meta-analysis found 72.0% reduction in the preterm birth in vaginal progestrone group and 46% in cervical cerclage group[10]. A recent study resulted that preterm birth is seen in 33.9% cases in progestrone group and 45.2%in cerclage group[11]. Previous studies showing controversial results made us to study and compare the efficacy of prophylactic vaginal

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progesterone with cervical cerclage in women with previous history of preterm birth in local population. It will help us to know the local statistics and to make the practical guidelines in our practice to prevent the preterm birth, perinatal mortality and morbidity.

MATERIALS AND METHODS

Study Design: Randomized controlled trial.
Setting: Department of Obstetrics & Gynecology, Shahida Islam Medical and Dental College, Lodhran.
Duration of Study: 27th April 2020 to 26th April 2021.
Sample Size: The calculated sample size was 120 i.e. 60 in each group with 5% level of significance, 90% power of study, taking percentage of preterm delivery as 72.0% in the vaginal progesterone and 46.0% in the elective cerclage group[10].
Sample Technique: Non-probability, consecutive sampling.
Sample Selection: All 18-40 years of age women presenting with gestational age 14-20 weeks (assessed on LMP) having previous history of preterm birth having were included in the study. Patients having twin and multiple pregnancy, antepartum haemorrhage and preterm premature rupture of membrane (PPROM) were excluded. The patients having severe intra-uterine growth retardation as assessed on ultrasonography were also excluded.
Data Collection Procedure: After taking approval from ethical review committee of SIMDC Lodhran, 120 patients presenting to out-patient department who fulfilled the inclusion criteria and gave informed consent were included in the study and divided in to two groups A & B by lottery method. 200mg vaginal progestrone daily at night till delivery was given to group A. In group B cervical cerclage (McDonald stich) with prolene 1-0 applied by researchers themselves after admission in SIMDC. Both groups were monitored till delivery and results were noted as per operational definitions mentioned previously.
Statistical Analysis: Data was analyzed by SPSS 25.0 version. Age of patient, parity, gestational age, BMI were presented as mean and standard deviation. Status of gestational diabetes, pregnancy induced hypertension, education, place of living, and efficacy were presented as percentage and frequency. Both groups were analyzed in terms of efficacy by Chi-square test. P value $\leq$ 0.05 showed statistically significant result. Chi-square was applied post stratification to see effect of these on efficacy. P value $\leq$0.05 was considered significant.

RESULTS

Distribution of patients according to age, gestational age, parity, BMI, place of living, education status, PIH and GDM in both groups is shown in Table 1 & 2 respectively. Efficacy (no preterm birth (<37 weeks)) was 38 (63.33%) in group A (vaginal progesterone) and 56 (93.33%) in group B (cervical cerclage) with p-value of 0.0001 as shown in Table 3.

Table No.1: Demographic Segmentation

		Group A	Group B	Total
Age(years)	18-30	32(53.3%)	36(60%)	68(56.67%)
	31-40	28(46.67%)	24(40%)	52(43.33%)
	Mean±SD	29.97±5.43	28.63±5.12	29.30±5.27
Gestational age(weeks)	14-17	35(58.33%)	33(55.0%)	68(56.67%)
	18-20	25(42.67%)	27(45.0%)	52(43.33%)
	Mean±SD	17.13±1.98	17.23±1.97	17.19±1.97
Parity	0-2	28(46.67%)	35(58.33%)	63(52.50%)
	3-4	32(53.33%)	25(41.67%)	57(47.50%)
	Mean ± SD	2.57 ± 0.77	2.30±0.79	2.43 ± 0.79
BMI(kg/m $^{2)}$	≤30	28(46.67%)	28(46.67%)	56(46.67%)
	>30	32(53.33%)	32(53.33%)	64(53.33%)
	Mean ± SD	29.75 ± 2.92	29.83 ± 3.30	29.81 ±3.11
Place of living	Rural	18(42.86%)	22(36.67%)	40(33.33%)
	Urban	42(57.14%)	38(63.33%)	80(66.67%)
Education	Uneducated	22(36.67%)	24(40.0%)	46(38.33%)
	Educated	38(63.33%)	36(60.0%)	74(61.67%)
GDM	Yes	10(16.67%)	14(23.33%)	24(20%)
	No	50(83.33%)	46(76.67%)	96(80%)

Table No.2: Association of Medical Disorders in Both Groups

PIH	Yes	15(25%)	18(30%)	33(27.50%)
	No	45(75%)	42(70%)	87(72.50%)

Table No.3: Comparison of Efficacy between both Groups

		Group A	Group B

		(n=60)	(n=60)
Efficacy	Yes	38(63.33%)	56(93.33%)
	No	22(36.67%)	04(6.67%)

P value is 0.0001 which is statistically significant

DISCUSSION

Factors which are responsible for the initiation of labour are targeted to prevent preterm birth. These include increased uterine contractility, preterm cervical ripening and/or activation of the membrane decidua. When compared with placebo or standard care, progesterone, cervical cerclage and cervical pessary were found to be effective in reducing preterm birth[12,13].

Aim of this study was the comparison between the efficacy of prophylactic vaginal progesterone and cervical cerclage in women with previous history of preterm birth. Efficacy was defined as no preterm birth at <37 weeks. Efficacy was 38(63.3%) in group A i.e. those women who were given vaginal progesterone and 56 (93.3%) in the group B i.e. those women in whom cervical cerclage was applied with p value of 0.0001. According to one study done by Abd Elaal NK et al[9], in the women who were given only vaginal progesterone, preterm birth was noted to be 40.5% but in those women in whom cervical cerclage was applied the rate of preterm birth was only 11.60%. One systematic review and network meta-analysis showed preterm birth rates in both groups to be 72.0% and 46.0%[10] respectively. Preterm delivery rate was 33.9% in the first group and 45.2% in the 2nd group (adjusted odds ratio: 1.72, 95% confidence interval: 0.52,5.66).[11]

Patients with or without history of preterm birth but short cervix as seen on ultrasound have reduced rate of preterm delivery and neonatal morbidity and mortality after receiving vaginal progesterone as shown by two independent randomized clinical trials[14-16] and an individual patient data meta-analysis. Patients with acute insufficiency of cervix[17] or with a previous history of preterm birth and short cervix of <25mm[18] on ultrasound were candidates of cervical cerclage. So vaginal progesterone and a cervical cerclage have a beneficial role in decreasing preterm birth in patients with previous history of preterm birth and short cervix<25mm.

Cerclage may be considered for women with singleton pregnancy, previous history of spontaneous preterm birth and cervical length of <25 mm before 24 weeks of gestation[19,20] as recommended recently by two professional organizations. The basis for this recommendation was that the individual patient data meta-analysis (IPD) of randomized control trials showed that the risk of preterm birth at <37,<35,<32,<28 and <24 weeks of gestation, total perinatal morbidity and mortality is reduced significantly in those women in whom cerclage was applied compared with no cerclage[21]. According to another IPD meta-analysis women who had a short cervix of <25 mm in the mid trimester were given vaginal progesterone which significantly decreased the risk of preterm birth at <35, <34, <33, <30 and <28 weeks of gestation, total neonatal morbidity and mortality as compared to placebo[16]. Risk of preterm birth at <33 weeks of gestation and total neonatal morbidity and mortality in women with a short cervix (<25mm), singleton pregnancy and previous spontaneous preterm birth was reduced significantly in a subgroup analysis[16].

Women who had a cervical length of less than 25 mm in the mid trimester singleton pregnancy and previous spontaneous preterm birth were given either vaginal progesterone or cerclage was applied and it was associated with decreased risk of preterm birth at less than 32 weeks of gestation [RR 0.47, 95% confidence interval (CI) 0.24-0.91, for vaginal progesterone, and RR 0.66, 895% CI 0.48-0.91, for cerclage] and total perinatal morbidity and mortality (response rate (RR) 0.43, 95% CI 0.20-0.94, for vaginal progesterone, and RR 0.64, 95% CI 0.45-0.91, for cerclage) when compared with placebo and no cerclage, respectively[22].

For prevention of preterm birth in singleton pregnancy, a cochrane review comparing cerclage with no treatment showed that there was less marked but statistically significant decrease in the preterm birth[16]. After application of cervical cerclage, the preterm births reduced consistently at all commonly reported gestational periods (<37, <34 and < 28 weeks), other clinically specified subgroups and in those women in whom cervical cerclage was applied. In a meta-analysis by Berghella et al[23], cerclage was found to be beneficial in women with singleton pregnancy, short cervix and preterm births**.**

CONCLUSION

According to this study prophylactic cervical cerclage was found to be more efficacious than prophylactic vaginal progesterone in women with previous history of preterm birth . In order to reduce perinatal mortality and morbidity in these women cervical cerclage should be applied according to our recommendations.

Author's Contribution:

Concept & Design of Study:	Sara Fayyaz
Drafting:	Joveria Sadaf, Sana Hafeez
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Final Approval of version:	Sara Fayyaz

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REFERENCES

1. Sanchez-Ramos L. Vaginal progesterone is an alternative to cervical cerclage in women with a short cervix and a history of preterm birth. Am J Obstet Gynecol 2018;219(1):5-9.
2. Manuck TA, Rice MM, Bailit JL. Preterm neonatal morbidity and mortality by gestational age: a contemporary cohort. Am J Obstet Gynecol 2016;215:103-14.
3. Allotey J, Zamora J, Cheong-See F. Cognitive, motor, behavioral and academic performances of children born preterm: a meta-analysis and systematic review involving 64,061 children. Br J Obstet Gyencol 2018;125:16–25.
4. Jarde A, Lutsiv O, Park CK, Beyene J, Dodd JM, Barrett J, et al. Effectiveness of progesterone, cerclage and pessary for preventing preterm birth in singleton pregnancies: a systematic review and network meta-analysis. Br J Obstet Gyencol 2017;124:1176–89.
5. Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Drake P. Births: final data for 2016 Natl Vital Stat Rep 2018;67:1.
6. Conde-Agudelo A, Romero R, Da Fonseca E, O'Brien JM, Cetingoz E, Creasy GW, et al. Vaginal progesterone is as effective as cervical cerclage to prevent preterm birth in women with a singleton gestation, previous spontaneous preterm birth, and a short cervix: updated indirect comparison meta-analysis. Am J Obstet Gynecol 2018;219(1):10-25.
7. Afridi N, Masood U, Baloch S, Khan S, Khan S. Comparison of oral progesterone (dydrogesterone) and Micronized progesterone (Cyclogest pessary), to reduce the incidence of spontaneous preterm births. J Ayub Med Coll Abbottabad 2019;31(2):248–51.
8. Khan Z, Khan R, Aitazaz F. Success rate of cervical cerclage in preventing preterm labour. Pak J Physiol 2016;12(3):33-6.
9. Abd Elaal NK, Sanad ZF, Dawod RM, Mnasir SM. Vaginal progesterone and cervical cerclage for preterm labor prevention and their impact on perinatal outcome. Menoufia Med J 2015;28: 864-72.

10. Jarde A, Lutsiv O, Beyene J, McDonald SD. Vaginal progesterone, oral progesterone, 17-OHPC, cerclage, and pessary for preventing preterm birth in at-risk singleton pregnancies: an updated systematic review and network meta-analysis. Br J Obstet Gynecol 2019;126:556–7.
11. Wood AM, Dotters-Katz SK1, Hughes BL. Cervical cerclage versus vaginal progesterone for management of short cervix in low-risk women. Am J Perinatol 2019;36(2):111-7.
12. Dodd JM, Flenady V, Cincotta R, Crowther CA. Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth. Cochrane Database Syst Rev 2013;7:CD004947.
13. Alfirevic Z, Stampalija T, Roberts D, Jorgensen AL. Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy. Cochrane Database Syst Rev 2012;4:CD008991.
14. Jain V, McDonald SD, Mundle WR, Farine D. Guideline no. 398: Progesterone for prevention of spontaneous preterm birth. J Obstet Gynaecol Canada 2020;42(6):806-12.
15. Hassan SS, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2011;38:18–31.
16. Romero R. Vaginal progesterone in asymptomatic women with a sonographic short cervix. Am J Obstet Gynecol 2012.
17. Daskalakis G, Papantoniou N, Mesogitis S, Antsaklis A. Management of cervical insufficiency and bulging fetal membranes. Obstet Gynecol 2006;107:221–6.
18. Owen J, Hankins G, Iams JD, Berghella V, Sheffield JS, Perez-Delboy A, et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. Am J Obstet Gynecol 2009;201:375, e1–8.
19. Committee opinion no. 522: incidentally detected short cervical length. Obstet Gynecol 2012;119:879.
20. Daskalakis G, Goya M, Pergialiotis V, Cabero L, Kyvernitakis I, Antsaklis A, et al. Prevention of spontaneous preterm birth. Archives Gynecol Obstet 2019;299(5):1261-73.
21. Romero R, Conde-Agudelo A, Da Fonseca E, O'Brien JM, Cetingoz E, Creasy GW, et al. Vaginal progesterone for preventing preterm birth and adverse perinatal outcomes in singleton gestations with a short cervix: a meta-analysis of individual patient data. Am J Obstet Gynecol 2018;218(2):161-80.
22. Conde-Agudelo A, Romero R, Nicolaides K, Chaiworapongsa T, O′Brien JM, Cetingoz E, et al. Vaginal progesterone vs. cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. Am J Obstet Gynecol 2013; 208 :42.e1-42.e18
23. Berghella V, Rafael TJ, Szychowski JM, Rust OA, Owen J. Cerclage for short cervix on Ultrasonography in women with singleton gestations and previous preterm birth: a meta-analysis. Obstet Gynecol 2011; 117:663-671.

Frequency of Complications of Ileostomy in the Management of Ileal Perforation Secondary to Typhoid Fever

Ileal Perforation Secondary to Typhoid Fever

Bakhtawar Urooj[1], Nadia Mehreen[2], Munazza Laraibe[1], Zarak Khan[1], Muhammad Anwar[3] and Zohra Samreen[4]

ABSTRACT

Objective: To determine the frequency of complications of ileostomy in the management of ileal perforation secondary to typhoid fever in a tertiary setting.

Study Design: Descriptive Study

Place and Duration of Study: This study was conducted at the Department of Surgery, Bolan Medical College, Quetta from February 2020 to February 2021 for a period of one-year.

Materials and Methods: Ninety patients with single or multiple ileal perforation due to typhoid fever confirmed by clinical features, laboratory tests and abdominal x-ray were included in this study. Patients were observed for complications of ileostomy like skin excoriation, stoma retraction, stenosis, prolapse, peristomal sepsis, parastomal hernia, necrosis and death for two months.

Results: The average age of the patients was 40.30±10.14 years. Skin excoriation was the commonest complication that was observed in 18.9% cases followed by stoma retraction 10%, parastomal hernia 10%, stenosis 4.4%, prolapse 3.3%, peristomal sepsis 6.7% and necrosis 2.2%. Mortality was observed in 6.67% (6/90) due to stoma.

Conclusion: In this study skin excoriation was the commonest complication**.** Early surgery and adequate resuscitation are the important factors for successful management of patients with ileal perforation. Primary closure of perforation is a preferred technique in clinically stable patients with a single perforation with minimal soiling of the abdominal cavity, to avoid complications related to stoma.

Key Words: Ileal, Perforation, Typhoid, Fever, Skin, Excoriation

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INTRODUCTION

Ileal perforation is a frequently encountered surgical emergency in the developing countries. It is a hole in the wall of ileum leading to signs and symptoms of peritonitis, including severe abdominal pain and tenderness. Ileal perforation due to typhoid fever is common in Pakistan due to high incidence of typhoid fever.[1,2] Complicated and untreated cases of typhoid fever usually results in single or multiple ileal perforations.[2] Typhoid fever is a severe febrile illness caused by ingestion of salmonella typhi, a gram negative bacillus. It has got an average incubation period of 10-14 days. Regions of the world like ours, lacking clean and safe drinking water supplies and adequate waste disposal system have increased incidence of typhoid fever.[2]

A recent study showed that up to 65 percent of ileal perforation results due to untreated typhoid fever.[2] Another study reported that 62 percent of solitary ileal perforations are due to typhoid fever and mortality is reported up to 32 percent if not treated.[3]

There are various surgical procedures for the management of ileal perforation. These include primary repair, primary ileostomy and segmental resection with end to end anastomosis. But ileostomy is a widely accepted surgical option and regarded more successful procedure as compared to primary repair in terms of overall mortality, morbidity and duration of hospital stay.[1] Ileostomy is life-saving surgical procedure in which the end or loop of ileum is diverted to an artificial opening of 2 to 3 cm usually on the lower right side of the anterior abdominal wall. Stoma is the end of the ileum which connects to the surface of the skin.

The complications of ileostomy are not just common but also difficult to manage. Serious complications may require reoperation. The main disadvantage of performing ileostomy is that it requires further surgical procedure for its closure and associated with nutritional disturbances and emotional trauma. Commonly

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reported complications of ileostomy are skin excoriation (17.64%), stoma retraction (3.50%), stenosis (1.17%), prolapse (2.94%), peristomal sepsis (5.80%) and necrosis (0.58 %).[4,5] Death has been reported worldwide due to ileostomy.[6]

However, in Balochistan, studies on estimation of stoma related complications secondary to typhoid fever, so far, have not been conducted as per our best knowledge. Most studies come from western countries which may not be true frequency of complications of ileostomy in Pakistan.

The aim of this study is to evaluate the frequency of complications of ileostomy in terms of stoma related complications and mortality. The result of this study will help the clinicians to estimate the frequency of complications and to promptly manage these complications in a less hygienic environment, prevailing at hospitals in Balochistan. This study will also help to enhance knowledge about the frequency of complications of stoma secondary to typhoid fever in our cross cultural settings.

MATERIALS AND METHODS

Study Design: Descriptive Study

Settings: Department of Surgery, Bolan Medical Complex Hospital, Quetta

Duration: One year from 3-Feb-2020 to 3 Feb-2021

Inclusion Criteria:

- Only adult cases, both gender, age ranging from 18 to 60 years.
- Patient with single or multiple ileal perforation due to typhoid fever confirmed by clinical features, laboratory tests and abdominal x-ray.

Exclusion Criteria:

Confounding conditions which can influence

- Ileal perforation due to tuberculosis
- Ileal Perforation due to trauma or gunshot cases
- Ileal Perforation due to ingestion of toxic substances and poisoning

Data Collection Procedure: A total of 90 cases that fulfill the inclusion criteria was enrolled in the study from Department of Surgery Bolan Medical Complex Hospital, Quetta. Informed consent about the surgical procedure and its complication was obtained and demographics were noted. A detailed history including general physical examination, abdominopelvic examination and associated symptoms, routine Laboratory investigations, Typhidot test and abdominal x-ray in standing position was taken to confirm the diagnosis. After establishment of diagnosis of ileal perforation secondary to typhoid fever, prompt surgical intervention was done. Patients was observed for complications of ileostomy.

Data Analysis Procedure: Data entry and analysis was on computer packages IBM SPSS version 20.0. Mean and Standard Deviation (S.D) was computed for quantitative variable like age and duration of typhoid fever. Frequency and percentage were calculated for gender and postoperative complications such as skin excoriation, stoma retraction, stenosis, prolapse, peristomal sepsis, parastomal hernia and death.

RESULTS

Most the patients were 31- 50 years of age. The average age of the patients was 40.30±10.14 years and mean duration of typhoid fever was 3.68±0.91 weeks as shown in Table-1.

Table No.1: Descriptive statistics analysis of data

Statistics		Age (Years)	duration of typhoid fever days/week
Mean		40.30	3.68
Std. Deviation		10.142	.910
95% Confidence Interval for Mean	Lower Bound	38.18	3.49
	Upper Bound	42.42	3.87

Rate of stoma retraction was high in above 45 years of age as compared to below and equal to 45 years of age cases (18.8% vs. 5.2%; p=0.04) while other complications were not statistically significant between age groups including the rate of skin excoriation 17.2% and 21.9% in ≤45 and >45 years of age respectively, stenosis 1.7% and 9.4% in ≤45 and >45 years of age respectively, prolapse rate 5.2% and 0% in ≤45 and >45 years age respectively, rate of peristomal sepsis 5.2% and 3.1% in ≤45 and >45 years of age respectively, necrosis 1.7% and 3.1% in ≤45 and >45 years of age respectively, rate of parastomal hernia was 12.1% and 6.3% in ≤45 and >45 years of age respectively and death rate was 3.4% and 12.5% in ≤45 and >45 years of age respectively as presented in Table-2.

Table No.2: Frequency of complications of ileostomy in the management of ileal perforation secondary to typhoid fever age groups

Complications	Age Groups (Years)		P-Value
	≤45 n=58	>45 n=32	
Skin excoriation	10 (17.2%)	7 (21.9%)	0.591
Stoma retraction	3 (5.2%)	6 (18.80%)	0.040
Stenosis	1 (1.7%)	3 (9.4%)	0.092
Prolapse	3 (5.2%)	0 (0%)	0.191
Peristomal sepsis	5 (5.2%)	1 (3.1%)	0.317
Necrosis	1 (1.7%)	1 (3.1%)	0.666
Parastomal hernia	7 (12.1%)	2 (6.3%)	0.378
Death	2 (3.4%)	4 (12.5%)	0.099

Rate of stoma retraction was also high in male as compared to female (18% vs 0%; p=0.005) and death was also significantly high in male than female (12% vs 0%; p=0.023) other complications rate including skin excoriation was 24% in male and 12.5% in females,

stenosis 6% in males and 2.5% in females , prolapse 4% in males and 2.55 in females, peristomal sepsis 6% in males and 7.5% in females, necrosis 2% in males and 2.5% in females and parastomal hernia 12% in males and 7.5% in females as shown in Table 3.

Table No.3: Frequency of Complications of Ileostomy in the Management of Ileal Perforation Secondary to Typhoid Fever by Gender

Complications	Gender		P-Value
	Male n=50	Female n=40	
Skin excoriation	15(24%)	5(12.5%)	0.166
Stoma retraction	9 (18%)	0(0%)	0.005
Stenosis	3(6%)	1(2.5%)	0.423
Prolapse	2(4%)	1(2.5%)	0.694
Peristomal sepsis	3 (6%)	3 (7.5%)	0.777
Necrosis	1 (2%)	1 (2.5%)	0.873
Parastomal hernia	6 (12%)	3 (7.5%)	0.480
Death	6 (12%)	0 (0%)	0.023

Rate of complications was not statistically significant with respect to duration of typhoid fever including skin excoriation 11.1% in <3 and 24.1% in >3, stoma retraction 16.7% in <3 and 5.6% in >3, stenosis 8.3% in<3 and 1.9% in >3, prolapse 5.6% in <3 and 1.9% in >3, peristomal sepsis 5.6% in<3 and 7.4% in >3,necrosis 5.6% in <3 and 0% in >3, parastomal hernia 2.8% in <3 and 14.8% in >3, death rate 11.1% in <3 and 3.7% in >3 as shown in Table-4.

Table No.4: Frequency of Complications of Ileostomy in the Management of Ileal Perforation Secondary to Typhoid Fever by Duration of Typhoid Fever

Complications	Duration of typhoid fever		P-Value
	≤3 n=36	>3 n=54	
Skin excoriation	4 (11.1%)	13 (24.1%)	0.124
Stoma retraction	6 (16.7%)	3 (5.6%)	0.085
Stenosis	3 (8.3%)	1 (1.9%)	0.144
Prolapse	2 (5.6%)	1 (1.9%)	0.338
Peristomal sepsis	2 (5.6%)	4 (7.4%)	0.730
Necrosis	2 (5.6%)	0 (0%)	0.080
Parastomal hernia	1 (2.8%)	8 (14.8%)	0.062
Death	4 (11.1%)	2 (3.7%)	0.168

Skin excoriation was the commonest complication that was observed in 18.9% cases followed by stoma retraction 10%, parastomal hernia 10%, stenosis 4.4%, prolapse 3.3%, peristomal sepsis 6.7% and necrosis 2.2%. Mortality was observed in 6.7% (6/90) due to stoma.

DISCUSSION

In this study the average age of the patients was 40.30±10.14 years and mean duration of typhoid fever was 3.68±0.91 weeks. There were 55.56% male and 44.44% female. In Rahman et al [7] the common age groups affected was 1-50 years' age group (5 patients) and 61-70 years age groups (5 patients).The incidence in males was slightly greater than females. Male to female ratio was 2.5:1.

Onset of symptoms and time of presentation in the hospital are important prognostic factors. An early presentation holds a good prognosis. Unfortunately, in developing countries, the presentation to hospital is usually late with fully blown peritonitis, some cases may present with septicemia and multi-organ failure. Current literature strongly favors the surgical management only of enteric ileal perforation.[8,9] The age incidence is more in second decade. The perforation is common in 2nd and 3rd decade as evidenced by other studies.[10] The commonest cause of ileal perforation in a series was typhoid fever accounting for 53.5% of cases. The other causes of ileal perforation in this study are 25% nonspecific, 17.8% traumatic, 3.5% TB. Typhoid fever accounted for 56.6% of cases of ileal perforation in the series by Karmakar.[11]

In present study frequency of complications of ileostomy in the management of ileal perforation secondary to typhoid fever, skin excoriation was the commonest complication that was observed in 18.9% cases followed by stoma retraction 10%, parastomal hernia 10%, stenosis 4.4%, prolapse 3.3%, peristomal sepsis 6.7% and necrosis 2.2%. In another study it was reported that the commonly reported complications of ileostomy are skin excoriation (17.64%), stoma retraction (3.50%), stenosis (1.17%), prolapse (2.94%), peristomal sepsis (5.80%) and necrosis (0.58 %).[4,5] Death has been reported worldwide due to ileostomy.[6] In Rahman et al study[7] the common complications are wound infection, burst abdomen, faecal fistula and respiratory complications. Wound infection is the commonest complication in his study, with a complication rate of 21.4% in six patients, Burst abdomen rates about 1 0.7%, faecal fistula rates about 3.5% and respiratory complications about 14.2%. Santillana in his series reported a rate of 71.9% in 96 patients.[12]

In this study mortality was observed in 6.67% due to stoma. The complications and mortality due to ileostomy have been reported up to 18.2 percent and 4 percent, respectively.[4] These figures are much lower than the rates reported other studies such as 6.8% from Nepal, and 10.5% from India in another study.[13] In Jain et al study[6] the mortality rate was 17.1% which was significantly affected by perforation- admission interval of more than 48 hours, number of perforations and occurrence of postoperative complications. In present study rate of stoma retraction was high in males as compare to female and death was also significantly high in male than female. Our study showed a male preponderance of ileal perforation; this observation was

similar to previous reports by Beniwal et al[13] and Ugochukwu et al.[14] but this was at variance with the report of Edino et al.[15] who reported more female predominance. The reason for this difference is not completely understood but Beniwal et al.[13] reported that males are more exposed to risk and genetic predisposition also heightens the risk of infection. Again, the majority of the cases were within the paediatric age range (first and second decade of life); this was similarly reported by Ugochukwu et al.[14] Edino et al[15] and Ahmed et al.[16]

In this series the outcome of best results in terms of mortality, morbidity and post-operative complications were found to be in patients with ileostomy. The primary closure of perforation was associated with an overall 32% complication rate whereas only 17% in ileostomy group. Ileostomy proved to be the most successful procedure in this study in terms of overall mortality and morbidity, this is supported by Bhansali et al study [17], Kalid et al study [1], Meh et al.[18]

CONCLUSION

In this study skin excoriation was the commonest complication that was observed followed by stoma retraction, parastomal hernia, stenosis, prolapse, peristomal sepsis and necrosis. Mortality observed in this study was 6.67% due to stoma**.** Early surgery and adequate resuscitation are the important factors for successful management of patients with ileal perforation. This study proposes that ileostomy may be given priority over other surgical options especially in those moribund patients who present late in the course of their illness, have more than one perforation with massive fecal contamination of the abdominal cavity. Primary closure of perforation is a preferred technique in clinically stable patients with a single perforation with minimal soiling of the abdominal cavity.

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REFERENCES

1. Khalid S, Burhanulhuq, Bhatti AA. Non-traumatic spontaneous ileal perforation: experience with 125 cases. J Ayub Med Coll Abbottabad 2014; 26(4):526-9.
2. Chatham-Stephens K, Medalla F, Hughes M, Appiah GD, Aubert RD, Caidi H, et al. Emergence of extensively drug-resistant salmonella typhi infections among travelers to or from Pakistan - United States, 2016-2018. MMWR Morb Mortal Wkly Rep 2019; 68(1): 11-3.
3. Wain J, Hendriksen RS, Mikoleit ML, Keddy KH, Ochiai RL.Typhoid fever. Lancet 2015;385: 1136-45.
4. Poskus E, Kildusis E, Smolskas E, Ambrazevicius M, Strupas K. Complications after loop ileostomy closure: a retrospective analysis of 132 patients. Viszeralmedizin 2014; 30(4): 276–80.
5. Löb S, Luetkens K, Krajinovic K, Wiegering A, Germer CT, Seyfried F. Impact of surgical proficiency levels on postoperative morbidity: a single centre analysis of 558 ileostomy reversals. Int J Colorectal Dis 2018;33(5):601-8.
6. Jain S, Meena LN, Ram P. Surgical management and prognosis of perforation secondary to typhoid fever. Trop Gastroenterol 2016;37(2):123-8.
7. Rahman K, Krishnaswamy J, Muthukumaran G, Prakash S. A comparative study on outcome of ileal perforation after primary perforation closure and resection and ileostomy. Inter Surg J 2018; 5(2):445-51.
8. Malik AM, Laghari AA, Mallah Q, Qureshi GA, Talpur AH, Effendi S, et al. Different surgical options and ileostomy in typhoid perforation. World J Med Sci 2006;1(2):112-6.
9. Farooq T, Rashid MU, Lodhi MF, Farooq A, Ahmad S. Enteric ileal perforation primary repair versus loop ileostomy. Infect 2011;3(13.04):9.
10. Koume J, Kouadio L, Turquin HT. Typhoid ileal perforation: surgical experience of 64 cases. Acta Chir Belg 2004;104:445-7.
11. Karmakar SR, Dwivedi Dr, Bhalerao RA. Perforations of terminal ileum. Indian J Surg 1972;34:422-6.
12. Santillana M. Surgical complications of typhoid fever: enteric perforation. World J Surg 1991; 15(2):170-5.
13. Beniwal US, Jindal D, Sharma J, Jain S, Shyman G. Comparative study of operative procedures in typhoid perforation. Ind J Surg 2003;65:172-7
14. Ugochukwu AI, Amub OC, Nzegwu MA. Ileal perforation due to typhoid fever – review of operative management and outcome in an urban centre in Nigeria. Inter J Surg 2013;11:218–22.
15. Edino ST, Yakubu AA, Mohammed AZ, Abubakar IS. Prognostic factors in typhoid ileal perforation, a prospective study of 53 cases. J Natl Med Assoc 2007;99:1042–5.
16. Amed HN, Niaz MP, Amin MA, khanMH, Parhar AB. Typhoidperforation still a common problem: situation in Pakistan in comparison to other countries of low human development. J Pak Med Assoc 2006;56:230e2.
17. Bhansali SK. Gastrointestinal perforation: a study of 50 patients, 42: clinical study of 96 cases. J Post Grad Med Inst 1967;395-9.
18. Meh EA, Dogo P. Comparison of three for typhoid enteric perforation, a technique favored by operations for typhoid perforation. BJS 1997;84:558.

Compare Oxidative Role of Beta-Carotene and Resveratrol (3 4 5 Hydroxystillbene) in Methotraxate Induced Hepatotoxicity on the Basis of Morphology and Catalase Activity

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ABSTRACT

Objective: Compare the oxidative role of β-carotene (BC) and Resveratrol (RSV) in Methotrexate (MTX) induced liver toxicity based on morphology and catalase activity.

Study Design: Experimental longitudinal study

Place and Duration of Study: This study was conducted at the Al-Tibri Medical College & Hospital from January 2021 to October 2021 for a period of 10 months.

Materials and Methods: 48 healthy Wistar albino rats were attained and then divided into 6 groups, Group I (Control Group) received normal saline, Group II was given BC, Group III was given RSV, Group IV was given MTX, Group V was given BC+MTX, and Group VI was given RSV+MTX for 24 days. On the 25th day the subjects were euthanized and liver sections for studying the nuclear diameter was fixed with formalin and stained using H&E staining. The nuclear diameter was measured with ocular counting scale on a light microscope. The liver homogenate was used to analyze catalase enzyme content. Data was analyzed using SPSS with all variables given in Mean± S.D. for statistical analysis paired-t test was done with the level of significance being P-value <0.05.

Results: Mean Nuclear Diameter of Hepatocytes were 5.067 ± 0.1256 in G-I, 5.233±0.0422 in G-II, 5.217±0.0601 in G-III, 5.733±0.0803 in G-IV, and 5.483±0.0307 in G-V, and 5.467±0.0494 in G-VI. Significant difference was seen when all the groups were compared with the MTX Group (G-I vs G-IV P=0.008, G-II vs G-IV P=0.002, G-III vs G-IV P=0.006, G-V vs G-IV P=0.048, & G-VI vs G-IV P=0.042). The level of CAT in each Group in (U/mg protein) were 143.5±3.21 in G-I, 143.15±2.87 in G-II, 149.17±3.85 in G-III, 92.71±1.93 in G-IV, 123.09±3.19 in G-V, and 125.5±1.95 in Group VI. Significant difference was seen when all the groups were compared with the MTX groups (G-I VS G-IV P=0.0001, G-II VS G-IV P=0.001, G-III VS G-IV P=0.001, G-V VS G-IV P=0.01, & G-VI VS G-IV P=0.01).

Conclusion: According to the study results both therapeutic agents were significantly effective in prevention of the toxic effects of methotrexate on liver. There potent antioxidant effect was evidenced through morphological restoration of liver architecture and catalase activity.

Key Words: methotrexate, liver, catalase

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INTRODUCTION

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Liver is the biggest organ of the human body. Its weight is approximately 1500 Gm. This organ is a wedge shaped. It placed in right hypochondria and epigastrium and extending into left hypochondria. Naturally it is protected by rib cage and maintains its position by peritoneal reflection, followed by ligamentous attachment.[1, 2] Drug induced injury as a prolong time concern and diverting the attention towards it as a serious health issue and threatening situation for public. Moreover, it was came up as a main reason for an approved drug for the withdrawn from the market or Tag with the black box warning. The liver is the most vulnerable organ being damage by drugs, which further developed hepatotoxicity. Drug induced hepatotoxicity is unpredictable, and acute injury with various serious health problems. Hence it is established that the reactive metabolites formed from drugs are responsible for most cases of hepatotoxicity. Which are accompanied by the two reactive small molecules Reactive oxygen species (ROS) and Reactive nitrogen

species (RNS).These are biomarkers to predict the drug induced hepatotoxicity.[3] One of the drug which creates hepatotoxicity is methotrexate. Methotrexate (MTX) is broadly used as second line of immunomodulation.[4] It is an antimetabolite and antifolate drug. The indication of methotrexate is in various diseases. It is used as a therapy of leukemia, lymphoma and in many solid tumors. It indicates in immune modulatory effects against inflammatory disease like psoriasis, inflammatory bowel disease and inflammatory arthritis. It is effective with combination of other drugs in the treatment of several neoplastic diseases.[5]Its immune modulatory effect it is use in the treatment of eczema. Methotrexate also used as a chemotherapy agent for decades, and selected for therapy of un-ruptured ectopic pregnancies.[6] And used in treatment of demyelinating polyneuropathy.[7] Methotrexate currently indicated in various pediatric cases like Hodgkin lymphoma, Osteosarcoma, brain tumors and meningeal leukemia.[8] Beta-carotene is a lipid soluble carotenoids and it has natural antioxidants pigment which is usually found in various vegetables and fruits. It is an originator of vitamin A with so much antioxidant and immune properties. It boost up the antioxidant defensive system by inhibiting the single oxygen and combating peroxide radicals, and reacting directly with Per oxy radical through stabilizing the lipids membrane from target of free radicals. Beta-Carotene (BC) obstructs and upgrades the effects of APAP on liver tissue. Many studies have shown that BC has anti carcinogenic properties. It inhibits the carcinogenic activity, genetic damage and caspase-3 activity. It reduces the risk of cancers.[9] The other antioxidant compound Resveratrol (3,4,5) Trihydroxistillbene (Rsv) (3,4,5 trihydrostillbene) is a bioactive compound found in a great variety of plants such as plums, blueberry, peanuts and grapes. Various studies were conducted on (Rsv) and suggests the benefits for healthy antioxidants, anti-Inflammatory and hepatoprotective effects. Regarding liver disease studies it is known that the proliferation of stellate cells which plays key role in liver injury aggravating via oxidative stress. For this effect the bioactive compound prevent the liver cell damage.[10]

MATERIALS AND METHODS

An experimental study was conducted on 48 healthy Wistar albino rats after attaining ethical approval from the institutional review board of the university. The study took place at Al-Tibri Medical College & Hospital from January 2021 for a period of October 2021. The subjects were acquired from the animal house of the institute weighting between 210-310 grams. All the animals were kept in clean cages in a well-ventilated room with adequate light and ambient temperature between 23-25◦C. food and water were available ad libitum. Methotrexate, B-carotene, and Resveratrol were purchased from a local pharmacy shop. The subjects were divided into 6 groups each consisting of 8 subjects. The following intervention was performed in each group:

- Group I (control) was administered similar amount of 0.9% Normal Saline Solution only. `
- Group II (🡅-carotene) was administered a solution of β-carotene (10mg/kg/ day intraperitoneally) for a period of 24 days.
- Group III (Resveratrol) rats received resveratrol (10mg/kg/ day intraperitoneal) for a period of 24 days.
- Group IV (MTX) rats were given MTX on the 21st day of the study as a one-time only injection intraperitoneally 20mg/kg.
- Group V (β-carotene + MTX) subjects were administered β-carotene by intraperitoneally (10 mg/kg/day) for a period of 24 days, and then on the 21st day of the experiment they were also given MTX at a dose level of 20 mg/kg.
- Group VI (Resveratrol + MTX) rats were given intraperitoneally (10mg/kg/day) for a period of 24 days, and then on the 21st day were given MTX at a dose level of 20 mg/kg on day.

On day 25th of the study, all the subjects were weighted and euthanized under anesthesia. A midline longitudinal incision was given to expose the organs... Liver tissues for Catalase were stored at -25◦C for quantitative analysis. Histological study was carried out at the institution. The liver extracted from the subjects was wash with normal saline and cut into small pieces, fixed into 10% formalin for PAS for 36 hours. The liver samples were then stained using H&E staining for histological study. The nuclear diameter was measured with ocular counting scale on a light microscope. The liver homogenate was used to analyze catalase enzyme content. The activity of catalase was measured at 37◦C by following the rate of disappearance of hydrogen peroxide at 240nm. SPSS was used to analyze the data. The results were compared with paired t-test with $p< 0.05$ considered as statically significant. All results were expressed as means ± standard error (SEM).

RESULTS

Table 1: Shows the Mean Nuclear Diameter (µm) of Each Group

Table 2: Shows the Statistical Comparison using Paired T-test of Nuclear Diameter among Various Groups I to VI

Table 3: Shows the Biochemical parameters Catalase (CAT) analyzed in liver homogenate of experimental animals (Albino rats = 250 Gm average), to assess the hepatotoxicity of Methotrexate and its attenuation by 🡅-carotene and Resveratrol.

Table 4: Shows the Comparative statistical analysis of CAT of various Groups I to VI by paired T-test.

Table No.1: Nuclear Diameter of Hepatocytes (µm) in Group I – VI

Groups	Mean ± Standard Error Mean (SE)
Group I (Saline)	5.067 ± 0.1256
Group II (β-Carotene alone)	5.233 ± 0.0422
Group III (Resveratrol alone)	5.217 ± 0.0601
Group IV (Methotrexate alone)	5.733 ± 0.0803
Group V (β – Carotene + MTX)	5.483 ± 0.0307
Group VI (Resveratrol + MTX)	5.467 ± 0.0494

Results are expressed as Mean ± SE (Standard Error Mean = SE) MTX = Methotrexate

Table No.2: Statistical Comparison using Paired T-test of Nuclear Diameter among Various Groups I to VI

Paired Samples Statistics (95% Confidence Interval of the Difference)	
Paired Comparison Groups	Sig.(2-tailed) (P< 0.05)
Group I (Saline) vs. Group IV (Methotrexate)	.008**
Group II (🡅-Carotene) vs Group IV (Methotrexate)	.002**
Group III (Resveratrol) vs Group IV (Methotrexate)	.006**
Group V (β – Carotene + MTX) vs Group IV (Methotrexate)	.048**
Group VI (Resveratrol + MTX) vs Group IV (Methotrexate)	.042**
Group V (β – Carotene + MTX) vs Group VI (Resveratrol + MTX)	.695*

Results were considered significant when P < 0.05
MTX = Methotrexate
KEY: ** = Significant * = non-Significant

Table No.3: Biochemical parameters Catalase (CAT) analyzed in liver homogenate of experimental animals (Albino rats = 250 Gm average), to assess the hepatotoxicity of Methotrexate and its attenuation by -carotene and Resveratrol

Biochemical parameters in liver homogenates (Mean ± SE)	
Groups	CAT (U/mg Protein)
Group I (Saline Control)	143.5 ± 3.21
Group II (🡅-Carotene alone)	143.15 ± 2.87
Group III (Resveratrol alone)	149.17 ± 3.85
Group IV (Methotrexate alone)	92.71 ± 1.93
Group V (🡅-carotene + MTX)	123.09 ± 3.19
Group VI (Resveratrol + MTX)	125.5 ± 1.95

Results are expressed as Mean ± Standard error of mean (SE).
MTX = Methotrexate, CAT = Catalase

Table No.4: Comparative statistical analysis of CAT of various Groups I to VI by paired T-test

Groups	Sigificance (2-tailed)
G-I vs G-II	0.11*
G-I vs G-III	0.09*
G-I vs G-IV	0.0001**
G-II vs G-V	0.03**
G-III vs G-VI	0.03**
G-IV vs G-II	0.001**
G-IV vs G-III	0.001**
G-IV vs G-V	0.01**
G-IV vs G-VI	0.01**
G-V vs G-VI	0.11*

G = group. Results were considered significant when P < 0.05
Statistical significance P < 0.0001, P < 0.001, P < 0.01, P < 0.03
KEY:** = Significant * = Non Significant

DISCUSSION

Methotrexate is a potent drug with multiple uses. Its association with the group of anti-folate and –anti-metabolite drugs allows it to be given in the treatment of leukemia, lymphoma, rheumatoid arthritis, and several other solid tumors. [11] Despite its many uses in medicine, side effects of high dose methotrexate can be life threatening. Side effects include renal toxicity, neurotoxicity, hematological toxicity, pulmonary toxicity, mucocutaneous toxicity, and gastrointestinal toxicity [12]. Drug interactions can also increase the risk of Methotrexate toxicity, as drugs such as sulfamethoxazole and Trimethoprim can all displace methotrexate from bound protein in the serum reducing methotrexate clearance. There for drugs which alter the rate of elimination of methotrexate must be recognized by the practitioner so that drug-drug interaction can be avoided. [13] The aim of our study was to see if β-carotene and Resveratrol can reduce the toxicity induced by Methotrexate. The study observed an increase in the nuclear diameter of hepatocytes in the methotrexate treated group. This was due to injury to the liver hepatocyte cells caused by methotrexate. [14] This can be explained on the basis of distortion and disintegration of hepatocytes architecture. Significant difference was observed in the mean nuclear diameter when all the groups were compared to the methotrexate only group. Our study showed that Resveratrol and β-carotene both prevented an increase in the mean nuclear diameter of hepatocytes thereby reducing the toxic potential of methotrexate. [15] This finding is similar to another study that showed that resveratrol protects against methotrexate induced hepatic injury.[16-17] Firdous et al (2011) also reported that β-carotene administration had a hepatoprotective effect against the generation of free radicals and reduced oxidative stress,

thereby leading to a reported improvement in the hepatocyte architecture. A decrease in the amount of catalase enzyme was seen in the methotrexate treated group with other groups showing a significant difference in the amount of catalase. Both the groups with Resveratrol and β-Carotene prevented a reduction in the amount of catalase enzyme when methotrexate was administered along with it. [18] This is similar to another study by Dalaklioglu (2013) which showed that resveratrol significantly improved the activity of catalase in liver when compared to methotrexate treated group only. [18] The increased level of catalase is also seen in another study by El-Demerdash et al (2004) by showing that β-carotene is a potent antioxidant that increases the level of Catalase. [19] Furthermore, it was reported by Cetin et al (2008) that Resveratrol reduces oxidative stress and increases the levels of Catalase. [21] Further studies can be done to study more histological and biochemical features that can be altered by the administration of Both Resveratrol and β-Carotene.[20]

CONCLUSION

According to the study results both therapeutic agents were significantly effective in prevention of the toxic effects of methotrexate on liver. There potent antioxidant effect was evidenced through morphological restoration of liver architecture and catalase activity.

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REFERENCES

1. Vinnakota S, Jayasree N. A new insight into the morphology of the human liver: a cadaveric study. Int Scholarly Research Notices 2013.
2. Kose E, Sapmaz HI, Sarihan E, Vardi N, Turkoz Y, Ekinci N. Beneficial effects of montelukast against methotrexate-induced liver toxicity: a biochemical and histological study. Sci World J 2012:1.
3. Li Y, Xie X, Li M, Jiao X, Sun Y, Wang X, Tang B. Two-photon fluorescent probe for revealing drug-induced hepatotoxicity via mapping fluctuation of peroxynitrite. Chem Sci 2017; 8(5): 4006-11.
4. Seitz M. Molecular and cellular effects of methotrexate. Current Opinion In Rheumatol 1999; 11(3):226-32.
5. Braun J, Rau R. An update on methotrexate. Current opinion in Rheumatol 2009;21(3):216-23.
6. Ripellino P, Fleetwood T, Cantello R, Comi C. Treatment of chronic inflammatory demyelinating polyneuropathy: from molecular bases to practical considerations. Autoimmune diseases. 2014 :2014.
7. Stika CS. Methotrexate: the pharmacology behind medical treatment for ectopic pregnancy. Clin Obstet Gynecol 2012;55(2):433-9.
8. Imtiaz S, Kazmi A. Patterns of care and outcomes of adult osteosarcoma in a tertiary care cancer centre in Pakistan. J Pak Med Assoc 2014; 64(10):1166-70.
9. Kuoti Al-Rekabi BK, Al-Shwilly HA. Comparative Study on the Protective Effect of L-Carnitine in Combination with Beta-Carotene against Overdose Acetaminophen Induced Hepatotoxicity and Nephrotoxicity in Adults Male Rats. Ind J Public Health Research Devel 2019;10(1).
10. Özgöçmen M, Yeşilot Ş. The role of resveratrol in hepatatoxicity caused by methotrexate. Vet J Mehmet Akif Ersoy University ;6(2):57-63.
11. Wang W, Zhou H, Liu L. Side effects of methotrexate therapy for rheumatoid arthritis: a systematic review. Eur J Med Chem 2018;158: 502-16.
12. Sakura T, Hayakawa F, Sugiura I, Murayama T, Imai K, Usui N, et al. High-dose methotrexate therapy significantly improved survival of adult acute lymphoblastic leukemia: a phase III study by JALSG. Leukemia 2018;32(3):626-32.
13. Ferreri AJ, Cwynarski K, Pulczynski E, Fox CP, Schorb E, La Rosée P, et al. Whole-brain radiotherapy or autologous stem-cell trans-plantation as consolidation strategies after high-dose methotrexate-based chemoimmunotherapy in patients with primary CNS lymphoma: results of the second randomisation of the International Extranodal Lymphoma Study Group-32 phase 2 trial. The Lancet Haematol 2017;4(11):e510-23.
14. Annest NM, VanBeek MJ, Arpey CJ, Whitaker DC. Intralesional methotrexate treatment for keratoacanthoma tumors: a retrospective study and review of the literature. J Am Acad Dermatol 2007; 56(6):989-93.
15. Gaies E, Jebabli N, Trabelsi S, Salouage I, Charfi R, Lakhal M, Klouz A. Methotrexate side effects: review article. J Drug Metab Toxicol 2012;3(4): 1-5.

16. Suzuki K, Doki K, Homma M, Tamaki H, Hori S, Ohtani H, et al. Co-administration of proton pump inhibitors delays elimination of plasma methotrexate in high-dose methotrexate therapy. Br J Clin Pharmacol 2009;67(1):44-9.
17. Tunalı-Akbay T, Sehirli O, Ercan F, Sener G. Resveratrol protects against methotrexate-induced hepatic injury in rats. J Pharm Pharmaceutical Sci 2010;13(2):303-10.
18. Dalaklioglu S, Genc GE, Aksoy NH, Akcit F, Gumuslu S. Resveratrol ameliorates methotrexate-induced hepatotoxicity in rats via inhibition of lipid peroxidation. Human Experimental Toxicol 2013;32(6):662-71.
19. El-Demerdash FM, Yousef MI, Kedwany FS and Baghdadi HH. Cadmium-induced changes in lipid peroxidation, blood hematology, biochemical parameters and semen quality of male rats: protective role of vitamin E and b-carotene. Food and Chemical Toxicol 2004;42:1563–71.
20. Cetin A, Kaynar L, Kocyigit I, Hacioglu SK, Saraymen R, Ozturk A, et al. Role of grape seed extract on methotrexate induced oxidative stress in rat liver. Am J Chinese Med 2008;36: 861–72.

Aerobic Exercise: A Potent Method to Improve Morphology of Bone

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ABSTRACT

Objective: To study the effect of aerobic exercise on histomorphometery of bone.
Study Design: Experimental study
Place and Duration of Study: This study was conducted in Ziauddin University, Karachi from February 2021 to April 2021 for a period of 8 weeks.
Materials and Methods: The study samples were 12 male Sprague Dawly Rats (SD) weighing 200-300gms, divided into two groups; 6 assigned to the experimental group and 6 to the control group. Data was collected through Maze Engineers Multilane rat treadmill and Nikon INTENSELIGHT C-HGFI. Data analyzation was done using SPSS version 25. Skewness and Kurtosis tests were applied in order to check the normality of data. Independent T-test was applied between both the groups to determine mean values on the similar outcome measures and a p-value of <0.05 was considered to be significant**.**
Results: The study observed a statistically significant increase in Haversian canal diameter, increase in area in the post-exercise group of rats, an increase in the number of lamellae per osteon with exercise and a greater average osteon area in the exercise group. However, a statistically significant difference could not be observed in the number of osteon per high power field (HPF) between the two groups.
Conclusion: Findings of this study suggest that weight-bearing exercises such as treadmill running help increasing the density and strength of the cortical bones, amplifying their morphology. Thus, the study concluded that seven weeks of aerobic training results in improved bone morphology parameters.
Key Words: Aerobic Exercise, Bone Health, Bone Morphology

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INTRODUCTION

Bone health is a major concern of the modern era. Due to increasingly sedentary lifestyles being adopted, degenerative changes in bone are becoming a more common feature of modern times.[1] Aerobic exercises in particular are considered to have a positive influence deteriorating bone health. Bone health starts declining when there is greater bone absorption as compared to bone formation resulting in diminished cortical width reduced trabecular volume.[2]

Animal studies have demonstrated that aerobic exercises such as treadmill running and swimming help to preserve the architecture and composition of bone eventually resulting in overall increased bone strength; a process called "remodeling". Studies on young mice and rats have shown to increase bone mineral density and periosteal thickness. [3, 4]

During remodeling, key cells known as osteoclasts, osteoblasts and osteocytes perform a role in maintaining the homeostasis of the bone. Osteocytes are the most abundant type of cells which sense mechanical loads placed on the bone.[5] Osteoblasts are bone forming cells responsible for production of collagen type I and they mature to become osteocytes which regulate the composition of bone during mechanical strains. Osteoclasts on the other hand are responsible for reabsorption of damaged bone components.[6]

Bone is composed of organic and inorganic components. The inorganic components of bone consist of hydroxypeptides, calcium, fluoride and sodium ions. The organic components of bone mainly consist of collagen type I and some percentage of non-collagenous proteins.[7] The quantity of collagen has a direct influence on the mechanical integrity of bone. Type I collagen is found to be the most important structural component of the extracellular matrix responsible for the mineralization of the bone.[8] Alteration in crosslinking of these collagen fibers in the extracellular matrix of bone occurs due to lack of physical activity, old age, osteoporosis and osteopenia

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which may eventually result in bone deterioration leading to loss of bone mass.[9] Decreased mechanical competence due to low bone strength in response to decreased minerals such as collagen and number of lamellae may result in increased risk of fractures.[10]

Bone mass can be increased by mechanical stimulation. This includes increased loading on the bone resulting in increase in the bone matrix and other structural components of bone.[11]

Aerobic exercise such as treadmill running can induce mechanical loading stress on the bone. This loading regulates osteoblastic differentiation by bone matrix signaling process. In a rat model study, treadmill training has been shown to increase the cell signaling in bone resulting in increased production of osteoblasts into the bone lamellae showing a direct relationship of exercise in the prevention of bone mass loss.[12] Obesity is one of the factors said to increase bone resorption and decrease bone formation thus resulting in reduced bone mass and strength. Studies conducted on obese rats suggests that involuntary wheel running exercise improves the bone quality by limiting bone resorption.[13] It was histologically noted that treadmill running resulted in increased thickness and number of the bone trabeculae with increase in the cortical bone mass.[14] Hence, this research suggests that increased loading on the bone can improve the bone mass resulting in decreased chances of bone health deterioration.

MATERIALS AND METHODS

This Randomized Controlled Trial was carried out at Ziauddin University, Karachi, Pakistan. The sample was collected by simple random sampling. The subjects were 12 healthy young male Sprague Dawly Rats (SD) weighing 200-300gms, divided into two groups; 6 were assigned to the running/experimental group and 6 to the sedentary/control group.[15]The rats were randomly divided into 2 groups (1 running and other sedentary) experimental and control groups. They were housed in individual cages and fed a standard laboratory stock feed and water. Adequate temperature and day night cycles were maintained. The experimental group was trained for a total of 29 days i-e 7 weeks excluding the weekends. In week 1 they were assigned an exercise program beginning with a 5 minutes warm up of low intensity on a multilane rat treadmill which consisted of a running belt of appropriate size and grip to prevent animal from slippage with a transparent wall in front to enable that the animal watches the surrounding. The warm up time was not included in the exercise session time length. After warm up, the speed was gradually increased to 0.30- 0.34 m/s for 25 minutes/session. Week 2 consisted of 2 sessions per day with speeds increasing up to 0.35-0.45 m/s with a duration of 30-32 minutes/session. Week 3 and 4 consisted of 2 sessions per day with a constant speed of 0.45 m/s for a duration of 30 minutes/session. Following the downhill protocol, 2nd day of week 5 was the day when the rats exercised to the level of exhaustion i.e. speed of 0.55 m/s for 45 minutes/session twice a day. Rest of the days of week 5 continuing into week 6 and 7 the session was conducted once a day. The rate of exercise was 0.30 m/s for 15 minutes.[16] At the end of week 7 after exercising, all rats of both experimental and control group were sacrificed anesthetically, after which bilateral tibia of all the rats were harvested and the transverse section at the level of mid-shaft of tibia was removed from the bone for histological examination. The harvested bone was kept in formaldehyde solution for few hours and then the process of bone demineralization and dehydration using isopropyl alcohol was followed. After the removal of alcohol using xyelene solution, sample fixation and overnight paraffin embedding was done. Finally, 5 micrometer size sectioning of samples was done. The samples were then stained with hematoxylin and eosin dye. 10 slides were made per mouse tibia. Once the slides were prepared we used Nikon INTENSELIGHT C-HGFI microscope with its built in calibrated software to determine the average number of osteons per hpf, number of lamellae per osteon, osteon thickness, Haversian canal diameter and Haversian canal area.

RESULTS

At the end of the 7th week all rats were dissected anesthetically and their bilateral tibia were harvested to study under the microscope. After the preparation of the microscopic slides, both groups were studied under the microscope to assess the post exercise outcomes in exercising group and non-exercising group including the number of osteons/ Hpf, number of lamellae per osteon, area of Haversian canal, diameter of Haversian canal and area of osteon. All these morphological differences can be visually examined in Figure 1.Data was analyzed using SPSS version 25. All variables included in this study were continuous thus these were expressed in mean and standard deviation. Skewness and Kurtosis test were applied to check the normality of the data, values of the test showed that the data was normally distributed, based on this Independent T-test was applied between both the groups to determine mean values on the similar outcome measures. In all calculations, a p-value of <0.05 was considered to be significant. Statistical analysis proved significant difference in mean of the bone parameters of exercising and non-exercising group of rats. When the number of osteon per high power field were compared between the two groups we found that this average count was higher (8.33±1.5) in the exercise group as compared to the control group (6.33±2.25) but the difference was not statistically significant (p-value=0.101). (Table-1). The number of lamellae per osteon showed a significantly greater (p-value=0.002) average number of lamellae in the exercise group (2.79±0.25) than the controls (1.89±0.45). (Table-1). The mean area of Haversian

canals of the exercise group also was calculated to be significantly more (p-value=0.001) in the exercise group (99.21±22.56 µm2) as compared to the controls (39.58±12.37 µm2). (Table-1). We found similar results for Haversian canal diameters too. Controls had significantly smaller (p-value=0.001) diameters (6.69±1.42 µm) as compared to the exercisers (10.78±22.56 µm). (Table-1). Lastly, we calculated osteon area found significantly thicker osteons (p-value=0.001) in the exercise group (582.93±106.67 µm2) than the controls (287.37±27.25 µm2) (Table-1).

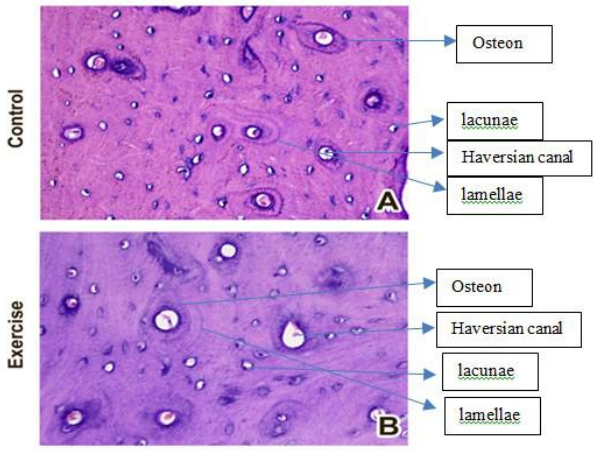

Figure No. 1: Post exercise outcomes in exercising group and non-exercising group including the number of osteons/ Hpf, number of lamellae per osteon, area and diameter of Haversian canal, diameter of Haversian canal and area of osteon.

Table No.1: Post-Training Analysis of the Exercise and Control Group

Variable	Group	N	Mean	Std. Deviation	p-Value
Number of Osteon / HPF	Control	6	6.33	2.25	0.101
	Exercise	6	8.33	1.50	
No of Lamella / Osteon	Control	6	1.81	0.45	0.002
	Exercise	6	2.79	0.25	
Haversian Canal Area (μm^2)	Control	6	39.58	12.37	0.001
	Exercise	6	99.21	22.56	
Haversian Canal Diameter (µm)	Control	6	6.69	1.42	0.001
	Exercise	6	10.78	1.26	
Osteon Area (μm^2)	Control	6	287.37	27.75	0.001
	Exercise	6	582.93	106.67	

DISCUSSION

In this study, we evaluated the histological changes induced by exercise on bone by assessing them visually and quantitatively using histological parameters. We demonstrate that seven weeks of aerobic training results in improved bone morphology parameters. We firstly observed a statistically significant increase in Haversian canal diameter and area in the post-exercise group of rats. This implies greater laying down of bone matrix in response to exercise resulting in increased blood supply to the bone which eventually results in greater diameter of vessels. In response, the matrix on the periphery of the Haversian canals undergoes resorption resulting in increase in their diameters. These findings are supported by those of Hart[17] which highlighted an increase in bone turnover markers. The author further supported our findings by underlining that moderate intensity aerobic training improves bone morphology and aids in slowing or inhibiting osteoporosis by causing a significant decrease in the rate of bone resorption.[17] However, in our study we exhibit direct visualization of these effects on the structural and functional unit of bone. Another important observation was an increase in the number of lamellae per osteon with exercise. It has been implicated by studies carried out previously that tensile strength of bones is directly proportional to the number of lamellae.[18-19] It is also reported that aerobic exercise has a significant impact on the morphology of bone by producing stimulatory signals for osteocytes. As a result, the osteocytes present a response of molecular signaling towards osteoclasts and osteoblasts thus resulting in bone matrix deposition ultimately leading to increased tensile strength. [20] In our study however, we could not find a statistically significant difference in the number of osteon per high power field (HPF) between the two groups. Though the difference being statistically non-significant, we observed that the mean values were greater in the exercise group. This may be due to the fact that minimal strain is sensed by the osteocytes at the front of the tunnel which are involved in laying down new osteon. [21] However, findings of the same study further added that increased mechanical loading in cortical bone leads to more bone remodeling with an increased yet smaller number of osteons and tinier Haversian canals. Finally, we found greater average osteon area in the exercise group. Our findings are consistent with the study of Harding & Beck [22] which revealed that weight-bearing exercises such as treadmill running help in increasing the density and strength of the cortical bones thus amplifying the morphology of bones. However, the study added that as compared to the lower impact aerobics such as walking, higher impact aerobics such as treadmill running yields a more profound effect on the morphology of bones. Moreover, the method used in this analysis was DEXA scan, whereas we directly measured the osteon area histologically.[22]

CONCLUSION

The findings of this study suggest that weight-bearing exercises such as treadmill running help in increasing

the density and strength of the cortical bones thus amplifying the morphology of bones.

Author's Contribution:

Concept & Design of Study:	Munira Mukadam
Drafting:	Kevin Joseph Jerome Borges, Sumaira Imran Farooqui
Data Analysis:	Rehan Ahmed Siddiqui, Syed Nudrat Shah, Amna Amir Khan
Revisiting Critically:	Munira Mukadam, Kevin Joseph Jerome Borges
Final Approval of version:	Munira Mukadam

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

REFERENCES

1. Winther A, Ahmed LA, Furberg AS, Grimnes G, Jorde R, Nilsen OA, et al. Leisure time computer use and adolescent bone health—findings from the Tromsø Study, Fit Futures: a cross-sectional study. BMJ Open 2015;5(6):e006665.
2. Santos L, Elliott-Sale KJ, Sale C. Exercise and bone health across the lifespan. Biogerontol 2017;18(6):931-46.
3. Gardinier JD, Rostami N, Juliano L, Zhang C. Bone adaptation in response to treadmill exercise in young and adult mice. Bone reports 2018;8:29-37.
4. Chen X, Li L, Guo J, Zhang L, Yuan Y, Chen B, Sun Z, et al. Treadmill running exercise prevents senile osteoporosis and upregulates the Wnt signaling pathway in SAMP6 mice. Oncotarget 2016;7(44):71072.
5. Arias CF, Herrero MA, Echeverri LF, Oleaga GE, López JM. Bone remodeling: A tissue-level process emerging from cell-level molecular algorithms. PloS one 2018;13(9):e0204171.
6. Han Y, You X, Xing W, Zhang Z, Zou W. Paracrine and endocrine actions of bone—the functions of secretory proteins from osteoblasts, osteocytes, and osteoclasts. Bone Res 2018;6(1): 1-1.
7. Farbod K, Nejadnik MR, Jansen JA, Leeuwenburgh SC. Interactions between inorganic and organic phases in bone tissue as a source of inspiration for design of novel nanocomposites. Tissue Engineering Part B: Reviews. 2014; 20(2):173-88.
8. Paola CM, Camila AM, Ana C, Marlon O, Diego S, Robin Z, et al. Functional textile finishing of type I collagen isolated from bovine bone for potential healthtech. Heliyon 2019;5(2):e01260.
9. Hammond MA, Laine TJ, Berman AG, Wallace JM. Treadmill exercise improves fracture toughness and indentation modulus without altering the nanoscale morphology of collagen in mice. PLoS One 2016;11(9):e0163273.
10. Saito M, Kida Y, Kato S, Marumo K. Diabetes, collagen, and bone quality. Current osteoporosis reports. 2014 Jun;12(2):181-8.
11. Skedros JG, Keenan KE, Williams TJ, Kiser CJ. Secondary osteon size and collagen/lamellar organization ("osteon morphotypes") are not coupled, but potentially adapt independently for local strain mode or magnitude. J Structural Biol 2013;181(2):95-107.
12. Yuan Y, Chen X, Zhang L, Wu J, Guo J, Zou D, et al. The roles of exercise in bone remodeling and in prevention and treatment of osteoporosis. Progress in Biophysics and Molecular Biol 2016;122(2): 122-30.
13. Cao JJ, Picklo MJ. Involuntary wheel running improves but does not fully reverse the deterioration of bone structure of obese rats despite decreasing adiposity. Calcified Tissue Int 2015;97(2):145-55.
14. Berman AG, Hinton MJ, Wallace JM. Treadmill running and targeted tibial loading differentially improve bone mass in mice. Bone reports 2019;10:100195.
15. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Ind J Psychological Med 2013;35(2):121.
16. Ríos-Kristjánsson JG, Rizo-Roca D, Kristjánsdóttir KM, Núñez-Espinosa CA, Torrella JR, Pagès T, et al. A three-criteria performance score for rats exercising on a running treadmill. Plos one 2019;14(7):e0219167.
17. Hart NH, Nimphius S, Rantalainen T, Ireland A, Siafarikas A, Newton RU. Mechanical basis of bone strength: influence of bone material, bone structure and muscle action. J Musculoskeletal Neuronal Interactions 2017;17(3):114.
18. Fonseca H, Moreira-Gonçalves D, Coriolano HJ, Duarte JA. Bone quality: the determinants of bone strength and fragility. Sports Med 2014;44(1): 37-53.
19. Osterhoff G, Morgan EF, Shefelbine SJ, Karim L, McNamara LM, Augat P. Bone mechanical properties and changes with osteoporosis. Injury 2016;47:S11-20.
20. Davison KS, Blimkie CJR, Faulkner RA, Giangregorio L. Bone Adaptation To Mechanical Loading: How Does Bone Sense The Need For Change to Loading From Exercise? Current Topics Osteoporosis 2005;118-143.
21. Smit TH. Closing the osteon: Do osteocytes sense strain rate rather than fluid flow? Bio Essays 2021;2000327.
22. Harding AT, Beck BR. Exercise, osteoporosis, and bone geometry. Sports 2017;5(2).

The Impact of Obstructive Jaundice on Quality of Life

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ABSTRACT

Objective: The purpose of the study is to assess the effects of gall bladder disease patients to maintain their quality of life of having obstructive jaundice.

Study Design: Case control study.

Place and Duration of Study: This study was conducted at the Civil Hospital's Outpatient Department of General Surgery, Unit-1, and Karachi from 18th December 2018 to June 2019.

Materials and Methods: It was conducted on 195 patients of both genders age 20yrs – 80yrs diagnosed with obstructive jaundice and underwent for biliary patenting. In those patients we assessed quality of life with the short form-36 (SF-36) which includes 8 domains. SPSS version-21 was used to analyze the data.

Results: The results of our study revealed statistically highly significant effect of cholelithiasis, chronic cholecystitis and gall bladder polyp on quality of life of obstructive jaundice patients ($p<0.001$*). Also patients with such diseases also had a significantly lower SF-36quality of life scores for both overall and in all eight individual domains than those patients who did not have those diseases, whereas it also indicated that the existence of gall bladder carcinoma in patients with obstructive jaundice didn't have a statistically significant effect on their quality of life ($p>0.05$).

Conclusion: Our study concludes that quality of life of those patients who were suffering from the benign causes of obstructive jaundice; such as cholelithiasis, chronic cholecystitis and gall bladder polyp were more significantly improved after therapy, whereas patients with gall bladder carcinoma had a worst effect on quality of life for both the genders.

Key Words: Cholelithiasis, Gallbladder polyp, Cholecystitis, Gall bladder carcinoma

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INTRODUCTION

Gallstone is a prolonged recurring hepato-biliary illness. It happens due to the spoiled cholesterol metabolic system, bile acids, and bilirubin.

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The prevalence of gallstone disease has stretched from 5.2% to 10% in Africa and 6.3% in Iran. The gold standard for diagnosing obstructive jaundice is Endoscopic Retrograde Cholangio Pancreatography (ERCP). ERCP can identify choledo-cholithiasis, common bile duct strictures and any other obstruction. Impairment of quality of life may be due to the biliary obstruction that results in cholangitis. [1-5].

MATERIALS AND METHODS

This study used non-probability, consecutive sampling to choose cases from the Civil Hospital Outpatient Department of General Surgery, Unit-1, Karachi. The study period was from 18-dec-2018 to june-2019. The study began when CPSP approved it. The Dow University Health Science, Civil Hospital ethical review committee approved the data gathering. The study included 195 patients aged 20 to 80 years of both sexes. Patients with obstructive jaundice and biliary patenting for more than 2 years were excluded from the research. The patients' age, duration since biliary patenting, and gender were collected. The SF-36 measures QoL in 8 domains: physical function, role-

physical, bodily pain, general health, vitality, social function, role-emotional, and mental health (MH).

This was done using SPSS version 21. Age, time since biliary patenting, serum bilirubin, and QoL evaluation score were expressed as Mean SD. The frequency and percentages of cholelithiasis, incidental gallbladder cancer, gallbladder polyp, and chronic cholecystitis were calculated.

Stratification controlled gender, age, cholelithiasis, incidental gallbladder cancer, gallbladder polyp, and chronic cholecystitis. Post stratification, a Mann-Whitney U-test was used. Statistical significance was defined as p 0.05 or less.

RESULTS

Data of total 195 patients were analyzed for the study. The mean age of patients was 55.85 ± 15.40 years whereas 98 (50.3%) of them were male while 97 (49.7%) of them were females. Furthermore, 36 (18.5%) of them had cholelithiasis, 24 (12.3%) of them had chronic cholecystitis, 16 (8.2%) of them had gall bladder polyp while 3 (1.5%) of them had incidental gall bladder carcinoma. Moreover, their mean total SF-36 quality of life score was 55.20 ± 12.50. The study results showed that there was a statistically significant effect of cholelithiasis on quality of life of obstructive jaundice patients (p<0.001) where patients who had cholelithiasis had significantly lower SF-36 quality of life scores, both overall and in all eight individual domains, than patients who did not have cholelithiasis (table-1).

The study results further showed that there was a statistically significant effect of chronic cholecystitis on quality of life of obstructive jaundice patients (p<0.001) where patients who had chronic cholecystitis had significantly lower SF-36 quality of life scores, both overall and in all eight individual domains, than patients who did not have chronic cholecystitis (table 2). The study results also showed that there was a statistically significant effect of gall bladder polyp on quality of life of obstructive jaundice patients (p<0.001) where patients who had gall bladder polyp had significantly lower SF-36 quality of life scores, both overall and in all eight individual domains, than patients who did not have gall bladder polyp (table 3). The study results further revealed that the presence of gall bladder carcinoma in obstructive jaundice patients did not have a statistically significant effect on their quality of life (p>0.05), though the patients with gall bladder carcinoma had lower SF-36 quality of life scores, both overall and in all eight individual domains (table 4).

Table No.1: Cholelithiasis and Quality of Life

Quality of Life (QoL) Domain	Cholelithiasis		Mann-Whitney U test
	No	Yes	p-value
N	159	36	-
Physical function (PF)			
Mean± SD	55.98±16.6	44.12±12.62	<0.001*
Median [IQR]	56.59[69.06-41.49]	41.35[49.66-32.31]	
Max – Min	94.27-25.3	71.83-27.52	
Role-physical (RP)			
Mean± SD	57.28±17.41	43.14±11.53	<0.001*
Median [IQR]	57.99[71.34-40.98]	42.78[48.02-34.76]	
Max – Min	89.18-25.29	76.42-25.42	
Body pain (BP)			
Mean± SD	62.36±17.41	51.11±14.66	<0.001*
Median [IQR]	62.57[76.89-48.13]	49.24[60.43-41]	
Max – Min	93.39-25.24	91.17-25.18	
General health (GH)			
Mean± SD	50.07±13.46	41.12±10.38	<0.001*
Median [IQR]	50.23[59.36-39.25]	40.41[45.91-32.01]	
Max – Min	87.01-25.88	69.4-25.59	
Vitality (VT)			
Mean± SD	55.32±16.41	44.87±14.85	<0.001*
Median [IQR]	54.76[69.05-42.83]	43.26[50.61-34.94]	
Max – Min	94.44-25.26	88.41-25.15	
Social function (SF)			
Mean± SD	63.15±16.02	51.23±13.74	<0.001*
Median [IQR]	63.45[74.85-51.47]	51.32[63.37-39.68]	
Max – Min	93.41-27.87	74.86-27.27	
Role emotional (RE)			
Mean± SD	61.32±17.89	43.33±12.97	<0.001*
Median [IQR]	62.34[76.48-46.67]	41.3[[53.79-35.7]	
Max – Min	93.54-25.31	78.31-26.92	
Mental health (MH)			
Mean± SD	53.81±15.65	42.75±12	<0.001*
Median	53.35[62.	40.66[51.81-	

[IQR]	99-39.62]	33.3]	
Max – Min	94.66-25.24	72.61-25.08	
Total SF-36-Qol Score			
Mean± SD	57.41±12	45.46±9.84	<0.001*
Median [IQR]	56.88[63.72-50.03]	47.2[50.88-38.27]	
Max – Min	92.2-26.99	64.15-26.32	

Table No.2: Chronic Cholecystitis and Quality of Life

Quality of Life (QoL) Domain	Chronic cholecystitis		Mann-Whitney U test
	No	Yes	p-value
N	171	24	-
Physical function (PF)			
Mean± SD	55.73±16.26	39.96±11.46	<0.001*
Median [IQR]	56.59[68.67-41.15]	35.52[50.47-29.81]	
Max – Min	94.27-25.3	63.1-27.52	
Role-physical (RP)			
Mean± SD	55.98±17.01	45.37±17.28	0.005*
Median [IQR]	56.54[69.98-40.92]	40.63[54.04-31.56]	
Max – Min	89.18-25.29	84.31-25.42	
Body pain (BP)			
Mean± SD	62.26±17.13	46.21±12.92	<0.001*
Median [IQR]	62.57[76.23-48.32]	44.37[55.86-36.92]	
Max – Min	93.39-25.24	72.29-25.18	
General health (GH)			
Mean± SD	49.54±13.17	40.41±12.34	0.002*
Median [IQR]	50[58.21-38.76]	40.65[46.3-29.97]	
Max – Min	87.01-25.88	75.28-25.59	
Vitality (VT)			
Mean± SD	54.96±16.62	42.27±11.71	<0.001*
Median [IQR]	54.45[69.05-42.07]	43.8[50.89-31.37]	
Max – Min	94.44-25.88	63.09-25.15	
Social function (SF)			
Mean± SD	62.25±15.96	51.66±15.71	0.003*
Median [IQR]	63.08[73.84-51.15]	50.73[61.85-37.03]	
Max – Min	93.41-27.27	86.8-29.68	
Role emotional (RE)			
Mean± SD	60.12±17.7	45.93±16.77	<0.001*
Median [IQR]	60.16[75.11-44.69]	40.05[56.52-32.12]	
Max – Min	93.54-25.31	86.84-26.92	
Mental health (MH)			
Mean± SD	53.84±15.19	37±9.62	<0.001*
Median [IQR]	53.35[62.9-40.45]	36.12[41.61-28.33]	
Max – Min	94.66-25.95	58.87-25.08	
Total SF-36-Qol Score			
Mean± SD	56.83±11.7	43.6±12.08	<0.001*
Median [IQR]	56.17[62.52-49.38]	44.23[52.52-33.02]	
Max – Min	92.2-29.31	64.99-26.32	

Table No.3: Gall bladder Polyp and Quality of Life

Quality of Life (QoL) Domain	Gall bladder Polyp		Mann-Whitney U test
	No	Yes	p-value
N	179	16	-
Physical function (PF)			
Mean± SD	54.51±16.46	45.76±16.07	0.043*
Median [IQR]	54.06[68.32-39.95]	41.9[55.68-31.59]	
Max – Min	94.27-25.3	86.11-28	
Role-physical (RP)			
Mean± SD	56.21±16.71	37.44±15.32	<0.001*
Median [IQR]	56.42[69.98-41.46]	31.81[40.82-27.27]	
Max – Min	89.18-25.42	80.91-25.29	
Body pain (BP)			
Mean± SD	61.4±17.12	47.76±16.7	0.003*
Median [IQR]	61.55[75.68-47.63]	45.26[57.85-34.51]	
Max – Min	93.39-25.18	91.63-27.47	
General health (GH)			
Mean± SD	49.15±13.1	40.23±14.18	0.010*
Median [IQR]	4869[57.95-38.76]	37.71[44.73-28.49]	
Max – Min	87.01-25.59	72.75-25.96	
Vitality (VT)			
Mean± SD	54.48±16.38	41.21±14.54	0.002*
Median [IQR]	53.74[66.11-42.07]	39.89[47.42-28.88]	
Max – Min	94.44-25.15	79.52-25.26	
Social function (SF)			
Mean± SD	61.85±16.09	50.84±15.17	0.009*
Median [IQR]	62.1[73.55-50.67]	50.41[64.57-36.34]	
Max – Min	93.41-27.27	73.11-30.25	
Role emotional (RE)			
Mean± SD	59.7±17.64	43.46±17.69	0.001*
Median [IQR]	59.3[74.95-44.38]	37.9[48.08-31.17]	
Max – Min	93.54-25.31	84.58-27.44	
Mental health (MH)			
Mean± SD	52.67±15.59	41.67±12.35	0.007*
Median [IQR]	52.57[62.48-39.33]	41.35[52.07-30.28]	
Max – Min	94.66-	62.34-25.24	

	25.08		
Total SF-36-Qol Score			
Mean± SD	56.25±12.1	43.55±11.25	<0.001*
Median [IQR]	56.08[62.24-48.48]	44.92[51.41-32.61]	
Max – Min	92.2-26.32	65.96-26.99	

Table No.4: Incidental Gall bladder Carcinoma and Quality of Life

Quality of Life (QoL) Domain	Incidental gall bladder carcinoma		Mann-Whitney U test
	No	Yes	p-value
N	192	3	-
Physical function (PF)			
Mean± SD	54±16.56	40.24±12.06	0.154
Median [IQR]	53.08[66.61-39.89]	34.76[54.06-31.89]	
Max – Min	94.27-25.3	54.06-31.89	
Role-physical (RP)			
Mean± SD	54.8±17.41	46.53±12.9	0.414
Median [IQR]	54.26[69.3-39.64	49.22[57.87-32.5]	
Max – Min	89.18-25.29	57.87-32.5	
Body pain (BP)			
Mean± SD	60.49±17.45	46.67±13.94	0.174
Median [IQR]	60.25[74.87-46.84]	42.95[62.09-34.97]	
Max – Min	93.39-25.18	62.09-34.97	
General health (GH)			
Mean± SD	48.52±13.42	42.1±10.75	0.412
Median [IQR]	47.99[57.85-38.33]	46.45[50-29.86]	
Max – Min	87.01-25.59	50-29.86	
Vitality (VT)			
Mean± SD	53.56±16.64	42.46±11.15	0.251
Median [IQR]	52.47[65.73-41.65]	38.39[55.07-33.92]	
Max – Min	94.44-25.15	55.07-33.92	
Social function (SF)			
Mean± SD	61.19±16.19	45.37±15.86	0.095
Median [IQR]	61.84[72.7-50.06]	38.83[63.45-33.83]	
Max – Min	93.41-27.27	63.45-33.83	
Role emotional (RE)			
Mean± SD	58.63±18.1	41.53±16.22	0.106
Median [IQR]	58.73[74.79-43.99]	33.94[60.16-30.5]	
Max – Min	93.54-25.31	60.16-30.5	
Mental health (MH)			
Mean± SD	51.97±15.6	38.65±12.08	0.143
Median [IQR]	51.87[61.62-39.15]	32.75[52.55-30.65]	
Max – Min	94.66-25.08	52.55-30.65	
Total SF-36-Qol Score			
Mean± SD	55.4±12.44	42.95±12.38	0.087
Median [IQR]	54.93[61.6-48.24]	38.61[56.91-33.32]	
Max – Min	92.2-26.32	56.91-33.32	

DISCUSSION

Most patients with biliary abrasions are old and unable to afford surgery. This study looked at how benign and malignant gallbladder problems affect quality of life. Patients with benign or malignant obstructive jaundice ranged in age from 29 to 70 years. In contrast, malignant etiologies were more common in people aged 50+. [23] Many studies have indicated that malignant obstructive jaundice increases with age [24,25]. Our study found that older patients were more likely to develop malignant obstructive jaundice. Men are more likely than women to have benign or malignant obstructive jaundice. Bodily jaundice male-female ratio was 1.33, while malignant obstructive jaundice was 1.23. [23] Gall stones are the most common cause of obstructive jaundice in females.[26,8] More study backed up the results. [24,26] Our study indicated that males had slightly more gall bladder disease than females in obstructive jaundice.

Bekele et al. found that benign obstructive jaundice was the most common etiology in Ethiopia. The study also found that benign causes of choledo-cholithiasis were more common, with 11 patients (22%) having common bile duct stricture and 2 (4%) having post cholecystectomy common bile duct stone. The most common cause of benign is choledocholithiasis. [24,27-29] This study found pancreatic head cancer (15%), gallbladder carcinoma (8%) and cholangio-carcinoma (5%). (8 percent). 4% The same was true with obstructive jaundice. [24,29] We found cholelithiasis to be the most common benign cause of obstructive jaundice, followed by chronic cholecystitis and gallbladder polyps, with 3 (1.5%) having incidental gallbladder malignancy. The most common benign cause of obstructive jaundice was cholelithiasis. Finan et al. studied gastrointestinal symptoms and QoL after cholecystectomy. In addition to the SF-36, the survey covered symptoms of biliary illness and other benign gastrointestinal problems. Patients with symptomatic gallstone disease benefitted from laparoscopic cholecystectomy. [30] Malignant incidental gallbladder carcinoma patients' quality of life increased while benign causes of obstructive jaundice including cholelithiasis and chronic cholecystitis worsened (p=0.087). Some studies combined the SF-36 and GIQLI, or a general health and postoperative QoL questionnaire. Quintana et al. (19) utilized the SF-36 to assess post-cholecystectomy patients. Their findings revealed that both the SF-36 and GIQLI were valid QoL measures. [31] With benign and malignant obstructive jaundice, the SF-36 Health Survey predicts Qol.

CONCLUSION

Obstructive jaundice is a common and difficult to treat condition. On the other hand, gallbladder cancer patients had greater quality of life than those with benign causes of obstructive jaundice, such as

cholelithiasis. This study demonstrates that early detection and treatment of obstructive jaundice is critical.

Author's Contribution:

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Final Approval of version:	Farhana Memon

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

REFERENCES

1. Schirmer BD, Winters KL, Edlich RF. Cholelithiasis and cholecystitis. J Long Term Eff Med Implants 2005;15:329-38.

2. Tazuma S. Gallstone disease: epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). Best Pract Res Clin Gastroenterol 2006;20(6):1075-83.

3. Sachdeva S, Khan Z, Ansari MA, Khalique N, Anees A. Lifestyle and gallstone disease: Scope for primary prevention. Ind J Community Med 2011;36:263-7.

4. Hou L, Shu XO, Gao YT, Ji BT, Weiss JM, Yang G, et al. Anthropometric measurements, physical activity, and the risk of symptomatic gallstone disease in Chinese women. Ann Epidemiol 2009;19(5):344-50.

5. Silva MA, Wong T. Gallstones in chronic liver disease. J Gastrointest Surg 2005;9(5):739-46.

6. Kratzer W, Mason RA, Kächele V. Prevalence of gallstones in sonographic surveys worldwide. J Clin Ultrasound 1999;27(1):1-7.

7. Farzaneh E, Zavvareh HT, Gharadaghi J, Sheikhvatan M. Prevalence and characteristics of gallstone disease in an Iranian population: A study on cadavers. Hepatobiliary Pancreat Dis Int 2007;6(5):509-12.

8. Channa NA, Khand FD, Bhangwer MI, Leghari MH. Surgical incidence of cholelithiasis in hyderabad and adjoining areas (Pakistan). Pak J Med Sci 2004;20(1):13-17.

9. Panpimanmas S, Manmee C. Risk Factors for Gallstone Disease in a Thai Population. J Epidemiol 2009;19(3):116-121.

10. Chandran AP, Sivarajan R, Srinivasan V, Srinivas M, Jayanthi V. Risk profile for gallstone disease in southern Indian population: Is there anything new? Ind J Gastroenterol 2014;33(3):254-257.

11. Jazrawi RP. Gallstones and their Complications. Medicine 2002;30(12):80-82.

12. Pacchioni M, Nicoletti C, Caminiti M, Calori G, Curci V, Camisasca R, et al. Association of Obesity and Type II Diabetes Mellitus as a Risk Factor for Gallstones. Digestive Diseasesand Sci 2000;45(10):2002-2006.

13. Roche SP, Kobos R. Jaundice in the adult patient. Am Fam Physician 2004;69(2):299-304.

14. Bekele Z, Yifru A. Obstructive jaundice in adult Ethiopians in a referral hospital. Ethiop Med J 2000;38(4):267-75.

15. Aziz M, Ahmad N. Incidence of malignant Obstructive Jaundice - a study of hundred patients at Nishtar Hospital Multan. Ann KE Med Coll 2016;10(1):71–3.

16. Hina H, Khan SA,Muneer S, Adil SA. Diagnostic accuracy of ultrasound in evaluation of obstructive jaundice with MRCP as gold standard. Pak J Med Sci 2020;36(4): 652–656.

17. Khurram M, Durrani AA, Hasan Z, Butt AUA, Ashfaq S. Endoscopic retrograde cholangio-pancreatographic evaluation of patients with obstructive jaundice. J Coll Physicians Surg Pak 2003;13(6):325–8.

18. Akhtar S, Mufti TS. Diagnostic accuracy of obstructive jaundice on ultrasonography at Ayub Hospital complex. J Ayub Med Coll Abottabad 1999;11(1):45–6.

19. Cheema KM, Ahmad F, Gondal SH. Evaluation of etiological incidence and diagnostic modalities in obstructive jaundice. Pak Postgrad Med J 2001;12(4):160–4.

20. Chu D, Adler DG. Malignant biliary tract obstruction: evaluation and therapy. J Natl Compr Canc Netw 2010;8(9):1033-44.

21. Sultana A, Smith CT, Cunningham D, Starling N, Neoptolemos JP, Ghaneh P. Meta-analyses of chemotherapy for locally advanced and metastatic pancreatic cancer. J Clin Oncol 2007;25(18): 2607-15.

22. Valle J, Wasan H, Palmer DH, Cunningham D, Anthoney A, Maraveyas A. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med 2010;362(14):1273-81.

23. Roy BC, Hanifa MA, Alam MS, Naher S, Sarkar P. Etiological Spectrum of Obstructive Jaundice in a Tertiary Care Hospital. Global Journal of Medical Research: I Surgeries and Cardiovascular System 2015;15(4):1-5.

24. Chalya PL, Kanumba ES, McHembe M. Etiological spectrum and treatment outcome of Obstructive jaundice at a University teaching Hospital in northwestern Tanzania: A diagnostic and therapeutic challenges. BMC Res Notes 2011;4:147.

25. Witwit RJ. Relation between the clinical presentation and etiology of obstructive jaundice. Kufa Med J 2011;14(1):209-213.

26. Siddique K, Ali Q, Mirza S, Jamil A, Ehsan A, Latif S, Malik AZ. Evaluation of the aetiological spectrum of obstructive jaundice. J Ayub Med Coll Abbottabad 2008;20(4):62-6.

27. Verma SR, Sahai SB, Gupta PK, Munshi A, Verma SC, et al. Obstructive Jaundice- Etiological Spectrum, Clinical, Biochemical and Radiological Evaluation: at a Tertiary Care Teaching Hospital. Int J Tropical Med 2010;7(2).

28. Saddique M, Iqbal SA. Management of Obstructive Jaundice: Experience in a Tertiary Care Surgical Unit. PJS 2007;23(1):23-25.

29. Khanzada TW, Samad A, Memon W, Kumar B. Etiological Spectrum of Obstructive Jaundice. JPMI 2008; 22(2):157-160.

30. Finan KR, Leeth RR, Whitley BM, Klapow JC, Hawn MT. Improvement in gastrointestinal symptoms and quality of life after cholecystectomy. Am J Surg 2006;192:196-202

31. Quintana JM, Cabriada J, Aróstegui I, Oribe V, Perdigo L, Varona M, et al. Health-related quality

of life and appropriateness of cholecystectomy. Ann Surg 2005;241:110-118.

The Pattern of Bacterial Isolates in Cases of Empyema Thoracic in Children

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ABSTRACT

Objective: To determine the frequency of pattern of bacterial isolates in children with thoracic empyema visiting to Children Hospital Larkana, Sindh.

Study Design: Cross sectional Descriptive Study

Place and Duration of Study: This study was conducted at the Department of Paediatric Medicine, Children Hospital CMC (H), SMBBMU, Larkana, Sindh, Pakistan from September, 2020 to March, 2021 for a period of six months.

Materials and Methods: All patients who implemented the inclusion criteria and admitted in Children Hospital CMC (H), Larkana were took in the study. The procedure, its risks and benefits of the study enlightened and then informed consent was received. Chest x-rays were taken in all patients at the time of admission, after intercostal tube drain (ICTD) introduction, its removal and at discharge, while ultrasound CT of chest were done when needed. Diagnostic thoracentesis was performed and pleural fluid was submitted for biochemical analysis (total and differential leukocyte count, protein, sugar, and LDH) and microscopic analysis (Gram staining, culture, and smear for AFB and Gen Expert). Outcome variable i.e. pattern of bacterial isolates was assessed. All the collected data were recorded into the proforma added towards the end and used electronically for research purpose.

Results: Mean ± SD of age was 5.1±2.3 years. Out of 128 patients, 77 (60.2%) were male while 51 (39.8%) were female. In distribution for pattern of bacterial isolates, staphylococcus aureus were noted in 23 (18%) patients, staphylococcus epidermidis was noted in 17 (13.5%), streptococcus pneumoniae was noted in 14 (10.9%), 09 (7%) had pseudomonas, 09 (7%) had Klebsiella pneumoniae, proteus in 5 (3.9%), E.coli in 4 (3.1%), 4 (3.1%) had mixed, tuberculosis was noted in 18 (14%) while 25 (19.5%) patients had no growth pattern of bacterial isolates.

Conclusion: It is to be concluded that staphylococcus aureus was the commonest organisms of bacterial isolates followed by mycobacterium tuberculosis in our study. Further research is required to better understand the factors associated with pattern of bacterial isolates in children with thoracic empyema.

Key Words: Bacterial Isolates, Thoracic Empyema, Staphylococcus Aureus

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INTRODUCTION

Pleural effusion (PE) is an excessive collection of fluid in the pleural space. It results from excessive formation or decrease fluid removal by the lymphatics. PE may be transudate or exudate in nature [1]. Para-pneumonic effusions are associated with bacterial pneumonia, bronchiectasis or lung abscess and are probably the most frequent source of exudative variety of pleural effusion [2].

The term Thoracic Empyema (ET) refers to accumulation of pus in the pleural space [3], which is related with morbidity and mortality in Pakistan. Even globally, PE is related with considerable amount of morbidity, although there is availability of rapid diagnostic tools, great coverage of immunization and extended antibiotics.[4] Incidence of pediatric empyema has risen over the last decade while pediatric pneumonia causing to ET accounts for 0.6%, affecting about 3.3 per 100,000 children [5]. Though, there is lack of literature on the topic of pediatric empyema incidence and prevalence in Pakistan [6]. Globally studies shown that the incidence of thoracic empyema is increasing, due to drug resistant bacteria, emergent non-vaccine replacement serotypes, specially serotype 19A after the introduction of PCV7, late diagnosis, failure to introduce appropriate antimicrobial therapy, malnutrition, co-morbidities, non-compliance attitude and costly treatment [1,6-13]. The characteristic bacterial pattern for diagnosis of thoracic empyema is direct a pleural fluid analysis and standard bacterial culture [14]. Pleural fluid analysis should be done with the detailed clinical manifestation and Chest x-ray to find out the etiology of a PE. Culture is crucial to verify

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antibacterial susceptibility. [15] The frequent organisms of thoracic empyema in pediatric group are Mycobacterium tuberculosis, Pneumococcus, Staphylococcus aureus and other gram negative bacteria[4,6]. Tuberculosis is commonest culprit of exudative pleural effusion followed by parapneumonic effusion in Pakistan and other developing countries [15, 16]. It is also assumed that pneumonia caused by fatal organisms like S.pneumoniae often presents with prominent symptoms at early phase of the disease. Thus, it is frequently treated in advance as the progression to PE is decreasing [17].

MATERIALS AND METHODS

Operational Definations:

Empyema: It is defined as, if pleural effusion will fulfill as a minimum one of the following criteria:

(1) The aspiration of frank pus on pleural tap;
(2) Positive Gram staining of pleural effusion;
(3) Existence of bacteria on culture pleural effusion;
(4) The presence of polymorph nuclear leukocytes ≥10,000/dl, LDH more than 200 U/L, glucose ≤40mg/dl and protein less than 3 g/dl in a pleural effusion [10, 11, 15].

Tuberculous Empyema: Tuberculous empyema is described as empyema with one of the following criteria:

(1) Acid fast bacilli (AFB) are present on pleural fluid smear;
(2) AFB is present in sputum and with sign of active parenchyma TB on chest x-ray/CT scan of thorax (nodular consolidation with or without cavity in apex, tree in bud appearance) [11].

Pattern of bacterial Isolates

Staining Reaction	Shape	Catalase	Coagulase	Oxidase	Additional Properties	Organism
Gram+ve	Cocci	+ve	+ve	-ve	DNase +ve	Sta. Aureus
Gram+ve	Cocci	+ve	-ve	-ve	DNase –ve	Coagulase –ve Staphylococci
Gram+ve	Cocci	-ve		-ve	Non motile, Nonsperforming CAMP +ve	GBS
Gram+ve	Rods	+ve	-ve	-ve	Motile, facultative Anaerobe	Listeria monocytogens
Gram+ve	Cocci	-ve	-ve	-ve	Esculine hemolysis +ve	Enterococci
Gram-ve	rods	+ve	-ve	-ve	Motile, glucose and lactose fermenter, indole +ve	E-coli
Gram-ve	rods	+ve	-ve	-ve	Non motile, glucose and lactose fermenter, ureas test +ve	Klebsiella species
Gram-ve	rods	+ve	-ve	-ve	Glucose fermenter, ureas test +vie, Swarming motility	Proteus species
Gram-ve	rods	+ve	-ve	+ve	Motile, glucose, lactose fermentation –ve	Pseudomonas aeruginosa

Data Collection: This study was carried out after approval of synopsis from Research Department of SMBBMU. All patients visited to department of Pediatrics Medicine, Children Hospital CMC (H) Larkana and fulfilling the inclusion criteria (Children below 15 years of age of either gender, presented with thoracic empyema in accordance with operational definition) were took in the study. A written informed consent was received from parents / guardian of patients. Empyema which was secondary to chest trauma or surgical procedure, excluded. Chest x-rays were taken in all patients at the time of admission, after intercostal tube drain (ICTD) introduction, its removal and at discharge, while ultrasound and CT of chest were done when needed. Diagnostic thoracentesis was performed and pleural fluid was submitted for biochemical analysis (total and differential leukocyte count, protein, sugar, and LDH) and microscopic analysis (Gram staining, culture, and smear for AFB and Gen Expert). Outcome variable i.e. pattern of bacterial isolates was assessed in accordance with operational definition. All information was recorded into the predesigned proforma (attached). Biasness and confounders of the study were managed by firmly following the inclusion and exclusion criteria.

Data Analysis: Data was analyzed on SPSS version 23.0. Mean ± standard deviation was calculated for quantitative variables like age, weight. Frequency and percentage were calculated for gender, site of chest and outcome variable i.e. pattern of bacterial isolates. Effect modifiers were controlled through stratification of age, gender and site of chest. Post stratification, Chi-square/Fisher's exact test as appropriate was applied using $P \leq 0.05$ as criteria of statistical significance.

RESULTS

In this study 128 patients were included to assess the pattern of bacterial isolates in children with thoracic empyema. Mean age was 5.1±2.3 years; these were of all age from 1 year to 15 years.

Table No.1: Frequency for Pattern of Bacterial Isolates n=128

Bacterial isolates	Frequency	% age
Staphylococcus Aureus	23	18%
Tuberculosis	18	14%
Staphylococcus Epidermidis	17	13.5%
Streptococcus pneumoniae	14	10.9%
Klebsiella pneumoniae	9	7%
Pseudomonas	9	7%
Proteus	5	3.9%
E. Coli	4	3.1%
Mixed	4	3.1%
No Growth	25	19.5%

Table No.2: Stratification for Age Group with Pattern of Bacterial Isolates n=128

Pattern of Bacterial Isolates	Age group [in years]		P-Value
	1 – 5	>5	
Staphylococcus Aureus	11(8.6%)	12(9.4%)	0.002
Tuberculosis	12(9.4%)	6(4.7%)	
Staphylococcus Epidermidis	14(10.9%)	3(2.3%)	
Streptococcus pneumoniae	11(8.6%)	3(2.3%)	
Klebsiella pneumoniae	1(0.8%)	8(6.3%)	
Pseudomonas	8 (6.3%)	1(0.8%)	
Proteus	3(2.3%)	2(1.6%)	
E. Coli	4(3.1%)	0(0.0%)	
Mixed	2(1.6%)	2(1.6%)	
No Growth	12(9.4%)	13(10.1%)	

Table No.3: Stratification for Gender with Pattern of Bacterial Isolates n=128

Pattern of Bacterial Isolates	Gender		P-Value
	Male	Female	
Staphylococcus Aureus	14(10.9%)	9(7.0%)	0.704
Tuberculosis	12(9.4%)	6(4.7%)	
Staphylococcus Epidermis	7(5.5%)	10(7.8%)	
Streptococcus pneumoniae	8(6.3%)	6(4.7%)	
Klebsiella pneumoniae	5(3.9%)	4(3.1%)	
Pseudomonas	6(4.7%)	3(2.3%)	
Proteus	2(1.6%)	3(2.3%)	
E. Coli	4(3.1%)	0(0.0%)	
Mixed	3(2.3%)	1(0.8%)	
No Growth	16(12.5%)	9(7%)	

Applied Chi-Square test

Table No.4: Stratification for Site of Chest Pain with Pattern of Bacterial Isolates n=128

Pattern of Bacterial Isolates	Site of Chest Pain		P-Value
	Right	Left	
Staphylococcus Aureus	16(12.5%)	7(5.5%)	0.955
Tuberculosis	14(10.9%)	4(3.1%)	
Staphylococcus Epidermidis	11(8.6%)	6(4.7%)	
Streptococcus pneumoniae	11(8.6%)	3(2.3%)	
Klebsiella pneumoniae	6(4.7%)	3(2.3%)	
Pseudomonas	5(3.9%)	4(3.1%)	
Proteus	4(3.1%)	1(0.8%)	
E. Coli	3(2.3%)	1(0.8%)	
Mixed	3(2.3%)	1(0.8%)	
No Growth	15(11.7%)	10(7.8%)	

61% of children were below 5 years where 39% of above 5 years. Male were n=77 (60.2%) and number of female was 51(39.8%). Right side of chest was affected in 68.8% (n=88) whereas left side was involve in 31.3% (n=40) no one has bilateral involvement. In distribution for pattern of bacterial isolates staphylococcus aureus were noted in 23 (18%) patients, staphylococcus epidermidis was noted in 17 (13.5%), streptococcus pneumoniae was noted in 14 (10.9%), 09 (7%) had pseudomonas, 09 (7%) had Klebsiella pneumoniae, proteus in 5 (3.9%), E.coli in 4 (3.1%), 4 (3.1%) had mixed, tuberculosis was noted in 18 (14%) while 25 (19.5%) patients had no growth pattern of bacterial isolates as shown in TABLE 1. Stratification of age, gender, and site of chest was done with respect to patterns of bacterial isolates as shown from Table [2-4]**.**

DISCUSSION

Quite a lot of studies from developed countries showed that the prevalence of ET and PE is increasing[18-22]. In these countries, childhood ET is frequently and rapidly recognized and managed quickly with drugs or surgical procedure[23,24]. Our study shows same results of ET in children that observed elsewhere in Asia [25, 26].

The mean age, in this study was 5.1±2.3 years, whereas Nyambat B, et al [12] noted age as 5.1 years. Another study noted as 7.9 years [27].

In present study, out of 128 patients, 77 (60.2%) were male while 51 (39.8%) were female, where Baranwal AK, et al [28] noted 70% male patients.

Our study reported the distribution of site of chest as 88 (68.8%) patients had right chest pain while 40 (31.3%) were involved with left site. Hardie W, et al[10] noted patients have 64% ET with right chest pain and 36% with left chest pain.

Current study reported the pattern of bacterial isolates as staphylococcus aureus was noted in 23 (18%) patients, staphylococcus epidermidis was noted in 17 (13.5%), Streptococcus pneumoniae was noted in 14 (10.9%), 09 (7%) had Klebsiella, 09 (7%) had pseudomonas, proteus in 5 (3.9%), E.coli in 4 (3.1%), 4 (3.1%) had mixed, tuberculosis was noted in 18 (14%) while 25 (19.5%) patients had no growth pattern of bacterial isolates. Nyambat B, et al[12] further reported the pattern of bacterial isolates as Staphylococcus Aureus in 126 (9.1%), E.coli 13 (0.9%), Klebsiella 35 (2.5%), pseudomonas 37 (2.7%) and staphylococcus epidermidis 01 (0.1%) Chonmaitree T, et al[27] noted S. Aureus as 35% whereas Baranwal AK, et al[28] reported to have 162 (67%) prevalence of staphylococcus.

In recent study, stratification of confounders / effect modifiers with respect to pattern of bacterial isolates, significant difference was noted in age group (P=0.002) whereas insignificant difference was found in gender (P=0.704), body mass index (P=1.000) and site of chest pain (P=0.955)**.**

CONCLUSION

It is to be concluded that Staphylococcus Aureus was the most frequent organism of causing empyema thoracic followed by mycobacterium tuberculosis in our study. Further research is needed to better understand the factors related with pattern of bacterial isolates in children with thoracic empyema. As the study was used only on single hospital, so results may not reveal the scenario of whole country. Epidemiological and research data on this problem should be expanded by further studies in multiple centers in Pakistan with larger sample in order to validate the findings of current study.

Author's Contribution:

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Data Analysis:	Abdul Rehman, Vijia Kumar Gemnani, Faisal Jamro
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REFERENCES

1. Light RW. Disorders of the pleura, mediastinum, diaphragm, and chest wall. Harrisons Principles Int Med 2005;16(2):1565.
2. Dutta V, Khyriem AB, Bora I, Barman H, Lyngdoh WV, Neigrihms S. Bacteriological profile of pleural fluid among the pediatric population in a tertiary care centre-a retrospective analysis. Int J Health Sci Res 2015;5(9):167-74.
3. Jiménez D, Díaz G, García-Rull S, Vidal R, Sueiro A, Light RW. Routine use of pleural fluid cultures. Are they indicated? Limited yield, minimal impact on treatment decisions. Respir Med 2006;100(11):2048-52.
4. Grijalva CG, Zhu Y, Nuorti JP, Griffin MR. Emergence of parapneumonic empyema in the USA. Thorax 2011;66(8):663-8.
5. Attia Bari AM, Naz S, Ahmad TM. Pleural empyema in children: prolonged clinical course. Proceeding SZPGMI 2012;26(1):1-7.
6. Ali Faisal S, Abdul Sattar S. Empyema Xhoracic in children: clinical presentation, Management and Complications. J Coll Physicians Surg Pak 2014;24(8):573-6.
7. Memon SA, Shaikh SJ. The etiology of pleural effusion in children: Hyderabad experience. Pak J Med Sci 2007;23:186-7.
8. Brims FJH. Review: empyema thoracis. Eur Respir Rev 2010;19(117):220-8.
9. Foglia RP, Randolph J. Current indications for decortication in the treatment of empyema in children. J Pediatr Surg 1987;22(1):28-33.
10. Hardie. Pneumoccocal pleural rimpyemasin children. Clin Infect Dis 1996;22:1057-63.
11. Kundu S, Mitra S, Mukherjee S, Das S. Adult thoracic empyema: a comparative analysis of tuberculous and nontuberculous etiology in 75 patients. Lung Ind 2010;27(4):196.
12. Nyambat B, Kilgore PE, Yong DE, Anh DD, Chiu CH, Shen X, et al. Survey of childhood empyema in Asia: implications for detecting the unmeasured burden of culture-negative bacterial disease. BMC Infec Dis 2008;8(1):90.
13. Middelkamp JN, Purkerson ML, Burford TH. The changing pattern of empyema thoracis in pediatrics. J Thorac Cardiovasc Surg 1964;47(2):165-73.
14. Lc Monnier. Diagnosis of pleural empyema in children. Clin Infect Dis 2006:42:1135-40.
15. Rehan M, Alam MT, Imran K, Farrukh SZ, Masroor M, Kumar P. The frequency of various diseases in patients presenting with pleural effusion. Gomal J Med Sci 2013;11(1).
16. Memon SA, Shaikh SJ. The etiology of pleural effusion in children: Hyderabad experience.Pak J Med Sci. 2007;23(1):86-7.

17. Finland M, Barnes MW. Changing ecology of acute bacterial empyema: occurrence and mortality at Boston City Hospital during 12 selected years from 1935 to 1972. J Infect Dis1978;137(3): 274-91.
18. Byington CL, Samore MH, Stoddard GJ, Barlow S, Daly J, Korgenski K, et al. Temporal trends of invasive disease due to Streptococcus pneumoniae among children in the intermountain west: emergence of nonvaccine sero groups. Clin Infect Dis 2005;41(1):21-9.
19. Eastham KM, Freeman R, Kearns AM, Eltringham G, Clark J, Leeming J, et al. Clinical features, aetiology and outcome of empyema in children in the north east of England. Thorax 2004;59(6): 522-5.
20. Finley C, Clifton J, Fitzgerald JM, Yee J. Empyema: an increasing concern in Canada. Can Respir J 2008;15(2):85-9.
21. Munoz-Almagro C, Jordan I, Gene A, Latorre C, Garcia-Garcia JJ, Pallares R. Emergence of invasive pneumococcal disease caused by nonvaccine serotypes in the era of 7-valent conjugate vaccine. Clin Infect Dis 2008;46(2): 174-82.
22. Spencer DA, Iqbal SM, Hasan A, Hamilton L. Empyema thoracis is still increasing in UK children. BMJ 2006;332(7553):1333.
23. Engum SA. Minimal access thoracic surgery in the pediatric population. Semin Pediatr Surg 2007;16 (1):14-26.
24. Ulku R, Onen A, Onat S, Kilinc N, Ozcelik C. Intrapleural fibrinolytic treatment of multiloculated pediatric empyemas. Pediatr Surg Int 2004;20(7): 520-4.
25. Avansino JR, Goldman B, Sawin RS, Flum DR. Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis. Pediatr 2005;115(6):1652-9.
26. Sonnappa S, Jaffe A. Treatment approaches for empyema in children. Paediatr Respir Rev 2007; 8(2):164-70.
27. Chonmaitree T, Powell KR. Parapneumonic pleural effusion and empyema in children: review of a 19-year experience, 1962-1980. Clin Pediatr 1983;22 (6):414-9.
28. Baranwal AK, Singh M, Marwaha RK, Kumar L. Empyema thoracis: a 10-year comparative review of hospitalized children from south Asia. Arch Dis Childhood 2003;88(11):1009-14.

The Frequency of Weight Gain in Children of Probable Tuberculosis under Treatment

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ABSTRACT

Objective: To determine the frequency of weight gain in children of probable Tuberculosis under treatment.
Study Design: Descriptive case series study
Place and Duration of Study: This study was conducted at the TB DOTS Clinic, CMC Children Hospital, Larkana from July 2017 to January 2019.
Materials and Methods: Total 100 children of age 6 months to 5 years age, both genders and new cases of probable tuberculosis were consecutively selected. Children with malnutrition, complain of Refusal to feed, convulsions, unconsciousness or having HIV co-infection were excluded.
Results: Mean age ± SD was 33.53 ± 12.56 months. (Ranged 07-60 months). Mean ± SD initial weight was 18.75 ± 6.33 Kgs while mean ± SD final weight was 25.36 ± 9.23 Kgs. Overall, net minimum & maximum weight gain were 0.5 to 15.6 Kgs with mean ± SD weight gain of 9.61 ± 4.03 Kgs. Male children were in almost two third majority i-e; 63% (n= 63). Sixty percent (60%, n= 60) children had confirmed tuberculosis. Weight gain in probable cases of TB after treatment given was found to positive among seventy nine percent (n= 79) children.
The stratification analysis showed that frequency of weight gain increased with increasing age, male children, rural living children and with taking four ATT drugs.
Conclusion: Tuberculosis is a great burden among our population especially children in whom diagnosis is difficult or late. Weight gain is main indicator of successful treatment. The current study highlighted the importance of TB occurrence in children by investigating one of its core issues. Further studies are warranted to understand other changing phenomenon of presentations, diagnosis and treatment effectiveness and compliance.
Key Words: Probable Tuberculosis, Antituberculous, Gain, Children, Malnutrition

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INTRODUCTION

Tuberculosis affected an estimated 8.8 million people and caused 1.4 million deaths globally in 2010, including at least 64000 children.[1]In one study from south Africa, children <13 years of age contributed to 14% of the burden, with a childhood tuberculosis incidence rate of 407 per 100,000 population per year.[2]
According to National Tuberculosis Control Programme (NTCP) has created guidelines for early diagnosis and management of Tuberculosis in children that consist of four criteria: suggestive clinical features, evidence of close contact with an adult case of tuberculosis, tuberculin skin testing and suggestive radiological findings.[3]
As in children there is difficulty in collection of respiratory specimens and there is low yield of organisms, therefore the diagnosis of Tuberculosis in children is difficult,[4,5]Investigations such as Gene Xpert help in diagnosing Tuberculosis[6]but in resource poor health facilities with limited access to these diagnostic investigations, diagnosis becomes an even greater challenge.[7] Tuberculosis is a wasting disease[8] and outcome of ATT can be predicted by body weight assessment.[9] Each child should be clinically assessed every 2 weeks during the intensive phase, and every 4 weeks during the continuation phase until treatment completion. The assessment should be done about symptoms, weight, treatment compliance and any side effects. Most children with Tuberculosis will start to show signs of improvement within 4-8 weeks of ATT.[10]
Weight gain is a sensitive indicator of good response to treatment. Treatment failure is considered if child is receiving ATT and there is no symptom resolution or symptoms are getting worse and continued weight loss. The bodyweight has been assessed in many studies during the intensive phase[11]and it is obvious from

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previous studies that there is an association between inadequate weight gain and poor outcome of ATT.[12]Assessment of weight is a cheap and easy method to see the outcome of ATT.[13]

As local data is deficient on weight gain in children having probable tuberculosis during ATT so rationale of this study is to determine the treatment outcome by monitoring weight in every new case of Probable Tuberculosis as weight is a cheap and easy method to determine the outcome of ATT. It will help to predict the treatment outcome clinically and prevent deaths and treatment failures by early interventions. It will further helps to adjust drug dosages in children who are gaining weight.

MATERIALS AND METHODS

Probable Tuberculosis: When a child got score of 5-6 by current National Tuberculosis Control Programme (NTCP) scoring chart.

Weight Gain: When the child had gained weight of ≥2kg at the 8 weeks of treatment as compared to baseline weight.

New cases of Probable Tuberculosis: Those cases which had been labelled probable and started antituberculous therapy (ATT) within previous 2 weeks, confirmed by taking proper history.

Compliance of drugs: Patient taking > 80% of medicine as physician advised was taken as good compliance.

Data Collection Procedure: Study was conducted in TB DOTS Clinic, CMC Children hospital, Larkana. All eligible and consented patients were selected according to selection criteria.

At the start of treatment, weight was noted and then weight was measured after every 2 weeks of initiating anti-tuberculous therapy given until 8 weeks of treatment.

Finally; the weight at the 8 weeks of treatment was compared to the baseline weight and seen that whether the child had gained weight or not.

Detailed information regarding age, initial weight, number of drugs and drug compliance as defined by operational definition were taken. Weight measurement was carried out on each visit. Weight was measured in kilograms after removing excessive cloths of children and compared to the baseline weight and if the child had gained weight of ≥ 2kg at the 8 weeks of treatment as compared to baseline weight then it was labelled as weight gain.

Data Analysis: Data were analyzed on SPSS version 21.0. Percentage and frequency were calculated for categorical variables. Mean and standard deviation were calculated for quantitative variables. Applying Chi-square test, P value ≤ 05 assumed as significant.

RESULTS

During study period 312 children were treated and out of these 100 children with probable TB were included in the study as per the selection criteria. The results on these patients are as under.

Mean age ± SD was 33.53 ± 12.56 months. Ages of these patients ranged from 07-60 months. (Table 1)

Table No.1: Baseline data of all participating children. (n= 100)

Viariable	Minimum	Maximum	Mean	Standard deviation
Age of child in months	07	60	33.53	12.56
Initial Weight (Kgs) (Before initiating treatment)	5	29	18.75	6.33
Weight on 1st visit	5.5	32	20.41	6.72
Weight on 2nd visit	5.7	34.8	22.14	7.17
Weight on 3rd visit	6.7	37.3	23.88	7.61
Weight on 4th visit	7	43.1	25.36	9.23
Net weight gain	0.5	15.6	9.61	4.03

Table No. 2. Effect of different variables of child on frequency of weight gain in probable Tuberculosis under treatment

Variable		Weight gain		Total	P value
		Yes	No		
Age of child (Years)	Upto 1 Year	2(66.6%)	1(33.3%)	3(100%)	0.348
	1-2 Years	23(88.5%)	3(11.5%)	26(100%)	
	2-3 Years	22(73.3%)	8(26.7%)	30(100%)	
	3-4 Years	18(69.2%)	8(30.8%)	26(100%)	
	4-5 Years	14(93.3%)	1(6.7%)	15(100%)	
Gender	Male	32(80%)	8(20%)	40(100%)	0.524
	Female	47(78.3%)	13(21.7%)	60(100%)	
Residence	Urban	29(78.4%)	8(21.6%)	37(100%)	0.549
	Rural	50(79.4%)	13(20.6%)	63(100%)	
Drugs	3 drugs	36(78.3%)	10(21.7%)	46(100%)	0.530
	4 drugs	43(79.6%)	11(20.4%)	54(100%	

Initial weight (before initiating treatment) ranged from 05 to 29 Kgs with a mean ± SD initial weight of 18.75 ± 6.33 Kgs. Weight on 4th visit was noted to minimum to maximum from 7 to 43.1 Kgs with mean ± SD final weight of 25.36 ± 9.23 Kgs. Overall, net minimum & maximum weight gain were 0.5 to 15.6 Kgs with mean ± SD weight gain of 9.61 ± 4.03 Kgs (Table 1). Measurement of weights on 1st visit, 2nd visit and 3rd follow up visits which gradually changed were recorded and are given in Table 1.

Age of children ranges mostly 1-4 years. Accordingly; children with age <1 year were 3% (n= 3), 1 to 2 years and 3 to 4 age were 26% (n= 26) each and 2 to 3 years, 4-5 age were 30% (n= 30) and 15% (n= 15) respectively.

Male children were in almost two third majority i-e; 63(63%), belong to rural areas; 63(63%).

After inclusion in the study and starting treatment for probable TB, it was observed that sixty percent (60%, n= 60) children had confirmed tuberculosis.

Forty six percent (n= 46) children were given three drugs while other 54% (n= 54) received four drugs as treatment of TB however; among to four drug therapy.

The actual outcome of this study was the weight gain in probable cases of TB after treatment given which was found to positive among seventy nine percent (n= 79) children.

In this study the stratification analysis showed that frequency of outcome variable (weight gain) increased with increasing age groups from in 66.7% in upto 1 year age to 93.3% in 4-5 years children; however these results did not accompany the significant p value. (P value 0.348, Table: 2).

Further it was noted that male children had slightly higher rates of weight gain (80%) compared to (78.3%) in the female children. (P value 0.524, Table: 2).

Likewise; there was slightly more frequency of weight gain in rural than the urban living children (79.4% vs 78.4%). (P value 0.549, Table: 2).

Finally; it was also noted that children taking four drugs were more toward to weight gain (79.6%) compared to those taking three drugs (78.3%) for TB; however these results too did not accompany the significant p value. (P value 0.530, Table: 2).

DISCUSSION

The burden of childhood TB in developed world is as high as 7% while, it triples in the developing nations reaching up to 20%.[14] Published reports are common in adults but there is a very little number of studies can be identified investigating this serious issue among children. One thing which raises the severity of this critical concern is that among adults, TB is easily and quickly identifiable through manifestation of its typical symptoms but the children with tuberculosis often pose diagnostic difficulties due to atypical features.[15-18]

Children with pulmonary TB present with a wide variety of signs and symptoms. Children may either be asymptomatic or, at the other extreme, present with severe weight loss and wasting in cases with disseminated TB.[19,20] An evident fact is that there is very strong association between malnutrition and TB in children as well as adults, though in children it direction of causality may be sometime misleading or confusing regarding weight loss and TB. This is because TB in itself causes wasting and malnutrition with poor weight gain makes child prone to attract TB. On the other hand children taking ATT show a progressive weight gain and are monitored for it as an indicator or treatment effectiveness.[10-13]

The current study was conducted to assess the children diagnosed with probable tuberculosis by investigating the frequency of weight gain under TB treatment. The results of the study show a clear picture of treatment effectiveness. A big majority of children (79%) showed weight gain ranging from 0.5 Kgs minimum to 15.6 Kgs maximum. This can be considered an enormous success and it had been more profound had there been a more compliance among the treated children. The compliance rate was 46%. There is only one study in comparison with our findings. The study by Mexitalia M, et al., [17] studied the effect of tuberculosis treatment on leptin levels & weight gain in Indonesian children and found that there were significant changes in weight gain of children having probable TB. Mean weight of children at baseline was 18.65 Kgs which increased upto 19.75 Kgs after intensive phase (P value < 0.001) and further to 20.85 kgs after continuation phase (P value < 0.001).

This shows resemblance in the two studies regarding effect of TB treatment on weight of children. However; the stipulated difference is due to the difference of selection criteria and the age ranges of the two studies. Mexitalia M, et al.,[17] in their study has taken children of age 5-14 years with a mean age of 6.8 years while in the current study the age range was set between 6 months to 60 months (5 years). Another study had taken children of age form 1 month to 15 years with mean age ± SD age of 105.2 ± 45.3 on patients of intrathoracic TB patients. The mean body weight of children documented in this study was 19.8 kg which is comparable with the current study. [18]

The current study also report that increasing age affects positively on weight gain with TB treatment. Likewise; male gender and rural living are also factors which favour more weight gain with ATT in children. No other contemporary study has evaluated these factors. Compliance to ATT is a critical issue not only in adults but in children also. In current study the compliance rate was only 46% however one study documented almost complete compliance (97%) among all groups of TB treatment.[22] We think that age, education, number of drugs given, counselling/ support and motivation for

treatment may be the reasons for difference of the compliance rates in the two studies. In case of children, it is their parents who need to be counseled and motivated for completion of treatment of their children. Directly Observed Treatment, Short Course (DOTS) is a useful measure in this regard however; patients loose compliance soon afterward which needs to be controlled. Poor adherence to drug therapy is the main barrier to cure. Co-operation and other strategies are required. [11,19,20,]

Treatment show signs of improvement after 2 to 4 weeks of anti-TB treatment in which if, there is continued weight loss then it is labeled as treatment failure. However; children should be monitored at least on a monthly basis for the first 2 months, thereafter every 2 months until completion of treatment. Children responding well to treatment will have resoluton of symptoms and gain weight.[19,20]

CONCLUSION

As infective but chronic disease, the Tuberculosis is a great burden among our population. The children are especially worse targets because of unclear manifestataion leading to late diagnosis and increasing morbidity. TB in children is known to present with weight loss or at least failure to gain weight. In the scenario of changing presentations a strict vigilance on the new cases especially among children is the need of hour. Strategies exist to address some of the challenges. Unfortunately, the hopes engendered by new diagnostic and therapeutic methods are tempered by the reality that most of the world's children with TB are excluded from them by poverty and poor medical infrastructure.

The current study highlighted the importance of TB occurrence in children by investigating one of its core issues. The study found that with good compliance the TB treatment bring about significant positive changes of weight gain in children. Elder age, male gender, rural living and use of four drugs leads to more frequency of weight gain among probable cases of TB.

Further studies are warranted to understand the changing phenomenon of TB in children.

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REFERENCES

1. Ewer K, Deeks J, Alvarez L, Bryant G, Waller S, Anderson P, et al. Comparison of T-cell-based assay with tuberculin skintest for diagnosis of Mycobacterium tuberculosis infection in a school tuberculosis outbreak. Lancet 2003;361(9364): 1168–73.
2. Curtis AB, Ridzon R, Vogel R, McDonough S, Hargreaves J, Ferry J, et al. Extensive transmission of Mycobacterium tuberculosis from a child. N Engl J Med 1999;341(20):1491–5.
3. World Health Organization. Global tuberculosis control: surveillance, planning, financing. Geneva, Switzerland: WHO; 2011.
4. Marais BJ, Hesseling AC, Gie RP, Schaaf HS, Beyers N. The burden of childhood tuberculosis and the accuracy of community-based surveillance data. Int J Tuberc Lung Dis 2006;10:259-63.
5. Ministry of Health, Government of Pakistan, PC-1 form from National Tuberculosis Program for 1996-2002, Islamabad: Ministry of Health, Government of Pakistan 1996;2-6.
6. Reports on National TB prevalence survey 1987-1988. Directorate of Tuberculosis control program. Islamabad: Ministry of health, Government of Pakistan; 1988.
7. National guidelines for diagnosis and management in children, National TB control Program, Ministry of Health, Government of Pakistan in collaboration with Pakistan Paediatric Association, first edition. Feb 2006.
8. López-Ávalos GG, Prado-Montesde OE. Classic and new diagnostic approaches to childhood tuberculosis. J Trop Med 2012.
9. Chiang SS, Swanson DS, StarkeJR. New Diagnostics for Childhood Tuberculosis. Infect Dis Clin North Am 2015;10.
10. Detien AK, DiNardo AR, Leyden J, et al. Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in children: a systematic review and meta-analysis. Lancet Respir Med 2015;3(6): 451–61.
11. Nelson LJ, Wells CD. Tuberculosis in children: considerations for children from developing countries. Semin Pediatr Infect Dis 2004;15 (3):150–4.
12. Baldwin MR, Yori PP, Ford C, et al. Tuberculosis and nutrition: disease perceptions and health seeking behavior of household contacts in the Peruvian Amazon. Int J Tuberc Lung Dis 2004;8:1484-91.
13. Gillespie SH, Kennedy N. Weight as a surrogate marker of treatment response in tuberculosis. Int J Tuberc Lung Dis 1998;2:522-3.
14. Dheda K, Gumbo T, Gandhi NR, et al. Global control of tuberculosis: from extensively drug-

resistant to untreatable tuberculosis. Lancet Respir Med. Author manuscript; available in PMC 25 Jul 2017.
15. Stephen M, Luis E. Cuevas, Jean-Philippe P, et al. Clinical Case Definitions for Classification of Intrathoracic Tuberculosis in Childrena:an update. Clin Infect Dis 2015;61(Suppl 3):S179–S187.
16. Venturini E, Turkova A, Chiappini E, Galli L, De-Martino M, Thorne C. Tuberculosis and HIV co-infection in children. BMC Infect Dis 2014;14 (Suppl 1):S5.
17. Mexitalia M, Dewi YO, Pramono A, Anam MS. Effect of tuberculosis treatment on leptin levels, weight gain, and percentage body fat in Indonesian children. Korean J Pediatr 2017; 60(4):118-23.
18. Lodha R, Mukherjee A, Singh V, Singh S, et al. Effect of micronutrient supplementation on treatment outcomes in children with intrathoracic tuberculosis:a randomized controlled trial. Am J Clin Nutr 2014;100:1287-97.
19. Anna M, Mandalakas H, Kirchner L, et al. Optimizing the Detection of Recent Tuberculosis Infection in Children in a High Tuberculosis HIV Burden Setting. Hesseling Am J Respir Crit Care Med 2015;191(7):820–30.
20. Szkwarko D, Hirsch-Moverman Y, Du-Plessis L, Du-Preez K, Carr C, Anna M. Child contact management in high tuberculosis burden countries: a mixed-methods systematic review. Mandalakas PLoS One 2017;12(8):e0182185.
21. Kennedy N, Ramsay A, Uiso L, Gutmann J, Ngowi FI, Gillespie SH. Nutritional status and weight gain in patients with pulmonary tuberculosis in Tanzania. Trans R Soc Trop Med Hyg 1996; 90:162–6.
22. Paton NI, Ng YM. Body composition studies in patients with wasting associated with tuberculosis. Nutrition 2006;22:245–51.

Impact of Nigella Sativa on Weight of Testis & Body Weight in Doxorubicin Treated Albino Rats

Ashok Kumar[1], Sadia Sundus[3], Mona Rani[2] and Saad Saleem[4]

ABSTRACT

Objective: To measure impact of nigella sativa (NS) on weight of testis & body weight and doxorubicin treated albino rats.

Study Design: Experimental work

Place and Duration of Study: This study was conducted at the BMSI animal House, Karachi from 1st March 2017 to 4 April 2017 (total 35 days).

Materials and Methods: Experimental work was take place on 40 animals of 16 weeks old in the animal house for 35 days. Animals were separated into 4 sets, A1, B2, C3 & D4. A1 served as control, B2 receive Doxorubicin 3 mg/kg /7 days intraperitonealy, C3 receive Nigella sativa 1000mg/kg everyday orally along with Doxorubicin 3 mg / kg /7 days intraperitonealy and D4 receive extract of Nigella sativa 1000mg/kg everyday orally. After completion of experiment, animals were sacrifice and tissue material were well-preserved for staining.

Results: In B2 body weight was noticeably reduced, bute amended in C3 which were given Nigella sativa along with Doxorubicin.

Conclusion: This study reveals that Nigella sativa amended the weight reduction.

Key Words: NS(nigella sativa), TQ (thymoquinone), doxorubicin (Dox), folkoric, KU (Karachi university)

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INTRODUCTION

Doxorubicin is an anthracycline antibiotic derivative came in knowledge as a anticancerous agent in 1969 for the management of numerous cancerous tumours like breast carcinoma, osteosarcomas, soft-tissue sarcomas, lymphomas, alopecia and ovary carcinoma but usage is limited because it can destroy both healthy as well as cancerous cells thus causing numerous side effects like cardiac, renal and testicular injuries by stimulating production of free radicals and nitrogen varieties.[1-4]

DXR was initially filtered from Streptomyces species, extremely hydrophilic, associated with Nausea, vomiting, and heart arrhythmias.[5] Cancer is the topmost reason of death in the world after cardiovascular diseases.

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It also causes male infertility by gonadal impairment due to antineoplastic drugs. Testicular weight became reduced due to decreased sperm cell count and motility. First indication of genotoxic impairment is increased apoptosis of spermatogonia and spermatocytes due to oxidative stress to testis by destruction of lipids in cell membrane.[6-10]

It can also stimulates oxidative damage to mitochondria which indicates manifestation of transcription factor.[11] Management for cancer is surgical procedure, chemo, radioactivity, hormone remedy, immunotherapy, targeted remedy, and marrow replacement.[12] Local procedures of treatment like; surgery and radiation are more successful when cancer cells are not metastasized, however systemic approach (chemotherapy) is required along with local procedures when early signs of micro metastasis are appeared.[13]

Archaeologically, medicinal plants were used to obtain food and herbal medicines. Nigella sativa is derived from Latin word, nigellus. It is a member of Ranunculaceae family, used globally for the treatment of various ailments. It is strongly recommended in Tibb-e-Nabwi as a healing medicine for several illnesses such as upper respiratory disorders like bronchitis, asthma. It is commonly taken as liver tonic, digestive, anti-diarrheal, hunger

stimulant and boost up immunity.[14,15] It is cytoprotective, inhibits cellular membrane oxidation, lipid peroxidation, free radicals neutralization, ROS suppression so it reduces serum lipids and increases body weight.[16] NS improve sperm counts, sperm viability & motility, weight of testis and reduces sperm abnormalities.[17-19] It is helpful in hypotension, digestive friendly, nephrocurative, antioxidant, hypoglycemia, hypolipidemia &liver friendly.[20-22]

MATERIALS AND METHODS

The study was conducted in BMSI on 40 albino rats which were 16 weeks old originally obtained from Brooklyn Laboratories, USA, hybridize at animal house B.M.S.I. for assessment of their health they were retained under observation for 1 week. Body weights were noted earlier and after completion of study. The standard food & water were given in libitum. Rats were alienated into four sets, each comprised of ten rats. Nigella sativa seeds extract obtained from KU and injectable Doxorubicin 50mg/25ml was obtained from Pfizer.

A1 = Control.

B2= Doxorubicin injection 3 mg/1000g/7days intraperitonealy for 35 days

C3= crushed Nigella sativa (1g/1000g everyday orally) & injection Doxorubicin 3 mg / 1000g /7 days intraperitonealy) for 35 days.

D4= crushed Nigella sativa 1g/1000g everyday orally for 35 days.

Animals were observed daily for their wellbeing. After completion of research rats were sacrificed after taking final weight with the help of Sartorius balance. Rats were cut in midline from thoracic region to scrotum. The testes were visualized and examined carefully for any change in contour, color, hemorrhage. Testes were detached and weights were noted.

Relative weights of testes were calculated

$$\text{Comparative weight of testis} = \frac{\text{Mean weight of testis (mg)} \times 100}{\text{Ultimate weight of animal (gm)}}$$

RESULTS

Body Weight

A1: Group A1 animals mean initial weight was 221.30±11.56 & mean final weight was 267.76±13.45. There was substantial raise in the mean final body weight in A1 ($p<0.0174$) as compared to its initial body weight (Table 1).

B2: Group B2 animals mean initial weight was 238.10±11.68 & Mean final body weight was 200.75±4.51.There was highly substantial reduction in the mean final body weight of B2 ($p<0.008$) as compared to its initial body weight(Table1). There was highly substantial reduction in the mean final body weight in B2 ($p<0.0036$) as compared to A1 (Table 2).

C3: Group C3 animals mean initial weight was 231.80±10.93 & mean final body weight was 215.70±11.56. There was inconsequential reduction in the mean final weight ($p<0.324$) as compared to its initial weight (Table1). There was inconsequential reduction in the mean final body weight ($p< 0.1006$) as compared to A1. There was substantial raise ($p< 0.0264$) in mean value of final body weight in C3 when compared with B2 (Table 2).

D4: Group D4 animals mean initial weight was 237.90±11.24 gm & mean final body weight was 281.43±12.56 gm. There was substantial raise in the mean final body weight ($p<0.0188$) as compared to its mean value of initial body weight (Table 1). There was inconsequential raise in the mean final body weight ($p< 0.2789$) as compared to A1. There was highly substantial raise in the mean final body weight ($p< 0.0001$) as compared to B2. There was substantial raise in the mean final body weight ($p<0.0012$) as compared toC3 (Table 2).

Absolute Testicular Weight

A1: In A1 animals mean absolute testicular weight was 1.653±0.098(Table 3).

B2: In B2 animals mean absolute testicular weight was 0.972±0.070. There was highly substantial reduction in the mean absolute testicular weight ($p< 0.0001$) in B2 as compared to mean absolute testicular weight in A1. (Table 3).

C3: In C3 animals mean absolute testicular weight was 1.423±0.021.There was inconsequential reduction in the mean absolute testicular weight in C3 ($p<0.0340$) as compared to the mean absolute testicular weight in A1 (Table 3). There was highly substantial raise in the mean absolute testicular weight in C3 ($p< 0.0001$) as compared to the mean absolute testicular weight in B2 (Table 3).

D4: In D4 animals mean absolute testicular weight was 1.907±0.041(Table 3). There was substantial raise in the mean absolute testicular weight in D4 ($p< 0.0279$) as compared to mean absolute testicular weight in A1. There was highly substantial surge in the mean absolute testicular weight in D4 ($p< 0.0001$) as compared to

mean absolute testicular weight in B2 while highly substantial raise was also showed in the mean absolute testicular weight in D4 ($p<0.0001$) as compared to the mean absolute testicular weight in C3. (Table 3)

Mean Relative Testicular Weight

A1: In A1 animals, mean relative testicular weight was 617.344±29.96 (Table 4).

B2: In B2 animals, mean testicular relative weight was 484.184±20.44 (Table 4). There was highly substantial reduction in the mean testicular relative weight in B2 ($p<0.0017$) as compared to the mean testicular relative weight in A1. (Table 4).

C3: In C3 animals, mean testicular relative weight was 659.712±35.68. There was inconsequential raise in the mean testicular relative weight in C3 ($p<0.375$) as compared to the mean testicular relative weight in A1. There was highly substantial raise in the mean testicular relative weight in C3 ($p<0.0005$) as compared to the mean testicular relative weight in B2 (Table 4).

D4: In D4 animals, mean testicular relative weight was 677.611±37.33. There was inconsequential raise in the mean testicular relative weight in D4 ($p<0.224$) as compared to the mean testicular relative weight in A1. There was highly substantial raise in the mean testicular relative weight in D4 ($p<0.0003$) as compared to the mean testicular relative weight in B2 and inconsequential raise in the mean testicular relative weight in D4 ($p<0.732$) as compared to the mean testicular relative weight in C3 (Table 4).

Table No.1: Evaluation of mean (Initial and Final) body weight in various Albino rats groups

SETS (n=40)	Management	Initial Weight	Final Weight	P-Value
A1	Control	221.30±11.56	267.76±13.45	0.0174*
B2	Doxorubicin	238.10±11.68	200.75±4.51	0.008**
C3	Doxorubicin and NS	231.80±10.93	215.70±11.56	0.324
D4	NS	237.90±11.24	281.43±12.56	0.0188*

n: number of albino rats Data: Mean±SEM P<0.05: significant
P<0.01: highly statistically significant

Table No.2. Evaluation of mean final body weight between various Albino rat groups

Sets	T	P-Value
A1 & B2	3.4393	0.0036**
A1 & C3	1.7305	0.1006
A1 & D4	1.1165	0.2789
B2 & C3	2.7144	0.0264*
D4 & B2	6.0456	0.0001**
D4 & C3	3.8506	0.0012**

T: t-test score P<0.01 (**) is highly statistically significant

Table No.3: Evaluation of mean absolute weight of testis in various Albino rat groups

Sets (n=40)	Management	Mean absolute weight of testis	Statistical comparison	P-Value
A1	Control	1.653±0.098	A1 & B2	0.0001**
B2	Doxorubicin	0.972±0.070	A1 & C3	0.0340
C3	Doxorubicin and NS	1.423±0.021	A1 & D4	0.0279*
D4	NS	1.907±0.041	B2 & C3	0.0001**
			D4 & B2	0.0001**
			D4 & C3	0.0001**

N: number of albino rats Data: Mean±SEM
P<0.05: statistically significant P<0.01: highly statistically significant

Table No.4: Evaluation of mean relative weight of testis in various Albino rat groups

SETS (n=40)	Management	Relative Weight	Statistical comparison	P-Value

A1	Control	617.344±29.96	A1 & B2	0.0017
B2	Doxorubicin	484.184±20.44	A1 & C3	0.375
C3	Doxorubicin and NS	659.712±35.68	A1 & D4	0.224
D4	NS	677.611±37.33	B2 & C3	0.0005
			D4&B2	0.0003
			D4&C3	0.732

n: number of albino rats **Data: Mean±SEM** **P<0.01:highly statistically significant**

DISCUSSION

Management of cancer comprises of surgical procedure, Radio & Chemotherapy. It is used for the management of numerous cancerous tumours but its usage is limited because it can destroy both healthy normal body cells too thus causing numerous side effects like cardiac, renal and testicular injuries by stimulating production of free radicals, reactive oxygen and nitrogen species.[1,2]

Nigella sativa belongs to the Ranunculaceae family and used globally as a therapeutic herb for the treatment of various ailments. It is strongly recommended in Tibb-e-Nabwi as a healing medicine for several illnesses such as upper respiratory disorders like bronchitis, asthma.[14,15]

The body weight of B2 animals in was decreased as compared to all other groups; due to anorexia and vomiting caused by doxorubicin as supported by.[1,2] Decrease in body weight is also reported by. [7] testicular weight was also became decreased as explained by [6]

C3 animals were looking active and healthy. Their appetite was good as compared to group B2 due to ameliorating effects of Nigella sativa. Our observations were supported by [14,15] who reported that Nigella Sativa decreases toxic side effects caused by several chemotherapeutic agents. Increase in testicular weight was also observed by [20-23]

CONCLUSION

Research determined that B2 animals had reduced body weight, absolute & relative wt of testis but in C3 animals we observe raise level of body weight, absolute & relative wt of testis as compared to B2. Therefore our hypothesis from this research work is that avoid the treatment of Doxorubicin and if mandatory don't use it without *nigella*, in order to minimize its harmful effects.

Author's Contribution:

Concept & Design of Study:	Ashok Kumar
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Revisiting Critically:	Ashok Kumar, Sadia Sundus
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Nimbal SK, Gadad PC, Koti BC. Effect of ethanolic extract of Rosa centifolia against doxorubicin induced nephrotoxicity in albino rats. J Ayurveda Integrative Med 2021,112-120.
2. Chaudhary D, Khatiwada S, Sah SK, Tamang MK, Bhattacharya S, Jha CB. Effect of doxorubicin on histomorphology of Liver of Wistar Albino Rats. J Pharmacy Pharmacol 2016;4:186-90.
3. Omobowale TO, Oyagbemi AA, Ajufo UE, Adejumobi OA, Ola-Davies OE, Adedapo AA, et al. Ameliorative effect of gallic acid in doxorubicin-induced hepatotoxicity in Wistar rats through antioxidant defense system. J Dietary Supplements 2018;15(2):183-96.
4. Benzer F, Kandemir FM, Kucukler S, Comaklı S, Caglayan C. Chemoprotective effects of curcumin on doxorubicin-induced nephrotoxicity in wistar rats: by modulating inflammatory cytokines, apoptosis, oxidative stress and oxidative DNA damage. Archives Physiol Biochem 2018;124(5): 448-57.
5. Mansy M, Malak S, Mubarak RT, Shamel M, Kamal S. The Effect of EGF on the Ultrastructure of Submandibular Salivary Glands of Albino Rats Receiving Doxorubicin. Annals Dental Specialty 2020;8(1):26-33.
6. Badkoobeh P, Parivar K, Kalantar SM, Hosseini SD, Salabat A. Effect of nano-zinc oxide on doxorubicin-induced oxidative stress and sperm disorders in adult male Wistar rats. Iranian J Reproductive Med 2013;11(5):355.
7. El-Sayed ES, Mansour AM, El-Sawy WS. Protective effect of proanthocyanidins against doxorubicin-induced nephrotoxicity in rats. J Biochemical Molecular Toxicol 2017;31(11): e21965.
8. Pugazhendhi A, Edison TN, Velmurugan BK, Jacob JA, Karuppusamy I. Toxicity of Doxorubicin (Dox) to different experimental organ systems. Life Sci 2018;200:26-30.
9. Khan TH, Ganaie MA, Alharthy KM, Madkhali H, Jan BL, Sheikh IA. Naringenin prevents doxorubicin-induced toxicity in kidney tissues by regulating the oxidative and inflammatory insult in

Wistar rats. Archives Physiol Biochem 2020;126(4):300-7.
10. Yarmohmmadi F, Rahimi N, Faghir-Ghanesefat H, Javadian N, Abdollahi A, Pasalar P, et al. Protective effects of agmatine on doxorubicin-induced chronic cardiotoxicity in rat. Eur J Pharmacol 2017;796:39-44.
11. Shaker RA, Abboud SH, Assad HC, Hadi N. Enoxaparin attenuates doxorubicin induced cardiotoxicity in rats via interfering with oxidative stress, inflammation and apoptosis. BMC Pharmacol Toxicol 2018;19(1):1-10.
12. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, et al. Cancer treatment and survivorship statistics, 2014. CA: a Cancer J Clinicians 2014;64(4):252-71.
13. Katzung BG, Masters SB, Trevor AJ, editors. Basic & clinical pharmacology. USA; McGraw Hill Companies: 2009.
14. Alghamdi SA. Effect of Nigella sativa and Foeniculum vulgare seeds extracts on male mice exposed to carbendazim. Saudi J Biological Sci 2020;27(10):2521-30.
15. Al-Seeni MN, El Rabey HA, Al-Hamed AM, Zamazami MA. Nigella sativa oil protects against tartrazine toxicity in male rats. Toxicol Reports 2018;5:146-55.
16. Assi MA, Hezmee MN, Abba Y, Rajion MA, Wahid H, Yusof MS. Assessment of therapeutic effects of Nigella sativa against chronic lead acetate-induced reproductive dysfunction in male Sprague-Dawley rats. Comparative Clinical Pathol 2017;26(1):87-97.
17. Elshama SS. The preventive and curative role of Nigella sativa in poisoning cases. J Clin Exp Tox 2018;2(2):18-24.
18. Hashem MA, Mohamed WA, Attia ES. Assessment of protective potential of Nigella sativa oil against carbendazim-and/or mancozeb-induced hematotoxicity, hepatotoxicity, and genotoxicity. Environmental Science and Pollution Res 2018;25(2):1270-82.
19. Tavakkoli A, Ahmadi A, Razavi BM, Hosseinzadeh H. Black seed (Nigella sativa) and its constituent thymoquinone as an antidote or a protective agent against natural or chemical toxicities. Iranian J Pharmaceutical Research: IJPR 2017;16(Suppl):2.
20. Mosbah R, Yousef MI, Maranghi F, Mantovani A. Protective role of Nigella sativa oil against reproductive toxicity, hormonal alterations, and oxidative damage induced by chlorpyrifos in male rats. Toxicol Industrial Health 2016;32(7):1266-77.
21. Abd-Elkareem M, Abd El-Rahman MA, Abou Khalil NS, Amer AS. Antioxidant and cytoprotective effects of Nigella sativa L. seeds on the testis of monosodium glutamate challenged rats. Scientific Reports 2021;11(1):1-6.
22. Mosbah R, Djerrou Z, Mantovani A. Protective effect of Nigella sativa oil against acetamiprid induced reproductive toxicity in male rats. Drug Chemical Toxicol 2018;41(2):206-12.
23. Sapmaz HI, Yıldız A, Polat A, Vardı N, Köse E, Tanbek K, Çuğlan S. Protective efficacy of Nigella sativa oil against the harmful effects of formaldehyde on rat testicular tissue. Asian Pacific J Tropical Biomed 2018;8(11):548.

Correlation Between Occupation and Azoospermia among Industrial Workers in District Faisalabad, Pakistan

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ABSTRACT

Objective: The main focus of study was to check the incidence of Azoospermia among these workers for any correlation with their occupation.
Study Design: A cross-sectional study
Place and Duration of Study: This study was conducted at the AS&RB of Khyber Medical University, Peshawar and Khyber Medical College, Peshawar from start of January to the end of June in year 2019.
Materials and Methods: After informed consent, semen samples were taken from married men who visited fertility clinics and laboratories for semen analysis. A questionnaire was made to input their data regarding their duration of their job, personal history and other medical condition. Semen analysis was performed by using computer assisted technique. Sample with zero sperm count was noted and presented in statistical analysis.
Results: Total 360 males were included in this study after applying exclusion criteria. These were evenly divided into three groups according to their occupation. From 360 samples, 51 were having zero sperm count, in which 11 were farmers (9.2%), 19 were textile industry workers (15.8%) and 21 belongs to oven workers (17.5%).
Conclusion: From result section it is concluded that incidence of Azoospermia was highest among oven workers followed by textile industry workers and farmers.

Key Words: Azoospermia, low sperm count, male infertility, semen analysis

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INTRODUCTION

Male fertility is a major concern these days. Incidence of poor semen parameters are increasing rapidly from past few years. This become a topic of interest among medical researchers to identify the environmental and nutritional factors causing poor semen parameters and total sperm count.[1,2] To check the fertility of male, a routine semen analysis test is performed at abstinence of 3-5 days in laboratory. Total active sperm count describes the fertility of a male. If this count falls below the optimal level (oligozoospermia) or become zero (azoospermia) as per WHO criteria.[3]

Studies done in the past identify that high heat effects normal spermatogenesis. High testicular temperature is hostile for sperm, this drastically decreased sperm counts which is reversible, and i.e. if high heat has been removed the total sperm count will be resumed. This has been studied in 2019.[4] Furthermore high heat also cause low sperm motility and affects its morphology.[5] Studies also revealed that some industrial chemicals which are used in coloring and dyeing of clothes in textile industries are also among toxic to spermatogenesis. Prolong exposure to these chemicals decreased sperm production and motility along with increased sperm mortality.[6,7] Similar studies also identify few pesticides are also considered to be one of the main cause of male infertility in farmers and gardeners.[8]

So after extensive review of literature a study was conducted to check the correlation between these risk factors related to different jobs and their impact on workers in district Faisalabad, Pakistan.

MATERIALS AND METHODS

After approval from AS&RB of Khyber Medical University, Peshawar and graduate committee of Khyber Medical College, Peshawar, a cross sectional study was performed on Pakistani married men from age 25 to 55 years, visited at different fertility clinics in Faisalabad, Punjab, Pakistan. After informed consent from patient and data collection via questionnaire semen samples were taken at lab in vicinity of fertility clinics under supervision of qualified lab technicians.

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One-time semen sample was considered as standard sample and exclusion criteria were applied. These samples were grouped according to occupation and computer assisted semen analysis was performed.

This study was performed from start of January to the end of June in year 2019. A Questionnaire was made which contains basic information regarding age, duration of marriage, occupational history, duration of occupation and time spend at working place, socioeconomic history and any past medical history.

The data was collected and analyzed as per WHO criteria. Statistical analysis was done by using SPSS v23. One-way ANOVA and LSD tests are used to compare means of each group for correlation.

RESULTS

Out of 360 semen samples, it was noted that 51 were having zero sperm account i.e. azoospermia. From these 51 azoospermic samples 11 were farmers (9.2%), 19 were textile industry workers (15.8%) and 21 belongs to oven workers (17.5%) as shown in following table.

Table No.1: Distribution of respondents regarding their sperm count and group type

			Group			Total
			Farmer/ Gardener	Industry Worker	Oven/ Baker Worker	
Sperm Count	No Sperm	Count	11	19	21	51
		% within Group	9.2%	15.8%	17.5%	14.2%
	Sperm Present	Count	109	101	99	309
		% within Group	90.8%	84.2%	82.5%	85.8%
Total		Count	120	120	120	360
		% within Group	100.0%	100.0%	100.0%	100.0 %

Chi Square value= 3.838^{NS} P-Value= 0.147 NS = Non-Significant (P>0.05)

Table shows the incidence of azoospermia among different groups and correlation of their mean values. This also calculates the percentage or azoospermia among each group.

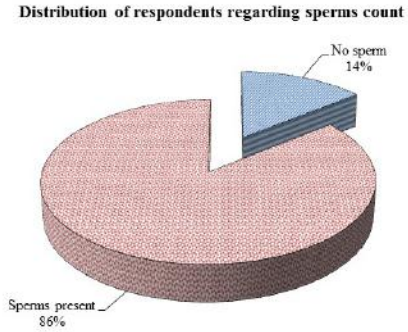

Figure No.1: Graphical representation of samples having sperms present vs no sperms

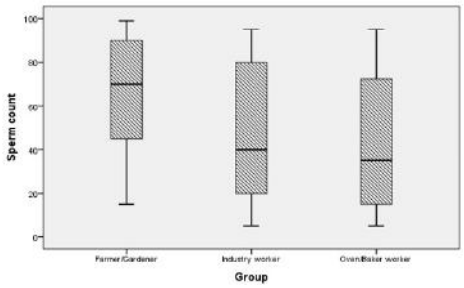

Figure No.2: Graphical representation of sperm counts and their mean values among different groups

DISCUSSION

Faisalabad is the largest and densely populated city of Pakistan. Most of its population is related to laborious jobs such as farmers, textile industry and oven workers. Prolong summer and increasing air and water pollution are the emerging problems of this city. Study shows that job related factors along with pollution effects male reproductive health.[9,10] In order to address this problem, a study was conducted on semen analysis of married men related to different occupations in district Faisalabad. Main aim was to check the incidence of azoospermia in correlation to their occupation as shown in Figure. 1.

Among all three groups, incidence of azoospermia was highest in oven/bakery workers. Decreased sperm count was also reported among them as shown in Fig. 2. These findings are in correlation with studies done worldwide.[11,12] This might be the fact that high heat has negative impact on spermatogenesis, furthermore prolong sitting on tandoor (stove for making traditional bread) might be a cause of zero or low sperm count among this community.[13]

Textile industry workers shows identical findings as compared to oven workers and bakers. Although their sperm count was better, but azoospermia was remarkably on higher side. These results were similar to the studies done internationally.[14,15] This might be due

to exposure of hazardous industrial chemicals. During study it was noted that most of industrial workers didn't follow safety protocols for toxic chemicals. No personal protective equipment usually practiced in small industries related to dyeing and coloring units, high heat and poor ventilation were also noted. According to different studies done in the past, these hazardous factors might be considered as the cause of azoospermia and decreased sperm count among them.[16,17]

Azoospermia among farmers and gardeners were only 9.2%. Comparatively better values than other two groups. But statistically highly significant as compared to total population. Our findings are in correlation with studies done in the past as the trend of azoospermia is increasing among farmers worldwide.[18] Hazardous pesticides may be the cause of low or zero sperm count among farmers.

The results of our study identifies the hazardous factors related to their job, such as high heat in extreme hot weather for oven workers and bakers, textile chemicals for textile industry workers and pesticides for farmers. Moreover, data also presents the number of sperms present in each group as well. Hence we did not rule out any anatomical defect for azoospermia such as obstructive cause. So a thorough study is advised in this direction for further analysis and root cause.

CONCLUSION

From result section it is concluded that incidence of Azoospermia was highest among oven workers followed by textile industry workers and farmers. Although a thorough study is advised for other factors such as smoker vs non-smoker and any underlying obstructive causes for azoospermia.

Author's Contribution:

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

REFERENCES

1. Danielewicz A, Przybyłowicz KE, Przybyłowicz M. Dietary patterns and poor semen quality risk in men: a cross-sectional study. Nutrients 2018;10(9): 1162.
2. Ajayi AB, Afolabi BM, Ajayi VD, Oyetunji I. Low Sperm Counts: Biophysical Profiles of Oligospermic Males in Sub-Saharan Africa. Open J Urol 2018;8(08):228.
3. Cooper TG, Noonan E, Von Eckardstein S, Auger J, Baker H, Behre HM, et al. World Health Organization reference values for human semen characteristics. Human Reproduction Update 2010;16(3):231-45.
4. Abdelhamid MHM, Esquerre-Lamare C, Walschaerts M, Ahmad G, Mieusset R, Hamdi S, et al. Experimental mild increase in testicular temperature has drastic, but reversible, effect on sperm aneuploidy in men: A pilot study. Reproductive biol 2019;19(2):189-94.
5. Aldahhan RA, Stanton PG. Heat stress response of somatic cells in the testis. Molecular and Cellular Endocrinol 2021;527:111216.
6. Oudir M, Chader H, Bouzid B, Bendisari K, Latreche B, Boudalia S, et al. Male rat exposure to low dose of di (2-ethylhexyl) phthalate during pre-pubertal, pubertal and post-pubertal periods: Impact on sperm count, gonad histology and testosterone secretion. Reproductive Toxicol 2018;75:33-9.
7. Sharma A, Mollier J, Brocklesby RW, Caves C, Jayasena CN, Minhas S. Endocrine-disrupting chemicals and male reproductive health. Reproductive Med Biol 2020;19(3):243-53.
8. Lwin TZ, Than AA, Min AZ, Robson MG, Siriwong W. Effects of pesticide exposure on reproductivity of male groundnut farmers in Kyauk Kan village, Nyaung-U, Mandalay region, Myanmar. Risk management and healthcare policy 2018;11:235.
9. Yucel C, Kozacioglu Z. Effect of seasonal variation on the success of micro-dissection testicular sperm extraction: A pilot study. Andrologia 2019;51(1):e13156.
10. Zou P, Sun L, Chen Q, Zhang G, Yang W, Zeng Y, et al. Social support modifies an association between work stress and semen quality: Results from 384 Chinese male workers. J Psychosomatic Res 2019;117:65-70.
11. Hasan FS, Yassin BAG. Seminal Fluid Abnormality among Infertile Males: A Two-Center Based Study in Baghdad. Iraqi Postgraduate Med J 2020;19(2).
12. Shah MAA, Inayat Q, Ali M, Mughal IA, Imdad L, Javed M. Correlation between Occupation and Sperm Morphology along with Sperm Count in Industrial Workers in District Faisalabad, Pakistan. Pak J Med Health Sciences 2021;15(2):324-6.
13. Hamerezaee M, Dehghan SF, Golbabaei F, Fathi A, Barzegar L, Heidarnejad N. Assessment of semen quality among workers exposed to heat stress: a cross-sectional study in a Steel Industry. Safety and health at work 2018;9(2):232-5.
14. Boulicault M, Perret M, Galka J, Borsa A, Gompers A, Reiches M, et al. The future of sperm: a biovariability framework for understanding global sperm count trends.Human Fertil 2021;1-15.
15. Abdollahi M-B, Dehghan SF, Balochkhaneh FA, Moghadam MA, Mohammadi H. Comparison of mice'sperm parameters exposed to some hazardous physical agents. Environmental Analysis, Health Toxicol 2021;36(3).
16. Ilieva I, Sainova I, Yosifcheva K. Toxic Effects of Heavy Metals (Lead and Cadmium) on Sperm

Quality and Male Fertility. Acta morphologica et anthropologica 2020;27:3-4.
17. Yang H, Wang J, Yang X, Wu F, Qi Z, Xu B, et al. Occupational manganese exposure, reproductive hormones, and semen quality in male workers: A cross-sectional study. Toxicol Industrial Health 2019;35(1):53-62.
18. Sunanda P, Panda B, Dash C, Padhy RN, Routray P. Semen quality among different professional groups: A retrospective study in a teaching hospital. Middle East Fertility Society J 2018;23(3):220-4.

Correlation Between Serum Calcium and National Institute of Health Stroke Score (NIHSS) in Ischemic Stroke Patients

Bushra Siddiqa[1], Syed Saif Ur Rehman[2], Adnan Ghafoor[5], Aisha Aslam[3], Ayesha Aftab[4] and Maria Sarfraz[6]

ABSTRACT

Objective: To determine correlation between serum Calcium and National Institute of Health Stroke Score (NIHSS) in ischemic stroke patients.

Study Design: Descriptive / Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine department Fauji foundation Hospital, Rawalpindil from 18th Sep, 2018 to 18th Mar, 2019.

Materials and Methods: The study was conducted after the approval of ethical committee. All the patients were educated and an informed consent was taken. All male and female patients of specified age group presenting to OPD/ emergency room & admitted in wards were evaluated. The diagnosis of acute ischemic stroke was based on symptoms of focal neurologic deficit and computed tomography (CT) brain evidence of ischemic infarct. Severity of stroke was assessed using National Institute of Health Stroke Score (NIHSS).

Results: Total 150 patients were included according to the inclusion criteria of the study. Mean age (years) in the study was 46.42±18.91 whereas there were 66 (44.0) male and 84 (56.0) female patients who were included in the study. There is a positive correlation (r=0.078) noted between serum calcium and NIHSS score in ischemic stroke patients.

Conclusion: There is a positive correlation between serum calcium and National Institute of Health Stroke Score (NIHSS) in ischemic stroke patients. Serum calcium levels may affect the severity of ischaemic injury.

Key Words: Calcium Serum Levels, Computed Tomography Scan, Ischemic Stroke, National Institute of Health Stroke Score, Severity

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INTRODUCTION

Stroke is characterized by acute onset of focal or diffuse impairement of cerebral functions more than 24 hours duration or leading to death secondary to a vacular aetiology with no other obvious cause[1,2]

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Multiple factors predispose towards stroke. Increasing age, high blood pressure, hyperglycemia, hyperlipidemia and artial fibrillations are major risk factors.[3,4] Smoking, raised inflammatory markers, Thrombophilia, metabolic syndrome, insulin resistance, microalbuminuria and serum calcium are increasingly correlated with ischaemic stroke.[5]

Ischemic injury of neurons initiates activation of multiple pathways leading to the loss of cell homeostasis. ischaemic injury catalyzes facilitates increased entry of calcium from the extracellular spaces into the neurons resulting in increased release of cytotoxic enzymes leading to cellular death.[6] Low calcium level at the time of acute ischaemic stroke results in more severe stroke as assessed by the National Institute of Health Stroke Score (NIHSS)[7,8]. Recent study showed patients with lower serum calcium have a correlation coefficient of r= -0.3 than those with high calcium levels[1].Studies also showed raised calcium levels through neuro-protective mechanisms lead to smaller size of infarcts[2,9].Patients found to have high levels of calcium at the time of acute ichaemic stroke tend to develop lesser complications[10,11]. Other studies indicated that Vitamin D and Calcium replacement in stroke patients leads to better outcome and lessens morbidity and mortality[12,13].

Awareness of the role of Calcium ions in the ischemic stroke has led to the development of such neuroprotective agents that modify the role of this ion in Cerebrovascular accidents[13]. This also helps to investigate further regarding the importance of improving dietary calcium in patients who are at risk of stroke.

Due to the massive burden that ischemic stroke shares, there is a huge need to develop prognostic markers for stroke survivors.[5] Serum calcium level can also be employed as a prognostic marker in patients with stroke. Current study was aimed to find association of calcium level with severity of ischaemic stroke in our population. Results of this study would help in executing better management plan for patients with ischaemic stoke.

MATERIALS AND METHODS

This Descriptive Cross-sectional study was conducted at outpatient department of General Medicine, Fauji Foundation Hospital, Rawalpindi for six months from 18th Sep, 2018 to 18th Mar, 2019 after approval from hospital ethical committee. The sample size was calculated (n=150) with anticipated population proportion of 14.7%, significance Level of 5% and with precision of 6%. Non probability purposive sampling technique was employed. Clinically diagnosed cases of patients having first episode of acute ischemic stroke presenting within 72 hours, with age 18 to 70 years of both genders are included in the study.

Patients with history of recurrent stroke, deranged liver function tests, chronic renal failure, aspiration pneumonia on chest X-ray, any malignancy, any autoimmune disorder determined with the help of ANA, recent trauma/ surgery and patients who were not willing to participate in the study were excluded.

Patients from outpatient department of FFH Rawalpindi who fulfilled criteria was included in the study. Detailed history regarding the illness was obtained from each patient. Complete clinical examination was performed by the trainee researcher. Diagnosis of acute ischaemic stroke was made on the basis of history, physical examination and findings of the CT scan of brain. 5cc blood sample was taken from all patients presenting with acute ischaemic stroke without applying tourniquet and was sent to laboaratory within 72 hours of their symptoms. Serum calcium level, Albumin and Rena function tests in addition to baseline investigations were measured under the supervision of a pathologist in FFH pathology lab. All these information were recorded on a preset Performa.

Data was entered and analyzed in SPSS version 20. Total 150 patients were included according to the inclusion criteria of the study.

RESULTS

Descriptive statistics of age (years) of patient was also calculated in terms of mean and standard deviation. Mean age (years) in the study was 46.42±18.91 with ranges from 18 to 70 years.

Distribution of gender of patient was also calculated in terms of frequency and percentage of male and female patients. There were 66 (44.0) male and 84 (56.0) female patients who were included in the study according to the inclusion criteria.

Descriptive statistics of serum calcium levels was measured in terms of mean and standard deviation. In our study, among acute ischemic stroke patients, mean serum calcium levels was 8.52±0.31, whereas mean NIHSS score was 21.84±5.83.

The objective of the study is to determine correlation between serum calcium and NIHSS score in ischemic stroke patients was r=0.078 as Pearson's correlation, as shown in Table 1.

Effect modifier like age stratification was stratified and compared with correlation between serum calcium and NIHSS score in ischemic stroke patients. Among patients with age 51- 70 years, there is a positive correlation r=0.011 was observed between serum calcium levels and NIHSS score, as shown in Table 2.

Effect modifier like gender stratification was stratified and compared with correlation between serum calcium and NIHSS score in ischemic stroke patients. Among male patients, there is a positive correlation r=0.231 was observed between serum calcium levels and NIHSS score, as shown in Table 3.

Effect modifier like hypertension, diabetes mellitus, hyperlipdemias & smoking stratification was stratified and compared with correlation between serum calcium and NIHSS score in ischemic stroke patients. Our Study findings showed that there is a positive correlation observed between serum calcium levels and NIHSS score among diabetes mellitus (r=0.076), hyperlipidemias (r=0.070) and smoking (r=0.091), as shown in Table IV. Post stratification chi-square test was applied and *P*-value ≤ 0.05 was considered as significant.

Sample Size: Calculated by WHO sample size calculator

Level of confidence	95%
Power of test	80%
Correlation Co-efficient	-0.3 [1]
Sample size:	150

Table No. I: Pearson's Correlation between Serum calcium and NIHSS in ischemic stroke patients (n=150)

		NIHSS score
Serum calcium levels	Pearson Correlation	0.078
	Sig. (2-tailed)	0.342
	N	150

Table. No. 2: Effect modifier like Age stratification with Pearson's Correlation between Serum calcium and NIHSS in ischemic stroke patients(n=150)

Age Groups		Pearson's Correlation (r)
18 – 50 years	Serum Calcium Levels & NIHSS score	0.123
51 – 70 years	Serum Calcium Levels & NIHSS score	0.011

Table. No. 3: Effect modifier like Gender stratification with Pearson's Correlation between Serum calcium and NIHSS in ischemic stroke patients(n=150)

Gender		Pearson's Correlation (r)
Male	Serum Calcium Levels & NIHSS score	0.231
Female	Serum Calcium Levels & NIHSS score	-0.043

Table. No. 4: Effect modifier like HTN, DM, Hyperlipidemias & Smoking stratification with Pearson's Correlation between Serum calcium and NIHSS in ischemic stroke patients (n=150)

Effect Modifiers		Pearson's Correlation (r)
Hypertension	Serum Calcium Levels & NIHSS score	-0.004
Diabetes Mellitus	Serum Calcium Levels & NIHSS score	0.076
Hyper-lipidemias	Serum Calcium Levels & NIHSS score	0.070
Smoking	Serum Calcium Levels & NIHSS score	0.091

DISCUSSION

Millions of stroke occur annually in world and has become one of the leading cause of death in world especially in developed countries.[1,8,12] Incidence of stroke is also increasing in third world countries. Stroke poses a huge ecnomic toll on already week health care system of poor countries but also has grave impact on the patient functional status and their family lives[8]. Stroke is considered to be one of major aetology leading to disability in adult population of the United states.[1,12] Although data about exact prevalance and incidence of stroke is not available but load can be assumed to be high due widely prevalent risk factors in the Pakistani population[8].

Our study was aimed to find correlation of calcium levels with severity of the acute ishaemic stroke. Current studies have shown association of high level of calcium to be associated with lesser severe stroke and improved prognosis[1,6,8,13-17].In our study, mean age in years was 46.42±18.91. Similarly, in a study conducted by Ishfaq et al,[1] mean age in years was 61.09±11.93.

In a study conducted in 2017[1] found that frequency and percentage of male and female patients were 71(51.4%) and 67(48.6%) respectively. Likewise, in our study, there were 66 (44.0) male and 84 (56.0) female patients.

In our study, among acute ischemic stroke patients, mean serum calcium levels was 8.52±0.31. Likewise, in a study conducted by Ishfaq et al,[1] mean serum calcium levels was 8.82±0.69.

In our study, correlation between serum calcium and NIHSS score in ischemic stroke patients was r=0.078 as Pearson's correlation. Consequently, in a study conducted in 2017[1] found that patients with lower serum calcium have a correlation coefficient of r= -0.3. Further prospective trials will be required to clarify the mechanism of this effect and to assess the role of serum calcium level as a prognostic variable and of calcium modulation as part of a strategy for prevention of stroke.

CONCLUSION

There is a positive correlation between serum calcium and NIHSS in ischemic stroke patients. serum calcium levels may affect the severity of ischaemic injury.

Author's Contribution:

Concept & Design of Study:	Bushra Siddiqa
Drafting:	Syed Saif Ur Rehman, Adnan Ghafoor
Data Analysis:	Aisha Aslam, Ayesha Aftab, Maria Sarfraz
Revisiting Critically:	Bushra Siddiqa, Syed Saif Ur Rehman
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Isfaq M, Ullah F, Akbar S, Rahim F, Afridi A. Correlation of Serum calcium with severity of acute ischemic stroke. JPMA 2017;67:1679.
2. Borah M, Dhar S, Gogoi DM, Ruram AA. Association of serum calcium levels with infarct size in acute ischemic stroke; Observation from Northeast India J Neurosci Rural Pract 2016;7: 41-45.
3. Chung J, Ryn W, Kim Beom, Yoon B. Elevated Calcium after cute Ischemic Stroke : Association with a poor Short- Term Outcome and Long-Term Mortality. J Stroke 2015;17(1): 54-59.
4. Liu J, Wang D, Xiong Y, Liu B, Wei C, Ma Z, et al. A cohort study of relationship between serum

calcium levels and cerebral microbleeds(CMBs) in ischemic stroke patients with AF and/or RHD. Medicine (baltimore) 2016;95(26): e4033.
5. Gupta A, Prabhakar S, Modi M, Bhadada S, Kalaivani M, Lal V, et al. Effect of Vitamin D and calcium supplementation on ischemic stroke outcome: a randomized controlled open label trial. Int J Clin Pract 2016;70(9):764-70.
6. Ovabiagele B, Starkman S, Teal P, Lyden P, Kaste M, Davis SM, et al. Serum calcium as prognosticator in ischemic stroke: Stroke 2008; 39:2231-6.
7. Venketasubramanian N, Yoon BW, Pandian J, Navarro JC. Stroke Epidemiology in South, East, and South-East Asia: A Review. J Stroke 2017; 19:286-94.
8. Zafar F, Tariq W, Shoaib RF, Shah A, Siddique M, Zaki A, et al. Frequency of Ischemic Stroke Subtypes Based on Toast Classification at a Tertiary Care Centrein Pakistan. Asian J Neurosurg 2018;13:984-9.
9. Radu RA, Terecoasa EO, Bajenaru OA, Tiu C. Etiologic classification of ischemic stroke: Where do we stand? Clin Neurol Neurosurg 2017;159: 93-106.
10. Labberton AS, Rønning OM, Thommessen B, Barra M. Changes in survival and characteristics among older stroke unit patients-1994 versus 2012. Brain Behav 2019;9:e01175.
11. Dibaba DT, Xun P, Fly AD, Bidulescu A, Tsinovoi CL, Judd SE, et al. Calcium Intake and Serum Calcium Level in Relation to the Risk of Ischemic Stroke: Findings from the REGARDS Study. J Stroke 2019;21:312-23.
12. Guven H, Cilliler AE, Koker C, Sarikaya SA, Comoglu SS. Association of serum calcium levels with clinical severity of acute ischemic stroke. Acta Neurol Belg 2011;111:45-9.
13. Larsson SC, Traylor M, Burgess S, Boncoraglio GB, Jern C, Michaëlsson K, et al. Serum magnesium and calcium levels in relation to ischemic stroke. Neurol 2019; 92:e944-50.
14. Wu J, Xie J, Zhao Y, Gong L, Liu X, Liu W. Serum Calcium is Related to the Degree of Artery Stenosis in Acute Ischemic Stroke. Cellular physiology and biochemistry: Cell Physiol Biochem 2018;46:1189-97.
15. Buck BH, Liebeskind DS, Saver JL, Bang OY, Starkman S, Ali LK, et al. Association of higher serum calcium levels with smaller infarct volumes in acute ischemic stroke. Arch Neurol 2007; 64:1287-91.
16. High Calcium Levels at Admission Linked to Better Stroke Outcomes [Online] [cited 2007 June 2].
17. Umesawa M, Iso H, Ishihara J, Saito I, Kokubo Y, Inoue M, et al. Dietary calcium intake and risks of stroke, Its Subtypes, and Coronary Heart Disease in Japanese: The JPHC Study Cohort I Stroke 2008; 39:2449-56.

To Evaluate the Patients of Puerperal Sepsis after Caesarean Delivery at Tertiary Care Hospital

Yasmeen Joyo, Saira Parveen, Samana Aleem, Shabana, Rozina Mujeeb and Madiha Rafique

ABSTRACT

Objective: The rationale of our study is to evaluate the outcome of puerperal sepsis in patients undergone for caesarean delivery and this study will help us to save the patients from developing the sepsis and lessen the rate of maternal mortality.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at the Department of Obstet and Gynae, Peoples Medical College Hospital (PMCH) Nawabshah from January 2019 to November 2021 for a period of 10 months.

Materials and Methods: Patients were admitted from Emergency Department. They were evaluated by taking detailed history and clinical examination. The patients having pyrexia/sepsis and delivered within 30 days were diagnosed on clinical examination apart from laboratory investigations. Patients were treated accordingly.

Results: The age of patients was between 17-45 years. 10 (16.5%) age was between 17-20 years. 15 (24.5%) patients age was 21-30 years and 36 (59%) were of 31-45 years. 57 (93.4%) patients presented with increased leucocyte count , decreased platelets 41(67.2%), fever in 60(98.3%), abdominal distention in 50(82%), anemia positive in 50(82%), wound infection in 30(49%) and positive vaginal swabs in 39(64%). Patients developed septicemia in 17(27.8%), peritonitis in 26(42.6%), DIC in 14(23%) and mortality in 9(14%).

Conclusion: It is concluded that patients presenting with puerperal sepsis after Caesarean delivery were of middle aged female, mostly un-booked, and complication commonly seen was peritonitis. As compared to other studies, mortality was decreased in our study.

Key Words: Peritonitis, Septicemia, Sepsis, Mortality

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INTRODUCTION

Puerperal sepsis is the fatal condition in surgical practice throughout world. Its incidence is highly increased particularly in developing countries due to multiple reasons. It is major cause of death in patients undergone for caesarean Section.[1] Peritonitis, Septicemia and Disseminated Intravascular Coagulation are the main three serious complications that , if controlled timely, have good otherwise very poor prognosis.[2]

Sepsis is the systemic inflammatory response to infection. Its incidence is increasingly continuously now days. It has been the common cause of death in developed countries.

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During pregnancy, the changes in women either physiological or anatomical enhance the risk of infection.[3] Maternal bacterial sepsis is the common disease related to pregnancy and is the leading cause of increased mortality throughout world. The mortality ratio in this connection is about 25% in United States of America (USA) and 1.4% women die of this disease in United Kingdom.[4]

Globally, the mortality rate due to Puerperal sepsis is about 15%. It is the 2nd leading cause of death of maternal mortality and accounts for 10% of deaths. In developed countries, ratio of puerperal sepsis has somewhat declined. It is 5.5% and 7.4% of vaginal deliveries and Caesarean section respectively. [5] The majority of patients develop puerperal sepsis due to infection of genital tract by pathogens which colonize the vagina and cervix and through amniotic fluid invade the devitalized uterine tissues. Other causes could be the severe maternal anemia, multiple vaginal examinations, prolonged membranous rupture and prolonged labor. However, the only risk factor for this sepsis is Caesarean Section.[6,7] Multiple pathogens are involved as causative agents of this disease. These are Streptococcus, Pseudomonas, Bactericides fragilis, Escherichia Coli, Klebshiella spp, Streptococci and Stapylococci.[8] In most of the countries, the sepsis is treated by broad spectrum antibiotics due to non-

availability of facilities if culture and sensitivity testing of pathogens. This causes contradictory effect and develops resistance to antibiotics.[9] So the patients have limited options of treatment and the results are insignificant. In a study, bacteraemia was reported in 11.2% and common organism involved was Klebshella.[10,11]

MATERIALS AND METHODS

This is a cross sectional study done at Department of Gyn/Obstetrics Peoples Medical College Hospital (PMCH) Nawabshah from January 2019 to November 2021. Patients were admitted from Emergency Department. They were evaluated by taking detailed history and clinical examination. The patients having pyrexia/sepsis and delivered within 30 days were diagnosed on clinical examination apart from laboratory investigations. Elevated temperature, abdominal distention, dehydration, leukocytosis, foul smelling, platelet count, serum electrolytes were also evaluated. Ultrasound was also done to know intra-abdominal collection and retained products of conception. Abdominal X Rays in erect and supine positions were taken. Malaria and typhoid fever were excluded from the study. All data was registered on case study Performa. Ethical approval was taken from the institutional ethical committee.

RESULTS

The age of patients was between 17-45 years. 10 (16.5%) age was between 17-20 years. 15 (24.5%) patients age was 21-30 years and 36 (59%) were of 31-45 years. 16% patients were primi, 33% were Para 1-4 and 51% were Para 5 and more (Chart No.1).

Table No.1: Age Difference

S.no:	Age of patients	No of patients	Percentage
1	17- 20 Years	10	16.5%
2	21-30 years	15	24.5%
3	31-45	36	59%
TOTAL	n=17-45	n= 61	100%

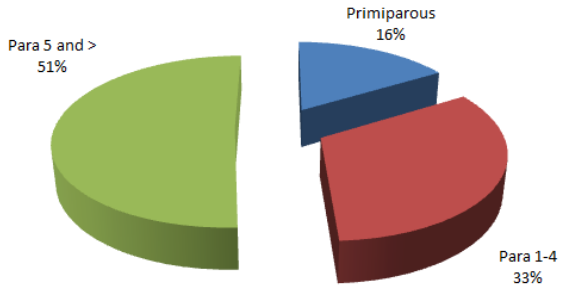

Figure No.1: Parity

42 (69%) patients were un-booked and 19 (31%) were booked (Chart No.2). 57 (93.4%) patients presented with increased leucocyte count, decreased platelets 41(67.2%), fever in 60(98.3%), abdominal distention in 50(82%), anemia positive in 50(82%), wound infection in 30(49%) and positive vaginal swabs in 39(64%) (Chart No.3). Patients developed septicemia in 17(27.8%), peritonitis in 26(42.6%), DIC in 14(23%) and mortality in 9(14%) (Chart No.4).

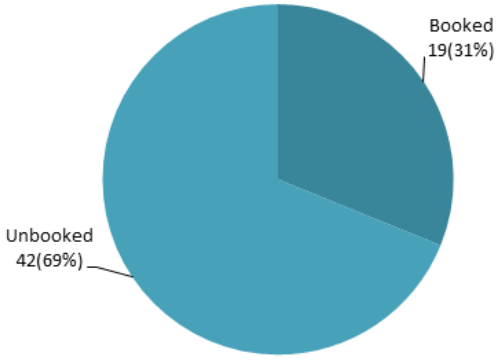

Figure No.2: Book Status

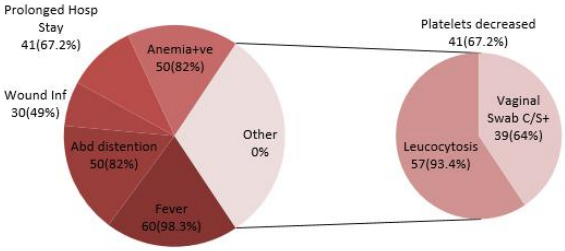

Figure No.3:Clinical, Biochemical and Histo-pathological Spectrum

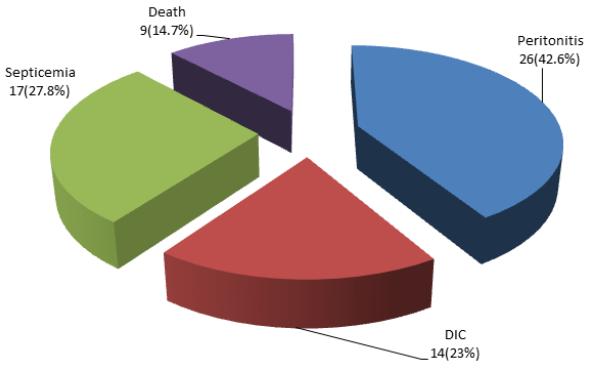

Figure No.4: Complications Of Peurperal Sepsis

DISCUSSION

Puerperal sepsis is one of the leading causes of maternal morbidity and mortality in clinical practice. It is still considered to be the 3rd common cause of maternal deaths. It ensues when streptococci colonizes in genital tract and invade endometrium along with adjacent structures, blood stream and lymphatic.[12] In a study, its incidence was seen among young patients of

15-25 years in 66.3% of all. In another study, the mean age of incidence was 25-35 years in 67% of all patients. In a study, the mean age was 31 years in about 71%. In our study, the major incidence was between 31-45 years and it was 59%.[13]

In a study, 58% patients of primi gravida developed puerperal sepsis. Multi-parous involved were 27% and grand multi were only 7%. But in our study, 16% primi, 33% multi parous and 51% grand multi developed Puerperal sepsis. In a study, majority of patients were un-booked. In our study, 69% patients were un-booked and 31% were booked. [14] In a study, 57.3% patients were anemic having hemoglobin level between 8.5-9 g/dl, 22.4% had Hb% level between 6-8 gms/dl and 21.5% had Hb% level below 5 gm/dl. Total leukocyte count (TLC) was more than 11000 cumm^2 in 72.09%. High vaginal swab C/S report was seen positive in 55.8%. Fever was seen in 90.6% cases and abdominal distention in 21.7% in our study, 82% had developed anemia, vaginal swabs positive in 64%, leucocytosis in 93.4%and fever was recorded in 98.3% patients. Abdominal distention was also seen in 82% cases. Platelets were decreased in 67.2%.[15]

In a study, 44.5% developed peritonitis, 4.3% septicemia, 4.3% endotoxic shock, 2.1% disseminated intravascular coagulation (DIC) and 10.8% pelvic abscess. Mortality was seen among 14.2%. In our study, peritonitis was noted in 42.6% patients, DIC in 23%, septicemia in 27.8% and mortality was noted in 14.7%. In a study, hospital stay was recorded more than 10 days in 85.2% patients. In our study, hospital stay more than 10 days was seen among 67.2%.[16]

CONCLUSION

It is concluded that patients presenting with puerperal sepsis after Caesarean delivery were of middle aged female, mostly un-booked, and complication commonly seen was peritonitis. As compared to other studies, mortality was decreased in our study.

Author's Contribution:

Concept & Design of Study:	Yasmeen Joyo
Drafting:	Saira Parveen, Samana Aleem
Data Analysis:	Shabana, Rozina Mujeeb, Madiha Rafique
Revisiting Critically:	Yasmeen Joyo, Saira Parveen
Final Approval of version:	Yasmeen Joyo

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

REFERENCES

1. Majangara R, Gidiri MF, Chirenje ZM. Microbiology and clinical outcomes of puerperal sepsis: a prospective cohort study. J Obstet Gynaecol 2018;38(5):635–41.
2. Fuchs A, Tufa TB, Hörner J, Hurissa Z, Nordmann T, Bosselmann M, et al. Clinical and microbiological characterization of sepsis and evaluation of sepsis scores. PLoS One 2021;16(3): 247-64.
3. Wilkie GL, Prabhu M, Ona S, Easter SR, Tuomala RE, Riley LE, et al. Microbiology and antibiotic resistance in Peripartum bacteremia. Obstet Gynecol 2019;133(2):269–75.
4. Ahmed MI, Alsammani MA, Babiker RA. Puerperal sepsis in a rural hospital in Sudan. Mater Soc 2013;25(1):19–22.
5. Demisse GA, Sifer SD, Kedir B, Fekene DB, Bulto GA. Determinants of puerperal sepsis among postpartum women at public hospitals in west SHOA zone Oromia regional STATE, Ethiopia (institution BASEDCASE control study). BMC Pregnancy Childbirth 2019;19(1):1–6.
6. Madhudas CKF, Sirichand P. Maternal morbidity and mortality associated with puerperal Sepsis. J Liquat Univ Med Heal Sci 2008;10(2):121–3.
7. Dare A BC. Puerperal sepsis:a preventable post-partum complication.. Aids Res Hum retroviruses 2015;15(4):92–95.
8. Mohamed IMA, Rabie A. Puerperal Sepsis in Rural Hospital Sudan. Mat Soc Med 2013;25(1):19–22.
9. Abebaw N. Assessment of the prevalence and associated factors of puerparal sepsis among PNC women during post -partum period at dessie referal hospital, Ethiopia. 2018.
10. Temesgen F. Incidence and determinants of puerperal fever among Parturients who gave birth in a tertiary teaching hospital. Addis Ababa: Addis Ababa University Institutional Repository; 2015.
11. Atlaw D, Seyoum K. Puerperal sepsis and its associated factors among mothers in University of Gondar referral hospital, Ethiopia, 2017. Int J Pregn Chi Birth 2019;5(5):190–5.
12. Admas A, Gelaw B, Worku A, Melese A. Proportion of bacterial isolates, their antimicrobial susceptibility profile and factors associated with puerperal sepsis among post-partum/aborted women at a referral Hospital in Bahir Dar, Northwest Ethiopia. Antimicrobial Resistance & Infection Control 2020;9(1):1–10.

13. Caughey AB, Cahill AG, Guise J-M, Rouse DJ. Obstetricians ACo, gynecologists. Safe prevention of the primary cesarean delivery. Am J Obstet Gynecol 2014;210(3):179–93.

14. Ezugwu FOOH. Prevalence and correlates of maternal morbidity in Enugu. AJOL 2010;3(1):121–30.

15. Khaskheli MNBS, Sheeba A. Risk factors and complications of puerperal sepsis at a tertiary healthcare Centre. Pak J Med Sci 2013;29(4): 972–6.

16. Maritim CVJN, Margaret K. Associated factors with puerperal Sepsis among reproductive age women in Nandi County, Kenya. J Midwifery Reproductive Health 2017;5(4):1032–40.

To Evaluate the Risk Factors and Prevalence of Endometrial Carcinoma in Patients of Endometrial Hyperplasia

Saira Parveen, Yasmeen Joyo, Shabana, Rozina Mujeeb, Resham Baloch and Samana Aleem

ABSTRACT

Objective: The rationale of our study is to find out the risk factors of developing in patients suffering from endometrial hyperplasia so that patients may be detected early and saved from developing cancer.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at the Department of Gyn & Obs at PMCH Nawabshah from January 2019 to December 2020 for a period of one-year.

Materials and Methods: Total patients included in this were 91. All the patients aged >40 to 65 years with any parity having complain of vaginal bleeding. Patients having uterine fibroids were excluded from the study. Detailed history regarding age, gravid parity and bleeding were taken apart from thorough clinical examination. Transvaginal sonography was performed using vaginal transducer of 6.5 MHz frequency. Endometrium hyperplasia was labeled as in the form of present or absent. If hyperplasia is found, endometrial tissue was taken to see its conversion into carcinoma through D&C.

Results: Total patients included in this study were 91. Of them 65 (71%) were nulliparous and 26 (29%) were multiparous. It ranged between 40 to 65 years with mean age of 48 years. 35 (38.5%) patients were of age40 to 50 years. 30 (33%) patients were aged from 51 to 55 years. 26 (28.5%) patients age was from 56 to 65 years. Only 20 (22%) patients were diagnosed as endometrial carcinoma on histopathology. Of 20, only 5 (22.7%) patients had simple hyperplasia and 15 (68%) had complex hyperplasia.

Conclusion: It is concluded that null parity is the most significant risk factor in our study and prevalence of EC is decreased in our study.

Key Words: Endometrial Carcinoma, Null parity, Obesity, Hyperplasia

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INTRODUCTION

Endometrial Carcinoma (EC) is the commonly reported gynecological malignancy in developed countries having annual incidence of 20 cases per 100,000 women. The report of American cancer Society shows probability of EC of 1 in 37 women. Increasing age, obesity and nulliparity are the significant risk factor of this disease in developing countries. The mortality of this disease accounted for 2.1% with good prognosis unless diagnosed at late stage.

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A risk factor is called when something enhances that gets the chance of getting converted disease such as cancer. Multiple diseases have varied risk factors. Some risk factors can be changed and some can't be. There are certain factors which increase the risk of endometrial cancer in women.[1]

The factors affecting the development of endometrial cancer includes obesity, estrogen taken after menopause, contraceptive pills, pregnancy, PCOS, ovarian tumors, age, diet, type 2 D.M, endometrial hyperplasia and radiotherapy. The factors like pregnancy, contraceptive pills/ IUD have lower risks.[2,3]

Endometrial hyperplasia is simply defined as the increased growth of endometrium. It is noninvasive proliferation of lining of uterus whose outcome is the series of glandular alterations. Endometrial Hyperplasia is classified into two types viz simple and complex based on the degree of structural complexity as seen by glandular crowding and with or without cytologic atypia.[4] Simple hyperplasia rarely transforms into cancer. Complex type commonly is converted to endometrial carcinoma and is commonly treated with progesterone and hysterectomy. According to cytology,

findings commonly are nuclear irregularity such as loss of axial polarity, rounded stratified nuclei and prominent nuclei. Hyperplasia Atypia is type of hyperplasia associate with increased risk of carcinoma and is usually treated by Hysterectomy.[5,6]

Endometrial hyperplasia occurs due to increased estrogen level by stimulating the growth of endometrial cells. Estrogen binds to nuclei of endometrial cells. This results in shedding of endometrial tissue because of effect of estrogen proliferating cells to progesterone. This occurs in two ways either by decreasing the number of estrogen receptors or increasing the conversion of estradiol to estrone.[7,8]

Abnormal vaginal bleeding is the common presentation unrelated to normal menstruation like heavy menstrual bleeding.[9] It is more than 80ml/period on three consecutive menstrual periods that is measured with help of soaked pad. Each soaked pad is about 10 m 0f blood. Diagnosis is usually done on trans-vaginal ultrasound.[10] It is considered to be hyperplasia if endometrial thickness is more than 5 mm.[11,12]

MATERIALS AND METHODS

This is a cross sectional study done at PMCH Nawabshah from January 2019 to December 2020. Total patients included in this were 91. All the patients were admitted from OPD Gyn/Obs and emergency Department of PMC Hospital Nawabshah. All the patients aged >40 to 65 years with any parity having complain of vaginal bleeding. Patients having uterine fibroids were excluded from the study.

Detailed history regarding age, gravid parity and bleeding were taken apart from thorough clinical examination. Routine investigations were done. trans-vaginal ultrasound was also done. Transvaginal sonography was performed using vaginal transducer of 6.5 MHz frequency. Endometrium hyperplasia was labeled as in the form of present or absent. If hyperplasia is found, endometrial tissue was taken to see its conversion into carcinoma through D&C.

RESULTS

Total patients included in this study were 91. Of them 65 (71%) were nulliparous and 26 (29%) were multiparous (Chart No.1). Age difference was also seen in all patients. It ranged between 40 to 65 years with mean age of 48 years. 35 (38.5%) patients were of age 40 to 50 years. 30 (33%) patients were aged from 51 to 55 years. 26 (28.5%) patients age was from 56 to 65 years (Table No.1).

Table No.1: Age Difference

S. No.	Age of patients	No of patients	Percentage
1	40-50 Years	35	38.5%
2	51-55	30	33%
3	56-65	26	28.5%
Total	40-65	n= 91	100%

Of 91 patients, only 20 (22%) patients were diagnosed as endometrial carcinoma on histopathology. Of 20, only 5 (22.7%) patients had simple hyperplasia and 15 (68%) had complex hyperplasia (Chart No.2).

Table No.2: Risk Factors of Endometrial Carcinoma

S.No.	Risk factors	No of patients	Percentage
1	Nulliparous	65	71%
2	Obesity	7	7.6%
3	D. M	6	6.5%
4	Estrogen taken after menopause	7	7.6%

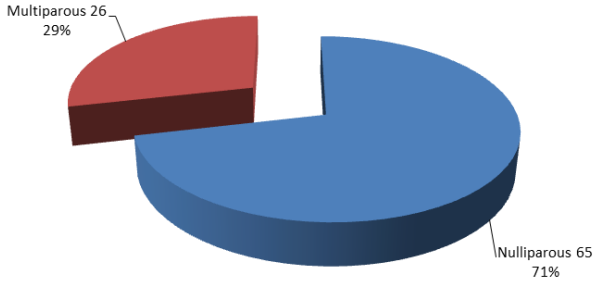

Figure No.1: Parity Prevalence

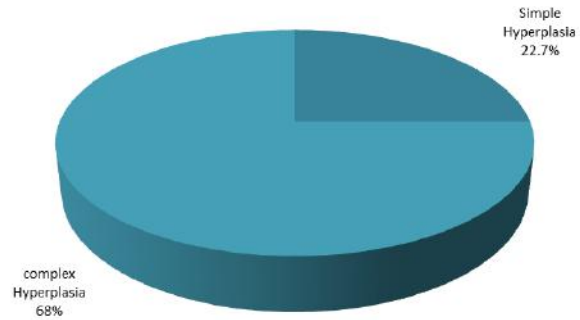

Figure No.2: Endometrial Carcinoma

DISCUSSION

Endometrial carcinoma (EC) is the common malignancy in females. Every year, more than 40 thousand new cases appear in United States of America.[13] This figure is increased as compared to prevalence of ovarian and cervical carcinomas. Approximately, 1 in 50 females develop endometrial carcinoma.[14]

This carcinoma occurs at reproductive age and menopausal stage. In a study, the median age endometrial carcinoma is 61 years. The most patients are between 50 and 59 years. In another study, 10% of women had developed EC before 40 years and 20-30% patients were diagnosed before the menopause. Another study has reported endometrial hyperplasia patients

aged between 40-59 had increased risk of developing EC. The risk was higher in patients aged above 60 years due to decreased immune system. In our study, the common age of incidence was 40-50 years.[15]

There is a close association of EC with parity. A total of 42 studies reported the association between parity for parous versus nulliparous for the development of EC. In a study, nulliparous women had more prevalence of endometrial carcinoma as compared to multiparous women. In our study, 65 (71%) patients were nulliparous and 26 (29%) were multiparous.[16]

Several studies concluded that patients having history of diabetes Mellitus and Obesity are associated with increased risk of endometrial carcinoma. But in another study, diabetes mellitus did not show any significant association but obesity showed association with development of EC. In our study, risk factor most commonly caused EC was null parity then DM and obesity.[17].

CONCLUSION

It is concluded that null parity is the most significant risk factor in our study and prevalence of EC is decreased in our study.

Author's Contribution:

Concept & Design of Study:	Saira Parveen
Drafting:	Yasmeen Joyo, Shabana
Data Analysis:	Rozina Mujeeb, Resham Baloch, Samana Aleem
Revisiting Critically:	Saira Parveen, Yasmeen Joyo
Final Approval of version:	Saira Parveen

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

REFERENCES

1. Vetter MH, Smith B, Benedict J, Hade EM, Bixel K, Copeland LJ, et al. Preoperative predictors of endometrial cancer at time of hysterectomy for endometrial intraepithelial neoplasia or complex atypical hyperplasia. Am J Obstet Gynecol 2020;222(1):60-67.
2. Doherty MT, Sanni OB, Coleman HG, Cardwell CR, McCluggage WG, Quinn D, et al. Concurrent and future risk of endometrial cancer in women with endometrial hyperplasia: a systematic review and meta-analysis. PLoS One 2020;15(4):232-237.
3. Jordan SJ, Na R, Weiderpass E, Adami HO, Anderson KE, van den Brandt PA, et al. Pregnancy outcomes and risk of endometrial cancer: a pooled analysis of individual participant data in the Epidemiology of Endometrial Cancer Consortium. Int J Cancer 2021;148(9):2068–78.
4. Clarke MA, Long BJ, Sherman ME, Lemens MA, Podratz KC, Hopkins MR, et al. Risk assessment of endometrial cancer and endometrial intraepithelial neoplasia in women with abnormal bleeding and implications for clinical management algorithms. Am J Obstet Gynecol 2020;223(4):541–549.
5. Padilla-Iserte P, Lago V, Tauste C, Diaz-Feijoo B, Gil-Moreno A, Oliver R, et al. Impact of uterine manipulator on oncological outcome in endometrial cancer surgery. Am J Obstet Gynecol 2021;224(1):61–65.
6. Kim S, Park J, Chen Y, Rowe K, Snyder J, Fraser A, et al. Long-term diabetes risk among endometrial cancer survivors in a population-based cohort study. Gynecol Oncol 2020;156(1):185–93.
7. Saleh M, Virarkar M, Bhosale P, El Sherif S, Javadi S, Faria SC. Endometrial cancer, the Current International Federation of Gynecology and Obstetrics Staging System, and the Role of Imaging. J Comput Assist Tomogr 2020;44(5): 714–29.
8. Association FRDGoPBoCM. Pathological diagnosis criteria for endometrial cancer. Chin J Pathol 2020;49(3):214–9.
9. Giannella L, Delli Carpini G, Sopracordevole F, Papiccio M, Serri M, Giorda G, et al. Atypical endometrial hyperplasia and unexpected cancers at final histology: a study on endometrial sampling methods and risk factors. Diagnostics (Basel) 2020;10(7):474-9.
10. Matsuo K, Ramzan AA, Gualtieri MR, Mhawech-Fauceglia P, Machida H, Moeini A, et al. Prediction of concurrent endometrial carcinoma in women with endometrial hyperplasia. Gynecol Oncol 2015;139(2):261–7.
11. Rakha E, Wong SC, Soomro I, Chaudry Z, Sharma A, Deen S, et al. Clinical outcome of atypical endometrial hyperplasia diagnosed on an endometrial biopsy: institutional experience and review of literature. Am J Surg Pathol 2012;36(11):1683–90.
12. Setiawan VW, Yang HP, Pike MC, McCann SE, Yu H, Xiang YB, et al. Type I and II endometrial cancers: have they different risk factors? J Clin Oncol 2013;31(20):2607–18.
13. Hutt S, Tailor A, Ellis P, Michael A, Butler-Manuel S, Chatterjee J. The role of biomarkers in endometrial cancer and hyperplasia: a literature review. Acta Oncol 2019;58(3):342–52.
14. Sanderson PA, Critchley HO, Williams AR, Arends MJ, Saunders PT. New concepts for an old problem: the diagnosis of endometrial hyperplasia. Hum Reprod Update 2017;23(2):232.
15. Travaglino A, Raffone A, Saccone G, Mollo A, De Placido G, Insabato L, et al. Endometrial hyperplasia and the risk of coexistent cancer: WHO versus EIN criteria. Histopathol 2019;74(5): 676–87.
16. Alcazar JL, Bonilla L, Marucco J, Padilla AI, Chacon E, Manzour N, et al. Risk of endometrial cancer and endometrial hyperplasia with atypia in asymptomatic postmenopausal women with endometrial thickness ≥ 11 mm: a systematic review and meta-analysis. J Clin Ultrasound 2018;46(9):565–70.

17. Rosen MW, Tasset J, Kobernik EK, Smith YR, Johnston C, Quint EH. Risk factors for endometrial cancer or hyperplasia in adolescents and women 25 years old or younger. J Pediatr Adolesc Gynecol 2019;32(5):546–9.

Prevalence of Urinary Tract Infection in Patients with Urinary Stone Disease and Their Antibiotic Sensitivities

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ABSTRACT

Objective: To find out the frequency of common bacteria causing urinary tract infection in patients with urinary stone disease and to determine the antibiogram of common bacteria causing urinary tract infection in patients with urinary stone disease.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at Urology Out-patient Department, Shaikh Zayed Hospital Lahore from 1st February 2020 to 30th July, 2020.

Materials and Methods: Sixty five patients with urinary stone diseases were enrolled. All urinary stone patients of both genders and 13-65 years were included. their clean-catch mid-stream urine samples were sent to microbiology laboratory for culture and sensitivity testing.

Results: The mean age was 45.09±15.49 years with 35 (53.8%) male and 30 (46.2%) female patients. The most common pathogens isolated were E. coli (61.5%), K. Pneumonia (9.2%), Enterococcus species (9.2%), methicillin-resistant Staphylococcus aureus (6.2%) and P. mirabilis (4.6%). Most of the isolates were found to be highly resistant to commonly prescribed antibiotics including cephalosporins, quinolones and penicillin-derivatives.

Conclusion: An overall high prevalence of E. coli causing UTI in patients with USD. For gram-positive isolates, low levels of resistance were detected against teicoplanin, linezolid and vancomycin while gram-negative isolates were most sensitive to colistin, meropenem and imipenem. Multi-drug resistant urinary tract bacteria are becoming widespread in patients with USD, probably due to frequent and unwarranted use of antibiotics. The surveillance of UTI and antimicrobial resistance patterns are essential to reduce the emergence of more resistant strains of these bacteria.

Key Words: Urinary Tract infection, Urinary stone disease, Urolithiasis, Bacteriuria

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INTRODUCTION

Urinary tract infection is very common in patients with urolithiasis. Persistent infections caused by urease-producing bacteria will form infection stones consisting of monoammoniumurate, struvite (magnesium ammonium phosphate), and/or carbonate apatite.[1]

Secondarily infected stones, the non-struvite and non–calcium carbonate apatite stones are also associated with UTIs.[2]

Complications of urolithiasis, i.e. asymptomatic bacteriuria, UTI, and sepsis have been recognized after treatment with extracorporeal shock-wave lithotripsy. Patients with severe or multiple stones might develop postoperative systemic inflammatory response syndrome after a percutaneous nephrolithotomy (PCNL), with a small percent progressing to urosepsis, which could lead to a catastrophic even, such as septic shock. All infections of the urogenital tract, pyelonephritis is very severe and leads to dangerous complications.[3] The frequency of urinary tract infection in stone disease, which has a high incidence in Pakistan need to be studied to find out the risk and help in the treatment of disease.[4]

In majority of studies, *E. coli* was found to be the most frequently encountered pathogen causing UTI and accounts for more than 50% of the isolates in several studies.[5-7] Similarly, in one of the studies, the majority of isolates were *E. coli* (52.7%) followed by Staphylococcus (21.4%), Moraxella (8%), Klebsiella

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(7.4%) and Enterococcus (5.9%). Other isolated organisms were Citrobacter (4%), Streptococcus (3.5%), Pseudomonas (2.4%), Sphingomonas (1.2%), Kocuria (0.8%), Acinetobacter (0.8%), Providencia (0.8%), Francisella (0.4%) and Morganella (0.4%).[8]

Ampicillin had the highest overall resistance rate (78.3%) whereas tazobactam/piperacillin combination had the highest overall sensitivity rate (17.7%). *E. coli*; the most commonly found uropathogen was most sensitive to nitrofurantoin (20%) while most resistant to ampicillin (77.8%).[8] While in another study the same organism was found to be most sensitive to imipenem (93%) followed by amikacin (78%), tazobactam (69%), fosfomycin (60%) and nitrofurantoin (59%). In this study similar patterns were shown by Klebsiella and Staphylococcus Aureus, the other two most common uropathogens of the study.[9]

The primary aim of this study is to identify the common pathogens associated with UTI in patients with urinary tract stone disease and to determine their sensitivity patterns. One of the main criteria for selecting antimicrobial drugs for treating UTI is data on the antibiotic resistance of uropathogens.[6] The results of this study will help the urologists and other doctors dealing with such infections especially locally to choose appropriate antibiotic regime at initial stage in the absence of culture and sensitivity reports and will also help in devising guidelines for appropriate empirical antibiotic therapy. Furthermore, as the pathogens causing urinary tract infections are developing resistance against commonly used antibiotics, this study will also shed light on the changing sensitivity patterns of these pathogens when compared to the previous studies.

MATERIALS AND METHODS

This cross-sectional study undertaken in the Department of Urology, Shaikh Zayed Hospital, Lahore from 01-02-2020 to 31-07-2020. Sixty five patients were included from 13 to 65 years of age and both genders with evidence of stone disease on CT-KUB plain. Those excluded from the study who refusing to give consent, patients with indwelling catheter or history of catheterization in past 6 weeks, with any history of instrumentation or surgery in past 6 weeks and with any history of antibiotic usage in last 3 days. The samples of mid-stream urine were sent to microbiology laboratory for culture and sensitivity testing. There urine samples were inoculated onto Cysteine Lactose Electrolyte Deficient medium using a calibrated loop with a capacity of 1µl in safety cabinet. All inoculated plates were incubated at 37 C for 24-48hours and the number of colonies were counted. Colony counts yielding bacterial growth of$>10^5$ per ml of urine (≥100,000 colonies) were regarded as significant for bacteriuria. Urine samples yielding more than 3 bacterial species were not considered for further investigation. Then gram staining of smear of the urine was prepared for identification of gram positive or negative bacteria. Specimen ID was confirmed by biochemical panel using api (analytical profile index) 20E and Whitek 2 system. The sensitivity of the isolated bacteria to specific antibiotics (as specified by CLSI (clinical and laboratory standards institute) 2019 guidelines for each bacterium) were then tested using NCCLS (National laboratory for Clinical Standards) Modified Kirby-Bauer disc diffusion technique and the bacteria were labelled sensitive(S) or resistant(R) after measuring zones of inhibition.

RESULTS

The age ranged from 15-65 years of patients with a mean of 45.09±15.49 years. Majority of the patients were in age group of 41-65 years (60.0%) followed by the age group of 15-40 years (40.0%).

Table 1: Frequency of different bacteria isolated (n=65)

Bacteria	Frequency	Percent
Escherichia coli	40	61.5
Klebsiella pneumonia	6	9.2
Enterococcus species	6	9.2
Methicillin-resistant Staphylococcus aureus	4	6.2
Proteus mirabilis	3	4.6
Pseudomonas aeruginosa	2	3.1
Coliform species	2	3.1
Serratia species	1	1.5
Acinetobacter species	1	1.5
Total	65	100.0

Table No.2: Antibiotics sensitivity and resistance patterns of gram-positive bacteria

Antibiotics	Gram Positive			
	Enterococcus species (%)		Staphylococcus aureus (%)	
	S	R	S	R
TPN	100	0	100	0
LNZ	100	0	100	0
VAN	100	0	100	0
NIT	83.3	16.7	100	0
FOS	60.0	40.0	100	0
AMX	50.0	50.0	0	100
AMP	50.0	50.0	0	100
AUG	50.0	50.0	0	100
PEN	40.0	60.0	0	100
GEN	-	-	33.3	66.7
AMK	-	-	0	100
IMI	-	-	0	100
CXA	-	-	0	100
CFX	0	100	0	100
CTR	0	100	0	100
CTX	0	100	0	100
CIP	0	100	0	100
CEF	0	100	0	100

There were 35 (53.8%) male and 30 (46.2%) female patients with a male to female ratio of 1.16:1.The most common pathogens isolated were *E. coli* (61.5%), K. Pneumonia (9.2%), Enterococcus species (9.2%), methicillin-resistant Staphylococcus aureus (6.2%) and P. mirabilis (4.6%). Other isolated pathogens were P. aeruginosa (3.1%), Coliform species (3.1%), Serratia species (1.5%) and Acinetobacter species (1.5%) (Table-1).

There were only 2 Gram-positive bacteria among the isolates: Enterococcus species and methicillin-resistant Staphylococcus aureus (MRSA). Both of these bacteria were found to be fully sensitive (100%) to Teicoplanin (TPN), Linezolid (LNZ) and Vancomycin (VAN) whereas both were highly resistant (100%) to ciprofloxacin (CIP) and most cephalosporins (Cefuroxime CFX, Ceftriaxone CTR, Cefotaxime CTX and Cephradine CEF). Moreover, Enterococcus was found to be resistant to half of the drugs tested while MRSA was found to be resistant to 2/3rd of the tested drugs (Table 2).

Among the 7 Gram-negative bacteria identified, percent of isolates sensitive to polymyxin B (PB), Colistin (CST), meropenem (MEM) and imipenem (IMI) were 96.1%, 90.6%, 88.2% and 87.0% respectively, whereas all gram-negative isolates were fully resistant (100%) to amoxicillin (AMX), ampicillin (AMP) and Cephradine (CEF) (Table 3).

Table No.3: Antibiotics sensitivity and resistance patterns of gram-negative bacteria

Antibiotics	Gram Negative						
	Escherichia coli	Klebsiella species	Proteus species	Pseudomonas aeruginosa	Coliform	Serratia species	Acinetobacter species
	S	S	S	S	S	S	S
CST	100	100	0	100	50	0	100
PB	100	100	100	100	50	0	100
MEM	97.3	60	100	50	50	100	0
IMI	95	66.7	100	50	50	-	0
AMK	91.7	33.3	100	50	50	-	0
ETP	89.2	60	-	0	100	100	0
NIT	80.6	0	0	0	0	0	0
FOS	79.4	0	-	-	-	-	-
SCF	75.7	33.3	100	50	50	100	0
TZP	73.7	40	100	50	50	100	-
GEN	54.1	33.3	100	50	50	-	0
AUG	28.9	0	0	-	0	0	0
CAZ	23.3	16.7	66.7	0	50	100	0
CT	18.9	20	66.7	-	10	100	0
X					0		
CTR	18.2	0	100	-	0	-	-
CIP	10.5	0	-	50	0	100	0
CFX	5.6	0	66.7	0	50	0	0
AMX	0	0	0	-	0	-	0
AMP	0	0	0	-	0	0	0
CEF	0	0	-	-	-	-	-

DISCUSSION

Urinary tract infection in patients with urinary stone disease is an increasing clinical problem. Urease producing bacteria have long been recognized to contribute to struvite stones and are almost always present in infection stones; however, the association of bacteria with other types of calcium and non-calcium stones has not been extensively investigated. Several findings do indicate a possible correlation between urinary stones and bacteria and higher rate of UTI in urinary stone patients.[10]

The incidence of urinary stone disease in males is 2 to 3 times higher than females as documented by many studies.[11-13] The lower male to female ratio in our study and other similar studies can be explained on the basis that although stone disease is more common in males, but urinary tract infection is very higher in females like to males.[14]

E. coli was the much frequent isolated pathogen causing UTI in patients with accounting for 61.4% of isolated pathogens. Although E.coli is the most frequent uropathogen in almost all studies, the prevalence of *E. coli* in our study was slightly less than its prevalence (64.41%) from a study in Jamshoro.[15] Whereas it is relatively higher when compared with the studies from Lahore and Karachi which identified *E. coli* isolates in 34.01% and 40% of the patients respectively.[16] This higher prevalence of *E. coli* in our study indicate that E.coli may be associated with urinary stone formation through unknown mechanism as also suggested by studies from Thailand and India.[17]E.coli is also the most prominent bacteria in urology.[18]

Other bacteria isolated in this study were K. Pneumonia (9.2%), Enterococcus species (9.2%), methicillin-resistant Staphylococcus aureus (6.2%), P. mirabilis (4.6%), P. aeruginosa (3.1%), Coliform species (3.1%), Serratia species (1.5%) and Acinetobacter species (1.5%). These findings are in line with the studies done in Jamshoro (K. Pneumonia: 11.31%, Enterobacter: 11.31%, P. mirabilis: 7.86%, P. aeruginosa: 3.27%, Citrobacter: 1.74%) and Thailand.[15,18] Another study done in Lahore showed similar trend with some variations (K. Pneumonia: 18.78%, S. aureus:6.6%, S. epidermidis: 4.57%, P. aeruginosa: 4.57%, P. mirabilis: 1.52%, Citrobacter: 1.52%) whereas the study from India identified isolates

with significantly different prevalence of (K. Pneumonia: 30%, P. aeruginosa: 19%, S. aureus: 5%, E. faecalis: 4%, P. mirabilis: 2%).[16] These differences could be due to the poor hygiene and sanitation in India.

The current study showed an alarmingly high percentage of resistance to commonly prescribed antibiotics. The all gram-negative isolates were fully resistant to at least 2 antibiotics (MDR). More isolates of Gram-negative bacteria revealed 100% resistance to ampicillin, amoxicillin and cephradine which is much higher than the resistance pattern of these antibiotics in previousstudies in Lahore, Jamshoro and Karachi.[15-16] Similar higher level of resistance among the gram-negative bacteria was also observed in this study against commonly used antibiotics such as ciprofloxacin (mean resistance of 87.8%), cephalosporins (cefuroxime (89.6%), ceftriaxone (81.3%), cefotaxime (75%), ceftazidime (72.7%)) and co-amoxiclav (77.6%). For comparison the mean resistance for some of these antibiotics in Jamshoro study was ciprofloxacin (27.4%), ceftriaxone (27%) and ceftazidime (24.5%) (16). Recently popular nitrofurantoin and fosfomycin were found to be effective against 2/3rd and 3/4th of the tested isolates. Most of the gram-negative isolates in our study were found to be sensitive to very few antibiotics namely polymyxin b, colistin, meropenem, imipenem, ertapenem and amikacin with mean resistance of only 3.9%, 9.4%,11.8%, 13%, 17.4% and 20% respectively.[19]

Only two species of gram-positive bacteria were identified in our study indicating high prevalence of mainly Gram-negative bacteria in causing urinary tract infection in patients with stone disease. Among Gram-positive bacteria evaluated for antimicrobial drug resistance enterococcus and only methicillin resistant strain of *S. aureus isolated.* Both of these bacteria were highly resistant to most first-line and commonly used antibiotics having zero susceptibility to ciprofloxacin and all tested cephalosporins (cephradine, cefotaxime, ceftriaxone and cefuroxime) while MRSA was also fully (100%) resistant to amikacin, imipenem and cloxacillin for which enterococcus were not tested. Both the strains were 100% susceptible to teicoplanin, linezolid and vancomycin. Although half of the isolates of enterococcus were also susceptible to ampicillin, amoxicillin, penicillin and co-amoxiclav but no isolate of MRSA was susceptible to any of these drugs. Again these findings indicate much higher levels of resistance among the Gram-positive isolates in patients with stone disease as compared to isolates identified in previous studies done in Lahore, Karachi and a similar study in Thailand.[16,17]

The role of typically cultured pathogens in pathologic calcification is largely unknown and unstudied, particularly in the case of kidney stone disease. Our data suggests that UTIs even in patients with stone disease are mainly caused by *E. coli* and not urease-splitting bacteria. Our findings also emphasize that UTIs in stone diseases is not limited to proteus or urease-splitting bacteria rather UTIs caused by other bacteria are more prevalent in the presence of stone disease. These observations could be due to either secondary infection of stones as suggested by a study in USA, alternatively these non-urease producing bacteria may be somehow involved in stone formation or propagation as suggested by a study in Thailand.[2,17]

UTIs associated with urolithiasis is a significant problem for the modern endo-urologist due to the high levels of resistance among the isolates as observed in this study. These bacteria continue to survive in the urine most likely due to multidrug resistance, thus becomes difficult to be eradicated. Another possible explanation of the persistence of these bacteria is that they may get entrapped in the stone periphery. Several factors may be responsible for this alarmingly increased prevalence of highly resistant organisms identified in this study. Most importantly, mis-use of antibiotics because of its easy availability over-the-counter without the requirement of any prescription have resulted in self-medication of these drugs for viral infections and for other irrelevant illnesses. Moreover, widespread quackery as well as failure to adhere to standard treatment guidelines and inadequate or absence of local antimicrobial drug resistance surveillance programs have allowed the pathogens to grow resistant to most antibiotics largely unnoticed.

CONCLUSION

An overall high prevalence of *E. coli* causing UTI in patients with USD. For gram-positive isolates, low levels of resistance were detected against teicoplanin, linezolid and vancomycin while gram-negative isolates were most sensitive to colistin, meropenem and imipenem. Hence, these could be used as empirical therapy for urinary stone patients having UTI in the study area. Multi-drug resistant urinary tract bacteria are becoming widespread in patients with USD, probably due to frequent and unwarranted use of antibiotics.

Author's Contribution:

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REFERENCES

1. Bichler KH, Eipper E, Naber K, Braun V, Zimmermann R, Lahme S. Urinary infection stones. In: Int J Antimicrobial Agents 2002;29: 488–98.
2. De Cógáin MR, Lieske JC, Vrtiska TJ, Tosh PK, E. Secondarily infected nonstruvite urolithiasis: A prospective evaluation. Urol 2014;84:1295–300.
3. Yongzhi L, Shi Y, Jia L, Yili L, Xingwang Z, Xue G. Risk factors for urinary tract infection in patients with urolithiasis - primary report of a single center cohort. BMC Urol 2018;18:1.
4. Khan FA, Siddiqui SH, Akhtar N. Urinary tract infection in stone patients and in patients with indwelling urethral catheters. JPMA 1981; 31(11): 254–8.
5. McAninch JW, Lue TF. Smith & Tanagho's General Urology, 18th ed. McGraw-Hill Co Inc pp; 2013;197–222.
6. Rafalskiy V. Resistance of urinary tract pathogens and the choice of antimicrobial therapy: deceptive simplicity. Urologiia 2017;3:104–10.
7. Acharya A, Gautam R, Subedee L. Uropathogens and their antimicrobial susceptibility pattern in Bharatpur, Nepal. Nepal Med Coll J 2011;13:30–3.
8. Bitew A, Molalign T, Chanie M. Species distribution and antibiotic susceptibility profile of bacterial uropathogens among patients complaining urinary tract infections. BMC Infect Dis 2017; 17:654.
9. Kidwai SS, Nageen A, Ghaznavi S, Bashir F, Ara J. Antibiotic susceptibility in commonly isolated pathogens from urinary tract infection in a cohort of subjects from low socioeconomic strata. Pak J Med Sci 2017;33(2):254–9.
10. Huang WY, Chen YF, Chen SC, Lee YJ, Lan CF, Huang KH. Pediatric urolithiasis in Taiwan: A nationwide study, 1997-2006. Urol 2012;79(6): 1355–9.
11. Ali SH, Rifat UN. Etiological and clinical patterns of childhood urolithiasis in Iraq. Pediatr Nephrol 2020;20(10):1453–7.
12. Geraghty RM, Jones P, Somani BK. Worldwide Trends of Urinary Stone Disease Treatment Over the Last Two Decades: A Systematic Review. J Endourol 2020;31(6):547–56.
13. Wang S, Zhang Y, Zhang X, Tang Y, Li J. Upper urinary tract stone compositions: The role of age and gender. Int Braz J Urol 2020;46(1):70–80.
14. McLaughlin S, Carson C. Urinary tract infections in women. Med Clin North Am 2004;88(2): 417–29.
15. Paryani JP, Memon S-R ur R, Rajpar ZH, Shah SA. Pattern and Sensitivity of Microorganisms Causing Urinary Tract Infection at Teaching Hospital. JLUMHS 2012;11(2):97–100.
16. Naeem SA, Batool U, Iram S, Wasim YN, Nadeem AM, Khan S, et al. "Prevalence of urinary tract infections and their antibiotic sensitivity in tertiary care hospital Lahore". J Dent Med Sci 2020;3:14.
17. Tavichakorntrakool R, Prasongwattana V, Sungkeeree S, Saisud P, Sribenjalux P, Pimratana C, et al. Extensive characterizations of bacteria isolated from catheterized urine and stone matrices in patients with nephrolithiasis. Nephrol Dial Transplant 2020; 27(11):4125-30.
18. Hannan TJ, Totsika M, Mansfield KJ, Moore KH, Schembri MA, Hultgren SJ. Host-pathogen checkpoints and population bottlenecks in persistent and intracellular uropathogenic Escherichia coli bladder infection. FEMS Microbiol Rev 2012;36:616–48.
19. Reza Mortazavi-Tabatabaei S, Ghaderkhani J, Nazari A, Sayehmiri K, Sayehmiri F, Pakzad I. Pattern of antibacterial resistance in urinary tract infections: A systematic review and meta-analysis. Int J Prev Med 2019;10:169.

Vitamin D Deficiency in Patients with Chronic Liver Disease

Vitamin D Deficiency with Chronic Liver Disease

Dilaram Khan, Fakhare Alam and Jan Dil Khan

ABSTRACT

Objective: To find the frequency of vitamin D deficiency in patients with chronic liver disease and evaluate the relationship of vitamin D deficiency with advancement in liver disease severity.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Lady Reading Hospital, Peshawar from August 2020 to February 2021.

Materials and Methods: One hundred and forty one patients with chronic liver disease were enrolled. Vitamin D level was measured in the blood sample of patients in the hospital laboratory. The cut-off value for vitamin D deficiency was set at Serum vitamin D [25 (OH) D] level <30 nmol/L.

Results: Ninety nine patients (70.2%) were males and 42 patients (29.8%) were females. The mean age was 53.40±12.19 years. Hepatitis C was the most common underlying cause of chronic liver disease observed in 80 patients (56.7%). 83 patients (58.9%) had Child-Pugh Class C chronic liver disease. Vitamin D deficiency was observed in 95 patients (67.4%). Gender and Child-Pugh Class had a significant association with vitamin D deficiency.

Conclusion: Vitamin D deficiency is a frequently occurring finding in patients. Female patients with advanced liver fibrosis are more likely to have vitamin D deficiency.

Key Words: Vitamin D deficiency, Fibrosis, End stage liver disease

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INTRODUCTION

Chronic liver disease is a multi-nutrient deficiency condition. Patients with Chronic liver disease are susceptible to micro and macronutrient deficiency ranging from protein and several vitamin deficiencies to minerals like zinc and selenium. Deficiency of fat-soluble vitamins is also frequently observed.[1] Vitamin D is one of the fat-soluble vitamins. Though deficiency of vitamin D is fairly common in advanced chronic liver disease, patients with a milder form of liver illness are also susceptible to a certain extent of vitamin D inadequacy.[2] Vitamin D deficiency has implications in terms of increased risk of mortality, morbidities, and precipitation of Chronic liver disease related complications, including recurrent bacterial infections and portal hypertensive complications.[3,4]

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The low level of vitamin D in chronic liver disease patients may be attributed to an imbalance in vitamin D metabolism in the liver. Synthesized in an inactive form (vitamin D2 and D3) in the skin under the effect of UV light, the inactive vitamin D is subjected to activation through hydroxylation in the liver. In liver fibrosis, the liver loses its ability to hydroxylase the inactive form of vitamin D leading to deficiency of active vitamin D, which is evident from the fact that the deficiency is more common in patients with Child-Pugh Class C liver disease.[5,6] Decreased dietary vitamin D, decreased intestinal absorption, and decreased exposure to sunlight further aggravate the condition of the patient[7]. Depending upon the severity of fibrosis, there are different reports about the prevalence of vitamin D deficiency in patients with chronic liver disease. There is lack of data about vitamin D deficiency in chronic liver disease patients in our country with respect to its prevalence and its association with disease severity.

The main aim of this study is to know the prevalence of vitamin D deficiency in chronic liver disease in our local set up so that to design strategies to prevent and treat vitamin D deficiency in patients suffering from chronic Liver disease.

MATERIALS AND METHODS

This descriptive study was conducted at the Department of Gastroenterology, Lady Reading Hospital Peshawar after approval from the ethical review board from 20th August 2020 to 20th February 2021. Patients in the age

range of 20 to 80, both genders with chronic liver disease (CLD) were included. Patients with a history of vitamin D deficiency prior to CLD, patients with a history of chronic kidney disease, vitamin D supplements, and steroid intake in the last six months were excluded. Patients were labeled as having CLD if they had one or more of the following features: (1) If they have biochemical abnormalities suggestive of CLD like deranged liver and synthetic functions and risk factors leading to CLD. (2) Sonographic features of CLD like surface nodularity, coarse heterogeneous echotexture, hypertrophic or atrophic liver segments.[9] (3) Liver biopsy findings of CLD or medical records were suggestive of CLD. Patients with CLD were classified into three classes based on their Child-Pugh score. Patients with a Child-Pugh score of six or less than six were classified as Child-Pugh Class A, those with a score of seven to nine as Child-Pugh Class B, and patients with a score of greater than nine were classified as Child-Pugh Class C. Patients with a history of vitamin D deficiency prior to CLD, patients with chronic kidney disease, vitamin D supplements, and steroid intake in the last six months were excluded. Data Collection: Demographics including age, gender, the underlying cause of CLD, duration of CLD, and Child-Pugh Class were noted from patients' records. Relevant history of vitamin D deficiency like bone fractures was taken, followed by detailed physical examination for any signs of vitamin D deficiency. Vitamin D level was determined in the hospital laboratory in the blood sample of the patient. Serum vitamin D [25(OH) D] levels less than 30nmol/L were labelled as deficient vitamin D. Analysis of the data was performed using SPSS-22.

RESULTS

There were 99 (70.2%) males and 42 (29.8%) were females. The male to female ratio was 2.4:1 (Table 1). The patient's age ranged from 20 to 80 years, while the mean age of the patients was 53.40±12.194 years. Majority of patients were in the age range of 46 to 60 (Table 2). Eighty three patients (58.9%) had Child-Pugh Class C chronic liver disease, while both Child-Pugh Class A and B were present in 29 (20.6%) patients each (Table 3). The most common underlying cause of CLD was chronic hepatitis C in 80 (56.7%), followed by chronic hepatitis B in 31 (22%), hepatitis B and hepatitis C co-infection in 11 (7.8%), PBC in 5 (3.5%) patients while in 14 patients (9.9%) patients, the underlying cause was either autoimmune hepatitis, non-alcoholic fatty liver, Wilson disease, hemochromatosis or the cause was unknown despite workup. The aetiology of these 14 patients was labelled as "miscellaneous" in this study (Table 4). Vitamin D deficiency was observed in 95 (67.4%) patients, 61 (64.21%) male and 34 (35.78%) female patients. Vitamin D deficiency was more common in patients with Child-Pugh Class C disease. Out of 83 Child Pugh Class C patients, 76 (91.56%), 11 (37.93%) child Pugh class B and 8 (27.58%) child Pugh class A chronic liver disease patients were having vitamin D deficiency (Table 5).

Table No.1: Frequency of genders (n=141)

Gender	No	%
Male	99	70.21
Female	42	29.79

Table No.2: Frequency of age (n=141)

Age	No.	%
20-30	21	14.89
31-45	40	28.36
46-60	80	56.73
61-80	20	14.18
Mean±SD	53.40±12.19	

Table No.3: Child class wise distribution of patients

Child class	No.	%
Child A	29	20.60
Child B	29	20.60
Child C	83	58.90

Table No.4: Aetiology wise distribution of chronic liver disease patients

Aetiology	**No.**	**%**
Hepatitis C	80	56.74
Hepatitis B	31	21.98
Hep B and C co-infection	11	7.80
Primary biliary cirrhosis	5	3.55
Miscellaneous	14	9.93

Table No.5: Vitamin D deficiency wise distribution of patients

Child class	**No.**	**%**
Child-A	8	27.58
Child-B	11	37.93
Child -C	76	91.56

DISCUSSION

The body's vitamin D requirement is fulfilled by absorption through the gut from dietary sources. Secondly, it is also predominantly synthesized endogenously in the skin's epidermal cells through exposure to ultraviolet radiation.[8] The inactive vitamin D thus synthesized is subjected to the liver for activation through hydroxylation via a protein called vitamin D binding protein (DBP) and an analog of albumin. In fibrotic diseases like chronic liver disease, where the normal parenchyma of the liver is replaced with fibrous tissue, the synthetic function of the liver is compromised, leading to reduction of DBP, which eventually leads to vitamin D deficiency.[9]

Our study showed high prevalence 76 (91.56%) of vitamin- D deficiency in cirrhotic patients of various aetiologies. These results of our study are almost similar to the study done by Arteh et al[5] in USA where 118 patients were studied and there was 92.4% prevalence of vitamin D deficiency in their patients.

Similarly the results of our study are also comparable to the study done Jamil et al[10] in Rawalpindi where total of 125 were studied and 88% had vitamin D deficiency. However the results of our study are somewhat different from the study done by Falak et al[11] in Faisalabad where vitamin D deficiency was reported in 76.5% of patients .The female gender and advanced chronic disease patients were more sufferer of vitamin-D deficiency in our study and same results were reported by Johnson and colleagues[12] in their study as well. Adults in our local population primarily consume proteinaceous diets, which may lead to dietary factors of deficiency as well. Moreover, females are less exposed to sunlight due to religious and socio-cultural concepts, which is also proven to lead to vitamin D deficiency.[13] Association of vitamin D deficiency was observed with the Child-Pugh score of the patients in inverse fashion. Vitamin D deficiency was more frequently observed as the patient's fibrosis score progressed from Class A and B to C. This effect could be explained due to reduction in the synthetic function of the liver, which is decreased as the fibrosis advances, eventually leading to reduction of DBP, which is necessary for activation of vitamin D. These results are in conformity with the results of the study conducted by Jamil et al.[10].

CONCLUSION

Vitamin D deficiency is a frequent finding in patients with chronic liver disease. Female patients and those with advanced fibrosis are more likely to have vitamin D deficiency.

Author's Contribution:

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REFERENCES

1. Zaina FE, Parolin MB, Lopes RW, Coelho JC. Prevalence of malnutrition in liver transplant candidates. Transplant Proc 2004;36(4):923-5.
2. Fisher L, Fisher A. Vitamin D and parathyroid hormone in outpatients with noncholestatic chronic liver disease. Clin Gastroenterol Hepatol 2007;5(4):513-20.
3. Zittermann A, Iodice S, Pilz S, Grant WB, Bagnardi V, Gandini S. Vitamin D deficiency and mortality risk in the general population: a meta-analysis of prospective cohort studies. Am J Clin Nutr 2012;95(1):91-100.
4. Anty R, Tonohouan M, Ferrari-Panaia P, Piche T, Pariente A, Anstee QM, et al. Low Levels of 25-Hydroxy Vitamin D are Independently Associated with the Risk of Bacterial Infection in Cirrhotic Patients. Clin Transl Gastroenterol 2014;5(5):e56.
5. Arteh J, Narra S, Nair S. Prevalence of vitamin D deficiency in chronic liver disease. Dig Dis Sci 2010;55(9):2624-8.
6. Heuman DM, Mihas AA, Habib A, Gilles HS, Stravitz RT, Sanyal AJ, et al. MELD-XI: a rational approach to "sickest first" liver transplantation in cirrhotic patients requiring anticoagulant therapy. Liver Transpl 2007; 13(1):30-7.
7. Stokes CS, Volmer DA, Grünhage F, Lammert F. Vitamin D in chronic liver disease. Liver Int 2013;33(3):338-52.
8. Zhang R, Naughton DP. Vitamin D in health and disease: current perspectives. Nutr J 2010; 9:65.
9. Konstantakis C, Tselekouni P, Kalafateli M, Triantos C. Vitamin D deficiency in patients with liver cirrhosis. Ann Gastroenterol 2016; 29(3):297-306.
10. Jamil Z, Arif S, Khan A, Durrani AA, Yaqoob N. Vitamin D Deficiency and Its Relationship with Child-Pugh Class in Patients with Chronic Liver Disease. J Clin Transl Hepatol 2018;6(2):135-40.
11. Falak S, Aftab L, Saeed M, Islam A. Prevalence of Vitamin-D deficiency is related to severity of liver damage in Hepatitis-C patients. Pak J Med Sci 2020;36(3):445-50.
12. Johnson LK, Hofsø D, Aasheim ET, Tanbo T, Holven KB, Andersen LF, et al. Impact of gender on vitamin D deficiency in morbidly obese patients: a cross-sectional study. Eur J Clin Nutr 2012;66(1):83-90.
13. Zargar AH, Ahmad S, Masoodi SR, Wani AI, Bashir MI, Laway BA, et al. Vitamin D status in apparently healthy adults in Kashmir Valley of Indian subcontinent. Postgrad Med J 2007; 83(985):713-6.

Effect of Dry Weight Reduction on Blood Pressure Control among End-Stage Renal Disease Patients on Maintenance Hemodialysis

Shahid Anwar[1], Tanzila Saleh[1], Abad-ur-Rehman[2], Zahid Anwar[3] and Mateen Akram[4]

ABSTRACT

Objective: To find mean change in post-dialysis blood pressure after dry weight reduction among patients on hemodialysis.
Study Design: Quasi-Experimental study
Place and Duration of Study: This study was conducted at the Dialysis Unit, Nephrology Department, Sir Ganga Ram Hospital, Lahore from June 2017 to March 2018.
Materials and Methods: Sixty patients were enrolled. The mean of the blood pressures was calculated as a baseline. Dry weight was reduced through ultrafiltration by additional weight loss of 0.9 kg/10 kg per dialysis. Follow-up was done after 4 weeks and a mean change in post-dialysis systolic and diastolic BP was recorded.
Results: Forty six (76.7%) were males and 14 (23.3%) were females. The mean age was 45.4±11.8 years. Mean SBP at baseline was 160.7±12.4 mmHg and 152.0±12.8 mmHg at 4 weeks, which is statistically significant (p=0.000).Mean DBP at baseline was 93.2±3.1 mmHg and 89.5±7.9 mmHg at 4 weeks, which is also statistically significant (p=0.000).
Conclusion: The reduction of dry weight is an effective maneuver to improve BP control in hemodialysis patients.
Key Words: Hemodialysis, Hypertension, Dry weight

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INTRODUCTION

World health organization considers hypertension (HTN) a major health ailment affecting 1.28 billion adult population worldwide, almost 46% of these individuals remain ignorant and undiagnosed, 42% get proper diagnosis and treatment, whereas only 21% achieve adequate control of HTN with treatment.[1]
Hypertension if left untreated or poorly controlled leads to weakening of blood vessels walls, formation of atherosclerotic plaques, and eventually leads to cerebrovascular accidents, acute coronary syndrome, and chronic kidney disease. Hypertension being a silent killer bags 9.4 million deaths yearly which accounts for 2.58% of all deaths.[2] In different parts of the world, many guidelines have been established based on age, race, and region but the American College of Cardiology (ACC)/American Heart Association (AHA) and European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines having little difference are widely followed. ACC/AHA 2017 guidelines suggest blood pressure (BP) more than 130/80 as HTN whereas the 2018 ESC/ESH report states >140/90 as HTN.[3] International Society of Hypertension 2020 report and 2017 JNC 8 endorse ≥140/90 blood pressure for labelling HTN.[4]
Chronic HTN leads to chronic kidney disease (CKD) and CKD itself develops secondary HTN. Prevalence of HTN is 60 to 90% at different stages of CKD being highest among patients of end-stage renal disease (ESRD) on hemodialysis (HD). Glomerulosclerosis, sympathetic over activity, hormonal imbalance, and atherosclerosis are important pathogenic mechanisms for the development of HTN in CKD patients, but fluid overload and salt retention play a vital role among HD patients.[5] Hypertension of HD patients is a risk factor for the development and progression of left ventricular hypertrophy (LVH), cardiovascular disease (CVD), and

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total mortality. More than 50% of HD patients have some form of CVD, 75% have LVH and overall cardiovascular mortality is 20 times higher than the normal population.[6] Surprisingly better survival is reported by some studies with high BP among HD patients.[7] Because of high mortality with very high and low BP, Kidney Disease Outcome Quality Initiatives (KDOQI) guidelines recommend pre hemodialysis and post hemodialysis blood pressure readings of <140/90 mmHg and <130/80 mmHg respectively.[8] Recent studies have proved the better quality of life among HD patients with adequate control of BP.[9]

Along with antihypertensive medications removing excess water from the body by HD is an effective way of managing hypertension among ESRD patients keeping in mind that >90% of HTN is due to hypervolemia.[10] Removal of excess body water depends upon a careful assessment of volume status and estimation of dry weight. There is no census on dry weight definition but generally, it is that post HD body weight at which patient remain normotensive until the next dialysis despite salt and water retention during the intradialytic period.[11] Reduction of dry weight to the point where a patient is not clinically hypovolemic helps in controlling BP and reduces hospitalization rates.[12]

This study is designed to find meaningful change in post-dialysis blood pressure after dry weight reduction among hypertensive end-stage renal disease patients on maintenance hemodialysis.

MATERIALS AND METHODS

This quasi-experimental study was conducted at Nephrology Unit, Sir Ganga Ram Hospital Lahore from 23rd June 2017 to 28th March 2018. Using the Non-Probability Consecutive Sampling technique, the sample size of 60 cases was calculated by using a 95% confidence level with a 10% margin of error.[13] End-stage renal disease hypertensive patients on thrice-weekly maintenance HD for more than 3 months were included**.** Patients with congestive cardiac failure and stroke in the previous six months and patients who failed to achieve a reduction in dry weight at 4 weeks were excluded from the study. Demographical characteristics and medication record was reviewed among patients already taking anti-hypertensive. At the start of the study post-HD, Systolic BP (SBP) and diastolic BP (DBP) were recorded from the non-arteriovenous access arm, 3 readings were taken for each patient, and the mean was calculated as baseline BP. All patients underwent thrice-weekly HD and the dry weight of the patients was reduced from 0.9 to 1 kg through ultrafiltration gradually over a period of 4 weeks. Follow-up was done after 4 weeks and a mean change in post-dialysis SBP and DBP was recorded. Data were entered and analyzed on SPSS-23. The difference between post-dialysis blood pressures was analyzed by using Paired sample t-test. Data were stratified for age, BMI, duration of ESRD, and gender. Post-stratification, a t-test was applied. A p-value ≤0.05 was considered significant.

RESULTS

Forty six (76.7%) were males and 14(23.3%) were females. 9(15.0%) were between 15-30 age group, while 22(36.7%), 29(48.3%) were between 31-45 years and >45 age groups respectively. The mean age of the patients was 45.4±11.8 years with 25 and 67 as the minimum and maximum ages. 39(65%) patients had normal weight, while 19(31.7%) and 2(3.3%) were overweight and obese respectively.

Table No.1: Demographic and statistical analysis of the data

Variable	No. (%)	SBP		P value	DBP		P value
		Baseline	At 4 weeks		Baseline	At 4 weeks	
Total	60 (100%)	160.7±12.4	152±12.9	0.000	93.2±3.1	89.6±7.9	0.000
Gender							
Male	46 (76.7%)	160.8±12.4	152.1±12.4	0.000	93.4±3.0	90.4±3.9	0.000
Female	14 (23.3%)	160.4±13.0	151.8±14.8	0.003	92.5±3.6	86.8.2±14.9	0.162
Age (years)							
15-30	9 (15%)	157.5±13.0	152.4±18.0	0.141	94.2±2.7	86.9±19.6	0.254
31-45	22 (36.7%)	164.7±15.0	154.7±12.3	0.000	94.2±4.3	90.7±3.1	0.001
≥45	29 (48.3%)	158.7±9.3	149.8±11.5	0.000	92.1±1.6	89.6±3.5	0.000
BMI (kg/m^2)							
Normal	39 (65%)	161.5±13.1	152.7±14.2	0.000	93.5±3.2	89.9±9.7	0.010
Overweigh t	19 (31.7%)	159.0±11.7	150.4±10.5	0.000	92.8±3.1	89.9±2.9	0.000
obese	2 (3.3%)	163.2±3.0	153.6±3.3	0.013	91.3±0.4	87.7±0.1	0.053
HD duration (months)							
10-48	20 (33.3%)	160.3±12.7	150.1±9.6	0.000	93.4±4.1	86.9±12.1	0.018
48-72	13 (21.7%)	162.0±13.6	150.0±15.5	0.000	93.5±2.7	89.7±3.7	0.002

>72	2 7(45%)	160.5±12.1	154.4±13.7	0.003	92.9±2.6	91.5±4.4	0.088

Among these patients, 20(33.3%) had ESRD from 10-48 months, while 13(21.7%), 27(45.0%) had 48-72 months, and >72 months respectively. The mean BMI of the patients was 22.9±4.4 with 17 and 36 as the minimum and maximum values. The mean duration of ESRD was 66.5±35.0 months with 10 and 132 as the minimum and maximum months. Mean SBP at baseline was 160.7±12.4 mmHg with 144 and 197.6 as the minimum and maximum values. Mean SBP at 4 weeks was 152.0±12.8 mmHg with 122.3 and 181.2 as the minimum and maximum values. Mean DBP at baseline was 93.2±3.1 mmHg with 90 and 104.3 as the minimum and maximum values. Mean DBP at 4 weeks was 89.5±7.9 mmHg with 87.6 and 98.5 as the minimum and maximum values. Mean SBP at baseline was 160.7±12.4 mmHg and 152.0±12.8 mmHg at 4 weeks, which is statistically significant (p=0.000). Mean DBP at baseline was 93.2±3.1 mmHg and 89.5±7.9 mmHg at 4 weeks, which is also statistically significant (p=0.000) [Table 1].

DISCUSSION

Management of HTN among HD patients is a difficult task and the target of BP in these patients is always a matter of debate. The first point of contention is the use of pre-dialysis, post-dialysis, or interdialytic BP readings as a target of HTN management. Pre-dialysis BP is affected by volume accumulation whereas post-dialysis BP is affected by ultrafiltration volume and rate, dialysate temperature, and food intake during dialysis. There are strong chances that patients are hypertensive pre-dialysis and develop hypotension after hemodialysis.[14] Contrary to that, in 10 to 15 % of patients excessive and rapid removal of water during HD leads to sympathetic overactivation resulting in post-dialysis HTN. In these individuals keeping pre-dialysis BP as a target may lead to serious consequences. It has been seen that pre-dialysis SBP <110 mm Hg or >150-159 mm Hg is associated with higher mortality.[15] BP readings of <140/90 pre-dialysis and <130/80 mmHg post-dialysis are endorsed by National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines as the target of HTN management.[16]

Removal of fluids during HD by ultrafiltration is an effective method of volume-dependent HTN. In 2009 DRIP trial was published, this experimental study has led to an important finding of lowering BP with the reduction in dry weight. In this study, 0.9 kg weight was lowered with ultrafiltration in 4 weeks resulting in a lowering of 6.9 mm Hg SBP and a lowering of 3.1 mm Hg in DBP. A recent study from China also reported lowering intradialytic BP with dry weight reduction.[17] Our study findings are in favor of previous research, SBP reduced to 8.7 mmHg and DBP reduced to 3.6 mmHg with 0.9 kg lowering of dry weight. Use of antihypertensive medication, salt restriction, and dry weight probing among HD patients improve quality of life and reduction in cardiovascular mortality.[18] However, using the Crit-Line Intradialytic Monitoring system for dry weight reduction and ultrafiltration may lead to the worst outcomes[19].

CONCLUSION

Dry weight reduction is a simple and well-tolerated method to control BP in hypertensive hemodialysis patients. Long-term control of BP will depend on continuous assessment and maintenance of dry weight.

Author's Contribution:

Concept & Design of Study:	Shahid Anwar
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Data Analysis:	Zahid Anwar, Mateen Akram
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REFERENCES

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol 2020;16(4):223–37.
2. Oparil S, Acelajado MC, Bakris GL, Berlowitz DR, Cífková R, Dominiczak AF, et al. Hypertension. Nat Rev Dis Primers 2018;4(1): 1–21.
3. Bakris G, Ali W, Parati G. ACC/AHA Versus ESC/ESH on Hypertension Guidelines: JACC Guideline Comparison. J Am Coll Cardiol 2019; 73(23):3018–26.
4. Shrout T, Rudy DW, Piascik MT. Hypertension update, JNC8 and beyond. Curr Opin Pharmacol 2017;33:41–6.
5. Ku E, Lee BJ, Wei J, Weir MR. Hypertension in CKD: Core Curriculum 2019. Am J Kidney Dis 2019; 74(1):120–31.
6. Cozzolino M, Mangano M, Stucchi A, Ciceri P, Conte F, Galassi A. Cardiovascular disease in dialysis patients. Nephrol Dial Transplant 2018;33(Suppl 3):28–34.
7. Udayaraj UP, Steenkamp R, Caskey FJ, Rogers C, Nitsch D, Ansell D, et al. Blood pressure and mortality risk on peritoneal dialysis. Am J Kidney Dis 2009;53(1):70–8.

8. Robinson BM, Tong L, Zhang J, Wolfe RA, Goodkin DA, Greenwood RN, et al. Blood pressure levels and mortality risk among hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study. Kidney Int 2012; 82(5):570–80.
9. Huang Y, Jia M, Li S, Lu G, Shen Y. The effects of pre-dialysis blood pressure targets on prognosis and health-related quality of life in haemodialysis patients. Int J Clin Pract 2021;75(7):e14177.
10. Gunal AI. How to determine 'dry weight'? Kidney Int Suppl 2013;3(4):377–9.
11. Agarwal R, Andersen MJ, Pratt JH. On the importance of pedal edema in hemodialysis patients. Clin J Am Soc Nephrol 2008;3(1):153–8.
12. Patel HP, Goldstein SL, Mahan JD, Smith B, Fried CB, Currier H, et al. A standard, noninvasive monitoring of hematocrit algorithm improves blood pressure control in pediatric hemodialysis patients. Clin J Am Soc Nephrol 2007;2(2):252–7.
13. Agarwal R, Alborzi P, Satyan S, Light RP. Dry-weight reduction in hypertensive hemodialysis patients (DRIP): a randomized, controlled trial. Hypertension 2009;53(3):500–7.
14. Inrig JK, Patel UD, Gillespie BS, Hasselblad V, Himmelfarb J, Reddan D, et al. Relationship between interdialytic weight gain and blood pressure among prevalent hemodialysis patients. Am J Kidney Dis 2007;50(1):108–18.
15. Ca S, Wc H, FT, D S, M R, S P, et al. Changing relationship of blood pressure with mortality over time among hemodialysis patients. J Am Soc Nephrol 2006;17(2):513–20.
16. K/DOQI Workgroup. K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. Am J Kidney Dis 2005;45(4 Suppl 3): S1-153.
17. Zhang Y, Zhang X, Li J, Liu X, Cui C, Yuan A, et al. Dry-weight reduction improves intradialytic hypertension only in patients with high predialytic blood pressure. Blood Press Monit 2019;24(4): 185-90.
18. Agarwal R, Flynn J, Pogue V, Rahman M, Reisin E, Weir MR. Assessment and management of hypertension in patients on dialysis. J Am Soc Nephrol 2014;25(8):1630–46.
19. Reddan DN, Szczech LA, Hasselblad V, Lowrie EG, Lindsay RM, Himmelfarb J, et al. Intradialytic blood volume monitoring in ambulatory hemodialysis patients: a randomized trial. J Am Soc Nephrol 2005;16(7):2162–9.

Frequency and Risk Factors of Hypoparathyroidism after Total Thyroidectomy

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ABSTRACT

Objective: To identify the frequency and risk factors of post-surgical hypoparathyroidism after total thyroidectomy.
Study Design: Randomized clinical study
Place and Duration of Study: This study was conducted at the Department of General Surgery, Jinnah Postgraduate Medical Centre Karachi from January 2020 to January 2021 for a period of one-year.
Materials and Methods: One hundred and sixty eight patients planned for total thyroidectomy were included. Frequency of hypoparathyroidism was noted at 6 months' follow-up. Risk factors of hypo-parathyroidism were determined by applying logistic regression.
Results: Transient hypoparathyroidism was seen more in carcinoma, thyroiditis and parathyroid disease patients, 44 (93.6%), 10 (21.2%) and 9 (19.1%) versus 94 (77.2%), 73 (60.2%) and 14 (11.57%, p-values 0.03, 0.048, and 0.001 respectively). Transient hypoparathyroidism seen more in lateral lymph node dissection patients including both central lymph node dissection and modified radical neck dissection, p= 0.002 and 0.03 respectively. Female gender was highly correlative with hypoparathyroidism with odds ratio OR= 2.246 (1.282–3.120, p=0.001), pathological condition of parathyroid gland OR= 1.620 (1.087–2.046, p=0.029) and extent of central lymph node dissection (bilateral) OR= 1.637 (0.081-2.231, p=0.018).
Conclusion: The independent risk factors for hypoparathyroidism after total thyroidectomy are; female gender, bilateral central lymph node dissection and extent of central lymph node dissection, pre-operative parathyroid gland pathology and malignancy.

Key Words: Hypothyroidism, Total thyroidectomy, Risk factors, Frequency

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INTRODUCTION

Hypoparathyroidism is one of the rare endocrine hormone deficiency diseases. The etiology of parathyroid deficiency due to genetic abnormality, consider as primary hypoparathyroidism, acquired or secondary hypoparathyroidism occurs due to ablate, extinguish, or functional impairment of parathyroid gland.[1] Secondary hypoparathyroidism is the most common character.

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Though, the diagnosis pattern is made by low serum calcium (Ca) levels, increased level of phosphorus, and abnormally low level of parathyroid hormone (PTH) in the blood circulation.[2] In the united states of America, the estimated prevalence rate of hypoparathyroidisms around 37 out of 100000 persons per year.[3]

Thyroidectomy surgery can be performed when thyroid cancer or goiter disease is identified. Post-surgery hypoparathyroidism is a regular complication resulting from total thyroidectomy. Hypoparathyroidism lasting less than 6 months (transient hypocalcemia) found in 25.4-83%, and 0.12–4.6% have lasting more than 6 months (permanent hypocalcemia).[4] Surgical injury, vascular compromise, and unintentional removal of the parathyroid gland are the primary causes of post thyroidectomy hypocalcemia. The type of surgical intervention and surgical expertise varies from center to center in secondary hypoparathyroidism. Worldwide, the prevalence rate of postsurgical hypoparathyroidism in 22 out of 100,000 patients.[5]

In post-operative period after total thyroidectomy, symptoms of hypocalcemia can be treated with calcium (Ca) supplementation abnormal level of hypocalcemia increases the patient's stay in the hospital, which is a financial burden to the hospital.

Though surgeons are concerned about hypocalcemia prediction and start treating early to avoid post-op complications as well as delay in discharge from the hospital. Patients pathological and clinical conditions and various dissection techniques might predict the hypocalcemia in post-surgical period.[5] Serum calcium values monitoring is a traditional method, even though absolute Ca values cannot sufficient to predict its development.[6] Some studies reported that intact parathyroid hormone (iPTH) values are important to predict the hypocalcemia post thyroidectomy but the drawback of iPTH is cost-effective and lacks convenience.[7-10]

Our present study goal was to identify the frequency and risk factors of post-surgical hypoparathyroidism after total thyroidectomy.

MATERIALS AND METHODS

In this randomized clinical study, we included 168 patients from the Department of General Surgery, Jinnah Postgraduate Medical Centre Karachi from 1st January 2020 to 1st January 2021. All patients planned for total thyroidectomy, male and female patients, age 18-60 years were included. All patients having renal disorders associated parathyroid disease, history of neck and thyroid surgery and who were unable to understand verbal and written commands were excluded.

After approval of the research proposal from the ethical review committee of the hospital, we included 168 patients who were scheduled for total thyroidectomy Written informed consent was taken from all patients before including in this study and thoroughly explaining to them the outcomes of the study. Data regarding the patient's age, gender, body mass index (BMI), hormonal status, Ca and phosphorus was recorded. During surgery, we noted the tumor size, operation time, need of lymph node dissection (LND), central neck dissection (CND), and modified radical neck dissection (MRND) and the underlying pathological condition was also included.

Data analysis was carried out by SPSS-23, quantitative variables were calculated as mean±SD, to compare these variables between the normal and transient hypo parathyroid group an independent sample t-test was applied. For qualitative variables frequency was calculated and Logistic regression was used to describe data and to explain the relationship between hypoparathyroidism and calcium dependency. Statistical P-value <0.05 indicated as significant.

RESULTS

There were 121 normal and 47 transient hypoparathyroidism patients identified. The mean age of the normal group was 52.2±3.25 years and 49.65±2.84 years in transient hypoparathyroidism (p-value < 0.0001). There were 145 (86.3%) females and 23 (13.7%) males. In comparison with males, transient hypothyroidism was significantly (p-value <0.0001) seen more in female patients, transient hypothyroidism was found in 4 (8.51%) males and 42 (89.3%) in female patients. Transient hypoparathyroidism was seen more in carcinoma, thyroiditis and Parathyroid disease patients, 44 (93.6%), 10 (21.2%) and 9 (19.1%) versus 94 (77.2%), 73 (60.2%) and 14 (11.57%, p-values 0.03, 0.048 and 0.001) respectively. Transient hypoparathyroidism seen more in LND patients; including both CND and MRND, p=0.002 and 0.03 respectively (Table 1).

All the parameters statistically analyzed following logistic regression to identify the correlation with hypocalcemia and based on that odds ratio was calculated. Female gender was highly correlative with hypoparathyroidism with odds ratio OR= 2.246 (1.282–3.120, p-value 0.001), pathological condition of parathyroid gland OR= 1.620 [1.087–2.046, p-value=0.029) and extent of CND (bilateral) OR=1.637 (0.081–2.231, p-value 0.018). These three parameters were statistically significant in evolving hypocalcemia in transient patients (Tables 2-3).

Table No.1: Basic characteristic and pathological condition developing in hypocalcemia (n=168)

Parameter	Normal (n=121)	Transient hypothyroidism (n=47)	P value
Age (years)	52.2±3.25	49.65±2.84	< 0.0001
BMI (kg/m^2)	24.76±4.94	25.32± 3.28	0.47
Gender			
Male	18(14.8%)	5 (10.6%)	<0.0001
Female	103(85.12 %)	42 (89.4%)	
Underlying pathology			
Carcinoma	94 (77.2%)	44 (93.6%)	0.03
Thyroiditis	73 (60.2%)	10 (21.2%)	0.048
Parathyroid present	14 (11.57%)	9 (19.1%)	0.001
LN dissection			
CND	95 (78.5%)	40 (85.1%)	0.002
MRND	9 (7.4%)	6 (12.76%)	0.03
Tumor size	3.6±4.4	4.2±5.4	0.45
Hormonal status			
Hypothyroid	13 (10.74%)	5 (10.63%)	0.39
Hyperthyroid	5 (4.1%)	3 (6.38%)	0.12
Calcium (mg/dl)	9.1±2.2	9.4±2.6	0.45
Phosphorous (mg/dl)	3.6±1.2	3.8±1.3	0.34
Surgery time	149.1±42.4	155.6±50.2	0.39

(min)			

Table No.2: Risk Factors of hypoparathyroidism based on Logistic regression

Variable	P-value	Odds ratio (CI)
Age	0.082	0.942 [0.910–1.021]
Gender(Female)	0.001	2.246 [1.282–3.120]
CND	0.631	1.143 [0.986–1.842]
MRND	0.054	1.162 [0.930–2.932]
Extent of CND (bilateral)	0.018	1.637 [0.081–2.231]
Operation time	0.312	0.983 [0.904–1.081]
Parathyroid gland in pathology	0.029	1.620 [1.087–2.046]

Table No.3: Hypoparathyroidism prevalence at different stages

Hypothyroidism stages	N=168	Prevalence	95% CI
At hospital discharge	72	42.8%	41.3 – 46.8
After 3 months follow-up	47	27.9%	24.2 – 29.8
After 6 months follow up	24	14.2%	12.8 – 15.8
Early recovery (transient)	39	23.2%	20.6 – 26.4

DISCUSSION

Hypoparathyroidism development in total thyroidectomy cannot be linked with a single risk factor, different studies have been conducted on various factors prone to hypoparathyroidism. Independent factors identifying is not an easy task. Different morbidities related to hypoparathyroidism are directly associated with hypocalcemia or hyperphosphatemia, indirectly deficient amount of Ca, and inactive vitamin D. When treatment is altered, due to hypercalcemia, neuromuscular excitability occurs then symptoms persist and hypercalciuria occurs when excessive Ca and vitamin D intake. Complications of hypoparathyroidism can cause ectopic calcification that happens in the gray-white matter and basal ganglia interface in the brain, decreased skeleton remodelling, and subcapsular cataracts are other complications related to hypoparathyroidism.

According to a study conducted post thyroidectomy approximately 33% of patients become hypoparathyroidism due to malignant diseases., 33% due to non-toxic goiter surgery, 10% due to primary hyperparathyroidism, and 25% due to toxic goiter.[11]

In the present study, there were 4 males and 42 females identified as transient hypoparathyroidism. The female gender shows a high frequency of hypoparathyroidism compares to males for postoperative hypocalcemia. Odds ratio = 2.246 [1.282–3.120] at 95% CI. Cho et al[2], the same kind of study conducted on 1030 patients, they described , the female gender is highest hazard ratio for hypoparathyroidism with (HR=2.285; 95% confidence interval = 1.391–3.751). Previous studies have the same concept on female gender prevalence. Because female diseases are linked to various hormones, indirectly interact with Ca or vitamin D. in this study due to limitation we did not include vitamin-D measurement.

In our study center, two-third of the surgical patients who underwent surgery due to carcinoma 94(77.2%).We found most of them proven for transient hypoparathyroidism. According to Page et al[4] and Shoback[14] study, transient hypoparathyroidism range between 6.9-46% after the thyroidectomy surgery. In LND surgery parathyroid dysfunction lasts long up to one year.[15] Surgery for graves' disease and anterior neck involving shown a high risk for postoperative hypoparathyroidism.

In post-operative patient, the calcium level found 9.4±2.6 mg/dl (transient), which almost mimic to the Ansari et al study[16], in their 170 patient total thyroidectomy study, they documented post-surgical calcium levels of <8.6mg/dl without symptoms and 2nd postoperative day it was 9.4 mg /dl with neuromuscular symptoms. after the total thyroidectomy, there was autoimmune hypoparathyroidism is most commonly occurs in an adult.[17]

Central lymph node dissection, MRND and extend of thyroidectomy are regular consider for the hypocalcemia. In our regression analysis malignancy, extend of bilateral CND was significantly associated with hypocalcemia. There was a controversial concept regarding the increase in surgical operating time directly caused by hypocalcemia. In our study, we have observed those who had longer surgical time, they developed hypocalcemia postoperatively. In our study, those patients having parathyroid pathology had a significantly high prevalence of hypocalcemia (Odds ratio = 1.620[1.087–2.046]).

The present study showed that a decrease in Ca and an increase in phosphorus levels were found on the first and the second postoperative days. Hypoparathyroidism prevalence has been gradually decreased at different stage periods (Table 3).

The limitation of this study was only a six months follow-up transient hypoparathyroidism study; we did not follow patients for a longer period. The study sample size was small, for fine results there is a need to conduct the study at a large center where a high volume of total thyroidectomy doing and document the long-term follow-up.

CONCLUSION

The independent risk factors for hypoparathyroidism after total thyroidectomy are; female gender, bilateral CND and extent of CND, pre-operative parathyroid gland pathology, and malignancy. Known of the above high-risk factor patient going to thyroidectomy surgery, care should be taken to preserve the parathyroid function during surgery. Special postoperative care has to be taken to prevent the risk of hypoparathyroidism by monitoring Ca and phosphorous levels.

Author's Contribution:

Concept & Design of Study:	Rizwan Khan
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REFERENCES

1. Bilezikian JP, Khan A, Potts Jr JT, Brandi ML, Clarke BL, Shoback D, et al. Hypoparathyroidism in the adult: Epidemiology, diagnosis, pathophysiology, target-organ involvement, treatment, and challenges for future research. J Bone Miner Res 2011; 26(10):2317-37.
2. Cho JN, Park WS, Min SY. Predictors and risk factors of hypoparathyroidism after total thyroidectomy. Int J Surg 2016;34:47-52.
3. Vadiveloo T, Donnan PT, Leese GP. A population-based study of the epidemiology of chronic hypoparathyroidism. J Bone Miner Res 2018; 33(3):478-85.
4. Page C, Strunski V. Parathyroid risk in total thyroidectomy for bilateral, benign, multinodular goitre: report of 351 surgical cases. J Laryngol Otol 2007;121(3):237.
5. Clarke BL, Leibson CL, Emerson JA, Ransom JE, Lagast H. Co-morbid medical conditions associated with prevelant hypoparathyroidism: a population-based study. London: Springer, 2012.
6. Underbjerg L, Sikjaer T, Mosekilde L, Rejnmark L. Cardiovascular and renal complications to postsurgical hypoparathyroidism: a Danish nationwide controlled historic follow-up study. J Bone Miner Res 2013;28(11):2277-85.
7. Lombardi CP, Raffaelli M, Princi P, Santini S, Boscherini M, De Crea C, et al. Early prediction of postthyroidectomy hypocalcemia by one single iPTH measurement. Surg 2004;136(6):1236-41.
8. Roh JL, Il Park C. Intraoperative parathyroid hormone assay for management of patients undergoing total thyroidectomy. Head & Neck: J Sci Specialties Head Neck 2006;28(11):990-7.
9. Zhou Y, Hartemink AE, Shi Z, Liang Z, Lu Y. Land use and climate change effects on soil organic carbon in North and Northeast China. Sci Total Environ 2019;647:1230-8.
10. Islam S, Al Maqbali T, Howe D, Campbell J. Hypocalcaemia following total thyroidectomy: early post-operative parathyroid hormone assay as a risk stratification and management tool. J Laryngol Otol 2014;128(3):274.
11. Clarke BL. Epidemiology and complications of hypoparathyroidism. Endocrinol Metab Clin North Am 2018;47(4):771-82.
12. Sands NB, Payne RJ, Côté V, Hier MP, Black MJ, Tamilia M. Female gender as a risk factor for transient post-thyroidectomy hypocalcemia. Otolaryngol Head Neck Surg 2011;145(4):561-4.
13. Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas J, Sancho J. Outcome of protracted hypoparathy-roidism after total thyroidectomy. Br J Surg 2010;97(11):1687-95.
14. Shoback D. Hypoparathyroidism. N Engl J Med 2008;359(4):391-403.
15. Falk SA, Birken EA, Baran DT. Temporary postthyroidectomy hypocalcemia. Arch Otolaryngol Head Neck Surg 1988;114(2):168-74.
16. Asari R, Passler C, Kaczirek K, Scheuba C, Niederle B. Hypoparathyroidism after total thyroidectomy: a prospective study. Arch Surg 2008;143(2):132-7.
17. Eisenbarth GS, Gottlieb PA. Autoimmune polyendocrine syndromes. N Engl J Med 2004;350(20):2068-79.
18. Lang BHH, Ng S-H, Lau LL, Cowling BJ, Wong KP, Wan KY. A systematic review and meta-analysis of prophylactic central neck dissection on short-term locoregional recurrence in papillary thyroid carcinoma after total thyroidectomy. Thyroid 2013;23(9):1087-98.
19. Baldassarre RL, Chang DC, Brumund KT, Bouvet M. Predictors of hypocalcemia after thyroidectomy: results from the nationwide inpatient sample. Int Scholarly Res Notices 2012.

Role of Hounsfield Unit in Predicting the Outcome of Treatment of Renal Calculi with Extracorporeal Shock Wave Lithotripsy (ESWL)

Zeeshan Shaukat[1], Abdul Rauf[2], Fazal-ur-Rehman Khan[2], Rana Atta ur Rehman[3] Hammad Shafi[4] and Muhammad Tayyab Naeem[2]

ABSTRACT

Objective: Objective of the study is to see the predictive accuracy of HU <934 in predicting the stone clearance in renal calculi with ESWL.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Urology Department at Shaikh Zayed Hospital, Lahore from October 2019 to April 2020.

Materials and Methods: This study was carried out in the Department of Urology. A written informed consent was taken from all the patients included in the study after discussing risk and benefit ratio. Patients with stone density of more than 934 HU were informed about the lower chances of stone removal. All the patients were diagnosed and followed on the same CT scan machine (Multi detector CT scanner; Light speed VCT; 140kv/3.91mm) and were given treatment on the same lithotripter (STORZ Medical MODULITH SLX; 4thGeneration). Post ESWL antibiotics were given for three days, with oral analgesics if required. Patients were followed after maximum 4 sessions of ESWL over a duration of three months.

Results: The mean age of patients was 44.54±9.16 years with minimum and maximum age as 18 and 60 years. There were 134(55.8%) male and 106(44.2%) female cases. There were 197(82.1%) cases who had stone clearance and 43(17.9%) cases did not have stone clearance. There were 187 cases who had density as <934 and had tone clearance and 35(81.4%) cases had density ≥934 and did not have stone clearance while there were 8(18.6%) false positive and 10(5.1%) cases had false negative. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of density <934 was 94.92%, 81.40%, 95.90%, 77.78% and 92.50% respectively.

Conclusion: HU can be used for multiple purposes as it not only identify tumor in the renal system also it could tell about the characteristics of urinary stone. CT scan is equally effective for the determination of the stone composition and also determination of the efficacy of ESWL for the stone clearance.

Key Words: ESWL, Renal Stone, Hounsfield Unit, Ureter, Bladder

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INTRODUCTION

Urinary stones are the third most common pathological disease of the urinary tract. The prevalence rate of stones vary from 1 to 20%.[1] In developed countries where hygienic life style is opted such as Sweden, Canada, USA stone prevalence is notably high (>10%).The incidence of stones in Pakistan is high.[2] Stone disease outpatient number is more than half of all of the patients in a urological setting. Dornier, a German aircraft corporation, was investigating the pitting on supersonic aircraft; they discovered that shock waves originating from passing debris in the atmosphere can crack something that is hard. First clinical application with the name of Human model-1, was used in 1980, with successful fragmentation of renal calculi.[3] Extracorporeal Shock Wave

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Lithotripsy(ESWL) is considered to be the first line of treatment for Renal stone and success rate is reported to be 80-90%.

Sir Godfrey Newbold Hounsfield was an English electrical Engineer, got Nobel Prize for physiology and medicine in 1979, for his part in developing CT scan. His name is immortalized in Hounsfield scale, a quantitative measure of radio-density used in evaluating CT scans.[6] Stone density in Hounsfield Units on Non-contrast computed tomography (NCT) found to be a prognostic feature for ESWL. El-Assmy et al used HU rate of stones to predict stone density and fragmentation success of ESWL and selected HU >1000 as their cut off value.[6] Ouzaid et al reported HU threshold of970 for the success of ESWL. Specifically stone free rate was96% and 38% with HU <970 and >970 respectively.[7] Foda et al demonstrated that stone dissolution unsuccessful if stone thickness was >934 HU.[8]

MATERIALS AND METHODS

Two hundred forty patients were taken using stone free clearance rate (successful ESWL) as 81.79% with sensitivity and specificity as 94.4% (assumed 90%) and 66.7% (assumed 90%) We used 95% confidence level and 10% margin of error. After approval from the hospital ethical committee, patients fulfilling the inclusion criteria were admitted on outpatient basis. A documented well-versed consent was taken from all the patients included in the study after discussing risk and benefit ratio. Patients with stone density of more than 934HU were informed about the lower chances of stone removal. All the patients were diagnosed and followed on the same CT scan machine (Multi-detector CT scanner; Light speed VCT; 140kv/3.91mm) and were given treatment on the same lithotripter (STORZ Medical MODULITH SLX; 4thGeneration). ESWL was performed by the Resident of Department of Urology. Post ESWL antibiotics were given for three days, with oral analgesics if required. Patients were followed after a maximum of 4 sessions of ESWL over a duration of three months. Stone clearance on HU and non- contrast was labeled (as per operational definition).

Results were generated with the use of Statistical Package for Social Sciences (SPSS) version 23.Mean± standard deviation was used for quantitative data. F(%) was used for qualitative data.2X2 contingency table was generated to determine diagnostic accuracy.

RESULTS

The mean age of patients was 44.54±9.16 years with minimum and maximum age as 18 and 60 years (Table 1).There were 134(55.8%) male and 106(44.2%) female cases(Table 2).The mean stone size was 13.76±3.78mm with minimum and maximum stone size as 6 and 20mm (Table 3).There were 85(35.4%) cases who had 6-12mm of stone size and 155(64.6%) cases had stone size as 12-20mm.There were 195(81.2%) cases who had <934 density and 45(18.8%) cases had density as ≥934. There were 187 cases who had density as <934 and had tone clearance and 35(81.4%) cases had density ≥934 and did not have stone clearance while there were 8(18.6%) false positive and 10(5.1%) cases had false negative. Diagnostic accuracy was estimated as 92.50%(Table 4). When diagnostic accuracy was estimated for age, it was observed that at age 18-40 year diagnostic accuracy was 97% and for age 41-60 years diagnostic accuracy was 90%. (Table5)Among male cases the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of density <934 was 94.69%, 76.19%, 95.54%, 72.73% and 91.79% respectively and among female cases the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of density <934 was 95.24%, 86.36%, 96.39%, 82.61% and 93.40% respectively. There was significant association with stone clearance and density with respect to gender, p<0.001 (Table 6).

Table No.1: Descriptive statistics of age (years) (n=240)

Age (years)	
Mean	44.54
S.D	9.16
Minimum	18.00
Maximum	60.00

Table No.2: Sex distribution of patients

Sex	No.	%
Male	134	55.83
Female	106	44.17

Table No.3: Descriptive statistics of stone size (mm)

Stone size (mm)	
Mean	13.76
S.D	3.78284
Minimum	6.00
Maximum	20.00

Among cases who had 6-12mm of stone size the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of density <934 was 100% for all and for patients who stone size 12-20mm the sensitivity, specificity, positive

predictive value, negative predictive value and diagnostic accuracy of density <934 was92.00%, 73.33%, 93.50%, 68.75% and 88.39% respectively. There was significant association with stone clearance and density with respect to stone size (Table 7).

Table No.4: Comparison of density in stone clearance

		Stone clearance		Total
		Yes	No	
Density	<934	187(94.9%)	8(18.6%)	195(81.2%)
	≥934	10(5.1%)	35(81.4%)	45(18.8%)
Total		197(100%)	43(100%)	240(100%)

P <0.001 (Highly Significant)

Sensitivity	94.92%
Specificity	81.40%
Positive Predictive Value	95.90%
Negative Predictive Value	77.78%
Diagnostic Accuracy	92.50%

Table No.5: Comparison of density in stone clearance with respect to age groups (years)

Age groups (years)	Density	Stone clearance		P value
		Yes	No	
18-40	<934	61(100%)	2(14.3%)	<0.001**
	≥ 934	0(0%)	12(85.7%)	
41-60	<934	126(92.6%)	6(20.7%)	<0.001**
	≥ 934	10(7.4%)	23(79.3%)	

**Highly Significant

	Age groups (years)	
	18-40	41-60
Sensitivity	100.0%	92.65%
Specificity	85.71%	79.31%
Positive predictive value	96.83%	95.45%
Negative predictive value	100.0%	69.70%
Diagnostic accuracy	97.33%	90.30%

Table No.6: Comparison of density in Stone clearance with respect to gender

Gender	Density	Stone clearance		P value
		Yes	No	
Male	<934	107(94.7%)	5(23.8%)	<0.001**
	≥ 934	6(5.3%)	16(76.2%)	
Female	<934	80(95.2%)	3(13.6%)	<0.001**
	≥ 934	4(4.8%)	19(86.4%)	

**Highly Significant

	Gender	
	Male	Female
Sensitivity	94.69%	95.24%
Specificity	76.19%	86.36%
Positive predictive value	95.54%	96.39%
Negative predictive value	72.73%	82.61%
Diagnostic accuracy	91.79%	93.40%

Table No.7: Comparison of density in Stone clearance with respect to Stone size (mm)

Stone size (mm)	Density	Stone clearance		P value
		Yes	No	
6-12	<934	72(100%)	0(0%)	<0.001**
	≥ 934	0(0%)	13(100%)	
12-20	<934	115(92%)	8(26.7%)	<0.001**
	≥ 934	10(8%)	22(73.3%)	

**Highly Significant

	Stone size (mm)	
	6-12	13-20
Sensitivity	100.0%	92.00%
Specificity	100.0%	73.33%
Positive predictive value	100.0%	93.50%
Negative predictive value	100.0%	68.75%
Diagnostic accuracy	100.0%	88.39%

DISCUSSION

The occurrence of nephrolithiasis is accounted for, expanding across the world. This expansion is considered notwithstanding to be factors, for example, sex, race and age. Weight, decreased liquid and calcium utilization, expanded oxalate, sodium and high protein intake are viewed as among the main natural risk factors.[9] Because of its recurrence, urolithiasis is of specific worry for health financial matters. An investigation of the 2009 French information, given from the national coding framework for in-clinic stays and surgico-drug management, utilizing the term 'urolithiasis' uncovered an all out expense of >168 million €.10.

Lotan et al, inspected treatment techniques for renal colic in the Emergency Room in 10 nations in Europe and the USA. The expenses went from $80 to $750 (American dollars).[11]The best extent of the all out expense was identified with radiological examinations in the Emergency Room (40.5%), trailed by treatment costs (19.7%). Consequently, booking the room for treatment of the illness is of most extreme significance in diminishing the resulting costs after confirmation of case of urolithiasis.[12]

The utility of the CT has further enhances in the last decade as it no more just a diagnostic tool. It has successfully helped the healthcare provider to attenuate the composition of the renal stone. This composition of renal stone helps to predict stone size as it was seen that a stone made up of uric acid has lower attenuation (200-400HU) while a stone with high composition of the oxalate and calcium has large attenuation (>1000HU). ESWL can only be successful if it comply to the stone composition and its hardness. NCCT can be helpful in

prior determination of the stone attenuation so that failure rate of the ESWL could be reduced.[13]

Recently, a study which is carried out with the objective of determination of success rate of ESWL by taking HU measurement in upper urinary calculi as standard. This study categorized cases in two group (A<750HU and B>750HU), It was further evaluated that there was no significant difference for size of stone in the both groups at the start of treatment viz. 1.51cm group A, group B was 1.59 (p 0.5346). After the ESWL, the stone was completely cleared in group A, but only 15% in other group got their stone cleared(p<0.001). HU measurement in the stone free group was (514.10 versus 970.36 HU, respectively, p<0.0001). Conclusively, it can be drawn that HU value ≥750HU is a good predictor for the bad outcome and low clearance of kidney stone.[14]

In another study on the same pattern which included 60 patients with stone size of ≤20mm size, subjected for ESWL. NCCT was used for the determination of stone density presented by HU measurement. After a two week follow up of the patients, X ray was done to assess the stone clearance. Chemical stone analysis kit was used later on to assess the removed stone composition. Furthermore, the study has calculated that 93% cases has complete stone cleanse97% success of ESWL was seen in stone size <15cm while lesser in larger stone size. They have concluded that for >1000HU stone a higher shock waves are required for the complete clearance. 29% cases has calcium oxalate stone while rest 20% has the other formalities of the stone. As the density of the stone is estimated it was observed that Calcium oxalate was most dense (902.73±425.23 HU) and uric acid stones lowest (364.00±115.17). ESWL wave have similar intensity of wave irrespective of the stone density. But it is important to mention that in order to give ESWL in any case with urinary stone, proper NCCT should be done to determine the actual intensity of wave to clear stone.[15]

In 2014, an examination was performed to assess the utility of the Hounsfield Unit (HU) values as a prescient factor of extracorporeal shock wave lithotripsy result for ureteral and renal stones. A review study was performed to quantify stone HU esteems in 260 patients who went through extracorporeal stun wave lithotripsy (ESWL) for singular renal and ureteral stones from July 2007 to January 2012. Stone volume, area, skin-to-stone distance, stone HU esteems, and stone synthesis were evaluated. Accomplishment of ESWL was characterized as: (1) being free stone or (2) remaining stone parts 815 HU (P <0.0265). HU of calcium oxalate and calcium phosphate stones were higher than those of uric corrosive stones, yet the investigation couldn't separate between calcium oxalate monohydrate and calcium oxalate dehydrate stones. Assessment of stone HU esteems before ESWL can anticipate treatment result and help in the improvement of treatment systems.[16]

In current study diagnostic accuracy was 92.50%, these results are supported by a study in 2013 which has calculated the same diagnostic accuracy. Hence, it is stated that if there is stone size and density is >934 HUs and SSD >99mm, case may be induced with higher waves of SW and so as of ET.

In 2012, another study was done on the same pattern.In this study the stone density was 970HU and clearance was considered at a size of stone of <4mm on CT. At this cute of the sensitive (100%) and specific (81%) point on the receiver-operating characteristic curve. 97% cases who have stone density <970HU were stone free after the session of the ESWL. So it could be stated that stone density calculation by using NCCT is necessary so that ESWL can be performed on the right patients. This can also help to take decision about the number of session required for a case with urinary stone to be stone free.

CONCLUSION

So, through findings of this study it is concluded that predictive accuracy of HU <934 is very good in predicting the stone clearance in renal calculi with ESWL. So, in future pre-procedural HU evaluation can help to select the best therapeutic option.

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REFERENCES

1. Trinchieri ACG. Epidemiology. Stone Disease. In: Segura JW, Pak CY, Preminger GM, Tolley D, editors. Health Publications: Paris; 2003.
2. Jan H, Akbar I, Kamran H, Khan J. Frequency of renal stone disease in patients with urinary tract infection. J Ayub Med Coll Abbottabad 2008; 20(1):60-2.
3. Jack WM, Tom FL.Smith and Tanagho's General Urology,Eighteenth ed.In:Marshall L. Stoller.Urinary stone disease.McGraw Hill Professional:New York; 2012.p.268.

4. Junuzovic D, Prstojevic JK, Hasanbegovic M, Lepara Z. Evaluation of extracorporeal shock wave lithotripsy (ESWL): Efficacy in treatment of urinary system stones. Acta Inform Medica 2014;22(5):309-14.
5. Park BH, Choi H, Kim JB, Chang YS. Analyzing the effect of distance from skin to stone by computed tomography scan on the extracorporeal shock wave lithotripsy stone-free rate of renal stones. Korean J Urol 2012;53(1):40-3.
6. el-Assmy A, Abou-el-Ghar ME, el-Nahas AR, Refaie HF, Sheir KZ. Multidetector computed tomography: role in determination of urinary stones composition and disintegration with extracorporeal shock wave lithotripsyan in vitro study. Urol 2011;77(2):286-90.
7. Ouzaid I, Al-qahtani S, Dominique S, Hupertan V, Fernandez P, Hermieu JF. A 970 Hounsfield units (HU) threshold of kidney stone density on non-contrast computed tomography (NCCT) improves patients' selection for extracorporeal shockwave lithotripsy (ESWL): evidence from a prospective study. BJU Int 2012;110:E438-E42
8. Foda K, Abdeldaeim H, Youssif M, Assem A. Calculating the number of shock waves, expulsion time and optimum stone parameters based on noncontrast computerized tomography characteristics. Urol 2013;82(5):1026-31.
9. Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. JAMA 2005;293(4):455-62.
10. Raynal G, Merlet B, Traxer O. In-hospital stays for urolithiasis: analysis of French national data. Prog Urol 2011;21(7):459-62.
11. Lotan Y, Cadeddu JA, Roerhborn CG, Pak CY, Pearle MS. Cost-effectiveness of medical management strategies for nephrolithiasis. Urol Res 2004;172(6 Part 1):2275-81.
12. Turkcuer I, Serinken M, Karcioglu O, Zencir M, Keysan MK. Hospital cost analysis of management of patients with renal colic in the emergency department. Urol Res 2010;38(1):29-33.
13. Naik D, Jain A, Hegde AA, Kumar AA. Determination of attenuation values of urinary calculi by non-contrast computed tomography and correlation with outcome of extracorporeal shock wave lithotripsy–A prospective study. Int J Anat Radiol Surg 2017.
14. Sharma K, Kumar PS, Gupta R, Mittal P. Correlation of stone attenuation measurement on non-contrast enhanced computed tomography with stone fragmentation using extracorporeal shock wave lithotripsy in upper urinary calculi. Int J Contemp Med Surg Radiol 2018;3(2).
15. Nasef AS, El-Feky MM, El-Shorbagy MS, ELZayat TM, Elguoshy FI. The relationship between renal stone radio-density, chemical composition, and fragmentation by extracorporeal shockwave lithotripsy. Al-Azhar Assiut Med J 2015;13(2):2.
16. Nakasato T, Morita J, Ogawa Y. Evaluation of Hounsfield Units as a predictive factor for the outcome of extracorporeal shock wave lithotripsy and stone composition. Urolithiasis 2015;43(1): 69-75.

Three Years' Experience of Senning Operation: Short Term Results

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ABSTRACT

Objective: To discuss three years' experience with Senning operation and its short-term results.
Study Design: retrospective study
Place and Duration of Study: This study was conducted at the Children's Hospital/ university of Child Health Sciences Lahore for a period of 03 years from January, 2019 to November, 2021.
Materials and Methods: Record of all the patients who underwent Senning operation was reviewed. Age, sex, weight, pre-operative diagnosis, concomitant procedures, cross clamp time, bypass time, ICU stay were noted for each patient.
Results: 41 patients had Senning operation for transposition of Great Arteries in last 3 years. 39 (95%) were successfully discharged home. Mean age was 4.2 years and mean weight was 10.5kg. Two patients died of low cardiac output.
Conclusion: In developing countries where diagnosis of TGA is delayed due to multiple reasons, the Senning operation can make significant difference in the life of these patients. In the expert hands, it is safe and reproducible operation with good outcome.

Key Words: Senning Operation, Short Term, Results

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INTRODUCTION

Dextro-transposition of the great arteries (D-TGA) is the second-most common cyanotic congenital heart defect, accounting for 5% of all congenital heart diseases. D-TGA has a prevalence of 20–30 per 100,000 live births. In D-TGA, the aorta arises from the right ventricle with the pulmonary artery arising from the left ventricle. That results in parallel circulation. [1] Ideal operation for TGA is arterial switch operation which is done at the age of less than 3 weeks.[2] In developing countries like ours, delayed presentation of TGA patients make arterial switch operation impossible. At delayed age, Senning operation is performed which is physiological repair of TGA.[3]

In 1958, Atrial switch operation, a radical surgical treatment for TGA, was introduced by Ake Senning. Since the advent of Senning operation, the prognosis of TGA patients improved dramatically.

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The Senning operation diverts deoxygenated blood coming from superior and inferior vena cavae toward mitral valve and into left ventricle. The pulmonary venous blood coming from pulmonary veins is diverted towards right ventricle thus making right ventricle a systemic ventricle. [4]

90 percent of TGA patients die within one year of life if left untreated.[5] with the help of Senning operation, most of these patients can reach adulthood .[6]

MATERIALS AND METHODS

Study design: It's a retrospective review of the patients who underwent Senning operation from January 2019 to November 2021 at children's hospital / university of child health sciences Lahore. Files of all the patients were reviewed. Age, sex, weight, pre-operative diagnosis, concomitant procedures, cross clamp time, bypass time, ICU stay were noted for each patient.

Operative procedure: After taking written informed consent from the parents, surgery was started with sternotomy. Thymus was removed in every patient. Aortic and bicaval cannulation with metal tipped canulae was made. DelNido cardioplegia was used in each operation. Right and left atria were then opened. After resecting the remanent of inter atrial septum, Coronary sinus was opened. 1st layer to isolate the pulmonary veins from mitral valve was made by inverting the left atrial appendage and sewing it to right margin of atrial septal defect thus making the floor of systemic venous baffle. 2nd layer was created with a autologous pericardial patch to divert superior and inferior vena caval blood towards mitral valve and left

ventricle. This completed systemic venous baffle. 3rd and last layer was completed by using the autologous pericardium to baffle the pulmonary venous blood toward tricuspid valve around the systemic venous baffle, as described by shumaker.[7]

Statistical Analysis: Data were analyzed by the Statistical Package for the Social Sciences. Results were shown in mean with range.

RESULTS

From January 2019 to November 2021, 41 patients underwent Senning operation. There were 31 male and 10 female patients. Mean age was 4.2 years. Mean weight was 10.5kg. 3 patients had concomitant left ventricular outflow tract obstruction, which was dealt with during the operation.

Table No.1: Demographic Details

N	41	
Gender	Male 31	Female 10
Age	Mean 4.2yaers	Range 1 to 14 years
Weight	Mean 10.5kg	Range 7 to 20kg
Previous Rashkind balloon atrial septostomy	22 pateints	
Mode of admission	Out patient clinic	

Table No.2: Surgical Details

Cross clamp time	71minutes (mean)	Range 35 to 135 minutes
Cardiopulmonary bypass time	93 minutes (mean)	Range 50 to 190 minutes
LVOT resection	3	
Accessory mitral tissue	1	
PDA ligation	2	

Table No.3: Short Term Results

Survival	39 (95%)	
Icu stay	52 hours	24 to 90 hours
Duration of mechanical ventilation	18 hours	4 to 60 hours
Duration of inotropic support	32 hours	24 to 90 hours
Arrhythmia	20%	
RV dysfunction	5%	
Re operation for bleeding	1	

Out of 41, 22 had Rashkind operation (balloon atrial sept ostomy) in their neonatal age. Rest of them had natural large atrial septal defect. All the patients had diagnosis of d TGA with intact ventricular septum. Average cross clamp time was 71 minutes and cardiopulmonary bypass time was 93 minutes. All the patients underwent intra operative echocardiogram to rule out baffle obstruction, left ventricular outflow obstruction and other lesions.

Average ICU stay was 52 hours. Average stay on ventilator was 18 hours. Inotropic support was required for the mean of 32 hours. 2 patients died because of low cardiac output. Rest of the patients were discharged home on mean of 5th post-operative day. See table 1, 2 and 3.

DISCUSSION

The modern cardiac surgery centers are now doing arterial switch operation in most of the cases of TGA. Because of antenatal diagnosis, early care of the patients, availability of rashkind atrial septostomy and prostaglandin, arterial switch has now become the standard of care [8-9]. In developing countries like Pakistan, the diagnosis of TGA is made late because of limited number of pediatric cardiac centers, birth in remote areas, home deliveries of the babies, reluctance to go to pediatricians and financial constraints. In cases of delayed diagnosis, when arterial switch operation is not possible, atrial switch is one option. Other option is two stage prep switch.

Senning performed the first 'complete' repair for TGA in 1957. In the Senning repair, a baffle is created within the atria that baffles the superior and inferior vena caval blood to the mitral valve and thus left ventricle and into pulmonary circulation for oxygenation and the oxygenated pulmonary venous blood to the tricuspid valve and thus right ventricle and into systemic circulation thus oxygenated blood in systemic circulation. This leads to anatomic left ventricle acting as the pulmonary pump and the anatomic right ventricle acting as the systemic pump.[10]

Because of technical difficulties, most of the surgeons at that time were reluctant to adopt this new technique. In 1970s Broom was the one who modified it and made it simpler. Due to surgical modifications, there was more acceptance for Senning operation.[11 -12]

More and more infants were getting Senning operation in 1980s. Long terms outcomes were available in 1990s. The long terms results were not very encouraging. The problems of baffle obstruction, arrhythmias, and right ventricle failure were apparent. This lead to fall in interest in Senning operation.[13-14]

With technical modifications, using in situ pericardium to make wider pulmonary venous baffle, [15] the problem of pulmonary venous baffle obstruction can be minimized. Results of the recent studies are encouraging. , Talwar et al[16] published there results of

Senning operation. In that study there was 100 percent survival and no one had venous baffle obstruction. All the patients were asymptomatic and were enjoying healthy life.

Results of our study are comparable to Helbing et al. [17], Wells and Blackstone [18] and Maluf [19]

With only 3 dedicated pediatric cardiac surgery centers in Pakistan and 45000 new congenital heart disease patients every year, Senning will have its important role to play in TGA patients at least for the next 10 years.

CONCLUSION

In developing countries where diagnosis of TGA is delayed due to multiple reasons, the Senning operation can make significant difference in the life of these patients . In the expert hands, it is safe and reproducible operation with good outcome.

Author's Contribution:

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REFERENCES

1. Haligheri G, Patel CR, Komarlu R. Prenatal Delineation of Coronary Anatomy in Dextro-Transposition of Great Arteries. J Cardiovasc Echogr 2021;31(3):171-174.
2. Salna M, Chai PJ, Kalfa D, et al. Outcomes of the Arterial Switch Operation in ≤2.5-kg Neonates. Semin Thorac Cardiovasc Surg 2019;31(3): 488-493.
3. Pathan IH, Bangash SK, Zaki SB, Sheikh AS. Senning Procedure for Transposition of the Great Arteries in a Patient with Situs Inversus Totalis and Dextrocardia. J Coll Physicians Surg Pak 2018;28(9):S154-S156.
4. Senning A. Surgical correction of Transposition of the great vessels Surg 1959;45(6):966-980.
5. Liebman J, Cullum L, Belloc NB. Natural history of Transposition of the great arteries. Anatomy and birth and death characteristics: Circulation 1969;40 (2):237-262.
6. Dos L, et al. Late outcome of Senning and Mustard procedures for correction of transposition of the great arteries: Heart 2005;91(5):652-656.
7. Shumaker HBI. A new operation for transposition of the great vessels. Surg 1961;50:773–777.
8. Jonas RA, Laussen P. Transposition of the great arteries. Comprehensive surgical management of congenital heart disease. Hodder Arnold Publication 2007.p.256–279
9. Mee LB. The arterial switch operation // In: Stark J, de Leval M, Tsang V, editors. Surgery for congenital heart defects. 3rd ed. Jonh wiley and sons Ltd 2006.p.471–487.
10. Hoque A, Moinuddin S. Patient with D transposition of Great Arteries Operated by Senning Procedure: A Case Report. J Curr Adv Med Res 2017;4(1):31-33.
11. Ilbawi MN, DeLeon SY, Backer CL. An alternative approach to the surgical management of physiologically corrected transposition with ventricular septal defect and pulmonary stenosis or atresia. J Thorac Cardiovasc Surg 1990;100: 410–415.
12. Karl TR, Weintraub RG, Brizard CP. Senning plus arterial switch operation for discordant (congenitally corrected) transposition, Ann Thorac Surg 1997;64:495–502
13. Jatene AD. Anatomic correction of transposition of the great arteries. J Thorac Cardiovasc Surg 1982; 83:20-26.
14. Gourav KP, Negi S, Damodaran S, Amburu V. Pulmonary venous baffle obstruction following senning procedure - Role of transesophageal echocardiography. Ann Card Anaesth 2020;23(2): 232-234.
15. Iyer KS. The modified Senning operation – surgical aspects. Ann Pediatr Card [serial online] 2021 [cited 2022 Jan 13];14:382-7. Available from: https://www.annalspc.com/text.asp?2021/14/3/382/324647
16. Talwar S, Kumar MV, Bhoje A, Choudhary SK, Kothari SS, Juneja R, et al. Atrial switch procedure in children more than 5 years of age: mid-term results Interact Cardiovasc Thorac Surg 2016;23(5):694-698.
17. Helbing WA, et al. Long term results of atrial correction for transposition of the great arteries. Comparison of Mustard and Senning operations J Thorac Cardiovasc Surg 1994;108(2):363-372.
18. Wells EJ, Blackstone E. Intermediate outcome after Mustard and Senning procedures: a study done by the congenital heart surgeons society Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2000;3(1):186-197.
19. Maluf MA. Senning operation for correction of the transposition of the great arteries, results, long-term outcome and quality of life. World J Cardiovasc Dis 2012;2:213-219.

Early Outcome of Repair of Supra Cardiac Total Anomalous Pulmonary Venous Connection

Repair of Supra Cardiac Total Anomalous

Faiz Rasool, Mohammad Asim Khan and Salman Ahmad Shah

ABSTRACT

Objective: To discuss the results of supra cardiac TAPVC repair in our setup.
Study Design: Retrospective study
Place and Duration of Study: This study was conducted at the Pediatric Cardiac Surgery Department of Children's Hospital Lahore for a period of 03 years from January, 2019 to November, 2021.
Materials and Methods: Age, weight, presenting symptoms, operative details (like cross clamp time and cardiopulmonary bypass time), peri operative mortality, ICU stay, and complications were studied.
Results: From January 2019 to November 2021, 48 patients under went repair of supra cardiac TAPVC at children's hospital Lahore. Mean age was 13months, mean weight was 7kg, 9 (18%) patients died preoperatively. Ascending vertical vein was ligated in all cases, but in 2 patients we had to re-open the ascending vertical vein
Conclusion: With only a few centers in Pakistan doing infant cardiac surgery, early outcome after repair of supra cardiac TAPVC is reasonable in our set up, but still far worse than that of modern centers. Good patient selection, and post-operative management of pulmonary hypertension can result in better outcome. In this series we did not present the follow up of the patients, which is drawback of this article.

Key Words: Early Outcome, Supra Cardiac Total Anomalous, Pulmonary Venous Connection

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INTRODUCTION

The diagnosis of total anomalous pulmonary venous connection (TAPVC) is made when all four pulmonary veins drain anomalously to the right atrium or to a tributary of the systemic veins. It accounts for 1% to 1.5% of all congenital heart diseases. Supra cardiac TAPVC is the most common type of TAPVC that accounts for 45 to 55% of all TAPVCs.

Total anomalous pulmonary venous connection (TAPVC) is a cyanotic congenital heart disease in which all the pulmonary veins don't enter left atrium but rather into right atrium directly or indirectly through a tributary. It has 4 types (supracardiac, 45%; infracardiac, 25%; cardiac, 25%; mixed, 5%). [1]To make life possible, right to left shunt through atrial septal defect is mandatory. Otherwise patient would die immediately after birth.[2]

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The most common type of TAPVC is supracardiac TAPVC[3-6]. The connection in supracardiac TAPVC is usually to a left vertical vein draining into the left brachiocephalic vein through which pulmonary venous blood reaches right atrium.

More than 75% of infants with supracardiac TAPVC would die in first year of life if left untreated [7]. Surgical repair should be performed at the time of diagnosis, as an elective procedure. Delaying the surgery leads to complication like right ventricle pressure and volume overload. In the last two decades, the improvement in surgical technique and improved postoperative management has resulted in improved survival of TAPVC patients,[8] however, repair does remain a challenge with early mortality reported in the literature in the range of <10% to 50%. TAPVC in biventricular anatomy, with no concomitant intra cardiac anomaly has the best prognosis .[9,10]

MATERIALS AND METHODS

It is a retrospective study. Files of all the patients who underwent supracardiac TAPVC repair at children's hospital Lahore in last 3 years (from January 2019 to November 2021) were reviewed. Age, weight, presenting symptoms, operative details (like cross clamp time and cardiopulmonary bypass time), peri operative mortality, ICU stay , and complications were studied.

Pre-operative evaluation: all the patients were admitted through OPD or emergency to cardiology/cardiac

surgery ward. They were discussed in the cath conference. Decisions to operate were made after reviewing the echo cardiogram. Where in doubt, CT Angio was performed to confirm the diagnosis.

Patients with single ventricle were excluded from the study.

Surgical Strategy: Patients were taken to the operation room after taking written informed consent. Standard anesthesia was given. Under sterile conditions, median sternotomy was made. Patients were put on cardiopulmonary bypass with standard aorto bicaval cannulation. In most of the patients temperature was cooled to 28 degree centigrade. 2 patients required deep hypothermic circulatory arrest.

After clamping the aorta and DelNido cardioplegia in the aortic root, TAPVC was repaired with standard bi atrial approach. In 5 patients, suture less technique[11] was used. The sutureless technique involves anastomosing the pericardium to the pulmonary venous confluence and no direct suturing of pulmonary venous chamber to left atrium. In 3 patients superior approach[12] was used to repair TAPVC.

Post operatively patients were shifted to cardiac surgical ICU on mechanical ventilation. Epinephrine and milrinone infusions were started intra operatively and were continued in post-operative period. No patient received nitric oxide.

Operative mortality was defined as death within 30 days of an operation or within the primary hospitalization[13].

RESULTS

48 patients under went repair of supra cardiac TAPVC at children's hospital Lahore.

Age: age of the patients ranged from 2 months to 12 years with the mean of 13 months.

Weight: weight ranged from 3.5 kg to 39 kg with the mean of 7 kg

Cyanosis, dyspnea, failure to thrive and multiple respiratory infections were the chief presenting complaints.

Table No.1: Demographical information

Total number	48
Age of the patients	Average 13 months (range 2 months – 12 years)
Weight of the patients	Average 7 kg (range 3.5kg -39kg)
Obstruction present	5 patients
Mechanical ventilation	Mean 38hours (6 hours – 15 days)
ICU stay	Mean 70 hours (1- 30 days)

Cardiopulmonary bypass time: 45 minutes to 241 minutes, with the mean of 81 minutes.

Cross clamp time: 22 minutes to 184 minutes, with the mean of 62 minutes.

Concomitant surgical procedures: atrial septal defect (ASD) was present in all cases that was closed intra operatively. One patient had ventricular septal defect (VSD) that was closed concomitantly.

Ascending vertical vein was ligated in all cases but in 2 cases we had to re-open the vertical vein by removing the ligature. These 2 patients developed low cardiac output after coming off cardiopulmonary bypass but the hemodynamics improved when ascending vertical vein was re-opened.

Table No.2: Surgical Details

CPB time	Mean 81 minutes (45-241 minutes)
Aortic cross clamp time	Mean 61 minutes (22-184 minutes)
Sutureless technique	5
Superior approach	2
Standard bi atrial approach	41
Ascending vertical vein left open	2
Concomitant VSD closure	1
Concomitant PDA ligation	20
Deep hypothermic circulatory arrest	2

Mortality: 9 patients died (18.75%) . 8 out of 9 patients were having weight <5 kg. 3 patients died due to low cardiac output. 5 died because of persistent pulmonary hypertension, prolonged mechanical ventilation and multi organ failure. 1 died of post-operative bleeding.

Mechanical Ventilation: Patients remained on mechanical ventilation for 6 hours to 15 days with the mean of 38 hours.

ICU stay: Average ICU stay was 70 hours (1 – 30 days)

Complications: Table 3 gives the details of all the complications that occurred in post-operative period.

Table No.3: Complications

Mortality	9 (18.75%)
Post-operative bleeding	1
Pulmonary hypertensive crisis	5
Low cardiac output	3
Pneumothorax	1
Renal failure requiring dialysis	2
Stroke	1

DISCUSSION

Congenital heart disease (CHD) is the most common birth defect.[14] It is estimated that every year 42000 babies are born with CHD in Pakistan.[15]

Children's hospital Lahore is one of the largest pediatric cardiac surgery centers in Pakistan. We are doing > 1000 pediatric cardiac surgeries per year. In last 3 years we did 48 supra cardiac TAPVC repairs.

Mortality: Although there are few series which had mortality of 3%[16, 17] other centers reported that repair of TAPVC carried a relatively high early mortality (10–20 %) [18,19]. Postoperative care for TAPVC is based mostly on preventing or treating pulmonary hypertension\ and maintaining systemic cardiac output. Ideally, the pulmonary artery pressure will decrease to less than half of the systemic pressure soon after separating from cardiopulmonary bypass. [20] nitric oxide and milrinine are used to treat pulmonary hypertension[21]

Keeping the Vertical Vein Open: Whether the vertical vein should be ligated repair is controversial. Our strategy is to keep the vertical vein open if there is low blood pressure after turning off cardiopulmonary bypass. Chowdhury et al recommended some adjustable devices to close the vertical vein[22]. Vertical vein ligation is advisable to close any left to right shunt, but in relatively small left ventricle, it can be left open [23]. Transcatheter vertical vein closure might render patients with high LAP suitable candidates for further hybrid approach.

Risk Factors: Weight less than 5 kg, pre-operative pulmonary venous obstruction, and persistent pulmonary hypertemsion were identified as risk factors.

CONCLUSION

With only a few centers in Pakistan doing infant cardiac surgery, early outcome after repair of supra cardiac TAPVC is reasonable in our set up, but still far worse than that of modern centers. Good patient selection, and post-operative management of pulmonary hypertension can result in better outcome. In this series we did not present the follow up of the patients, which is drawback of this article.

Author's Contribution:

Concept & Design of Study:	Faiz Rasool
Drafting:	Mohammad Asim Khan Salman Ahmad Shah
Data Analysis:	Salman Ahmad Shah, Mohammad Asim Khan
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REFERENCES

1. Kanter KR. Surgical repair of total anomalous pulmonary venous connection. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2006: 40-4.
2. Stein P. Total anomalous pulmonary venous connection. AORN J 2007;85:509–20.
3. Shi G, Zhu Z, Chen J, Ou Y, Hong H, Nie Z, et al. Total anomalous pulmonary venous connection: the current management strategies in a pediatric cohort of 768 patients. Circulation 2017;135(1): 48–58.
4. Harada T, Nakano T, Oda S, Kado H. Surgical results of total anomalous pulmonary venous connection repair in 256 patients. Interact Cardiovasc Thorac Surg 2018.
5. Chowdhury UK, Airan B, Malhotra A, Bisoi AK, Saxena A, Kothari SS, et al. Mixed total anomalous pulmonary venous connection: anatomic variations, surgical approach, techniques, and results. J Thorac Cardiovasc Surg 2008;135(1):106–16.
6. Sakamoto T, Nagashima M, Umezu K, Houki R, Ikarashi J, Katagiri J, et al. Long-term outcomes of total correction for isolated total anomalous pulmonary venous connection: lessons from 50-years' experience. Interact Cardiovasc Thorac Surg 2018;27(1):20–6.
7. Burroughs JT, Edwards JE. Total anomalous pulmonary venous connection. Am Heart J 1960; 59:913-31.
8. Zhao K, Wang H, Wang Z, Zhu H, Fang M, Zhu X, Zhang N, Song H. Early and intermediate-term results of surgical correction in 122 patients with total anomalous pulmonary venous connection and biventricular physiology. J Cardiothorac Surg 2015;10:172.
9. Hancock Friesen CL, Zurakowski D, Thiagarajan RR, Forbess JM, del Nido PJ, Mayer JE, et al. Total anomalous pulmonary venous connection: an analysis of current management strategies in a single institution. Ann Thorac Surg 2005;79: 596-606.
10. Morales DL, Braud BE, Booth JH, Graves DE, Heinle JS, McKenzie ED, et al. Heterotaxy patients with total anomalous pulmonary venous return: improving surgical results. Ann Thorac Surg 2006; 82:1621-7.
11. Menon S, Mathew T, Karunakaran J, Dharan BS. Modified closed chamber sutureless technique for anomalous pulmonary venous connection. Ann Pediatr Cardiol 2017;10(1):58-60.
12. Okonta KE, Agarwal V, Abubakar U. Superior repair: A useful approach for some anatomic variants of total anomalous pulmonary venous connection. Afr J Paediatr Surg 2013;10(2):131-4.
13. Van Praagh R, Harken AH, Delisle G, Ando M, Gross RE. Total anomalous pulmonary venous drainage to the coronary sinus. A revised procedure

for its correction. J Thorac Cardiovasc Surg 1972; 64:132-5.
14. Pate N, Jawed S, Nigar N, Junaid F, Wadood AA, Abdullah F. Frequency and pattern of congenital heart defects in a tertiary care cardiac hospital of Karachi. Pak J Med Sci 2016,32:79-84.
15. Christianson A HC, Modell B. March of Dimes. Global report on birth defect. The hidden toll of dying and disabled children. New York; 2006.
16. Jang SI, Song JY, Kim SJ, Choi EY, Shim WS, Lee C, Lim HG, Lee CH. The recent surgical result of total anomalous pulmonary venous return. Korean Circ J 2010;40(1):31-5.
17. Liufu R, Shi G, Zhu F, Guan Y, Lu Z, Chen W, Zhu Z, Chen H. Superior Approach for Supracardiac Total Anomalous Pulmonary Venous Connection. Ann Thorac Surg 2018;105(5): 1429-1435.
18. Michielon G, Di Donato RM, Pasquini L, Giannico S, Brancaccio G, Mazzera E, et al. Total anomalous pulmonary venousconnection: long-term appraisal with evolving technical solutions. Eur J Cardiothorac Surg 2002;22:184–91.
19. Kirshbom PM, Myung RJ, Gaynor JW, Ittenbach RF, Paridon SM, DeCampli WM, et al. Preoperative pulmonary venous obstruction affects long-term outcome for survivors of total anomalous pulmonary venous connection repair. Ann Thorac Surg 2002;74:1616–20.
20. Kaiser L, Kron I, Spray T. Mastery of cardiothoracic surgery. Lippincott Williams & Wilkins, Philadelphia; 2007.
21. Franco K, Thourani V. Cardiothoracic surgery review, 1 Har/Psc edn. Lippincott Williams & Wilkins, Philadelphi; 2011.
22. Chowdhury UK, Subramaniam KG, Joshi K, Varshney S, Kumar G, Singh R, et al. Rechanneling of total anomalous pulmonay venous connection with or without vertical vein ligation: results and guidelines for candidate selection. J Thorac Cardiovasc Surg 2007;133:1286–1294.
23. Cope JT, Banks D, McDaniel NL, Shockey KS, Nolan SP, Kron IL. Is vertical vein ligation necessary in repair of total anomalous pulmonary venous connection? Ann Thorac Surg 1997;64: 23–8.

Evaluate the Assessment of Correlation of Uterine Fibroids with Adverse Pregnancy Outcomes: A Prospective Study

Nadia Taj, Sadia Zafar, Afshan Mehvish, Munazza Munir, Abeera Ashfaq and Maria Siddiqui

ABSTRACT

Objective: To evaluate the assessment of pregnancy outcomes among women with uterine fibroids.
Study Design: A prospective observational study
Place and Duration of Study: This study was conducted at the Gynecology department of Nishtar Medical University & Hospital Multan from April 2020 to April 2021 for a period of one-year.
Materials and Methods: The study included pregnant women with uterine fibroids. Each woman underwent a detailed clinical check-up and routine laboratory testing at each hospital visit. Moreover, fetal health was also assessed regularly through ultrasonography. Parameters including maternal age, size and number of fibroids, obstetric complications, parity, and delivery mode were observed.
Results: A total of 60 pregnant women with uterine fibroids were included in the study. The participants had a mean age of 31.56±4.3 years. Primigravida was reported in 25.03% of women while multigravida in 74.97%. 75% of women had spontaneous conception and 25% utilized different treatments for conception. Only 23.2% of women delivered through normal route and C-section was performed in 76.98% of women. 8% of women had a miscarriage, 12% had a postpartum hemorrhage, and only 3% had placenta previa associated antepartum bleeding. 15.4% had premature delivery while 75.2% completed the normal gestation period. Multiple fibroids and intramural location posed a high risk of C-section than single fibroids or sub-serosal fibroids.
Conclusion: Uterine fibroids can cause severe pregnancy outcomes. Therefore, it is advised to evaluate the complications regularly during the antenatal period and manage them effectively to avoid adverse obstetric outcomes.
Key Words: Uterine fibroids, obstetric outcomes, pregnancy

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INTRODUCTION

Uterine fibroids are one of the most prevalent benign tumors reported in the female reproductive system[1]. However, the burden of the disease remains underestimated as the majority of fibroids are asymptomatic [2]. The data suggest that 1% to 10.7% of pregnant women report the presence of uterine fibroids [3,4] while the incidence rate is constantly on the rise due to delayed childbearing age [5].

Despite the acknowledged increase in prevalence, the association between uterine fibroids and worse obstetric outcomes couldn't be established.

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The already established has reported the relation of uterine fibroids with many pregnancy complications including puerperal infection, dysfunctional labor, premature membrane rupture, preterm birth, fetal malpresentation, antepartum hemorrhage, placental abruption, spontaneous abortion, postpartum hemorrhage, and cesarean sections[6,7,8]. The study, therefore, aimed to assess the pregnancy outcomes among women with uterine fibroids.

MATERIALS AND METHODS

A prospective observational study was conducted at the gynecology department of Nishtar Medical University & Hospital Multan for 1 year from 19th April 2020 to 19th April 2021. Women regularly visited the gynecology department and had ultrasonography (USG) confirmed uterine fibroids were consecutively enrolled in the study. Keeping 95% confidence interval and 80% power of the study, 60 patients were included in the study. The women with previous caesarian section,

prior surgery, chronic diseases such as hypertension and diabetes, and those with uterine malformation were excluded from the study. All participants were informed of the study's objectives and consent was obtained. Ethical approval was sought from the ethical committee of the hospital.

Patients' data registry was assessed to obtain their history whereas data acquired from clinical examination and diagnostic investigations were recorded side-by-side. Fibroids were diagnosed in the scan of 1st-trimester. Ultrasonography was performed at successive visits to assess fetal health and variation in size of fibroid or any related complication. The following variables were analyzed during the study: maternal age, parity, gravidity, gestational age, size and number of fibroids, and obstetric complications.

SPSS (version 18.0) was used for statistical analysis. Quantitative data were presented as mean along with standard deviation whereas qualitative as frequency and percentages. Chi-square and student's t-test were used for comparison of sub-classes of quantitative and qualitative study data, respectively. P-value<0.05 was considered statistically significant.

RESULTS

A total of 60 pregnant women with uterine fibroids were enrolled in the study. The enrolled women had a mean age of 31.56±4.3. 35 (58.3%) women were reported to have single fibroids while multiple fibroids were found in 25 (41.6%) women. 49 (81.6%) women had intramural fibroids while sub serosal were found in 19 (31.6%) women. 15 (25.03%) women were Primigravida and 45 (74.97%) were multigravid. 45 (75%) women reported having spontaneous conception while the remaining 15 patients acquired medical assistance for fertility (Table 1).

Table (2) presents the observed obstetrics outcomes among evaluated women. 6 (10%) had threatened abortion, 5 (8%) had a miscarriage, 9(15.4%) had a preterm abortion, 2 (3%) had an antepartum hemorrhage. The majority of women had full-term delivery (92%) whereas 46 (76.98%) had to undergo a caesarian section. Post-partum hemorrhage was reported in 7 (12%) women.

Table (3) shows the association between obstetric outcomes and fibroid number. The route of delivery was significantly different between the women with a single fibroid compared to the one with multiple fibroids. 8 (13.3%) women with single fibroids had a vaginal route of delivery while only 1 (1.6%) with multiple fibroids (p=0.02). Whereas, 27 out of 35 patients with single fibroids had cesarian section compared to those with 24 out of 25 multiple fibroids patients (p=0.01). There was no significant difference between the two sub-classes in terms of other complications (Table 3).

Table IV shows the association between obstetric outcomes and fibroid location. Similar to the association with fibroid number, fibroid location significantly affects the route of delivery.

Table No.1: Clinical characteristics of patients

Variables	Data
Age, years (mean ± SD)	31.56±4.3
Gravidity (N, %)	
Primigravida	15 (25.03%)
Multigravida	45 (74.97%)
Spontaneous conception	45(75%)
Assisted conception	15 (25%)

Table No.2: Obstetric outcomes among patients

Outcomes	Data (N, %)
Threatened abortion	6 (10%)
Miscarriage	5 (8%)
Preterm delivery	9(15.4%)
Antepartum hemorrhage	2 (3%)
Abruption	3 (4.2)
Placenta Previa	2 (3%)
Full-term delivery	51 (92%)
Vaginal delivery	14 (23.2%)
Cesarean delivery	46 (76.98%)
Postpartum hemorrhage	7 (12%)

Table No.3: Association between obstetric outcomes and fibroid number

Variables	Single fibroid (n=35)	Multiple fibroids (n=25)	p-value
Placental distortion	2(3.33 %)	4 (6.66%)	.73
Placenta previa	-	2 (3.33%)	.23
Preterm delivery	4 (6.66%)	5 (8.33%)	.51
Vaginal delivery	8 (13.3%)	1 (1.66%)	.02
Cesarean delivery	27 (77.1%)	24 (40%)	.01
Postpartum hemorrhage	3 (5%)	4 (6.66%)	.8

Table No.4: Association between obstetric outcomes and fibroid location

Variables	Subserosal fibroid(s) (n=19)	Intramural fibroid (s) (n=49)	p-value
Placental distortion	2 (3.33%)	3 (5%)	.89
Placenta previa	-	2 (3.33%)	.3
Preterm delivery	3 (5%)	6 (10%)	.52
Vaginal delivery	11 (18.3%)	3 (5%)	.004

Cesarean delivery	8 (13.3%)	46 (76.6%)	.001
Postpartum hemorrhage	3 (5%)	4 (6.6%)	.9

Majority of women with sub serosal fibroids (18.3%) delivered through the vaginal route compared to women with intramural fibroids (5%) (p=0.04%). Consequently, the majority of the later class went through the cesarian section (76.6%). Whereas, no significant difference was found in terms of the incidence of other complications between the two groups (Table 4).

DISCUSSION

The study aimed to evaluate the obstetric outcomes of uterine fibroids. The enrolled women had a mean age of 31.56±4.3, similar to the ones reported in earlier studies such as by Egbe et al[9] and Saleh et al[2]. This indicates the higher association of uterine fibroids with advancing gestation age. Similarly, increased gravidity and incidence of fibroids are found to be correlated in our study which is supported by findings of Sheiner et al[10] and Saleh et al[2]. Our study reported that 12% of women had postpartum hemorrhage (PPH). A closely similar incidence of postpartum hemorrhage (PPH) in women with uterine fibroids was observed by Parazzini et al[11] and Febo et al[12]. However, few studies have reported contradictory results and found no relation between uterine fibroids and risk of postpartum hemorrhage such as the study by Coronado et al[13].

In our study, it was found out that uterine fibroids impede the normal mode of delivery (vaginal route). In compliance with this, Qidwai et al[7] and Stouts et al[6] also reported a higher CS rate in pregnant women with uterine fibroids. However, contradictory results, where no association between fibroids and CS was found, are also established in the literature[14].

We also established an association between several fibroids and obstetric complications. It was found that several fibroids increase the risk of caesarian delivery. Similar results were found by Qidwai et al[7]; however, despite the increased incidence of CS in women with more fibroids, the enhanced risk was not statistically significant. However, Lam et al[15] and Ciavattini et al[16] have observed a significant association between CS and preterm delivery. CS delivery was also significantly associated with intramural fibroid location as found by Zhao et al [21]. However, contrary results were found. The study was found to be limited in terms of study size, limited postpartum follow-up, and lack of control group comparison.

CONCLUSION

Uterine fibroids can cause severe pregnancy outcomes. Therefore, it is advised to evaluate the complications regularly during the antenatal period and manage them effectively to avoid adverse obstetric outcomes.

Author's Contribution:

Concept & Design of Study:	Nadia Taj
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Data Analysis:	Munazza Munir, Abeera Ashfaq, Maria Siddiqui
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REFERENCES

1. Harmon QE. The burden of uterine fibroids: a search for primary and secondary prevention. Fertil Steril 2019;111(1):50-1.
2. Saleh HS, Mowafy HE, Hameid AA, Sherif HE, Mahfouz EM. Does uterine fibroid adversely affect the obstetric outcome of pregnancy? BioMed Res Int 2018;2018:8367068.
3. Ouyang D, Norwitz ER. Pregnancy in women with uterine leiomyomas (fibroids). Up to Date 2017.
4. Sundermann AC, Edwards DR, Bray MJ, Jones SH, Latham SM, Hartmann KE. Leiomyomasin Pregnancy and Spontaneous Abortion: A Systematic Review and Meta-analysis. Obstet Gynecol 2017;130(5):1065.
5. Drayer SM, Catherino WH. Prevalence, morbidity, and current medical management of uterine leiomyomas. Int J Gynecol Obstet 2015;131(2):117-22.
6. Stout MJ, Odibo AO, Graseck AS, Macones GA, Crane JP, Cahill AG. Leiomyomas at routine second-trimester ultrasound examination and adverse obstetric outcomes. Obstet Gynecol 2010;116(5):1056-63.
7. Qidwai GI, Caughey AB, Jacoby AF. Obstetric outcomes in women with sonographically identified uterine leiomyomata. Obstet Gynecol 2006;107(2):376-82.
8. Ezzedine DNE. Are Women With Uterine Fibroids at Increased Risk for Adverse Pregnancy Outcome? Clin Obstet Gynecol 2016;59(1): 119–27.
9. Egbe TO, Badjang TG, Tchounzou R, Egbe EN. Uterine fibroids in pregnancy: prevalence, clinical presentation, associated factors and outcomes at the Limbe and Buea Regional Hospitals, Cameroon: a cross-sectional study. BMC Res Notes 2018;11 (1): 889.
10. Sheiner E, Bashiri A, Levy A, Hershkovitz R, Katz M, Mazor M. Obstetric characteristics and

perinatal outcome of pregnancies with uterine leiomyomas. J Reprod Med 2004; 49 (3):182–6.

11. Parazzini F, Tozzi L, Bianchi S. Pregnancy outcome and uterine fibroids. Best Pract Res Clin Obstet Gynaecol 2016;34:74–84.
12. Febo G, Tessarolo M, Leo L, Arduino S, Wierdis T, Lanza L. Surgical management of leiomyomata in pregnancy. Clin Exp Obstet Gynecol 1997; 24(2):76–8.
13. Coronado GD, Marshall LM, Schwartz SM. Complications in pregnancy, labor, and delivery with uterine leiomyomas: a population-based study. Obstet Gynecol 2000; 95(5):764–9.
14. Noor S, Fawwad A, Sultana R, Bashir R, Quratul a, Jalil H, et al. Pregnancy with fibroids and its and its obstetric complication. J Ayub Med Coll Abbottabad 2009; 21(4):37–40.
15. Lam SJ, Best S, Kumar S. The impact of fibroid characteristics on pregnancy outcome. Am J Obstet Gynecol 2014; 211(4): 395.
16. Zhao R, Wang X, Zou L, Li G, Chen Y, Li C, eCiavattini A, Clemente N, Delli Carpini G, Di Giuseppe J, Giannubilo SR, Tranquilli AL. Number and size of uterine fibroids and obstetric outcomes. J Matern Fetal Neonatal Med 2015;28(4): 484–8.
17. Zhao, et al. Adverse obstetric outcomes in pregnant women with uterine fibroids in China: A multicenter survey involving 112,403 deliveries. PLoS ONE 2017; 12(11): e0187821.

A Diagnostic Study of 150 Cases of Gliomas Based on Immunohistochemical Profile

Nadeem Reyaz[1], Muhammad Ejaz Butt[3], Muhammad Bahadur Baloch[4], Moniba Zafar[1], Ali Afzal[1] and Naveed Lodhi[2]

ABSTRACT

Objective: To present an overview of the relative frequency of gliomas in the light of expression of biomarkers relevant to the tumor grade.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Department of Pathology, Gulab Devi Teaching Hospital Lahore from February 2018 to December 2020.

Materials and Methods: 150 glioma samples were obtained from the pathology department of Lahore General Hospital by convenience sampling techniqueto be evaluated histologically for grading of the types of a tumor subsequent to hematoxylin & eosin staining. For tumor markers, immunohistochemistry was performed to assess the levels of glial fibrillary acidic protein (GFAP), nestin, and vimentin. The basic and immunostained sections were then assessed by three pathologists deprived of the pathological and clinical data of patients` parameters in a blinded manner. The outcomes of staining were semi-quantitatively scored. The data of incidence rates by histologic type, age, and gender was collected.

Results: The mean age of patients with gliomas was 21.71±16.9. The benign astrocytoma was the most frequent glioma making 52% of all the tumors. The males were on an average 59.34% and the females were 40.66%. The expression level of GFAP staining was considerably lower in high-grade glioma tissues as compared to low-grade glioma tissues. The majority of gliomas revealed moderation expression of nestin around 53.4%. The mean score of vimentin was 8.3 indicating its high expression for the grade IV gliomas.

Conclusion: The expression of biomarkers for gliomas correlated with the grade of the tumor. The mean age revealed gliomas occurring in the younger age group without a major difference in gender distribution.

Key Words: Gliomas, Astrocytoma, Immunohistochemistry, Biomarkers, Glial fibrillary acidic protein, Nestin, Vimentin

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INTRODUCTION

Glioma exist as the predominant type of adult chief glial tumors of the central nervous system. Despite being <1% of the brain tumors, glioma have an association with high mortality within first twenty-four months following the diagnosis.[1,2,3] The poor prognosis associated with glioma is attributed to their high capability of unregulated mitosis and metastasis.

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Their origin is assumed from the supporting glial constituents of CNS i.e. astrocytes, oligodendrocytes, and ependymal cells.[2] Based on the origin, the glioma is classified based on the World Health Organization 2007 recommendations into numerous morphological subtypes corresponding to the overall appearance of the tissue of origin: oligodendroglioma, astrocytoma ependymoma, and mixed oligoastrocytoma.[4]

A histopathological evaluation has been traditionally utilized for determining the types, subtypes, and tumor grade of gliomas. WHO categorized them into I, II, III, and IV grading criterion based on the level of malignant changes in the perikaryon.[5] The grading of diffuse glioma relies on certain relatively subjective features, for example, the existence or absence of atypical nuclei, endothelial proliferation, high cellular content, mitosis, and necrosis.[1]Despite the criterion, there is subjective variability of astroglial neoplasia which affects the

assessment of the survival rates within grades significantly. The histopathologists, therefore, investigated the markers of the related subpopulation of cells. Recognition of such analogous markers would greatly benefit diagnostics.[6]

Biomarkers like GFAP and vimentin are intermediate filament (IF) of class III category whereas nestin is a class IV IF with significance in assessing the prognosis of patients with gliomas.[7,8]GFAP was isolated and specified for the first time by Eng and Bignami in 1969 as an intermediate filament protein III constituent of glial cells` cytoskeleton. It is being applied as a biomarker ever since.[6]Nestin was initially designated as a progenitor neural stem cell marker and it has been revealed to completely down-regulate to the extent of extinction during differentiation into mature cells.[7] Vimentin has attained more consideration as the biomarker for the epithelial transition into mesenchymal cells responsible for the attainment of the characteristic tumor based invasiveness and mobility.[8,9,10]

The expression of GFAP, vimentin, and nestin in gliomas differs substantially in terms of their metastatic activity.[6] The rationale of our study was to associate the expression of these biomarkers through immuno-staining in gliomas with histopathological diagnosis and correlate our findings with the age and gender distribution along with the relative frequency of the tumors. Knowledge of variation in the expression of these biomarkers may highlight their regional significance for clinical utilization as markers for diagnosis.

MATERIALS AND METHODS

Hundred and fifty cases of space-occupying lesions previously diagnosed as primary neurological tumors at Pathology Department, General Hospital, Lahore were selected by convenience sampling technique from February 2018 to December 2020. Endorsement of the study was obtained from the institutional ethical committee. Tumor masses were evaluated histologically for glioma diagnosis and grading of their types following hematoxylin & eosin staining. All tumors other than gliomas were excluded from the study.

Deparaffinized slides stained with hematoxylin-eosin for tumor grade assessment and were utilized for immunohistochemistry.

A mouse monoclonal antibody for cytoskeletal filaments and interstitial proteins against GFAP. The cellularity and cytomorphological features were evaluated located in the neoplastic representative area under magnification of X40.[1,3] For nestin immunohistochemistry (IHC), an avidin-biotin-peroxidase complex method was utilized with 1:150 dilution from the monoclonal antibody of mouse against human nestin and mouse VIM Elisa kit for Vimentin IHC.[7]

The patient data was gathered from hospital record for analysis of frequency of age, gender and tumor distribution. The basic and immunostained sections were assessed by three pathologists deprived of the clinical and pathological data of patients` parameters in a blinded manner. The results of staining were semi-quantitatively scored based on Bei, Huang scoring.[1]

The immunoreactive score (IRS) for GFAP, nestin, and vimentin was determined by the estimation of the percentage of the immunoreactive cells along with an estimate of the staining intensity. The percentage of cells was scored as follows: 1 (0-49 % tumor cells stained), 2 (50–74 % tumor cells stained), and 3 (75–100 % tumor cells stained). The intensity of staining was coded as follows: 0= negative staining, 1 = staining weak, 2 = staining moderate, and 3 staining strong. Then the two subsequent scores were multiplied and the mean was classified into two groups: low expression (0–4.5) and high expression (4.5–9).[1]

Statistical Analysis: Data was evaluated through SPSS version 21. Chi-square test was applied to correlate the GFAP score with the grades of the tumors with the biomarkers and to trace the relation between grading of the tumor to age and gender distribution. The p-value of > 0.05 was considered statistically significant.

RESULTS

In a total of 150 cases of space-occupying lesions intra-cranially, 89 cases included males and 61 were females, with a male / female ratio of 1.46:1 as depicted in Table-1. Of all the 150 cases, benignglial tumors had relatively high frequency than tumors with malignant characteristics with p-value = 0.12 (Figure -1). The benign astrocytoma was the most frequent glioma making 52% of all the tumors; 23 cases were found underneath the age of twenty, while most of the cases (52) were found in the third decade. The mean age of patients with glioma was 21.71±16.9. A moderate number of tumors were found in the fourth and fifth decades, with numbers 12 and 20 respectively. Aprecipitous up surge in the number of cases in the sixth decade was noticed. These observations are depicted in Table2. Astrocytoma was found to be the most frequent tumor, ependymomas ranked second, whereas oligodendro-gliomas and glioblastomas multiforme had third and fourth respective prevalence (Table-3, Figure 3)

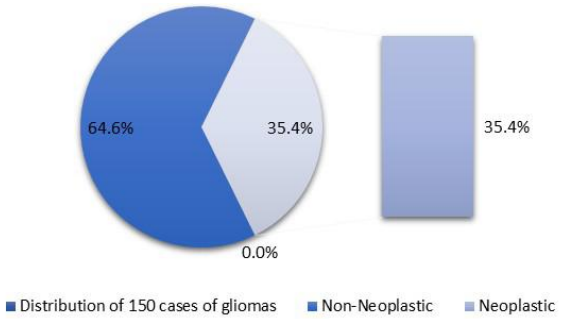

Figure No.1: Distribution of 150 cases of gliomas

Table No.1: Age and Sex distribution of 150 cases of gliomas.

Age group (years)	Sex		Total
	Male	Female	
0 – 9	3	2	5
10–19	11	7	18
20–29	32	17	52
30 – 39	4	9	12
40 – 49	11	7	20
50 – 59	22	17	37
60 – 69	6	2	8
Total	89	61	150

Table No.2: Relative frequency of the different types of neuro-epithelial tumors.

Types of Tumor	Sex*		Total	(%)
	Male	Female		
1.Benign Astrocytomas	52	26	78	52%
2.Anaplastic Astrocytomas	21	11	32	21%
3. Ependymomas	12	10	22	15%
4. Oligodendrogliomas	2	8	10	7%
4. Glioblastomas Multiforme	2	6	8	5%
Total	89	61	150	(100%)

*Difference between males and females for all age groups (P = 0.39)

Of the total 150 cases, 70 were of astrocytic tumors, 12 ependymoma cases, and 6 glioblastoma multiforme were positive for GFAP. Four cases of oligodendro-glioma were negative for GFAP along with 1 case of GFAP-positive oligodendrocytes. The GFAP stain revealed intense immunostaining to the subependymal and subpial networks of glial fibers. The expression level of GFAP staining was considerably lower in high-grade glioma tissues as compared to low-grade glioma tissues and normal brain tissues (Figure - 2). In the cases of the grades I & II glioma, the GFAP had a high expression average score >7 whereas tumors of III & IV grading had expression scores between 3-4. Double immunostaining with anti-vimentin and anti-GFAP antibodies emphasized the occurrence of both antigens in the same zones of the tumor (Figure 4)

The nestin expression was not found in 2.1% of the samples, 18.3% revealed low expression, and the majority revealed moderation expression 53.4% whereas 26.2% had high levels of expression. The average IHC nestin score for astrocytes was 5.3 with medulloblastoma 7.2, and 8.7 for glioblastoma multiforme. The nestin was found negative for ependymoma, oligodendroglioma, and choroid plexus papilloma. The vimentin was negative for oligodendrocytomas, however, its positivity increased with the grading of malignancy (p =0.414) (Table 3).

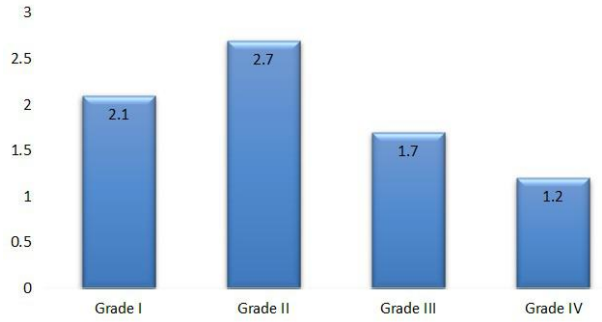

Figure No.2: Glial Fibrillary Acidic Protein Score

Figure 1 Mean Glial Fibrillary Acidic Protein Immunoreactive Score of gliomas from I to IV grading based on Bei, Huang (1) scoring system. The mean score is the sum of the percentage of immunohistochemistry staining and intensity staining of individual grade.

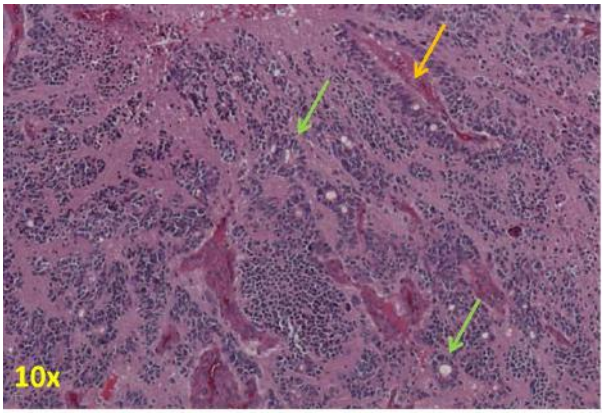

Figure No.3: Hematoxylin and eosin (H&E) staining showing anaplastic ependymoma features. Formation of true rosettes (green arrows) surrounding the microvascular proliferation within ependymal tumors, usually signifies anaplastic transformation which is characteristic of ependymomas. Pseudo palisading necrosis, characterized by a garland-like structure of hypercellular tumor nuclei lining up around irregular foci of tumor necrosis (yellow arrow)

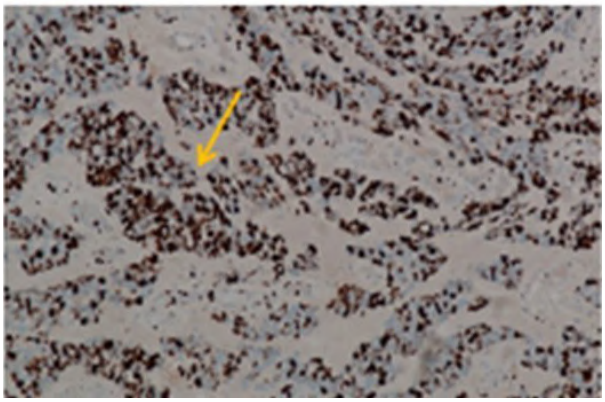

Figure No.4: Photomicrographs of Ki-67, vimentin, GFAP, and EMA immunostaining of the ependymal tumor (yellow arrow). Ki-67 immunostaining indicates a high proliferation index in the tumor (70%)

Table No.3: Correlation of Immunohistochemistry score with the expression of vimentin

Grades	Vimentin IHC Score (mean)	Vimentin Expression
Grade I	3.4	Low
Grade II	3.5	low
Grade III	5.5	Moderate to high
Grade IV	8.3	high

DISCUSSION

Gliomas are the principal tumors of the central nervous system with high morbidity and mortality.[1,6] Glioblastoma account for the majority of gliomas responsible for mortality.[11] However, the incidence of benign vs malignant gliomas varies considerably in the literature.[12]

There were more benign gliomas diagnosed in the 150 cases on histopathology. The mean age of most frequent gliomas diagnosed in our study was similar to the reported age with a peak of benign astrocytomas commencing in the twenties. However, the number of malignant tumors was less, particularly of glioblastoma multiforme, peaking at 50s contrary to 60s and 70s documented by Davis (2018).[13] The high frequency of benign tumors in children and adolescents is commensurate with the possible childhood exposure to the 30 kHz to 300 kHz frequency range of the radiofrequency electromagnetic fields. The intermittent occurrence, on the other hand, debunks the notion of genetically associated risk factors despite the advancement in molecular genetics. The immense inconsistency in the occurrence of types of gliomas is, therefore, bewildered by variations in approach to histopathological diagnosis, medical imaging, and surveillance. Forthcoming studies associating genetic, environmental, and regional lifestyle risk factors amongst and within countries will be significant to comprehend these differences.[13]

Ionizing radiation through mutations and DNA damage has the potential to induce oncogenesis. Early exposure to ionizing radiation as early as the first 7-9 years, either therapeutic or environmental, contributes to neurological tumor formation through aberrations in the cell cycle. Various new risk factors discovered in the past decade besides the neutral stem-like cells in the subventricular zone give rise to atleast a subset of gliomas. Moreover, transformed blood immune cells profile with CD4+ T-cell deficiency and mutation of the isocitrate dehydrogenase gene have been associated with gliomas.[2, 14]

Most epidemiological studies reveal that, along with the differences in geography, glioma incidence varies by age, sex, origin, and tumor subtype.[7] According to Molinaro, Taylor (2019)[2], women bear 50-60% less incidence of developing gliomas at all ages. The more incidence of cancer in men and its probable association with hormone lacks proper scientific evidence. Proposing unidentified risk factors being the root-cause.[2] The more occurrence at the young age could be the new norm of exposure to the cellular non-ionizing radiofrequency electromagnetic fields.[12, 13]

The interobserver and intraobserver variability in the histopathological diagnosis of glioma belies the exceptional limit of its utility. This led to the advancement in the new diagnosis and extensive research on the utilization of biomarkers for therapeutic and prognostic strategies.[7]There is substantial association of the expression of biomarkers with clinical outcome.[6] GFAP is recurrently designated for the visualization of astrocytes and tumors of glial origin. Glial fibrillary acidic protein (GFAP) is recurrently used as a dependable marker for visualization of astrocytes and glial-derived tumors.[4] The isolation followed by the development of antibodies has paved way for GFAP positivity assessment using immunohistochemical staining.[6] GFAP is the indicator of glial cells differentiation. The more pronounced the staining of GFAP is believed to mark less malignant and more differentiated tumors. The mature astrocytes and radial glia, therefore, express more GFAP.[1]

The evident levels of GFAP in the serum of grade II astrocytoma patients were significantly higher which could be attributed to the higher rate of cellular mitosis of astrocytes.[6, 15]Furthermore, there is formation of aggregates in astrocytes with the excessive translation of GFAP genes leading to neurodegeneration.[10]The lower expression of GFAP in dedifferentiated tumor of grade IV could be the consequence of decrease stimulatory response of glial cells to endocrine hormones of progesterone and dihydroprogesterone on GFAP gene.[16]A few examinations exhibited reformist loss of GFAP articulation with ascending astrocytoma grade similar to our findings.[6]

The expression of nestin and vimentin demonstrates an undifferentiated, more stemcell-like condition of these cells.[10] The vast majority of the gliomas that communicated elevated levels of nestin were high-grade gliomas.[17] The association between nestin expression and grade of the tumor has been proposed to be linked to dedifferentiation, enhanced motility of cell, ability to invade locally, and augmented malignant potential.[7]It triggers the activity of phosphorylated focal adhesion kinase (pFAK) on the cell membrane. Phosphorylated FAK degrades the transmembrane linker integrin and promotes tumor formation at the cellular level.[18]The outflow of vimentin was greater in high-grade glioma in correlation with low-grade samples. It is a major marker of epithelial-mesenchymal transition (CMT) through up regulating the receptor tyrosine kinase Axl expression and loss of E-cadherin.[8,19] This makes it effective indicator of the malignancy due to its role in regularization of cellular integrity.[20] It is, therefore, indispensable to recognize the underlying mechanisms at the molecular level. This will further define the biologic behavior of glioma cells, and then and there, take advantage of new beneficial strategies to regulate the progression of glioma.[3]

CONCLUSION

It is basic to look for efficient biomarkers for the prognosis of glioma to manage the clinical treatment including GFAP, vimentin, and nestin.

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

REFERENCES

1. Bei Y, Huang Q, Shen J, Shi J, Shen C, Xu P, et al. Igfbp6 regulates cell apoptosis and migration in glioma. Cell Mol Neurobiol 2017 Jul;37(5):889-98.
2. Molinaro AM, Taylor JW, Wiencke JK, Wrensch MR. Genetic and molecular epidemiology of adult diffuse glioma. Nat Rev Neurol 2019;15(7): 405-417.
3. Zhao C, Ban N, Dai S, Zhang, X, Zhang L, Xu P, et al. The role of Alix in the proliferation of human glioma cells. Hum Pathol 2016;52:110-118.
4. Kishore S, Thakur B, Bhardwaj A, Kusum A. Diagnostic accuracy of squash cytology and role of GFAP immunoexpression in glial tumors. Ind J Pathol Oncol 2018;5(1):12-17.
5. Lv D, Lu L, Hu Z, Fei Z, Liu M, Wei L, Xu, J. Nestin expression is associated with poor clinicopathological features and prognosis in glioma patients: an association study and meta-analysis. Mol Neurobiol 2017;54(1):727-735.
6. Ahmadipour Y, Gembruch O, Pierscianek D, Sure U, Jabbarli R. Does the expression of glial fibrillary acid protein (GFAP) stain in glioblastoma tissue have a prognostic impact on survival? Neurochirurgie 2020;66(3):150-154.
7. Abdelkareem RM, Elnashar AT, Fadle KN, Muhammad EMS. Immunohistochemical expression of nestin as cancer stem cell marker in gliomas. J Neurol Sci Disord 2019;5(1):047-051.
8. Lin L, Wang G, Ming J, Meng X, Han B, Sun B, Cai J, Jiang C. Analysis of expression and prognostic significance of vimentin and the response to temozolomide in glioma patients. Tumor Biol 2016;37(11):15333-15339.
9. Sofroniew MV. Stem-cell-derived astrocytes divulge secrets of mutant GFAP. Cell stem cell 2018;23(5):630-631.
10. Hol EM, Capetanaki Y. Type III intermediate filaments desmin, glial fibrillary acidic protein (GFAP), vimentin, and peripherin. Cold Spring Harb Perspect Biol 2017;9(12):a021642.
11. Bark JM, Kulasinghe A, Chua B, Day BW, Punyadeera C. Circulating biomarkers in patients with glioblastoma. Br J Cancer 2020;122(3): 295-305.
12. Ostrom QT, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2011-2015. Neuro-Oncol 2018;20 (suppl_4):iv1-iv86.
13. Davis ME. Epidemiology and overview of gliomas. In Seminars in oncology nursing. WB Saunders; 2018.p.420-429.
14. Van den Bent MJ, Chang SM. Grade II and III Oligodendroglioma and Astrocytoma. Neurol Clin 2018;36(3):467-84.
15. Kiviniemi A, Gardberg M, Frantzen J, Parkkola R, Vuorinen V, Pesola M, et al. Serum levels of GFAP and EGFR in primary and recurrent high-grade gliomas: correlation to tumor volume, molecular markers, and progression-free survival. J Neuro-Oncol 2015;124(2):237-45.
16. Morita K, Arimochi H, Itoh H, Her S. Possible involvement of 5α-reduced neurosteroids in adrenergic and serotonergic stimulation of GFAP gene expression in rat C6 glioma cells. Brain Res 2006;1085(1):49-56.
17. Ludwig K, Kornblum HI. Molecular markers in glioma. J Neuro-Oncol 2017;134(3):505-12.
18. Schmitt M, Sinnberg T, Nalpas NC, Maass A, Schittek B, Macek B. Quantitative Proteomics

Links the Intermediate Filament Nestin to Resistance to Targeted BRAF Inhibition in Melanoma Cells. Mol Cell Proteomics 2019; 18(6):1096-109.

19. Yin S, Chen F-f, Yang G-f. Vimentin immunohistochemical expression as a prognostic factor in gastric cancer: A meta-analysis. Pathol - Research Practice 2018;214(9):1376-80.
20. Lu W, Luo J-y, Wu M-h, Hou J-y, Yang X, Chen G, et al. Expression of vimentin in nasopharyngeal carcinoma and its possible molecular mechanism: A study based on immunohistochemistry and bioinformatics analysis. Pathol – Res Prac 2019; 215(5):1020-32.

Standardized and Competent Cost-Conscious Practice of Medical Students during Clinical Clerkship

Cost-Conscious Practice of Medical Students

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ABSTRACT

Objective: To assessed the perception of medical students regarding cost conscious practices in healthcare.
Study Design: A Retrospective qualitative study
Place and Duration of Study: This study was conducted at the Al-Tibri Medical College and Hospital, between the duration from September 2021 to October 2021 for a period of 03 months.
Materials and Methods: An electronic survey was prepared and sent to total 460 participants out of which 145 were practicing physician and 315 were medical students of 4th and 5th year. This survey included 39 close- and open ended questions that was prepared after extensive literature review. Questions were asked in which respondents were requested to agree, disagree, or don't know. Student's responses were compared to practicing physician using Chi square test.
Results: We observed from our data that practicing physician were comparably well aware about cost effective procedures than medical students. In our context the expert physicians were more likely to aware about cost reduction expenditure and electronic health records that can be effective way to reduce the cost on the other hand medical students were less aware about this strategy.
Conclusion: The provision of resources that can be easily adopted by various institutions can help to speed the widespread adoption of HVC curriculum in medical schools. Moreover there is need to emphasize the curriculum to advance their knowledge against cost conscious care. Even with minimal clinical experience, medical students were able to identify instances of lack of attention to cost-conscious care as well as potential solutions.
Key Words: Cost-Conscious Care, Healthcare, Medical Students, Physician, Clerkship

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INTRODUCTION

High Value Care (HVC) or Cost Conscious Care is a notion that refers to healthcare that gives the most benefit in relation to cost and damage. Despite the fact that affecting an HVC cultural shift has become a key objective in medical education, it is still unknown to what degree HVC has infiltrated in the curriculum and clinical experiences of medical students [1]. All healthcare facilities are directed by physicians, numerous studies have suggested that their lack of knowledge deliberately caused cost of medical care.

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Moreover, traditional training program for medical students did not provide instructions on cost effective awareness. It is obvious that learners will definitely adopt the wrong practice without proper education regarding cost conscious care[2]. The students will follow the same practice whatever followed by their supervising physician. Usually, most of the physicians follow a same approach which is "more is better", which is then automatically adopted by their students in clerkship [3].

Control the cost of healthcare system has become a challenge for many countries. Research have suggested that education regarding cost conscious care has positive impact on residents that will motivate them to continue their work in cost conscious manner after completing their clerkship[1,4]. The emphasis on the next generation of physicians is also based on the idea that motivated learners may effect change by rethinking the medical system and addressing local system concerns by implementing creative initiatives to enhance healthcare practices, thereby serving as change agents[5, 6].

Residency training is viewed as critical in teaching a new generation of doctors to offer high-value care while keeping costs down [7].

Although the role of education in addressing these issues is becoming more widely acknowledged, there remains a lag in implementation. According to empirical research, medical residents cite time constraints, medical uncertainty, fear of missing something, and concern of malpractice responsibility as impediments to resource stewardship [8, 9].

Furthermore, due to a hierarchy in teams, a dearth of clinical role models, and teachers who penalize "sins of omission" excessively, the existing teaching environment may offer challenges to enhancing high-value treatment [10, 11].

By conducting a system analysis that considers the environment in which High value cost conscious care (HVCCC) must work, the goal of this study was to determine the standardize cost conscious practice among the residence and physicians at Al-Tibri Medical College and Hospital ATMC&H.

MATERIALS AND METHODS

Ethical Approval: This web-based survey study was conducted after ethical approval from concerned authority of Al-Tibri Medical College and Hospital, Isra University Karachi.

Study Design: This survey was carried out over a period of 03 months September 2021 to October 2021. It was conducted at Al-Tibri Medical College and Hospital, Isra University Karachi (ATMC&H).This survey comprised of 39 questions that was proposed to take about 5-7 minutes to fulfil the survey. Students of MBBS and residence Doctors were asked about their experience to indulgent towards High Cost Care. Questions were asked in which respondents were requested to agree, disagree, or don't know.

We assessed trainees for their exposure to high value care and barriers during their clerkship. We also surveyed the level to which the residents and MBBS student want to include high value care training courses in their educational curriculum. The demographic data was also asked including gender, profession and ethnic group.

This survey was filled by 460 participants. The mean age of the participants was 31.16 ± 5.68 years.

Data Analysis: Our data were analyzed by using statistical software SPSS version 22.00. The relationship between groups were analyzed by using chi-square and One Way ANOVA. The p - 0.05 was considered as statistically significant.

RESULTS

A total of 460 participants were enrolled in our survey, out of which 145 were practicing physician and 315 were medical students of 3rd and 4th year. The demographic data was also recorded include age, gender, ethnicity, and nationality. As our study is independent of sex and gender so we didn't discuss their frequency here.

Table No.1: Attitudes of Practicing Physicians and Medical Students toward Cost-Conscious Care

Questionnaire	Responses	Practicing physicians (n=145) %	Medical Student (n=315) %	p-value
Do you think high quality healthcare minimizes the overall cost burden of the caretakers?	Agree	84.44	34.23	< 0.005
	Disagree	12.8	51.54	
	Don't Know	2.8	15.23	
Do you think effective patient care may contribute to the cost-conscious strategy?	Agree	89.7	56.30	< 0.005
	Disagree	8.97	20.55	
	Don't Know	1.33	23.15	
Do you believe that cutting down the expenditures without sacrificing patient care, can help in cost-reduction?	Agree	95.23	88.50	< 0.871
	Disagree	1.50	9.00	
	Don't Know	4.27	2.5	
Do you think generating electronic health records (EHRs) of patients can be a step towards cost-conscious care?	Agree	84.61	67.50	0.067
	Disagree	15.39	25.20	
	Don't Know	0	7.30	
Do you think pre-planning and strategic budgeting can contribute to an effective cost-conscious care?	Agree	94.92	78.56	0.850
	Disagree	5.08	15.90	
	Don't Know	0	5.54	
Do you think reducing medical waste can help in	Agree	77.66	56.66	< 0.005
	Disagree	16.23	28.20	

overall cost-reduction?	Don't Know	6.11	15.14	
Do you believe that conscious cost care requires extra efforts?	Agree	84.56	89.90	0.985
	Disagree	10.22	8.44	
	Don't Know	5.22	1.66	
Do you believe adequate staff schedules can help in cost-conscious care?	Agree	92.33	45.67	< 0.005
	Disagree	7.67	34.56	
	Don't Know	0	19.77	
Do you believe that healthcare products and services must be transparent in price for cost-effectiveness?	Agree	84.66	72.56	0.075
	Disagree	12.33	23.55	
	Don't Know	3.01	3.94	
Do you think innovative thinking and dedication to researching new trends or best practices can help in overall cost-conscious care?	Agree	78.45	84.56	0.891
	Disagree	21.55	15.44	
	Don't Know	0	0	
Do you think providing proactive and coordinated services timely to severely ill patients (for e.g., ER beds) can help in cost-reduction?	Agree	82.56	75.23	0.715
	Disagree	15.67	19.2	
	Don't Know	1.77	5.57	
Do you think that overall cost-conscious care fosters patient trust and satisfaction	Agree	87.45	86.75	0.905
	Disagree	12.55	12.00	
	Don't Know	0	1.25	

At the time of the survey, 33% (48/145) of physician respondents were between the ages of 30 and 40, 67% (97/145) were between the ages of 41 and 50, whereas 94 %t (296/315) of medical student respondents was between the ages of 21 and 26.

The questionnaire was designed to get maximum answer regarding their knowledge of high value cost conscious care as shown in Table 1.

While it was observed from our data that practicing physician were comparably well aware about cost effective procedures than medical students. For the first two question, when participants were asked that they could play an important role in minimizing the caretaker's total financial burden with high-quality healthcare. More than 84% physicians and 34% medical students were agreed with statically significant difference ($P<0.005$). In our context the expert physicians were more likely to aware about cost reduction expenditure and electronic health records that can be effective way to reduce the cost on the other hand medical students were less aware about this strategy. Use of pre-planning strategic budget can also help out in cost reduction, which is supported by our 94% physician and 78% students with no significant difference (i.e. $P>0.005$). In response to our question no. 7 regarding cost conscious care require extra effort, most of doctors were agreed to this statement and they think that it is an additional work more or less students had also the same response.

Similarly, most of the physician (92%) believed that there is a need to appropriately schedule the staff so that it can aid in cost effective measurements. In contrast, medical students were not well aware. Moreover, according to our practicing physician and medical students it is essential to make innovative thinking and dedication towards the new trends and best practices in coordinating with ill patient which ultimately reduce the cost of caretakers also help in treating seriously ill patients timely by arranging emergency bed for them. Our both group were agreed (86%) that cost conscious care also care fosters patient trust and satisfaction.

DISCUSSION

To our knowledge this is the first ever survey taken place in ATMC&H Karachi. The result of our qualitative analysis towards medical students' attitudes of cost-conscious care during their clerkship is presented in our study. We have studied numerous articles to find out the data regarding cost conscious care standardization Pakistan, but unfortunately we couldn't find out the data.

Many respondents said that cost education was critical for increasing physicians' cost awareness and encouraging more judicious resource utilization.

Moreover it was observed from our study that learners are not properly guided by expert physicians regarding cost effective treatment which is reflecting from their responses.

A few studies have been undertaken at specific residency programs to address the inadequacy of HVC instruction in the curriculum, despite the necessity for it. Traditionally, HVC education has not been addressed at the undergraduate medical college level, however it has been included in the curriculum of few institute in United States [12, 13].

The establishment of an online module to teach trainee doctors about the financial structure of the healthcare system was one of the initiatives to educate trainee doctors about healthcare expenditures [14].

A major contributor to healthcare waste is the over and misuse of laboratory testing and treatment with expensive medicines. This cost can be reduced when students were trained to be HVC officers during their clerkship [15].

This study, on the other hand, gives insight into the perspectives of early clinical learners on the importance of cost effective healthcare. Though some of Medical students instinctively identified reasons of low-value treatment as well as potential remedies even with limited clinical experience, however, the other needs the guidance from their instructor.

We believe that a reflective assignment that encourages medical students to think of ways they may be more cost-conscious would create a consciousness of healthcare value because medical students do not commonly make orders [16, 17].

CONCLUSION

The challenge is to provide high-quality, ethical, useful, and cost-effective way of treating patient. We must be aware of the financial implications of each clinical choice, and we must encourage this culture by providing proper advice to our trainees in the use of healthcare resources**.** As research improves and new issues relevant to health care emerge, medical colleges are always pushed to balance curricular time and resources**.** The provision of resources that can be easily adopted by various institutions can help to speed the widespread adoption of HVC curriculum in medical schools.

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REFERENCES

1. Sager A, Socolar D. Health Costs Absorb One-Quarter of Economic Growth, 2000–2005. Health (San Francisco) 2005;2:2000-05.
2. Moriates C, Dohan D, Spetz J, Sawaya GF. Defining competencies for education in health care value: recommendations from the University of California, San Francisco Center for Healthcare Value Training Initiative. Academic Med 2015; 90(4):421-4.
3. Qaseem A, Alguire P, Dallas P, Feinberg LE, Fitzgerald FT, Horwitch C, et al. Appropriate use of screening and diagnostic tests to foster high-value, cost-conscious care. Annals Internal Med 2012;156(2):147-9.
4. Sirovich BE, Lipner RS, Johnston M, Holmboe ES. The association between residency training and internists' ability to practice conservatively. JAMA Int Med 2014;174(10):1640-8.
5. Levy AE, Shah NT, Moriates C, Arora VM. Fostering value in clinical practice among future physicians: time to consider COST. Academic Med 2014;89(11):1440.
6. Leep Hunderfund AN, Dyrbye LN, Starr SR, Mandrekar J, Tilburt JC, George P, et al. Attitudes toward cost-conscious care among US physicians and medical students: analysis of national cross-sectional survey data by age and stage of training. BMC Med Educ 2018;18(1):1-1.
7. Courtright KR, Weinberger SE, Wagner J. Meeting the milestones. Strategies for including high-value care education in pulmonary and critical care fellowship training. Annals Am Thoracic Society 2015;12(4):574-8.
8. Ackerman SL, Gonzales R, Stahl MS, Metlay JP. One size does not fit all: evaluating an intervention to reduce antibiotic prescribing for acute bronchitis. BMC Health Services Res 2013; 13(1):1-9.
9. Manja V, Monteiro S, You J, Guyatt G, Lakshminrusimha S, Jack SM. Incorporating content related to value and cost-considerations in clinical decision-making: enhancements to medical education. Advances Health Sciences Educ 2019; 24(4):751-66.
10. Tilburt JC, Wynia MK, Sheeler RD, Thorsteinsdottir B, James KM, Egginton JS, et al. Views of US physicians about controlling health care costs. JAMA 2013;310(4):380-9
11. Moleman M, van den Braak GL, Zuiderent-Jerak T, Schuitmaker-Warnaar TJ. Toward High-Value, Cost-Conscious Care–Supporting Future Doctors

to Adopt a Role as Stewards of a Sustainable Healthcare System. Teaching and Learning in Med 2021:1-5.
12. Korenstein D, Kale M, Levinson W. Teaching value in academic environments: shifting the ivory tower. JAMA 2013;310(16):1671-2.
13. Post J, Reed D, Halvorsen AJ, Huddleston J, McDonald F. Teaching high-value, cost-conscious care: improving residents' knowledge and attitudes. Am J Med 2013;126(9):838-42.
14. Sirovich BE, Lipner RS, Johnston M, Holmboe ES. The association between residency training and internists' ability to practice conservatively. JAMA Int Med 2014;174(10):1640-8.
15. Brandes ER. High-value, Cost Conscious Care in Medical Education (Doctoral dissertation, Harvard University) 2018.
16. Muntz MD, Thomas JG, Quirk KL, Thapa B, Frank MO. Clerkship students as high-value care officers increased awareness and practice of cost-conscious care. In proceedings of the 2014 Annual Meeting of the Clerkship Directors of Internal Medicine (CDIM). Teach Learn Med 2015;27(3): 349-350.
17. Patel MS, Reed DA, Loertscher L, McDonald FS, Arora VM. Teaching residents to provide cost-conscious care: a national survey of residency program directors. JAMA Internal Med 2014; 174(3):470-2.

Compliant Prescription Writing-Dilemma or Reality?

Compliant Prescription Writing-Dilemma or Reality

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ABSTRACT

Objective: To better understand the idea of good prescription writing practices and to provide awareness to medical science students and clinicians of Al-Tibri Medical College and Al-Ibrahim Eye Hospital, Isra University Karachi.
Study Design: Cross-sectional / observational study
Place and Duration of Study: This study was conducted at the Al-Tibri Medical College and Karachi Hospital (ATMCH) and Al-Ibrahim Eye Hospital (AIEH) from August 2021 to November 2021 for a period of 04 months.
Materials and Methods: It consisted of two sections such that the first section discussed the demographic data of the participants including age, gender, field of specialization, Medicine professional year, relationship status etc. While, the other section evaluated the skill set. Data was analyzed using SPSS Version 20.0 with level of significance being kept at P-value ≤0.05.
Results: A total of 160 responses were generated. Out of which 90 respondents (56.25%) were male while remaining 70 participants (43.75%) were females with the mean age of 22.0 ± 3.0 years. It has also analyzed the understanding of compliant prescription writing and provided awareness in this regard to the participating individuals (i.e., 6.62% on average with a Standard deviation of 5.0 ± 0.3). About 74.7% (n=119) from 160 participants believed that there is a lot of malpractice to write a good prescription by the practitioners while only 7.6% (n=12) disagreed with the idea. However, to our surprise, a good amount of people i.e., 17.7% (n=29) were have no clue about compliant prescription writing ability.
Conclusion: Compliant prescription writing is a skill which should be acquired by every clinical practitioner and they should have complete knowledge including pharmacodynamics of the therapeutic drug to avoid any inevitable circumstances in the clinical set-up.

Key Words: Prescription, compliance, graduate, medicine, clinicians, therapy, drug.

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INTRODUCTION

A well-written prescription is an authorized set of instructions by a healthcare professional to its patients consisting of essential directions to treat a specific condition. Medical students strive to learn a good prescription writing because of the fact that many consultations end on that and do not require any further medical surveillance. However, it is becoming difficult day-by-day because of the poor knowledge and malpractice of the medical practitioners.

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The key factors contributing to a well-structured prescription includes (i) Accuracy in diagnosis (ii) Authorized practitioners (iii) Efficacy and specificity of a drug (iv) Precision drug delivery (v) Clinical expertise (vi) Legibility of a prescription (vii) and Data records of patients. Failing to any one of the components may lead to unforeseen medical negligence. [(1)]

According to the Drug and Cosmetic Act, there are two types of prescriptions legally. One that is prescribed by a health professional only, while the other can be obtained without prescription, usually termed as over-the-counter drugs or non-prescribed medics (such as paracetamol, cough syrup etc.)[(2)]. A standard prescription should address patient's demographic data (i.e., name, age, sex, ethnicity, blood groups, cast, weight etc.). While a proper medication should be prescribed by the consultant keeping allergic status and medical complexities in mind. Effective and safe dose of drug should be prescribed [(3)].

The World Health Organization defines a balanced prescription which defines patients' identity, mode of drug administration as well as pharmaceuticals basic principles including the form of drug, frequency and dose of drug, sequels of drug, and its duration in accordance with the patients' health standing [(4)]. The authorities should train medical students by arranging

learning opportunities, assessments, tutorials, seminars, and problem-related workshops to acquire the skill of writing a good prescription. These complications arise due to the lack of command, competency and knowledge of clinical pharmacology or pharma-cotherapy [5]. Cognitive abilities to think out-of-the box and differently for every patient can reduce these malpractices. Inappropriate prescription has been observed in South-Asian countries more therefore, Drug Regulatory Authority of Pakistan (DRAP) has established a guideline for treatment, control and management of drugs and its prescription to prevent unavoidable circumstances [6].

Unnecessary complications (for instance drug mortality or toxicity) and suffering can be avoided in this manner by omitting the basic errors by the healthcare professionals. Drug prescription is a common practice among clinicians which further decides the subsequent clinical procedures. Unregularized or inappropriate prescription can cause great harm to the end user. Therefore, rational treatment that is best effective drug in the least time to cure a disease and that too if cost-effective can reduce these burdens [7].

To better understand the idea of good prescription writing practices and to provide awareness to medical science students and clinicians of Al-Tibri Medical College and Al-Ibrahim Eye Hospital, Isra University Karachi.

MATERIALS AND METHODS

This cross-sectional study was designed and conducted at Al-Tibri Medical College and Karachi Hospital (ATMCH) and Al-Ibrahim Eye Hospital (AIEH) from August 2021 to November 2021. Medicine students (of M.B.B.S. 3rd year, 4th year, and 5th year) and Clinicians were included as participants. Participants were asked to fill e-forms discussing their perception of compliant prescription writing after their consent. The survey-based cross-sectional observational study consisting of two sections such that the first section discussed the demographic data of the participants including age, gender, field of specialization, Medicine professional year, relationship status etc. While, the other section analyzed the understanding of compliant prescription writing and provided awareness in this regard to the participating practitioners. Data was analyzed using SPSS Version 20.0 with 95% level of significance i.e., P-value ≤ 0.05.

RESULTS

A total of 160 individuals from different years of medicine of Al-Tibri Medical College including M.B.B.S. third year, fourth year, and final year students (86.1%) along with various clinicians (13.9%) from Al-Ibrahim Eye Hospital had participated in the proposed study. The demographic data included name, age, gender, marital status, and contact details of the respondents. Out of 160 participants, 90 respondents (56.25%) were male while remaining 70 participants (43.75%) were females.

Maximum responses were generated from a mean age group of 20-24 years (82.4%) which suggested that young doctors or clinicians wanted to know more about compliant prescription writing unlike others falling under the age of 22.0 ± 3.0 on average. Table 1 also suggested that the clinicians of AIEH of various specialization fields (~5.6% each) such as Pharmacology, Dermatology/Gastroenterology, Family Medicine, General Physician, General Surgery, Pediatrics, Neurosurgery, Urology, Pathology have attempted this survey whereas, the maximum number of clinical participants were from neurosurgery department (i.e., 11.1%).

Question 1 till 12 were asked to evaluate the good prescription writing skills among the responsible authorities and especially to the young doctors/graduates. And according to the data generated from this survey indicated by Table 2, 80.7% from a total of (n=160) respondents were aware about the compliance and importance of prescription writing in the clinical set-up while 19.3% clinicians and medical graduates did not know the value of a compliant prescription writing, thus encounter difficulties in prescribing the effective medication.

Table No.1: Demographic Status of the participants (n=160)

Variables	Characteristics	Frequency (n=160)	(%) age
Gender	Male	90	56.25%
	Female	70	43.75 %
	Others (Transgenders)	0	0%
Age	19-24 years	103	64.1 %
	25-30 years	10	6.5%
	>30 years	47	29.4%
Relationship Status	Married	28	17.7%
	Single	126	78.5%
	Engaged	2	1.2%
	Others (Divorced, widowed)	4	2.6%
Medical Student	Yes	138	86.1%
	No	22	13.9%
Professional year (M.B.B.S.)	3rd year	75	46.8%
	4rth year	57	35.5%
	Final year	6	3.8%
	Not applicable	22	13.9%
Clinician	Yes	18	11.4%
	No	142	88.6%
Specialization (Clinicians)	a) Pharmacology	1	5.6%
	b) Dermatology/ Gastroenterology	1	5.6%
	c) Family Medicine	1	5.6%
	d) General Physician	1	5.6%
	e) General Surgery	1	5.6%
	f) Pediatrics	1	5.6%
	g) Neurosurgery	1	11.1%

	h) Urology	1	5.6%		i) Pathology	1	5.6%

Table No.2: Perception and Practice about Drug Prescription among Atmch and Aieh Fellows (N=160)

S. No.		Questionnaire	Agree (%)	Disagree (%)	Don't know (%)	P-values
1.	1.	Do you think a good prescription should be legible (i.e., hand-written, dated, duly signed)?	98.7	1.3	0	≤0.05
2.	2.	Do you think a good prescription must contain patient's basic information (i.e., name, age, sex, address, weight, contact details etc.)?	91.1	6.3	2.5	≤0.05
3.	3.	Do you think a good prescription must state all the information regarding dosage (i.e., quantity, route, timings, and frequency)?	98.7	0	1.3	≤0.05
4.	4.	Do you think if a previously prescribed medicine has been changed for some reason, the old entry must be discontinued?	65.8	22.8	11.4	≤0.05
5.	5.	Do you think a good prescription must be signed by an authorized prescriber?	88.6	2.5	8.9	≤0.05
6.	6.	Do you think a practitioner should prescribe a formulation with its generic name?	48.1	41.8	10.1	≤0.05
7.	7.	Do you think a practitioner should prescribe a formulation with its trade (common) name?	43	44.3	12.7	≤0.05
8.	8.	Do you think if a combination of medicine must be clearly stated or not in a prescription?	87.3	6.3	6.3	≤0.05
9.	9.	Do you think a medical practitioner must prescribe a medicine keeping the allergic status of patient in mind?	91.1	6.3	2.5	≤0.05
10.	10.	Do you think the prescription must be written on an official registered note pad?	82.3	12.7	5.1	≤0.05
11.	11.	Do you think a consultant should prescribe an effective medicine to cure the disease?	94.9	3.8	1.3	≤0.05
12.	12.	Do you think the dose should be prescribed in International Unit (such as g, mg, mL, and L)?	83.5	10.1	6.3	≤0.05
13.	13.	Do you think there is a lot of malpractice to write a good prescription by the practitioners?	74.7	7.6	17.7	≤0.05

Mean= 80.7%, Chi-square test is applied.

Question 6 and 7 were asked to evaluate the sense of generic and trade name among the medical graduates and young practicing doctors. The data suggested that practitioners have not much aware about the difference

between the generic and brand name of a drug. About 41.8% participants believed that doctors should not prescribe the drug with its generic name (i.e., real formulation) and about 10.1% partakers didn't actually know the difference between the two determinants.

The proposed study has also provided awareness to the clinical practitioners about the authorized drug prescriber and registered drugs. Question 1, 5, and 10 were asked to analyze the knowledge about the said parameters and legibility of a prescription or a prescriber. On average 89.87% participants agreed to the authorization and legalization of a prescription while the rest 11.23% either disagreed or have no clue about the regularization of a standard medicine. Despite of having a clear basic understanding of the mode of action of drug, these young practitioners or clinicians don't know about the legibility of prescription and prescriber could be a matter of serious concern. So, this survey provides a detailed responsiveness on such important subject.

Question 3 and Question 12 evaluated the most frequent problem of the clinicians i.e., regarding effective dosage including quantity, route, timings, and frequency of a therapeutic dose. It has been observed that young doctors who are new to the clinical practises were encountering much difficulty in prescribing an effective dose. According to this survey, 98.7% participant agreed to the prescription of an effective dose while 1.3% were totally unaware of its importance.

Table No.3: Frequent errors or problems in compliant prescription writing

Errors	Frequency (f)	Percent (%)
Inappropriate dosage	61	37.8
Ineffective duration of treatment	32	20.0
Malpractises in taking history of a patient	39	24.4
Incompliant Prescription writting.	14	8.9
Knowledge of drug interaction (mode of action etc)	14	8.9

DISCUSSION

The World Health Organization stated the rational use of drugs such that the patient should receive prompt, accurate and appropriate therapeutic dose to ease his/her clinical need. According to them, this should meet their utter necessity within an adequate time period plus cost-effective [8].

In this proposed study, only 6.62% on average medical science students and clinicians of ATMCH and AIEH, Isra University Karachi don't know about the compliant prescription writing and its importance with a Standard deviation of 5.0 ± 0.3. This shows that the newly graduated students and young practitioners should be given proper trainings and workshops to reduce the burden of incompliant prescription writing by increasing the skill set.

Moreover, Pharmacological trainings under the professional and experienced practicing seniors should be increased to cater a broad spectrum of patients varying in age, gender, socio-economic and cultural status to provide them with the best available treatment timely [9]. This will offer the young lot with the different treatment options as to why and when a particular drug is prescribed for a specific time duration to reduce the ailment [10]. Table 3 highlighted the frequent errors in prescription writing among which 37.8% (f=61) were facing problem in dosage recommendation resulting in recurrent and unavoidable errors. Whereas, 24.4% (f=39) errors in submissive prescription writing were due to incomplete or improper history taking from a patient. About 74.7% (n=119) from 160 participants believed that there is a lot of malpractice to write a good prescription by the practitioners while only 7.6% (n=12) disagreed with the idea. However, to our surprise, a good amount of people17.7% (n=29) were have no clue about compliant prescription writing.

CONCLUSION

Medical science students and clinicians of Al-Tibri Medical College and Al-Ibrahim Eye Hospital, Isra University Karachi, however, are very well aware of the importance of good prescription writing practices but still requires better skill development trainings and courses to make a strong grip of clinical pharmacology, rational therapeutics and compliant prescription writing. For this purpose, the new batches should be provided with case-based scenarios and teacher-student group discussions especially during the early professional years and they must be incorporated in their curriculum to limit the errors and medical negligence.

Author's Contribution:

Concept & Design of Study:	Hina Khan
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Revisiting Critically:	Hina Khan, Syed Muhammad Masood Ali
Final Approval of version:	Hina Khan

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REFERENCES

1. James H, Tayem YI, Al Khaja KA, Veeramuthu S, Sequeira RP. Prescription writing in small groups as a clinical pharmacology educational intervention: perceptions of preclerkship medical students. J Clin Pharmacol 2016;56(8):1028-34.
2. Stith SS, Vigil JM, Adams IM, Reeve AP. Effects of legal access to cannabis on scheduled II–V drug prescriptions. J Am Med Directors Assoc 2018; 19(1):59-64.
3. Evans SB, Martin DD, Kudner R. The Standard Prescription and APEx Accreditation: One Hand Washes the Other. Practical Radiation Oncol 2019; 9(6):389-91.
4. Yimenu DK, Emam A, Elemineh E, Atalay W. Assessment of antibiotic prescribing patterns at outpatient pharmacy using world health organization prescribing indicators. J Primary Care Comm Health 2019; 10:2150132719886942.
5. James H, Tayem YI, Al Khaja KA, Veeramuthu S, Sequeira RP. Prescription writing in small groups as a clinical pharmacology educational intervention: perceptions of preclerkship medical students. J Clin Pharmacol 2016;56(8):1028-34.
6. Latif A, Ansari MS, Ansari MI, Malik R, Sohoo AA, Sohoo F, et al. The Influences of Pharmaceutical Industry on Prescription Practices in Public and Private Hospitals of Islamabad-Pakistan. Pak J Public Health 2021;11(1):24-9.
7. Horn D. Learn from someone else's mistakes: Community pharmacy malpractice cases with error prevention recommendations. Pharm Today 2019; 25(7):40-54.
8. Panchbhai AS. Rationality of prescription writing. Ind J Pharmaceutical Educ Res 2013;47(4):7-15.
9. Widiyanto B, Riza M. The Effectiveness of Learning Methods by Measuring Accuracy and Rationality in Prescription Writing by Medical Students. J Health Policy Management 2021; 6(1):74-80.
10. Indriyanti RA, Awalia F, Kharisma Y. Assessing medical students' pharmacological therapy ability through a mobile application. J Physics: Conference Series 2020;1469(1):012058.

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