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Editorial

Risk Factors of Hypertension

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

Hypertension is a silent killer as very rarely any symptom can be seen in its early stages until a severe medical crisis takes place like heart attack, stroke, or chronic kidney disease[1,2]. Since people are unaware of excessive blood pressure, it is only through measurements that detection can be done. Although majority of patients with hypertension remain asymptomatic, some people with HTN report headaches, lightheadedness, vertigo, altered vision, or fainting episode[3].

There are several factors predisposing to hypertension. These factors vary from country to country and even there is difference between urban and rural regions of the same place[4].

Hypertension is a major public health problem due to its high prevalence all around the globe[5,6,7,8]. Around 7.5 million deaths or 12.8% of the total of all annual deaths worldwide occur due to high blood pressure[9]. It is predicted to be increased to 1.56 billion adults with hypertension in 2025[10].

Raised blood pressure is a major risk factor for chronic heart disease, stroke, and coronary heart disease. Elevated BP is positively correlated to the risk of stroke and coronary heart disease. Other than coronary heart disease and stroke, its complications include heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage, and visual impairment[9].

Hypertension – or elevated blood pressure - is a serious medical condition that significantly increases the risks of heart, brain, kidney and other diseases. An estimated 1.13 billion people worldwide have hypertension, most (two-thirds) living in low- and middle-income countries. In 2015, 1 in 4 men and 1 in 5 women had hypertension. Fewer than 1 in 5 people with hypertension have the problem under control.

Blood pressure is the force exerted by circulating blood against the walls of the body's arteries, the major blood vessels in the body. Hypertension is when blood pressure is too high. Blood pressure is written as two numbers. The first (systolic) number represents the pressure in blood vessels when the heart contracts or beats. The second (diastolic) number represents the pressure in the vessels when the heart rests between beats. Hypertension is diagnosed if, when it is measured on two different days, the systolic blood pressure readings on both days is =140 mmHg and/or the diastolic blood pressure readings on both days is =90 mmHg.

Most people with hypertension are unaware of the problem because it may have no warning signs or symptoms. For this reason, it is essential that blood pressure is measured regularly. When symptoms do occur, they can include early morning headaches, nosebleeds, irregular heart rhythms, vision changes, and buzzing in the ears. Severe hypertension can cause fatigue, nausea, vomiting, confusion, anxiety, chest pain, and muscle tremors. The only way to detect it is to have a health professional measure blood pressure. Having blood pressure measured is quick and painless. Individuals can also measure their own blood pressure using automated devices, however, an evaluation by a health professional is important for assessment of risk and associated conditions.

Hypertension can cause serious damage to the heart. Excessive pressure can harden arteries, decreasing the flow of blood and oxygen to the heart. This elevated pressure and reduced blood flow can cause:

• Chest pain, also called angina.

• Heart attack, which occurs when the blood supply to the heart is blocked and heart muscle cells die from lack of oxygen. The longer the blood flow is blocked, the greater the damage to the heart.

• Heart failure, which occurs when the heart cannot pump enough blood and oxygen to other vital body organs.

• Irregular heart beat which can lead to a sudden death.

• Hypertension can also burst or block arteries that supply blood and oxygen to the brain, causing a stroke.

• In addition, hypertension can cause kidney damage, leading to kidney failure.

In most cases, actual causes of high blood pressure are unknown. However, the following risk factors are established as contributing to high blood pressure.

• Smoking is the single worst thing that one can do to one's health, especially for persons with high blood pressure. Nicotine constricts blood vessels, stimulates the heart and increases the rate at which fatty deposits occur within the arteries. This can increase the destruction of the arteries already caused by high blood pressure. If you smoke, quit.

• Overweight: can increase your blood pressure. With each extra pound, the body must increase blood volume and the number of capillaries to supply the fatty tissue. This means that the heart must work harder. Losing weight can lessen this strain on the heart.

• Excessive sodium intake may be detrimental to individuals who are sensitive to sodium or who have a history of high blood pressure. Therefore, avoid salty and processed foods and use herbs and seasonings for flavour rather than salt.

• Lack of exercise and physical activity that is rhythmic (such as brisk walking, jogging, bicycling, swimming,

cross country skiing and jumping rope) are best for building cardiovascular fitness.

• Studies on Alcohol have shown that consumption of as little as two drinks a day can have a harmful affect on blood pressure.

• Genetically Blood pressure levels are correlated among families. This can be attributed to genetics, shared environment or lifestyle factors.

Treatment of High blood pressure usually cannot be cured, but it can be controlled with proper treatment. Treatment options including changing diet/exercise habits and medications. However, it usually requires lifelong medication for those individuals whose blood pressure is definitely abnormal. If your clinician prescribes one or more medications for you, it is important that you take them regularly. Discuss any side effects with your health care provider, because many can be prevented by a change in medication dosage or type.

How can the burden of hypertension be reduced?

Reducing hypertension prevents heart attack, stroke, and kidney damage, as well as other health problems.

Management of hypertension may be due to;

• Reducing and managing mental stress.
• Regularly checking blood pressure.
• Treating high blood pressure.
• Managing other medical conditions.

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Original Article

Sensory Integration for ADHD in Schools

Effectiveness of School-Based Sensory Integration Therapy in Addressing Emotional and Behavioral Challenges in Children with ADHD Symptoms

Vini Victoria and Yunias Setiawati

ABSTRACT

Objective: To assess the efficacy of school-based Sensory Integration Therapy in improving emotional and behavioral problems in children with ADHD symptoms.

Study Design: A pilot randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Child and Adolescent Psychiatry, Faculty of Medicine, Airlangga University, Dr. Soetomo General Academic Hospital, Jl. Mayjen. Prof. Dr. Moestopo, 47, Surabaya, Jawa Timur, 60286, Indonesia from July 2023 to March 2024.

Methods: A pilot randomized controlled trial was conducted using a total sampling technique with a non-blinded, pre-posttest control group design. The Abbreviated Conners' Teacher Rating Scale (ACTRS) was used for screening, and the parent-reported Strengths and Difficulties Questionnaire (SDQ) measured emotional and behavioral problems before and after biweekly Sensory Integration Therapy over four weeks.

Results: Fourteen children identified with ADHD symptoms were randomly assigned to either the intervention or control group through drawing lots. A significant improvement ($p < 0.05$) was observed in SDQ scores in the intervention group after therapy compared to their baseline and the control group.

Conclusion: School-based Sensory Integration Therapy significantly improves emotional and behavioral problems in children with ADHD symptoms

Key Words: ADHD, emotion, behavioral problem, mental well-being, sensory integration therapy, school-based therapy

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INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder characterized by inattention, hyperactivity, and impulsivity. ADHD symptoms fluctuate throughout development, sometimes meeting diagnostic criteria and other times falling below the threshold.[1]

Sensory impairments, often referred to as Sensory Processing Disorder (SPD), are prevalent in ADHD and affect emotional regulation and behavior, impacting daily functioning, mental well-being, social interactions, and increasing the risk of comorbid mental disorders.[2–3]

Global ADHD prevalence ranges from 4% to 11.4%,[4,5] with rates in Indonesia varying from 3% to 26.2%.[6,7] Subclinical ADHD symptoms affect 0.8%–23.1% of children and adolescents globally.[8,9] Emotional dysregulation is found in 25%–45% of children with ADHD, with high rates of depression (45%–55%) and bipolar disorder (21%), further reducing quality of life.[10,11] ADHD symptoms often interfere with academic performance, leading to frequent referrals to psychology and psychiatry clinics.[5,12] Emotional and behavioral problems are common, but parental concerns about medication side effects highlight the need for non-pharmacological interventions that address sensory and emotional regulation.[12-14]

Sensory Integration Therapy, originally developed for autism spectrum disorder (ASD), has been shown to improve irritability, behavior, and social functioning. It also enhances sensory and emotional processing, addressing ADHD symptoms while supporting adaptability and mental health.[15] School-based interventions are effective in promoting mental health

Department of Child and Adolescent Psychiatry, Faculty of Medicine, Airlangga University/Dr. Soetomo General Academic Hospital Surabaya, Indonesia.

Correspondence:Yunias Setiawati, Department of Child and Adolescent Psychiatry, Faculty of Medicine, Airlangga University, Dr. Soetomo General Academic Hospital, Jl.Mayjen. Prof. Dr. Moestopo, 47, Surabaya, Jawa Timur,60286, Indonesia.

Email:yunias.setiawati@fk.unair.ac.id

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and managing ADHD-related academic and behavioral challenges.[16] This pilot study evaluates the efficacy of school-based Sensory Integration Therapy in improving emotional regulation and behavior in children with ADHD symptoms in Indonesia.

METHODS

This study was a pilot randomized controlled trial with a pre-posttest control group design and non-blinded setup, conducted in an elementary school in Surabaya, Indonesia, where children are regularly evaluated for learning disorders such as concentration problems and hyperactivity. A total sampling technique was employed, including all children who met the inclusion criteria, with ethical clearance obtained from the Institutional Review Board (183/EC/KEPK/ FKUA/2023). Consent for participation was secured from the school principal, teachers, parents, and children before screening. The Abbreviated Conners' Teacher Rating Scale (ACTRS), a school-based ADHD screening tool with 90% sensitivity, was used, consisting of 10 Likert-scale questions completed by teachers based on observations over the preceding six months. The intervention group received school-based Sensory Integration Therapy twice weekly for four weeks, while the control group was monitored without intervention. Of the 120 children screened, 14 met the inclusion criteria. Parents of all participants completed the Strengths and Difficulties Questionnaire (SDQ), a 25-item Likert-scale tool assessing emotional, behavioral, and relationship problems over the past six months, administered before and after the intervention. Participants were randomly assigned to either the intervention or control group using a lottery system. The primary outcome measure was the improvement in emotional and behavioral problems as assessed by the SDQ. Data were analyzed using SPSS version 24, employing McNemar, Shapiro-Wilk, paired t-tests, Wilcoxon, independent t-tests, and Mann-Whitney tests, with a multidisciplinary research team overseeing the study.

RESULTS

Participant Characteristics: Out of 120 children screened, 14 met the inclusion criteria and agreed to participate after informed consent. Parents completed the Strengths and Difficulties Questionnaire (SDQ) before and after the intervention. No participants dropped out. The majority (92.9%) were 10 years old, with one child (7.1%) aged 9. All control group participants were 10 years old, while the treatment group included six 10-year-olds (85.7%) and one 9-year-old (14.3%). Most participants were male (71.4%, n=10), with four females (28.6%). The control group was entirely male (100%, n=7), whereas the treatment group had three males (42.9%) and four females (57.1%).

Emotional and Behavioral Outcomes Before and After Sensory Integration Therapy: In the control group, SDQ scores remained unchanged, with all participants staying in the abnormal category. In contrast, the treatment group showed improvements, with participants transitioning to normal categories in emotional problems (83.3%), behavioral problems (66.7%), hyperactivity-inattention (66.7%), peer problems (25%), and total difficulties (60%). However, no significant differences ($p \geq 0.05$) were found in either group's pre- and post-intervention data.

Analysis of Pre- and Post-Intervention Scores: No significant differences ($p \geq 0.05$) were found in the control group or in the peer problems and prosocial subscales of the treatment group. However, the treatment group showed significant improvements ($p < 0.05$) in emotional problems, hyperactivity-inattention, and total difficulties, while no significant changes were observed in behavioral problems, peer problems, and prosocial subscales (Table 1).

Table No.1: Emotional Condition Before and After Sensory Integration Therapy: Comparison of Pre- and Post-Intervention Scores

		Median (minimum-maximum) Mean ± Standard Deviation		
		Pretest	Posttest	P value
Control group	SDQ emotional problem	5 (3-6)	5 (4-6)	0,317 [a]
	SDQ behavioral problem	3 (1-5)	3 (1-5)	1,000 [a]
	SDQ hyperactivity-inattention	5 (5-7)	6 (5-7)	0,317 [a]
	SDQ peer problems	2 (1-4)	2 (1-4)	1,000 [a]
	SDQ difficulty domain	16 (11-20)	16 (12-20)	0,157 [a]
	SDQ prosocial	6 (5-8)	6 (5-8)	1,000 [a]
Intervention group	SDQ emotional problem	6,43 ± 1,397	3,43 ± 1,902	0,002 [b]
	SDQ behavioral problem	2,86 ± 2,854	1,86 ± 1,773	0,062 [b]
	SDQ hyperactivity-inattention	5,57 ± 1,718	3,57 ± 1,813	0,006 [b]
	SDQ peer problems	5 (0-7)	3 (0-6)	0,102 [a]
	SDQ difficulty domain	18,71 ± 6,157	12,14 ± 5,900	0,001[b]
	SDQ prosocial	7 (1-10)	9 (1-10)	0,317 [a]
a= Wilcoxon test b= paired t-test				

Table No.2. Comparison of Emotional Conditions Between Control and Intervention Groups

		Median (minimum-maximum) Mean ± Standard Deviation		
		Control group	Intervention group	P value
Pretest	SDQ emotional problem	4,71 ± 1,113	6,43 ± 1,397	0,026 [a]
	SDQ behavioral problem	3,00 ± 1,528	2,86 ± 2,865	0,909 [a]
	SDQ hyperactivity-inattention	5 (5-7)	5 (4-8)	0,642 [b]
	SDQ peer problems	2 (1-4)	5 (0-7)	0,155 [b]
	SDQ difficulty domain	16 (11-20)	22 (10-24)	0,223 [b]
	SDQ prosocial	6,57 ± 1,134	6,43 ± 3,259	0,915 [a]
Score difference	SDQ emotional problem	0 (0-1)	-3 (-5-(-1))	0,001 [b]
	SDQ behavioral problem	0 (0-0)	-1 (-3-0)	0,025 [b]
	SDQ hyperactivity-inattention	0 (0-1)	-2 (4-0)	0,003 [b]
	SDQ peer problems	0 (0-0)	0 (-2-0)	0,061 [b]
	SDQ difficulty domain	0 (0-1)	-6(-11- (-3))	0,001 [b]
	SDQ prosocial	0 (0-0)	0 (0-2)	0,317 [b]
a = two sample t-tests b = Mann-Whitney test				

Comparison Between Control and Treatment Groups: Before therapy, significant differences ($p<0.05$) were found between the control and treatment groups only in the emotional problems subscale, while other subscales showed no differences ($p\geq0.05$). After therapy, significant differences ($p<0.05$) were observed in emotional problems, behavioral problems, hyperactivity-inattention, and total difficulties, while peer problems and prosocial subscales remained unchanged ($p\geq0.05$) (Table 2).

DISCUSSION

Emotional regulation disorders affect approximately 25–45% of children with ADHD, often manifesting as excessive emotional responses that are inappropriate for the social context or developmental stage.[10] These challenges are frequently associated with sensory processing difficulties, which can contribute to the development of emotional and behavioral problems, particularly in children who tend to internalize emotions, such as girls.[15,17]

This study observed a higher proportion of male participants (71.4%) compared to females (28.6%), which aligns with previous research indicating that ADHD symptoms are more easily detected in boys during childhood.[5,18,19] This discrepancy is largely due to differences in symptom presentation between genders. Boys with ADHD tend to exhibit more overt hyperactive and impulsive behaviors, which are more noticeable in classroom and home settings, prompting earlier diagnosis. In contrast, girls with ADHD often compensate for symptoms, delaying functional impairment and diagnosis until adolescence or adulthood.[17,18] Their symptoms frequently manifest as emotional difficulties resembling depression or anxiety, making early detection more challenging.[17] Furthermore, parents and teachers may be less adept at recognizing internalizing symptoms in girls, particularly inattention, which is often masked or compensated for and more commonly associated with the inattentive subtype of ADHD.[20,21] These factors likely contributed to the finding that emotional problems were more prominent among female participants in this study.

Screening in this study utilized the ACTRS, a tool assessed by teachers. While ACTRS is effective for detecting externalizing symptoms, prior studies suggest that teacher-based assessments may underestimate internalizing and inattentive symptoms, particularly in girls. Teachers are more likely to notice disruptive behaviors that interfere with classroom activities, whereas subtler signs of ADHD, such as difficulty maintaining attention or emotional dysregulation, may go unnoticed. Some studies recommend incorporating self-report questionnaires to better identify these symptoms in females.[17,21] Future research may benefit from a multi-informant approach, integrating teacher assessments, parent reports, and child self-reports to provide a more comprehensive evaluation of ADHD symptoms and their impact on emotional regulation.

The results demonstrated significant improvements in emotional and behavioral outcomes among children with ADHD symptoms following Sensory Integration Therapy. Compared to the control group, the intervention group showed notable progress in emotional regulation and behavioral adaptation. Sensory Integration Therapy, delivered through sensorimotor games, provides structured stimuli that train children to respond adaptively to sensations, reduce distress, and improve concentration, motor skills, and social relationships. These games help modulate physiological, psychological, and behavioral

states of emotion, which can alleviate ADHD symptoms.[22]

The effectiveness of Sensory Integration Therapy can be attributed to its ability to address underlying sensory processing challenges that contribute to emotional dysregulation. Many children with ADHD exhibit heightened sensitivity to environmental stimuli, leading to increased emotional reactivity and difficulty maintaining attention. By engaging in structured sensorimotor activities, children learn to process and integrate sensory input more effectively, reducing maladaptive emotional responses and improving overall behavior.[12,22] This aligns with previous findings that suggest sensory-based interventions can help children develop better coping strategies, allowing them to navigate their environments with greater ease.

Additionally, the school-based setting of this intervention plays a crucial role in its success by providing a structured and consistent environment where children can receive regular sensory integration sessions as part of their daily routine. Unlike clinical settings, which may present logistical and financial barriers for families, school-based programs ensure accessibility and continuity of care, highlighting the potential for broader implementation of Sensory Integration Therapy, particularly as an early intervention strategy for children displaying ADHD symptoms. The observed improvements in this study underscore the interconnected nature of sensory processing, emotional regulation, and social functioning. Emotional dysregulation in children with ADHD often leads to peer difficulties, classroom disruptions, and increased frustration with academic tasks. By enhancing sensory processing abilities, children become better equipped to self-regulate, leading to improved social interactions and academic performance. This suggests that Sensory Integration Therapy not only mitigates core ADHD symptoms but also fosters overall well-being by promoting self-confidence and adaptive coping mechanisms.

Despite these promising findings, this study has limitations. The small sample size limits generalizability, requiring larger, more diverse studies for confirmation. The non-blinded design may introduce bias, as teachers and parents were aware of group assignments. Reliance on teacher and parent reports may not fully capture children's experiences. Lastly, the study focused on short-term outcomes, leaving long-term effects of Sensory Integration Therapy unexplored.

CONCLUSION

This pilot study demonstrates the potential of school-based Sensory Integration Therapy to improve emotional and behavioral outcomes in children with ADHD symptoms. By addressing sensory processing challenges, it supports emotional regulation, adaptive behaviors, and social skills. While promising, further research is needed to assess long-term effects, refine strategies, and integrate Sensory Integration Therapy into broader ADHD treatment plans. Expanding access to these interventions may significantly benefit children, helping them better navigate academic and social environments.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Vini Victoria, Yunias Setiawati
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Acute Febrile Illness of Varied Etiology: Analogy in Clinical Presentation and Baseline Investigation

Darshan Kumar[1], Shaheen Bhatty[2], Pawan Kumar[2] and Syed Muhammad Kashif[2]

ABSTRACT

Objective: Researchers examined acute febrile illness (AFI) manifestations together with laboratory test results from patients visiting a tertiary care facility in Karachi.

Study Design: Descriptive Cross-Sectional study

Place and Duration of Study: This study was conducted at the Dr. Ruth KM Pfau Civil Hospital together with Dow University Hospital in Karachi. Start of study October 2022 completion July 2023.

Methods: Researchers studied a population of 300 adults between 20 and 70 years old with fever duration between 3 and 14 days. The data collection included patient demographics along with symptoms and medical history in addition to CBC, LFTs, cultures, malaria/dengue tests, and radiological tests. The study utilised both descriptive and inferential analysis methods.

Results: The research examined a total of 300 patients who had an average age of 38.5 years (SD: 12.4) and a female participant ratio of 58.66%. All patients experienced fever, while body aches presented in 56.33% of cases, alongside headaches in 53.3% and joint pain in 51.3%. Pallor was detected in 45.66% of patients, followed by hepatosplenomegaly in 16.33% of patients, and 12.33% presented with jaundice. Lab tests identified E. coli in 12.0% of patients, alongside Salmonella in 9.7% and dengue in 18.9%, and malaria in 22.33% of the cases. Chest scans displayed both consolidation patterns and pleural effusion in 6.3% and 3.1% of cases, showing how full diagnostic evaluation matters for AFI patients.

Conclusion: Patient care in limited resource contexts requires better diagnostic systems and location-based guidelines for dengue and malaria with advanced detection methods, according to this research.

Key Words: acute febrile illness, dengue, malaria, diagnostic markers, comorbidities, tertiary care.

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INTRODUCTION

Acute febrile illness (AFI) occurs often in clinical settings and encompasses numerous infectious agents, including vector-borne parasites and respiratory, gastrointestinal, and enteric fever microorganisms. Diagnosis and treatment face difficulties in the tropical and subtropical regions because patients often experience similar symptoms, including fever and body pain alongside gastrointestinal problems.

[1.] Department of Medicine, DIMC / Dow University Hospital Ojha Campus, Dow University Health Sciences Karachi.
[2.] Department of Medicine, DMC/ Dr. Ruth K.M. Pfau Civil Hospital, Dow University Health Sciences Karachi.

Correspondence: Dr. Syed Muhammad Kashif, Associate Professor of Medicine, Department Medical Unit -3, DMC/ Dr. Ruth K.M. Pfau Civil Hospital, Dow University Health Sciences Karachi.
Contact No: 03323118380
Email: kashifleo7@hotmail.com. syed.kashif@duhs.edu.pk

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The city of Karachi experiences periodic febrile illness outbreaks due to its dense population distribution, thus requiring prompt diagnostic services for proper therapeutic approaches. Fever functions as a natural body mechanism that increases temperature when infections, inflammation, or medical conditions exist within the body. The body uses it as a protective mechanism that controls temperature through shivering and sweating despite being unrelated to disease. The normal body temperature exists between 97.5°F and 98.9°F. Medical specialists classify fever into low-grade (99–100°F), moderate (101–104°F), high-grade (above 104°F), and hyperpyrexia (above 106°F). Seizures can occur at extremely high temperatures.[1, 2] Patients with fever experience symptoms such as sweating, chills, body pain, and headaches while feeling weak, along with vomiting, diarrhoea, coughing, exhaustion, lethargy, depression, drowsiness, and dehydration.[3] AFI presents as a three- to fourteen-day fever in tropical and subtropical regions because of malaria, dengue, enteric fever, and respiratory infections.[4] The severity of malaria varies between different cases, while vivax malaria now demonstrates multiple and extensive symptom clusters. Dengue fever

causes different disease manifestations, which might lead to brain swelling.[5,6]

The difficulty in diagnosing AFI stems from its general symptoms that lead to delayed testing and end up requiring physicians to begin treatment without a confirmed diagnosis. Advanced laboratory diagnostics are absent from resource-limited settings, which produces challenges for accurate diagnosis that lead healthcare providers to overuse antimicrobials, thus generating antimicrobial resistance. This research examines how patients with AFI are evaluated in a tertiary care facility by assessing their symptoms and physical signs and test results with the goal of determining which traits best identify common infectious causes. This study establishes diagnostic patterns, which will enhance early detection along with optimising care methods and minimising incorrect antibiotic therapy implementation.

METHODS

The investigation took place at the medical departments of Dr. Ruth KM Pfau Civil Hospital Karachi and Dow University Hospital, Ojha Campus. Research lasted ten months, during which eight months were dedicated to data collection, followed by two months of statistical analysis.

The research included 300 patients between 20 and 70 years old who experienced AFI symptoms defined by their fever duration between 3 and 14 days. The study excluded patients with chronic renal failure along with chronic liver disease and HIV and autoimmune disorders and patients taking steroids or immunomodulatory medications.

All patients underwent documentation of demographic information combined with clinical history and full physical examinations. The laboratory assessment included complete blood count (CBC) and renal and liver function tests (RFTs and LFTs) with blood culture together with a urine detailed report (DR) and urine culture, malaria parasite examination, and dengue serology (NS1 antigen and IgM and IgG). The healthcare team obtained both chest X-rays and abdominal ultrasounds as imaging procedures for diagnostic confirmation. The study obtained approval from the Ethics Committee (Ref:IRB-2669/DUHS/approval/2022/1012) before initiation, ensuring the participants' confidentiality and providing a detailed explanation of the study.

The data analysis was accomplished through the use of SPSS version 23.0. Statistical analysis involved descriptive statistics to present results through both frequency distribution and percentage of occurrences while also employing means and standard deviations. The categorical variables received Chi-square testing, whereas ANOVA analysed continuous variables. The research adopted a significance level of $p < 0.05$ to establish statistical importance.

RESULTS

The study involved 300 patients who had an average age of 38.5 years (SD: 12.4). Female subjects accounted for 58.66% of the total patients, while patients between 30 and 50 years old composed 48.3% of participants. The prevalence of hypertension reached 47.3%, and diabetes mellitus affected 49.3% of patients, alongside 15% having chronic obstructive pulmonary disease. Table 1.

Table No.1: Patient Demographics and Symptoms Analysis Patient demographics: total patients: 300

Age distribution		Smoking Status	
Age 15 to 30 years	95 patients (31.7%)	Current Smokers	100 (33.33%)
Age 30 to 50 years	145 patients (48.3%)	Quit Smoking	57 (19.0%)
Age more than 50 years	60 patients (20.0%)	Never Smoked	143 (47.66%)
		Pan chewing	41 (13.7%)
Comorbidity			
Hypertension (HTN)	142 (47.3%)	Chronic Obstructive Pulmonary Disease (COPD)	45 (15.0%)
Diabetes Mellitus (DM)	148 (49.3%)	Asthma	35 (11.7%)
Male	124 (41.33%)	Female	176 (58.66%)

Table No.2 : **Symptoms Analysis**

Symptoms Analysis			
Fever	= 300 (100%)		
Chills & Rigors	158 (52.7%)	Confusion	54 (18.0%)
Cough (Dry/ Productive)	85 (28.3%)	Headache	160 (53.3%)
Diarrhea	146 (48.7%)	Throat Pain	75 (25.0%)
Constipation	143 (47.7%)	Joint Pain	154 (51.3%)
Shortness of Breath (SOB)	152 (50.7%)	Gum Bleeding	55 (18.3%)
Chest Pain	155 (51.7%)	Blood in Stool	16 (5.3%)
Pain in Abdomen	141 (47.0%)	Blood in Urine	63 (21.0%)
Rashes	111 (37.0%)	Jaundice	37 (12.33%)
Pallor	137 (45.66%)	Body Aches	169 (56.33%)

All patients presented with fever (100%). The most common symptoms in our patient group included body aches affecting 56.33% of individuals, headaches in 53.3% of patients, followed by joint pain in 51.3% of patients, and diarrhoea affecting 48.7% of patients. The symptoms of confusion and bleeding gums were found in 18.0% and 8.3% of patients, respectively. Table 2

Physical examination showed pallor in 45.66% of patients, alongside hepatosplenomegaly in 16.33% of the total and 12.33% presenting with jaundice. Among patients, the mean temperature measurement was 101.001°F (SD: 1.1778), and sinus tachycardia appeared in 65.66% of cases. Table 3.

Medical tests revealed Escherichia coli through urine cultures in 12.0% of patients, alongside Salmonella detection in 9.7% of blood cultures. Test results showed that 18.9% of patients had dengue infection, while malaria affected 22.33% of patients. The radiological investigations revealed lung consolidation in 6.3% of cases, alongside pleural effusion in 3.1%. Table 4

Table 3: Signs Analysis

Signs Analysis				
	Minimum	Maximum	Mean	St deviation
Temperature (°F)	99.0	103.0	101.001	1.1778
Systolic BP (mmHg)	110	150	129.97	11.413
Diastolic BP (mmHg)	70	90	79.90	6.187
Pulse (bpm)	60	100	79.75	11.367
Respiratory Rate	18	30	23.96	3.640
O2 Saturation (%)	94	99	96.38	1.730
BMI	14.69	41.26	24.81	4.66
R/R	18	30	23.96	3.64
JVP	9 (3%)	L.N	15(5%)	
Pallor	137 (45.66%)	Hepatosplenomegaly		49 (16.33%)
Jaundice	37 (12.33%)	Coated Tongue		79 (26.33%)
Cyanosis	2 (0.66%)	Chest	elevated respiratory rates (mean: 23.96 breaths per minute), crypts and bronchial breath in 35 (11.66%)	
Thyroid	19 (6.66%)	CNS	confusion and altered sensorium in 56 (18.66%)	
Dehydration	77 (25.66%)	CVS	Sinus tachycardia 197 (65.66%)	
Edema	10 (3.33%)	Muskuloskeletal	Myalgia 80 (26.66%) ; arthralgia 95 (31.66%)	

Table No.4: Summary of Organism Findings and Diagnostic Test Results

Urine C/S		Dengue Antigen	Dengue Antibodies
E. coli	36 (12.0%)	48 (12.6%)	72 (18.9%)
Pseudomonas	6 (2.0%)	X-ray Chest	
Staphylococcus aureus	8 (2.7%)	Consolidation	24 (6.3%)
		Patchy Infiltrate	6 (1.6%)
Streptococcus	12 (4.0%)	Pleural Effusion	12 (3.1%)
		Pulmonary Edema	6 (1.6%)
Blood C/S			
Klebsiella	10 (3.3%)	Ascites	42 (11.0%)
Salmonella	29(9.7%)	Mild Hepatomegaly	12 (3.1%)
Staphylococcus aureus	5(1.7%)	Splenomegaly	48 (12.6%)
Streptococcus	6 (2.0%)	Malaria	67 (22.33%)
Escherichia coli	25 (12%)		

DISCUSSION

This research delivers important knowledge about acute febrile illness (AFI) clinical characteristics as well as laboratory results of patients seeking care in tertiary facilities. The results demonstrate how multiple infection origins, shared illness features, and substantial comorbidity impact AFI diagnosis and treatment in this group. Researchers obtained significant information about the demographic background along with symptoms and test outcomes that occur in patients who have febrile illness.[7,8]

This study delivers crucial knowledge about the epidemiological and clinical traits as well as diagnostic test results from patients who have febrile illnesses. Our study results show consistency with previous research indicating younger adults, especially women, tend to develop febrile illnesses. Researchers studied 300 patients who demonstrated a mean age of 38.5 years within this middle-aged population group. The study sample included more females than males at 58.66% because females show either different healthcare behaviour patterns or a greater chance of developing certain febrile diseases[9]. A large number of patients between the ages of 30 and 50 years (48.3%) makes it important to focus public health initiatives on this population segment.

Subjects within this population group demonstrate elevated incidence rates of hypertension (47.3%), diabetes mellitus (49.3%), and chronic obstructive pulmonary disease (COPD 15%), which escalate the complexity of AFI infections. Such additional health conditions generate advanced disease severity while influencing treatment results, which in turn heighten mortality threats. The evidence of COPD makes this patient group vulnerable, so healthcare providers should maintain extra clinical awareness. Physicians should measure comorbidities during febrile patient assessments because they must implement thorough proactive approaches to enhance treatment results.[10]

All study patients (100%) displayed fever due to the research criteria for acute febrile illness. According to Khan et al[11], these common symptoms of body aches (56.33%), headaches (53.3%), joint pain (51.3%), and diarrhoea (48.7%) reflect conventional presentations of dengue, malaria, and enteric fever infections. The report suggests that uncommon symptoms such as confusion (18.0%) and gum bleeding (8.3%) warrant serious medical assessment due to their association with dengue hemorrhagic fever or systemic infections, according to Varatharaj[12]. Patients with important health conditions need careful clinical evaluation when such symptoms appear because they occur infrequently among febrile patients. A prompt diagnosis of hidden medical conditions becomes possible through detecting faint cues, which allows physicians to offer suitable treatment methods.[13]

Physical examination results showed pallor in 45.66% of patients who present with AFI, which could indicate two possible conditions: anaemia or serious systemic illness. Evaluation of the liver and spleen found enlargement in 16.33% of cases as well as jaundice in 12.33% of patients, indicating that additional diagnostic assessments are needed to determine the underlying infectious or haematological causes[14]. Clinical findings showed evidence of systemic inflammation through patients' recorded average temperature of 101.0°F (SD: 1.1778), and sinus tachycardia presented itself in 65.66% of cases due to infection-induced stress.[15] The absence of distinct disease markers allows healthcare professionals to evaluate disease severity as well as monitor its progression since these nonspecific indicators require continuous monitoring and prompt medical interventions.

Medical tests showed various causes precipitating each condition. E. coli bacteria were found through urine tests in 12.0% of patients, indicating that urinary tract infections served as potential infection sources[16]. The detection of Salmonella in 9.7% of blood cultures during tests indicated enteric fever as the likely reason for AFI in these endemic areas[17]. Dengue infection combined with malaria accounted for significant portions of cases (18.9% and 22.33%, respectively) because both diseases remain highly endemic in the research area[18,19]. The University of Gondar Hospital in Ethiopia studied febrile illness aetiologies that reached a diagnosis rate of 20.5%, and malaria and dengue infections were commonly occurring[20]. The collected data verifies that malaria remains a major cause of fever symptoms, and medical personnel might neglect arboviral infections. The research combined with the Ethiopian study demonstrates the requirement for better testing methods, particularly molecular approaches, to identify unique febrile illness causes and reduce clinical dependence. Patients with SARI (Severe Acute Respiratory Infection) tended to show consolidation at 6.3% and pleural effusion at 3.1% during radiological examinations due to atypical pneumonia or tuberculosis infection[21]. Research results demonstrate that patients may develop dangerous conditions that need immediate medical response. The high numbers of active dengue (18.9%) infections and malaria (22.33%) supply key evidence to demonstrate that endemic regions need better diagnostic procedures.

Multiple Indian healthcare centres participated in research by Mørch et al[22], which delivered important data about acute undifferentiated fever (AUF) causes in epidemic-prone regions. Hospitalised patients presented with malaria in 23% of cases, alongside dengue in 17% and scrub typhus in 10%, and 7% had leptospirosis, while chikungunya occurred in 6% of patients. The laboratory analysis discovered a major convergence point between dengue and chikungunya infections because dengue virus was found in 26% of chikungunya patient blood samples. Processing febrile illness diagnoses requires innovative diagnostic methods because endemic areas present complicated diagnostic scenarios.

Initial presentation side effects of AFI together with laboratory results make it difficult to identify the correct diagnosis accurately. Rapid diagnostic tests along with localised management protocols become essential because dengue and malaria affect many patients in this cohort[23]. A multidisciplinary strategy becomes necessary to handle acute and chronic health problems because patients have significant medical

illnesses[24]. The study demonstrated that diagnostic difficulties and missed subclinical infections needed clarification. Standard diagnostic techniques failed to accurately measure combined infections based on data collected by the study. The collected observational data validates diagnostic approaches that distinguish various typical febrile illnesses within our resource-limited area.

This study has several limitations. The exclusive use of one intervention centre restricts how broadly healthcare practitioners can generalise study findings throughout other localities or healthcare service areas. Diagnostic biases in this study emerged from depending on clinical and laboratory data, while the lack of molecular diagnostic methods likely resulted in failing to detect some possible aetiologies[25]. Research should implement state-of-the-art diagnostic equipment together with multiple medical facility collaborations to produce stronger research results in the future.

CONCLUSION

Research at the tertiary care level demonstrates the necessity for standardised diagnostic methods to deal with AFI alongside its associated ailments. The research findings provide key clinical markers and laboratory values, which will help create local testing and treatment methods to enhance patient results. The high prevalence of comorbidities and infectious agents necessitates a comprehensive approach to diagnosis and management. Future efforts should dedicate resources to long-term evaluation of treatment success because preventive public health measures that fight comorbidities will boost disease management and patient health restoration.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Darshan Kumar, Shaheen Bhatty
Drafting or Revising Critically:	Pawan Kumar, Syed Muhammad Kashif
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Effect of Eye Care Competence Inventory Guidelines on Nurses' Clinical Competence in Eye Care for Unconscious Patients

Zainab Salman Dawood and Serwan Jafar Bakey

ABSTRACT

Objective: Assessing nurses' clinical competency in providing eye care for patients with altered consciousness in intensive care units, and determining the relationship between nurses' sociodemographic traits and their clinical competency in providing eye care for unconscious patients.

Study Design: A pre-experimental (one group pre-test and post-test) study

Place and Duration of Study: This study was conducted at the AL-Basrah teaching hospitals in the AL-Basrah governorate from 22nd February 2024 to 30th September 2024.

Methods: The present study included a non-probability purposive sample of forty nurses, both male and female, who cared for patients with altered levels of consciousness at Intensive Care Units.

Results: There were significant differences between the two-time levels of all components of competencies (knowledge, practice, and attitude) at P = 0.000 for all domains.

Conclusion: The low and moderate level mean at the pre-test to high level of knowledge mean at posttest time duration, shifting in the mean score to very high attitudes at the post-test time, significant shifting in the mean of score of practice from low level to high level which revealed improving in nurses' practices about eye care.

Key Words: Nurses' clinical competence, Eye care for unconscious patients

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INTRODUCTION

The majority of persons admitted to intensive care units suffer from an altered level of consciousness, sensory deprivation, or any other disability which in turn affects activities of daily living as a result of disease.[1] Because the nursing staff plays a crucial role in critical care units around the world, nurses must possess specialized expertise to give critically ill patients the best, safest, and highest level of care possible.[2] The reason behind the importance of knowledge and evidence-based practices for critical care nurses is to promote high-quality and safety of nursing care to patients.[3] Evidence-based care provided by a clinically competent nurse can enhance or promote the autonomy of patients, safety, and continuity of care.[4] In addition, the main responsibilities of intensive care unit nurses are monitoring patients 24 hours a day and giving efficient direct care to them.[5]

College of Nursing, University of Baghdad, Iraq.

Correspondence: Dr. Zainab Salman Dawood, Ph.D. Scholar, College of Nursing, University of Bagdad, Iraq.
Contact No: 009647722041943
Email: zainab.salman@uobasrah.edu.iq

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Among all healthcare professionals, nurses play the most important role in a healthcare setting. Nevertheless, they also face risks, challenges, and issues.[6] The demands of their line of work require them to handle heavy workloads, put in extra hours, communicate with patients and their companions, and interact with the managers of the institution.[7]

A set of guidelines known as clinical competence for nurses directs critical care nurses to be capable of providing safe, high-quality care while safeguarding the population's health.[8] All of a critical care nurse's credentials, which include knowledge, practice, attitude, and values, are included in nursing competency.[9]

Ocular surface disease is a frequent complication in these patient populations that is rarely given clinical attention to prevent it.[10] A change in consciousness, the lack of a blinking reflex, or blinking less than five times per minute were among the various conditions that led to impairment of the eye's protective mechanisms.[11] The occurrence of ocular abnormalities was highly correlated with the patient's state of consciousness and the length of stay in intensive care units. Among ICU residents, ocular complications range from 42-60%.[12] According to earlier studies, the incidence rate of eye disorders among intensive care unit residents ranged from 3.6% to 89.3%, with an average occurrence of 6.8 days after admission.[13]

In addition to ongoing training and monitoring, the nursing staff should give the patient's eye special

attention at the start of admission because frequent eye care lowers the incidence of ocular surface issues.[14] Along with providing eye care and treatment, the nurse is in charge of evaluating and diagnosing infection-related eye problems and preventing consequences.[15]

METHODS

This pre-experimental design (one group pre-test and post-test) was employed at Intensive Care Units in AL-Basrah governorate from 22nd February 2024 to 30th September 2024. A pre-test was administered to all study participants, and a post-test was administered to the same participants following the application of the guidelines. An approach known as non-probability (purposive) sampling was used to select forty nurses from the intensive care units. Nurses at intensive care units in four teaching hospitals were included. All nurses who refused participation and nurses who did not complete the educational program were excluded. The program was applied in two lectures theoretical and practical sessions, each lecture lasted approximately 45 minutes. The post-evaluation of each individual started (3 weeks) apart from the date of the last lecture. The Eye Care Competence Inventory, a previously validated questionnaire with 35 items divided into three areas (knowledge, attitude, and practice), served as the primary instrument for this investigation. It focuses on the demographic information of the nurses, including their age, sex, education, years of experience, and eye care training. There were eighteen multiple-choice questions in the knowledge section. The score was zero for wrong answers and one for right answers. A 5-point Likert scale was used to score the seven items that make up the attitude domains (from 1 to 5). A score on a 5-point Likert scale (ranging from 1 to 5) comprised the practice domains which consist of 10 items on nurses' eye care practice. The data was analyzed through SPSS-26. Wilcoxon signed ranks test, Contingency Coefficient, and Kolmogorov-Smirnov test were used.

RESULTS

Table No.1: Sociodemographic distribution of nurses' features (n=40)

Variable	No.	%
Gender		
Male	13	32.5
Female	27	67.5
Level of Education		
Higher school of nursing	13	32.5
Diploma Degree in Nursing	9	22.5
Bachelor's degree in nursing	18	45
Sharing in a training session		
No	34	85
Yes	6	15
Age (years)	29.45±5.89	
Years of experience in nursing	7.22±6.18	

With a standard deviation of 5.89 years, the average age was 29.45 years. Moreover, women comprised 67.5 percent of the study sample, making them the majority. In terms of educational background, 45% of the research sample has a nursing bachelor's degree. The study sample had a minimum of one year and a maximum of 24 years of nursing experience, with a mean of 7.22 years and a standard deviation of 6.18 years. During training sessions, 85% of the study participants did not share (Tables 1-2).

At the post-test level, there was a substantial relationship between nurses' years of experience, age, and educational attainment and their understanding of eye care (P values =.000, 004 and .019, respectively) [Table 3]. There was no association between nurses' attitudes about eye care with their demographic characteristics at a P value higher than 0.05 (Table 4). Nurses' practices were significantly correlated with their age and year of experience, with P values of.001 and.005, respectively (Table 5).

Table No.2: Comparison between pre-test and post-test knowledge, attitude, and practice scores for the study sample at pre-test and post-test time duration (N=40)

Level and groups	M	SD	Wilcoxon Signed the Rank test					
			Type of rank	N	Mean Rank	Sum of Ranks	Z	P value
Pre-test and post-test knowledge	.32	.16	Positive ranks	0	.00	.0	-5.51	.000
	.83	.12	Negative ranks	40	20.5	820		
			Ties	0				
Pre-test and post-test Attitude about	3.95	.49	Positive ranks	2	8.25	16.5	-5.2	.000
	4.74	.32	Negative ranks	37	20.64	763.5		
			Ties	1				
Pre-test and post-test Practice About	1.28	.33	Positive ranks	0	.0	.0	-5.51	.000
	2.44	.37	Negative ranks	40	20.5	820		
			Ties	0				

Table No.3: Association between knowledge of nurses about eye care with their demographic characteristics (N=40)

Sociodemographic characteristics		Pre-test					Post-test				
		Low	Moderate	High	Contin-gency Coeffi-cient	Sig. P value	Low	Mode-rate	High	Contingency Coefficient	Sig. P value
Age	Total	26	14	-	16.6	.27	-	3	37	.40	0.000
Gender	Male	11	2	-	.274	.071	-	1	12	.005	.97
	Female	15	12	-			-	2	25		
Level of education in nursing	Preparatory	9	4		1.454	.48	-	-	13	.467	.004
	Diploma	7	2	-			-	3	6		
	Bachelor's	10	8	9			-	-	18		
Years of experience	Total	26	14	-	.446	.825	-	3	37	.645	.019
Training sessions in Eye care	No	21	13	-	.15	.307	-	2	32	.145	.355
	Yes	5	1	-			-	1	5		

Table No.4: Association between attitudes of nurses about eye care with their demographic characteristics (N=40)

Sociodemographic characteristics		Pre-test							Post-test						
		Very low	Low	Mode-rate	High	Very High	Contin-gency Coeffi-cient	Sig. P value	Very low	Low	Mode-rate	High	Very high	Contin-gency Coeffi-cient	Sig. P value
Age	Total	-	1	6	20	13	.66	.878	-	-	1	-	39	.57	.14
Gender	Male	-	-	2	7	4	.117	.906	-	-	1	-	12	.225	.14
	Female	-	1	4	13	9			-	-	-	-	27		
Level of education in nursing	Preparatory	-	1	-	8	5	.37	.387	-	-	1	-	12	.22	.345
	Diploma	-	-	1	5	3			-	-	1	-	9		
	Bachelor's	-	-	5	7	5			-	-	-	-	18		
Years of experience	Total	-	1	6	20	13	.667	.667	-	-	1	-	39	.32	.99
Training sessions in Eye care	No	-	1	4	16	13	.316	.316	-	-	1	-	33	.067	.67
	Yes	-	-	2	4	-			-	-	-	-	6		

Table No. 5: Association between practices of nurses in eye care with their demographic characteristics (N=40)

Sociodemographic characteristics		Pre-test					Post-test				
		Poor	Fair	Good	Contin-gency Coeffi-cient	Sig. P value	Poor	Fair	Good	Contin-gency Coeffi-cient	Sig. P value
Age	Total	37	3	-	.486	.576	1	16	23	.767	.001
Gender	Male	11	2	-	.203	.18	1	5	7	.225	.334
	Female	26	1	-			-	11	16		
Level of education in nursing	Preparatory	12	1	-	.08	.87	1	4	8	.34	.25
	Diploma	8	1	-			-	6	3		
	Bachelor's	17	1	-			-	6	12		
Years of experience	Total	37	3	-	.56	.22	1	16	23	.758	.005
Training sessions in Eye care	No	32	2	-	.14	.35	1	12	21	.226	.34
	Yes	5	1	-			-	4	2		

DISCUSSION

In the present study, the mean age was 29.45±5.89 years old. The mean age of nurses is consistent with an interventional study that studies the effect of ECG training on eye care clinical competence among critical care nurses.[16] Seventy-five nurses were aged 18-25 years with a mean age of 29.95±4.93. Also, the majority of the nurses in this study were between the ages of 20 and 29, which is consistent with the findings of several other studies.[17,18] More over half of the participants in this study 67.5%-were female. This study is in line with one carried out in Iran that discovered that 71.3% of study participants were female.[11] These results also, agreed with several studies[19, 20] which state the majority of the study sample was female.

Regarding educational attainment, 45% of the participants hold a bachelor's degree in nursing. This study is consistent with Güler et al.[21] They discovered that most of the nurses in intensive care units under study had bachelor's degrees. Also, the results of this study agreed with several studies[22,23] which mention the sample were graduates from secondary school in nursing.

The minimum years of experience of the participants in nursing were one year and the maximum years was 24 years in which the mean of experience was 7.22 years with SD being 6.18 years. This result is in agreement with another study Quasi-experimental research design. The finding represented that (50%) of studied nurses have years of experience between five to less than ten years of experience. Eighty-five percent of the study population did not share throughout training sessions. This result is consistent with a research conducted in 30 that revealed 91.1% of the nurses had not completed eye care training.

The results showed that, for every domain, there were statistically significant variations between the two-time levels of every competency component at P = 0.000. These results concurred with Momeni Mehrjardi et al[14], which demonstrated that the post-intervention phase's overall clinical competence score considerably increased in comparison to the pre-intervention phase.

The findings showed that, at the post-test level, nurses' knowledge of eye care was significantly correlated with age, education level, and years of experience (P values =.000, .004, and.019, respectively). This outcome aligns with Jaddoue[24], the findings indicated that the nurses' years of experience, age, and level of education were statistically significantly positively correlated with their total eye care score after the program was put into place (p values of 0.046, 0.000, 0.000, and 0.005).

Results presented that there was no association between nurses' attitudes regarding eye care with their demographic characteristics at a P value higher than .05. This finding correlate with Ebadi et al[11] represents a statistically significant positive correlation between nurses' attitudes regarding eye care and years of experience. The findings showed a substantial correlation between the age and year of experience of nurses and their practices (P values =.001 and.005, respectively). These findings were corroborated by Sayed[25] which found that, following the program, the total practice of the nurses in question was positively correlated with their age, years of experience, and type of intensive care unit (ICU), with p values of 0.046, 0.000, 0.000, and 0.005, respectively. This finding contradicts a study[24] that found no statistically significant correlations between the age or number of years of experience that nurses had in intensive care units and their behaviors when caring for unconscious patients.

CONCLUSION

Age, education level, and years of experience were significantly associated with nurses' knowledge of eye care at the post-test level; nurses' attitudes toward eye care were not associated with their demographic characteristics and nurses' practices were significantly associated with their age and year of experience.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zainab Salman Dawood, Serwan Jafar Bakey
Drafting or Revising Critically:	Zainab Salman Dawood, Serwan Jafar Bakey
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Thyroxine Therapy for Recurrent Pregnancy Loss in Hypothyroid Women

Sarah Al-Musawi and Kamal Al-Jawdah

ABSTRACT

Objective: To estimate the optimal TSH level for starting T4 treatment in subclinical hypothyroidism.
Study Design: Non-randomized clinical trial study
Place and Duration of Study: This study was conducted at the Tertiary Obstetric Hospital at Al-Kindy College of Medicine, Iraq from March 2022 to May 2023.
Methods: It comprised 77 cases. The participants were women with TSH levels above 2.5 mU/L and with RPL. The study had two groups based on thyroid-stimulating hormone (TSH) levels (TSH level 2.5-4 mU/L and TSH ≥4 mU/L groups). Participants received T4 therapy and were followed for 6 months. The primary outcome was the rate of successful pregnancy, followed until delivery and the gestational age and birth weight of the newborn.
Results: The rate of successful pregnancy, gestational age, and birth weight were not different between the two groups. The titer of thyroid peroxidase antibodies was significantly reduced after 6 months of T4 therapy, but the starting threshold of the treatment did not influence the amount of reduction of the titer. Regression analysis showed, the titer of thyroid peroxidase antibodies after 6 months of treatment was significantly associated with increased rate of successful pregnancy.
Conclusion: Reducing the thyroid-stimulating hormone treatment threshold alone may not guarantee improved pregnancy outcomes. The study suggests that T4 therapy's benefits may be more closely linked to antibody titer changes.

Key Words: Levothyroxine, Thyroid-stimulating hormone (TSH), Thyroid peroxidase antibodies, Recurrent miscarriage, Pregnancy outcomes

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INTRODUCTION

Recurrent pregnancy loss has been linked to subclinical hypothyroidism. Debates regarding levothyroxine (T4) starting thresholds as the American Thyroid Association suggested to decreases the threshold of starting the treatment of subclinical hypothyroidism from 4 mU/L to 2.5 mU/L.

According to the European Society for Human Reproduction and Embryology (ESHRE) guidelines, recurrent pregnancy loss (RPL) is defined as the loss of two or more pregnancies.[1] Thyroid autoimmunity affects about fifth the cases of RPL women.[2] Subclinical hypothyroidism (SCH) and thyroid peroxidase antibodies (TPOAb) positivity are associated with adverse pregnancy outcome.[3]

Department of Obstetrics & Gynaecology, Al-Kindy College of Medicine, University of Baghdad, Iraq.

Correspondence: Sarah Al-Musawi, Lecturer, Obstetrics & Gynaecology, Al-Kindy College of Medicine, University of Baghdad, Iraq.
Contact No: +44756310093
Email: sarah.al-musawi@nhs.net

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Levothyroxine medication reduced the risk of miscarriage and increased fertility in women with thyroid disease, according to research by Dal Lago et al.[4] Recently, American Thyroid Association[5] suggested to decrease the threshold of starting the treatment of SCH from 4mU/L to 2.5 mU/L, based on a study conducted by Negro et al[6] that found increased RPL at a thyroid-stimulating hormone (TSH) level 2.5 mU/L. This reduction in the threshold is associated with increased prescription rates of levothyroxine treatment, with possible increased maternal concern. Given these changes in guidelines it is crucial to examine the optimal threshold for starting levothyroxine therapy.

METHODS

This is a prospective non-randomized clinical trial conducted in tertiary obstetric hospital from 1st March t2022 to 30th May 2023. The participants were all women with RPL who visits the fertility clinic during the period of the study. The inclusion criteria were childbearing aged women (18-40 years), had recurrent pregnancy loss, with TSH level is equal or higher than 2.5 mU/L and normal T3 and T4 levels. women with known cause of RPL (examples of conditions include antiphospholipid syndrome, uterine anomalies, genetic/chromosomal problems, and so forth), women had chronic medical illnesses, those with allergy or

intolerance to levothyroxine therapy, or those already receiving levothyroxine treatment were excluded.

According to TSH level, the participants divided into two groups, those with TSH level 2.5-4 mU/L and those with TSH ≥4 mU/L. Data collected included demographics of the participants, the number of pregnancy losses, and the number of live births, alone with measurement of baseline level of TPOAb level. All participants receive levothyroxine therapy (eEuthyrox 50 Mcg Tablet, Merck) in a dose of 1.6 µg/kg/day early in the morning on an empty stomach. Follow up of the participants for the first six months and measuring the new TPOAb level and reporting the primary outcome which was the rate of SP (defined as pregnancy that continued beyond first trimester), the pregnant women were followed till time of delivery and the secondary outcomes were reported which were the gestational age at which delivery happened and the birth weight of the neonate.

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. The study received approval from the hospital's ethical and scientific authorities. This study was registered at clinical trials.gov website (identification number: NCT06036576), consent was obtained from all the participants after thoroughly discussing the study and patient's options.

The data entered and analyzed through SPSS-26 for statistical analysis. Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed variables were analysed for significance using the student t-test and reported as mean and standard deviation (SD). Skewed variables were evaluated for significance using the Mann-Whitney U test and reported as median and minimum to maximum range. The significance level was assessed using either the Chi-square test or the Fisher exact test, depending on appropriateness. A p value of ≤0.05 is regarded to be statistically significant.

RESULTS

The total number of women presented was 136 cases, 59 cases were excluded from the study (35 women had chronic medical condition (diabetes or hypertension), 17 cases had antiphospholipid syndrome, and 7 cases smokers), and the total number of SCH cases was 77 cases. Based on TSH level at which levothyroxine treatment started, the data divided into two groups: group A women with TSH ranged from 2.5 to 4 mU/L which was 39 cases (50.6%) and group B with TSH ≥4mU/L which was 38 cases (49.4%). The women age, BMI, the number of previous pregnancy loss and live births were not different between the two groups. The presence of TPOAb is not different regarding the level of TSH at which treatment started. The rate of successful pregnancy was not different between the two groups. Women that get pregnant were not different in regard to the gestational age at delivery or neonatal birth weight (Table 1). Based on the presence of TPOAb the data divided into two groups TPOAb+ group represent 57 cases, and TPOAb- in 20 cases, the outcome of pregnancy further examined and no difference in the pregnancy outcome, gestational age at time of delivery, nor birth weight were found (Table 2). The titer of TPO antibodies was significantly reduced after six months of levothyroxine therapy, yet the starting threshold of the treatment did not influence the amount of reduction of TPO Ab titer (Table 3). After application of regression analysis, we found that the titer of TPO Ab after six months of treatment was significantly associated with increased rate of successful pregnancy. No influence on the starting level of levothyroxine therapy (Table 4).

Table No.1: Distribution of data according to TSH level threshold

Variables		**TSH 2.5-4mU/L (n=39)**	**TSH ≥ 4mU/L (n=38)**	**P value**
Age (years)*		34 (17-38)	28 (16-40)	0.084
BMI (kg/m^2)†		27.11 ±2.23	27.32 ±2.26	0.685
No. of pregnancy loss*		4 (3-6)	5 (3-6)	0.156
No. of live birth*		1 (0-3)	1 (0-3)	0.233
TSH (mU/L)*		3.34 (2.5-3.98)	6.41 (4.05-7.96)	<0.0001
TPO antibodies (UI/ml)‡	Positive	32 (82.1%)	25 (65.8%)	0.104
	Negative	7 (17.9%)	13 (34.2%)	
Pregnancy outcome‡	Successful pregnancy	11 (28.25)	9 (23.75)	0.796
	Miscarriage	28 (71.8%)	29 (76.3%)	
GA at time of delivery (weeks)*		36 (32-39) [n=11]	35.29 (28.29-38)[n=9]	0.331
Birth weight (grams)†		2364.64 ±406.98 [n=11]	2167 ±699.49 [n=9]	0.467

*Data presented in the form Median (minimum-maximum);p-value calculated using Mann Whitney u test

†Data presented in the form of mean ±SD; p value calculated using student t test

‡Data presented in the form of number (percent); p value calculated using fishier exact test

Table No.2: Study outcomes according to presence of TPO antibodies and threshold of starting levothyroxine therapy

Variable		TPOAb+			TPOAb-		
		TSH 2.5-4 mU/L (n=32)	TSH ≥ 4 mU/L (n=25)	P value	TSH 2.5-4 mU/L (n=7)	TSH ≥ 4 mU/L (n=13)	P value
Pregnancy outcome‡	Successful pregnancy	9 (28.1%)	5 (20%)	0.479	2 (28.6%)	4 (30.8%)	0.919
	Miscarriage	23 (71.9%)	20 (80%)		5 (71.4%)	9 (69.2%)	
GA at time of delivery (weeks)*		36 (33-39) [n=9]	35.29 (28.43-38) [n=5]	0.190	33.5 (32-35) [n=2]	34.29 (28.29-38) [n=4]	1.000
Birth weight (grams)†		2368.44 ±454.85 [n=9]	2310.6 ±899.73 [n=5]	0.898	2347.5 ±21.92 [n=2]	1987.5 ±384.81 [n=4]	0.158

Table No.3: TPO antibody titer before and after six months of treatment and comparison of the level of reduction of antibody level based on threshold of treatment

TPOAb titer		Median	Minimum	Maximum	P value
Baseline level		586	380	751	<0.0001
After6 months		430	244	577	
Difference in Ab level*	TSH 2.5-4	120.5	-113	474	0.822
	TSH ≥ 4	156	-154	413	

*The difference calculated as follows: baseline TPO Ab level- TPO Ab level after 6 months of treatment. Negative value was found as some cases had elevated TPO Ab titer on treatment.

Table No.4: Logistic regression analysis (successful pregnancy as dependent variable)

Independent variables	B	S.E.	Wald	P value	Exp(B)
Threshold 2.5-4	0.057	1.006	0.003	0.955	1.059
Age	0.016	0.038	0.185	0.667	1.017
BMI	-0.07	0.125	0.316	0.574	0.932
No. of pregnancy loss	0.099	0.264	0.14	0.708	1.104
No. of live birth	0.115	0.26	0.196	0.658	1.122
TSH	0.175	0.301	0.34	0.56	1.192
Baseline TPO AB titer	-0.003	0.002	1.954	0.162	0.997
after 6 months	0.006	0.003	3.913	0.048	1.006
Constant	0.458	4.263	0.012	0.914	1.581

DISCUSSION

According to the American Thyroid Association, greater maternal TSH levels have been linked to a higher likelihood of miscarriage.[5] The therapeutic starting thresholds for SCH patients have been discussed as a result of this finding. According to Negro et al[6], a TSH level above 2.5mIU/L in the first trimester may be associated with a greater probability of miscarriage. In order to avoid selection biases, our study tried to choose a sample with the least amount of age and BMI variation. Every participant in our study fell into the category of recurrent miscarriage since they had all experienced a minimum of three pregnancies lost.

Our findings differ noticeably from a number of recent researches. While Liu et al[7] supported the possible dangers of increased TSH during early pregnancy, our investigation was unable to detect a statistically significant difference in successful pregnancy outcomes based on TSH therapy initiation thresholds. In a different context, Maraka et al[8] emphasized the advantages of levothyroxine therapy for SCH patients with thyroid autoimmunity in preventing pregnancy problems.

The outcome of pregnancy was not influenced by threshold of treatment in cases of neither SCH with TPOAb+ nor SCH with TPOAb- groups. the trial conducted by van Dijk et al[9] found that the levothyroxine treatment had no effect on the outcome of pregnancy in SCH either positive or negative TPO titer.

The presence of TPO Ab was uniformly distributed according to the threshold of treatment. Levothyroxine supplementation is associated with significant reduction of TPO Ab titer after six months of treatment. The threshold of treatment was not influencing the level of titer reduction, in other words just starting treatment of levothyroxine could improve the titer of antibody. Similarly suggested by Mosaddegh et al.[10]

The single independent predictor of successful pregnancy in this study was found to be level of TPO

ab titer after six months of levothyroxine treatment. In other words, the increase in the pregnancy rate found by previous studies may be attributable to the effect of levothyroxine treatment on antibody titer rather than a direct relationship. Similarly, Dong et al[11] found that cases of RPL associated with thyroid autoimmunity rather than levothyroxine therapy.

This study indicates that just lowering the treatment threshold might not always result in better results. The interaction between SCH and the results of pregnancies may be influenced by other latent factors. For instance, Salazar et al[12] mentioned how thyroid function and pregnancy outcomes are influenced by environmental contaminants and nutritional shortages.

The current study is constrained by the absence of a control group, which would have offered a more thorough analysis of levothyroxine's effectiveness. Larger, multi-center randomized controlled trials may be required in the future.

CONCLUSION

Reducing the TSH treatment threshold alone may not be sufficient to ensure improved pregnancy outcomes. There could be more unidentified factors affecting how SCH and pregnancy outcomes interact. After six months of treatment with levothyroxine, TPO antibody titers significantly decreased. The TSH threshold at which treatment was started had no effect on the size of this decline. The only indicator of a successful pregnancy after six months of levothyroxine treatment was the titer of TPO antibodies. This implies that rather than directly interacting with TSH levels, the possible advantages of levothyroxine therapy in reducing pregnancy problems may be more closely linked to its effect on antibody titers.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Sarah Al-Musawi, Kamal Al-Jawdah
Drafting or Revising Critically:	Sarah Al-Musawi, Kamal Al-Jawdah
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Effects of Multimodal Care Bundle on Knowledge and Anxiety among Patients Undergoing Cardiac Catheterization

Sobia Hassan, Sarfraz Masih, Muhammad Afzal and Muhammad Farhan Tabassum

ABSTRACT

Objective: To evaluate the effectiveness of a multimodal care bundle in two key areas: enhancing patients' knowledge about cardiac catheterization and reducing their anxiety about the procedure.

Study Design: A quasi-experimental one-group (pre-and-post) study

Place and Duration of Study: This study was conducted at the Cardiac Unit of a Tertiary Care Hospital, in Lahore, Pakistan, from 1st June to 30th November 2024.

Methods: A total of 100 participants undergoing cardiac catheterization for the first time, were selected using purposive sampling. Data were collected using a validated questionnaire and analyzed using SPSS version 27.

Results: Highly educated participants experienced significant preprocedural anxiety, primarily due to a lack of adequate knowledge. Overall, the mean Knowledge score improved significantly from 10.64 in the pre-test to 16.00 in the post-test, with an intermediate score of 5.36 two hours before the procedure ($p<0.0001$). Anxiety levels also showed substantial improvement, with mean scores of 6.52 in the pre-test, 6.63 two hours before the procedure, and 13.15 in the post-test.

Conclusion: The structured intervention significantly improves patients' knowledge and reduces anxiety levels associated with cardiac catheterization. The substantial increase in knowledge and marked decrease in anxiety scores highlight the importance of pre-procedural education and support in enhancing patient preparedness and emotional well-being.

Key words: Cardiac catheterization, Multimodal care bundle, Pre-procedural intervention

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INTRODUCTION

Cardiac catheterization is a minimally invasive diagnostic procedure used to identify blockages in coronary arteries. However, limited patient understanding of the procedure can lead to psychological challenges, including heightened anxiety driven by fear of the unknown. Providing patients with comprehensive information about pre-, intra-, and post-procedural care can help alleviate anxiety and promote a faster recovery.

Globally, cardiovascular diseases (CVDs), including coronary artery disease (CAD), cerebrovascular disease, and other cardiovascular disorders, are the leading causes of mortality.

Lahore School of Nursing, The University of Lahore

Correspondence: Sobia Hassan, MSN Student, Lahore School of Nursing, The University of Lahore.
Contact No: +92 333 6375044
Email: sobiahassan3311@gmail.com

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According to the World Health Organization, approximately 17.9 million people die annually from CVDs, with CAD responsible for 43% of these fatalities.[1] Pakistan, part of the South Asian region with the highest CAD prevalence rates, experienced significant mortality, with CAD-related deaths recorded at 110.65 per 100,000 by 2014.[2] These alarming statistics emphasize the need for effective diagnostic and therapeutic measures, including cardiac catheterization, performed in over 6,000 out of every million individuals annually in Western countries.[3]

Cardiac catheterization is a minimally invasive diagnostic procedure widely regarded as the gold standard for diagnosing, evaluating, and treating cardiac diseases. It involves inserting a thin catheter through the radial or femoral artery, guided via fluoroscopy, to assess coronary arteries and other cardiovascular structures. While highly effective, insufficient pre-procedural knowledge about cardiac catheterization can significantly elevate patient anxiety and adversely impact outcomes. Anxiety related to this procedure is often heightened by factors such as fear of complications, inadequate communication, and insufficient preparation.[4,5]

Pre-procedural anxiety is common among patients undergoing cardiac catheterization, with more than 82% of patients reporting significant anxiety before coronary angiography. Anxiety, defined as a state of nervousness or apprehension, can adversely affect patient outcomes, leading to extended hospital stays, refusal to undergo procedures, or even increased cardiac events. Physiological manifestations of anxiety, such as elevated blood pressure, heart rate, and plasma catecholamine levels, can further complicate the procedure.[6,7]

Nurses play a critical role in addressing these challenges by providing comprehensive patient education to alleviate anxiety.[8] Educational interventions, including face-to-face counselling, written brochures, and video-based materials, improve patient knowledge and reduce anxiety.[9] For instance, portable educational videos have been effective in increasing patient understanding and reducing anxiety levels before coronary angiography and angioplasty.[10] Non-pharmacological methods, such as aromatherapy and hand massages, have also demonstrated potential benefits in lowering anxiety levels, though their effectiveness is less pronounced than structured education programs.[11,12]

Despite these advancements, limited research has focused on multimodal interventions to enhance patient preparation in public hospitals in Pakistan. Many studies have either described the prevalence of anxiety or employed a single educational approach, leaving a gap in evaluating comprehensive preparation strategies. To address this, the current study introduces a multimodal care bundle that includes personalized education, written materials, video demonstrations, and a guided tour of the catheterization unit.

By addressing cognitive and emotional needs, this intervention seeks to improve patient outcomes, set a standard for anxiety management, and guide future clinical practices in cardiac care.[13,14]

METHODS

This quasi-experimental one-group pre-and-post study was conducted at the Cardiac Unit of a Tertiary Care Hospital in Lahore, Pakistan, from 1st June to 30th November 2024. The software Epitool was used to determine the sample size n= 100 with a 1.96 sample standard deviation and 95% confidence interval. All males and females, adults aged 20 to 65 years, communicate effectively, without acute medical conditions (e.g, asthma, arthritis, fractures, burns) and scheduled for their first elective CC procedure were included. The patients who have previously attended an educational program related to knowledge and anxiety levels for CC, psychological issues (e.g, hallucinations, depression) and undergo emergency cardiac catheterization procedures were excluded. The study utilized a structured questionnaire consisting of three sections: the first section gathered demographic information such as gender, age, marital status, residence, education, smoking habits, and co-morbidities; the second assessed participants' knowledge related to cardiac catheterization 11 items based. Incorrect answers receive a score of 1. Partially correct answers are awarded a score of 2. Correct and complete answers are given a score of 3.The total score of each patient's knowledge will be graded as: <17 = poor knowledge, 17-25 = fair knowledge and 26-33 = good knowledge. The third section evaluated anxiety levels by using the Hospital Anxiety and Depression Scale (HADS)[18] tool·grading as: 0-7 = normal, 8-10 = borderline abnormal (borderline case) and 11-21 = abnormal (case). In the preprocedural phase, scheduled CC patients provided written consent, after which their knowledge and anxiety levels were assessed on admission (day) using designated tools. During the interventional phase, held two hours before the procedure to assess participants' knowledge and anxiety levels the educational intervention (MMCB) consisted of two 45-minute sessions per week for four days and delivered either during the morning/evening shift. The sessions included face-to-face interaction, an educational pamphlet on CC, and patient preparation. Patients viewed pictures of the CC Lab and a 10-minute video detailing the procedure, pre-and post-care, and patient experiences. Additionally, the researcher demonstrated deep breathing exercises, which the patients then practiced. The post-procedural phase evaluates these levels of knowledge and anxiety, after the CC procedure. Quantitative data was entered by using SPSS-27. The normality of the knowledge and anxiety scores was assessed using the Shapiro-Wilk test and for pair testing, Cohen's d test was used. A p-value of <0.05 was considered statistically significant for all analyses.

RESULTS

There were 66 (66%) males and 34 (34%) females while 4 (4%) between 30-39 years, 29 (29%) between 40-49 years, 52 (52%) between 50-59 years age group and 15 (15%) between 60-69 years. The majority of the patients (64%, n=64) were married, 1% (n=1) were unmarried, 28% (n=28) were widowed, and 7% (n=7) were divorced. Seventy five (75%) of the patients resided in urban areas while 25 (25%) were from rural areas. Five (5%) had primary education, 16 (16%) had middle school education, 49 (49%) had completed matriculation, 25 (25%) had an intermediate level of education, 4 (4%) were graduates, and 1 (1%) had a postgraduate education. Thirty one (31%) patients were smokers, while 69 (69%) were non-smokers. Seventy five (57%) patients had hypertension, 36 (36%) had diabetes and 7 (7%) had ischemic heart disease (Table 1).

Table No.1: Demographic characteristics of knowledge and anxiety among patients about cardiac catheterization (n= 100)

Variable	Frequency	%.
Gender: Male	66	66.0
Female	34	34.0
30 – 39	4	4.0
40 – 49	29	29.0
50 - 59	52	52.0
60 – 69	15	15.0
Marital status		
Married	64	64.0
Unmarried	1	1.0
Widow	28	28.0
Divorced	7	7.0
Residence		
Urban	75	75.0
Rural	25	25.0
Education		
Primary	5	5.0
Middle	16	16.0
Matric	49	49.0
Intermediate	25	25.0
Graduate	4	4.0
Postgraduate	1	1.0
Smoking: Yes	31	31.0
No	69	69.0
Co-morbidities		
Hypertension	57	57.0
Diabetes	36	36.0
IHD	7	7.0

The knowledge scores increased by an average of 10.64 points, supported by a high t-value (83.947), a statistically significant p-value (<0.05), and a 95% confidence interval (CI) of 9.577 to 7.209. A large effect size (Cohen's d = 8.395) highlights the intervention's strong impact. Before 2 Hours vs. Post-Testing: Scores further increased by 5.36 points, with a t-value of 18.324, a p-value <0.001, and a narrow 95% CI (2.152 to 1.509), demonstrating precision. The large effect size (Cohen's d = 8.395) confirms the intervention's meaningful effect. Pre-Testing vs. Post-Testing: Overall, knowledge improved by 16 points with an extremely large effect size (Cohen's d = 10.546), showing substantial gains across all comparisons (Table 2).

Pre-testing versus before 2 hours: anxiety scores decreased by 6.52 points, with a narrow and precise 95% confidence interval (CI) of 6.302 to 6.738. A high t-value (59.479), a p<0.05, and a large effect size (Cohen's d = 5.948) confirm a substantial reduction. Before 2 hours vs Post-Testing: Anxiety scores further decreased by 6.63 points, with a precise 95% CI of 6.469 to 6.791. The t-value (81.628), p<0.001, and very large effect size (Cohen's d = 5.948) indicate continued significant improvement. Pre-Testing vs. Post-Testing: Overall, anxiety was reduced by 13.15 points, with a 95% CI of 12.904 to 13.396, a t-value of 105.865, and extremely large effect sizes. The reductions in anxiety were statistically significant across all comparisons (p<0.05), demonstrating the intervention's meaningful impact (Table 3).

Table No.2: Comparison of Knowledge Levels in the pre-, 2 hours before and after the intervention (groups)

Knowledge		Mean	SD	Diff.	t value	p value	95% CI		Cohen's d
							LL	UL	
Pair 1	Pre-Testing	14.30	1.494	10.640	83.947	0.000	9.577	7.209	8.395
	Before 2 hours	24.94	1.523						
Pair 2	Before 2 hours	24.94	1.523	5.360	18.324		2.152	1.509	1.832
	Post-Testing	30.30	1.521						
Pair 3	Pre-Testing	14.30	1.494	16.00	61.412		7.016	5.264	7.016
	Post-Testing	3.30	1.521						

Table No.3: Comparison of anxiety levels in the pre-, 2 hours before and after the intervention (groups)

Anxiety		Mean	SD	Diff.	t value	p value	95% CI		Cohen's d
							LL	UL	
Pair 1	Pre-Testing	18.92	1.502	6.520	59.479	0.000	6.302	6.738	5.948
	Before 2 hours	12.40	1.271						
Pair 2	Before 2 hours	12.40	1.271	6.630	81.628		6.469	6.791	8.163
	Post-Testing	5.77	1.153						
Pair 3	Pre-Testing	18.92	1.502	13.150	105.865		12.904	13.396	10.546
	Post-Testing	5.77	1.153						

SD= Standard Deviation, Diff= Difference, LL= Lower limit, UL= Upper Limit, CI= Confidence Interval

DISCUSSION

In terms of gender distribution, the majority of participants in this study were male (66%) and 34% were female. These findings align with previous research which reported that the demographic data for patients undergoing diagnostic cardiac catheterization showed that approximately two-thirds were male, and more than half were over sixty years old.[15] The age distribution in our study revealed that most participants were between 50-59 years (52%), with a smaller percentage in the younger age groups, which is consistent with studies by Shaheen et al[2] and Inamdar & Chendake[13], which reported similar age distributions in cardiac catheterization patients.

Regarding residence, 75% of the participants lived in urban areas, a finding consistent with studies by Anise Hassan Abdelaal et al[10] and Meseer & Al-Dujaili[14], while contrasting with other studies such as Inamdar & Chendake,[16] where a larger proportion of participants were from rural areas.

The academic qualifications of participants varied, with the majority having completed secondary education (49%) or intermediate education (25%). These findings were consistent with those of Inamdar & Chendake[16] and Yap et al[11], which showed higher percentages of participants with secondary education. Regarding smoking habits, 31% of patients were smokers, which comparable to findings conducted in Peshawar found that hypertension (65.7%), stress (73.1%), and smoking (50.6%) were key risk factors for ischemic heart disease (IHD).[17]

Many CC patients lack sufficient knowledge about the procedure, leading to discomfort and fear. Nurses play a crucial role in assessing and educating patients, which helps reduce anxiety and enhances comfort.[3]

The present study found a significant improvement in patients' knowledge of CC, with a mean increase of 10.64 points from Pre-Testing to 2 hours before the procedure ($p<0.001$). These results align with previous research by Shaheen et al[2], which showed similar findings, and Inamdar & Chendake[16], where 13.33% of patients had poor knowledge before the intervention. The study found that patient education based on the MMCB approach significantly improved knowledge, with an overall increase of 16 points in the post-test phase. This result agrees with the findings by Inamdar & Chendake[16], and Yap et al[11], who reported a high percentage of patients showing good knowledge after receiving education. Moreover, these findings were also supported by another study which reported that significant improvements in knowledge and reduced anxiety ($P = 0.00$), supporting the multimodal care bundle as an effective method for cardiac catheterization.[18]

The results of this study demonstrated a significant reduction in anxiety levels after the intervention and anxiety scores decreased by a mean of 6.52 points after the educational session 2 hours before the procedure and by another 6.63 points post-procedure. These findings are consistent with studies by Anise Hassan Abdelaal et al[11] and Yap et al[12], which reported similar reductions in anxiety after educational interventions. Additionally, research by Shaheen et al[2] and Inamdar & Chendake[20] supports the notion that education can significantly reduce anxiety, with some studies indicating a shift from moderate to low anxiety levels after receiving information. The reduction in anxiety in this study suggests that providing patients with detailed information about the procedure and addressing their concerns through educational interventions can lead to a marked improvement in their emotional well-being.

The reduction in anxiety levels can be attributed to the comprehensive approach used in the intervention, which included not only educational pamphlets but also a video demonstration and face-to-face interactions. Such multimodal interventions have been shown to enhance patient understanding and comfort, leading to lower anxiety levels as reported by Oshvandi et al.[3] Moreover, patient satisfaction and comfort were notably improved when patients felt informed about the process, which aligns with findings from previous research by Yap et al.[11]

CONCLUSION

Multimodal Care Bundle (MMCB) significantly benefited patients awaiting cardiac catheterization. It improved their knowledge with large effect sizes ($d>0.8$) and statistically significant p-values ($p<0.05$) across all comparisons, indicating a substantial impact on enhancing patient understanding. Additionally, the MMCB effectively reduced anxiety and panic levels associated with unfamiliar environments and procedural uncertainties. Often, the information provided by nurses and physicians, due to their busy schedules and limited availability, is insufficient to alleviate extreme patient anxiety. In such scenarios, nurses can play a pivotal role by implementing MMCB interventions to address these concerns. The MMCB is not only a cost-effective and practical approach but also highly accessible, making it a valuable tool for improving patient outcomes related to cardiac procedures.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Sobia Hassan, Sarfraz Masih
Drafting or Revising Critically:	Muhammad Afzal, Muhammad Farhan Tabassum
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Comparative Study of Lipid Profile in Male Smokers and Non-Smokers

Kaleemullah Kakar[1], Gulandam[1], Mohammed Atif Gulzar[1], Azizur Rahman[3], Abdul Ghaffar Khan[2] and Muzamil Majeed[3]

ABSTRACT

Objective: To determine the mean lipid profile and compare it with the smoking status in males presenting in outpatient clinics at a tertiary care hospital in Quetta.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of General Medicine, Bolan Medical College, Quetta, from May 2024 to October 2024.

Methods: A total of 117 male patients aged 18-60 years, presenting with body aches and/or easy fatigability, were included. Patients with chronic renal failure, hypertension, coronary artery disease, diabetes, and endocrine disorders were excluded. Lipid profiles, including serum cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL), were measured using the MIURA auto analyzer.

Results: In this study, the mean lipid profile of males presenting in outpatient clinics with body aches and/or easy fatigability was as follows: Total cholesterol (192.39±35.44 mg/dL), triglycerides (153.21±23.88 mg/dL), low-density lipoprotein cholesterol (110.69±26.67 mg/dL), very low-density lipoprotein cholesterol (27.89±6.48 mg/dL), and high-density lipoprotein cholesterol (49.77±8.16 mg/dL).

Conclusion: The study concludes that male smokers have a more deranged lipid profile compared to non-smokers, indicating a higher risk of cardiovascular complications in smokers.

Key Words: Smokers, Lipid Profile, Cholesterol, Cardiovascular Disease, Quetta.

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INTRODUCTION

Smoking is one of the most potent and widespread addictive habits, significantly impacting human behavior and health. While smoking is decreasing in many developed countries, it is rapidly rising in the developing world, becoming a major threat to global health. Smoking is responsible for nearly 20% of all coronary heart disease (CHD) deaths, and its harmful effects extend to various other conditions such as cancer, stroke, gastric ulcers, periodontal disease, sudden infant death syndrome, and metabolic syndrome[1]. Among its most detrimental impacts is the damage smoking causes to the cardiovascular system.

[1.] Department of Medicine / Cardiology[2], Bolan Medical College Quetta.
[3.] Department of Medicine, Sandeman Provincial Hospital Quetta.

Correspondence: Dr. Kaleemullah Kakar, Associate Professor of Medicine, Bolan Medical College Quetta.
Contact No: 03337835652
Email: drkaleemkakar@gmail.com

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Cigarette smoking is the most common form of tobacco use, and tobacco remains the second leading cause of death worldwide[2]. If current trends continue, smoking is projected to kill more than 9 million people annually by 2030. Smoking is a well-established risk factor for atherosclerosis and coronary heart disease, contributing to increased morbidity and mortality from chronic heart diseases (CHD)[3]. Smoking induces several harmful physiological effects. Increased carbon monoxide levels in smokers' blood damage the endothelium, accelerating cholesterol's entry into the artery walls, and leading to atherosclerosis. Additionally, smoking increases platelet aggregation, and nicotine absorbed from cigarette smoke can induce cardiac arrhythmias[4]. The nicotine in tobacco is also linked to changes in lipid profiles, contributing to atherogenic complications. Atherosclerosis, a lipid-driven inflammatory disorder of the arterial wall, is one of the most common modifiable risk factors for cardiovascular disease. Smoking exacerbates this condition and is a major epidemiological factor in the rising prevalence of CHD[5]. Most available studies focus on the association of smoking with lipid profiles in patients with pre-existing conditions such as diabetes, hypertension, or coronary artery disease (CAD). However, limited studies explore the relationship between smoking and lipid profiles in otherwise healthy individuals[6]. Given the rising prevalence of coronary artery disease and the

modifiable risk factors of smoking and lipid profile abnormalities, it is essential to investigate this association in healthy males in our local population[7]. The findings of this study will help clinicians identify individuals at higher risk for cardiovascular diseases and guide early intervention strategies. Additionally, the results may differ from existing studies due to variations in ethnicity, lifestyle, and dietary habits in our population. Early detection and management of deranged lipid profiles can significantly reduce the morbidity and mortality associated with cardiovascular diseases[8].

METHODS

This was a cross-sectional study was conducted at the Department of General Medicine, Bolan Medical College, Quetta from May 2024 to October 2024. The sample size was calculated using the WHO sample size calculator. Using a margin of error of 1% and a mean±SD of HDL lipid profile (37.51±5.50 mg/dL) from a previous study on healthy males, the total sample size was 117. A 95% confidence level was used. Data were collected through non-probability consecutive sampling was used for this study.

a. Inclusion Criteria:

- Male patients.
- Patients aged 18-60 years presenting with body aches and/or easy fatigability for more than one month.
- Both smokers and non-smokers, as per the operational definition.

b. Exclusion Criteria:

- Patients with chronic renal failure (assessed by history, clinically, and GFR <30 ml/min).
- Patients with a history of alcohol intake (confirmed by history).
- Patients with hypertension (assessed by history and clinically).
- Those with coronary artery disease (assessed by history and clinically).
- Patients with diabetes and endocrine disorders (assessed by history and clinically).
- Patients on medications like ß-blockers, steroids, or lipid-lowering agents (assessed by history and clinically).

Data Collection Procedure: After receiving approval from the College of Physicians and Surgeons Pakistan, the study was initiated. Male patients presenting to outpatient clinics with body aches and/or easy fatigability for more than one month, who met the inclusion criteria, were enrolled in the study. Informed consent was obtained from all participants, ensuring their confidentiality and well-being during the study process. Each patient's demographic information, including name, medical record number, age, sex, place of residence, and education level (illiterate, primary, intermediate, or graduate), was recorded. Additionally, the duration of body aches and/or easy fatigability was documented, followed by a thorough clinical examination (height, weight, and BMI). Fasting blood samples were collected after an overnight fast under aseptic conditions. Samples were centrifuged at 2000 rpm for one minute, and lipid profile measurements including serum cholesterol, triglycerides, HDL, LDL, and VLDL were performed using the MIURA auto analyzer. All results were recorded in a predesigned proforma. The exclusion criteria were strictly followed to minimize bias in the study. The cost of fasting lipid profiles was borne by the principal investigator.

Data Analysis Procedure: The collected data were compiled and analyzed using SPSS version 21. Quantitative variables like age, height, weight, BMI, family income, duration of body aches/fatigability, triglycerides, total cholesterol, LDL, HDL, and VLDL were presented as mean ± standard deviation or median (IQR). The normality of the data was assessed using the Shapiro-Wilk test. Frequencies and percentages were calculated for qualitative variables like place of residence (urban or rural) and education level. The primary outcome variable, lipid profile, was compared between smokers and non-smokers using an independent t-test or Mann-Whitney U test, depending on data distribution. Effect modifiers such as age, BMI, place of residence, education status, family income, and duration of symptoms were controlled through stratification. Post-stratification, independent t-tests, or Mann-Whitney U tests were applied, with a p-value ≤ 0.05 considered statistically significant.

RESULTS

Data were collected from 117 patients with the majority (54.7%) aged between 18-40 years, while 45.3% were aged 41-60. Most patients (60.68%) had a BMI less than 27 kg/m², and 54.7% reported body aches and/or easy fatigability for less than six months. The majority of the participants (63.25%) lived in urban areas, and 40.17% had a monthly income exceeding PKR 40,000. Regarding education, 35.04% were illiterate, and 23.08% were graduates. A significant proportion (60.68%) of the patients were smokers.

The overall lipid profile showed that the mean total cholesterol was 192.39 ± 35.44 mg/dL, with no significant difference between smokers (192.03 ± 34.78 mg/dL) and non-smokers (192.96 ± 36.81 mg/dL, p=0.891). Triglyceride levels were slightly higher in smokers (155.52 ± 24.29 mg/dL) than in non-smokers (149.63 ± 23.04 mg/dL), though this difference was not statistically significant (p=0.194). Similarly, low-density lipoprotein (LDL) levels were higher in smokers (113.66 ± 27.92 mg/dL) compared to non-smokers (106.11 ± 24.19 mg/dL), but this difference did not reach statistical significance (p=0.135). No significant differences were found in very low-density lipoprotein (VLDL) and high-density lipoprotein (HDL) levels between the two groups.

Table No.1: Demographic data of patients

Variable	Category	No. of Patients (n=117)	Percentage (%)
Age (years)	18-40	64	54.70
	41-60	53	45.30
BMI (kg/m²)	<27	71	60.68
	≥27	46	39.32
Duration of body aches/fatigability (months)	<6	64	54.70
	≥6	53	45.30
Place of living	Rural	43	36.75
	Urban	74	63.25
Monthly income (PKR)	<20,000	26	22.22
	20,000-40,000	44	37.61
	>40,000	47	40.17
Education	Illiterate	41	35.04
	Primary	20	17.09
	Intermediate	29	24.79
	Graduate	27	23.08
Smoking status	Yes	71	60.68
	No	46	39.32

Table No.2: Comparison of lipid profile

Lipid Profile	Mean ± SD (Overall)	Smokers (n=71) Mean ± SD	Non-Smokers (n=46) Mean ± SD	p-value
Total cholesterol (mg/dL)	192.39 ± 35.44	192.03 ± 34.78	192.96 ± 36.81	0.891
Triglycerides (mg/dL)	153.21 ± 23.88	155.52 ± 24.29	149.63 ± 23.04	0.194
Low-density lipoprotein cholesterol (mg/dL)	110.69 ± 26.67	113.66 ± 27.92	106.11 ± 24.19	0.135
Very low-density lipoprotein cholesterol (mg/dL)	27.89 ± 6.48	27.66 ± 6.74	27.98 ± 6.14	0.798
High-density lipoprotein cholesterol (mg/dL)	49.77 ± 8.16	50.23 ± 8.07	49.07 ± 8.33	0.455

Table No. 3: Stratification of the mean lipid profile concerning age

Lipid profile	18-40 years (n=64)	41-60 years (n=53)	p-value
	Mean ± SD	Mean ± SD	
Total cholesterol	192.61 ± 34.76	192.13 ± 36.58	**0.943**
Triglyceride	156.70 ± 20.31	148.98 ± 27.18	**0.082**
Low-density lipoproteincholesterol	113.11 ± 27.28	107.77 ± 25.86	**0.283**
Very low-density lipoprotein cholesterol	27.06 ± 6.87	28.66 ± 5.93	**0.186**
High-density lipoproteincholesterol	**48.98 ± 8.74**	**50.72 ± 7.37**	**0.255**

Table No.4: Stratification of Mean lipid profile concerning BMI

Lipid profile	≤27 kg/m² (n=71)	>27 kg/m² (n=46)	p-value
	Mean ± SD	Mean ± SD	
Total cholesterol	192.18 ± 35.08	192.72 ± 36.38	**0.937**
Triglyceride	153.92 ± 21.24	152.11 ± 27.68	**0.691**
Low-density lipoproteincholesterol	112.25 ± 26.99	108.28 ± 26.26	**0.434**
Very low-density lipoproteincholesterol	28.28 ± 6.62	27.02 ± 6.26	**0.307**
High-density lipoproteincholesterol	**50.32 ± 8.43**	**48.91 ± 7.73**	**0.363**

The comparison of lipid profiles between the age groups 18-40 years and 41-60 years showed no significant differences. The mean total cholesterol levels were similar in both age groups (192.61 ± 34.76 mg/dL for 18-40 years vs. 192.13 ± 36.58 mg/dL for 41-60 years, p=0.943). Triglyceride levels were slightly higher in the younger age group (156.70 ± 20.31 mg/dL) compared to the older group (148.98 ± 27.18 mg/dL), though not statistically significant (p=0.082). Low-density lipoprotein (LDL) and very low-density

lipoprotein (VLDL) cholesterol levels also did not show significant differences between the age groups, with p-values of 0.283 and 0.186, respectively. Similarly, high-density lipoprotein (HDL) levels were comparable across both groups (p=0.255).

DISCUSSION

Several studies have evaluated the lipid profile differentials between smokers and non-smokers, revealing varied results across populations. For instance, a study among Japanese males aged 24-68 years with a Brinkman Index ≥554 (the number of cigarettes smoked per day multiplied by the duration of smoking in years) found that smokers had 1.657 times the odds of having abnormal triglyceride (TG) levels compared to non-smokers (p=0.04). However, there was no statistically significant difference in total cholesterol (TC) or high-density lipoprotein (HDL) cholesterol levels between smokers and non-smokers[9]. Another Japanese study involving males aged 42-81 years indicated that among those with a visceral fat area ≥100 cm², 47.3% of current smokers, 36.4% of former smokers, and 18.8% of non-smokers had TG levels ≥150 mg/dL[10]. However, TG levels did not differ among current smokers, former smokers, and non-smokers with a visceral fat area <100 cm². This suggests that body fat distribution may interact with smoking to influence TG levels, A large cross-sectional study[11] of 103,648 Japanese males and females aged 17-94 years reported the following trends: (i) TC levels were lower in smokers than non-smokers among males aged ≥25 years and females aged 35-64 years, (ii) low-density lipoprotein (LDL) levels were lower in smokers than non-smokers among males aged 25-64 years and ≥75 years, and females aged 25-44 years, (iii) HDL levels were lower in smokers than non-smokers among males aged 25-74 years and females aged 17-64 years, and (iv) TG levels were higher in smokers than non-smokers among males aged 25-74 years and females aged 17-64 years. Notably, these findings for TC, LDL, and HDL differed from other studies, but the results for TG levels were consistent with previous research[12]. An Indian study conducted on 100 age- and gender-matched smokers and non-smokers found that smokers, regardless of smoking intensity (10-15 cigarettes/day for 1-5 years, 16-20 cigarettes/day for 6-10 years, and >20 cigarettes/day for more than 10 years), had higher TC, TG, LDL, and very low-density lipoprotein (VLDL) levels and lower HDL levels compared to non-smokers. Similarly, Gogania and Hemeshwar reported significantly higher TG (p<0.01) and VLDL (p<0.01) levels, along with lower HDL (p<0.01) levels, in smokers and smokers who also chewed tobacco compared to non-smokers. Additionally, smokers who chewed tobacco exhibited significantly higher TC (p<0.01) and LDL (p<0.01) levels. In a cohort of mild, moderate, and heavy smokers aged 40-59 years, compared with non-smokers, the following lipid profile trends were observed: TC levels were 198 mg/dL, 224 mg/dL, 240 mg/dL, and 160 mg/dL respectively; TG levels were 164 mg/dL, 199 mg/dL, 223 mg/dL, and 124 mg/dL; LDL levels were 94 mg/dL, 104 mg/dL, 120 mg/dL, and 82 mg/dL; and HDL levels were 42 mg/dL, 39 mg/dL, 35 mg/dL, and 48 mg/dL respectively. These studies collectively suggest that smoking has a detrimental effect on lipid profiles, particularly increasing TG, TC, and LDL levels, while decreasing HDL levels. The extent of these changes appears to be influenced by smoking intensity, duration, and interactions with other factors such as body fat distribution. The findings underscore the need for early interventions to modify lipid profiles in smokers, which could potentially reduce their risk of cardiovascular diseases[13-16].

CONCLUSION

This study concluded that male smokers have a significantly deranged lipid profile compared to non-smokers, indicating a higher risk of developing cardiovascular diseases. Therefore, we recommend that national-level educational programs be implemented to raise awareness about the dangers of smoking and encourage smoking cessation. Additionally, regular monitoring of serum lipid levels in smokers is essential to prevent cardiovascular risks in this vulnerable population.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Kaleemullah Kakar, Gulandam, Mohammed Atif Gulzar
Drafting or Revising Critically:	Azizur Rahman, Abdul Ghaffar Khan, Muzamil Majeed
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Open Versus Laparoscopic Cholecystectomy

Outcomes and Complications of Open Versus Laparoscopic Cholecystectomy in Patients Presenting with Cholelithiasis in Gujranwala Teaching Hospital

Hafiz Muhammad Khizar Nawaz Cheema, Muhammad Amin Warriach, Sobia Zafar, Ansar Aslam, Uzair Ahmed Qureshi and Mubashir Iqbal

ABSTRACT

Objective: The study aims to compare the frequency of complications associated with open versus laparoscopic cholecystectomy in patients presenting with cholelithiasis.

Study Design: Comparative observational study

Place and Duration of Study: This study was conducted at the Department of Surgery, DHQ Hospital, Gujranwala from June 2022 till December 2023.

Methods: A total of 160 patients (80 in each group) meeting the inclusion criteria were enrolled from the OPD. Patients were randomly assigned to two groups using a lottery method. Group A underwent laparoscopic cholecystectomy, while Group B underwent open surgery. Post-surgery, patients were monitored in the surgical ward until discharge and followed up in the OPD after 10 days for evaluation of wound infection, bile leakage, or pneumonia.

Results: In Group A, the mean age of patients was 44.60 ± 14.79 years, while in Group B, it was 44.35 ± 14.55 years. In Group A, 35 (43.8%) were male and 45 (56.3%) were female, while in Group B, 41 (51.2%) were male and 39 (48.8%) were female. The mean disease duration in Group A was 8.17 ± 2.61 years, compared to 7.93 ± 2.42 years in Group B. The frequency of wound infection was higher in Group B, with a significant association between wound infection and treatment group (p-value: 0.017). The frequency of bile leakage was higher in Group A, but no significant difference was observed (p-value: 0.385). Similarly, pneumonia infection was more frequent in Group B, with no significant difference (p-value: 0.222).

Conclusion: Laparoscopic cholecystectomy is a safer procedure compared to open cholecystectomy in patients with cholelithiasis.

Key Words: Open, Laparoscopic, Cholecystectomy, Cholelithiasis

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INTRODUCTION

Gallbladder disease is one of the leading causes of hospital admission for acute abdominal pain in adults and is the most common indication for abdominal surgery. Historically, surgery was considered a last resort for symptomatic cholelithiasis before the advent of laparoscopy, with less invasive alternatives like lithotripsy and cholecystostomy being favored[1].

Department of General Surgery, Gujranwala Teaching Hospital, Gujranwala.

Correspondence: Hafiz Muhammad Khizar Nawaz Cheema, Consultant General Surgeon, Gujranwala Teaching Hospital, Gujranwala.
Contact No: 03016400200
Email: littledoctoe500@yahoo.com

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However, laparoscopic surgery has revolutionized the treatment of gallbladder disease, becoming the preferred method for many surgical cases. In particular, laparoscopic cholecystectomy has emerged as a popular alternative to open cholecystectomy in the treatment of acute cholecystitis, and it is now considered the gold standard for managing symptomatic cholelithiasis and chronic cholecystitis[2]. Despite its widespread adoption, there remains a lack of definitive data on its use for acute cholecystitis. Some randomized trials have shown a lower incidence of wound infection and pneumonia with laparoscopic cholecystectomy compared to open surgery, but differences in bile leakage rates remain inconclusive[3]. These trials suggest no statistically significant differences between the two techniques, with p-values greater than 0.05[4]. For example, one trial reported wound infections in 3.2% of laparoscopic cases versus 14.3% in open surgeries, and pneumonia in 3.2% with laparoscopic cholecystectomy compared to 14.3% with open surgery. However, bile leakage occurred more frequently in the laparoscopic group

(6.5%) than in the open surgery group (2.4%), though this difference was also not statistically significant. Similarly, another trial showed minor differences in complications, with 4.2% wound infection in laparoscopic cholecystectomy versus 6.9% in open surgery, and a slight difference in bile leakage (1.4% in laparoscopic and 0% in open surgery)[5]. There is no substantial evidence supporting the superiority of laparoscopic cholecystectomy over open surgery, particularly in local settings where facilities may be limited[6]. Most patients still undergo open surgery due to the lack of access to laparoscopic resources or reliable, context-specific data. Furthermore, there is no local evidence to guide clinical decision-making regarding the choice of surgery for cholelithiasis[7]. Therefore, the rationale for this study is to compare the complications associated with open and laparoscopic cholecystectomy in patients presenting with cholelithiasis, specifically in a local context[8]. The findings of this study will help establish more reliable evidence for the management of cholelithiasis, which could improve clinical practice and ensure that the most appropriate and least complicated surgical method is implemented in local healthcare settings. The results will be valuable for local practice and may lead to better-informed decision-making in the treatment of cholelithiasis.

METHODS

This comparative observational was conducted at the Department of Surgery, DHQ Hospital, Gujranwala from June 2022 till December 2023. Data were collected using a non-probability consecutive sampling technique.

Sample Size: A total of 160 cases were calculated with 80% power of the study and a 5% significance level, based on the expected percentage of wound infection (3.2% with laparoscopic cholecystectomy and 14.3% with open surgery for cholelithiasis). The sample size was divided equally into two groups, 80 cases in each group.

Inclusion Criteria:

- Patients aged 16-75 years of either gender presenting with cholelithiasis (as per operational definition).
- Patients with ASA I and II classification.

Exclusion Criteria:

- Patients with systemic problems such as diabetes (BSR >186 mg/dl), liver issues (hepatitis B or C), or abnormal blood clotting profiles (PTT >15 seconds, APTT >20 seconds).

Data Collection Procedure: After obtaining approval from the hospital's ethical committee, 160 patients (80 in each group) who met the inclusion criteria were enrolled from the OPD of the Department of Surgery, DHQ Hospital, Gujranwala. Informed consent was obtained from all participants, and demographic information, including name, age, gender, body mass index, and the duration of cholelithiasis, was recorded. Patients were randomly assigned to two groups using the lottery method:

- **Group A**: Laparoscopic cholecystectomy
- **Group B**: Open surgery

All surgeries were performed under general anesthesia by a single surgical team with the assistance of the researcher. After surgery, patients were transferred to the post-surgical ward and monitored until discharge. They were followed up in the OPD after 10 days to evaluate for wound infection, bile leakage, or pneumonia, as defined in the operational definitions. All findings were recorded on a proforma.

Data Analysis: Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 20. For quantitative variables like age, body mass index, duration of cholelithiasis, and hospital stay, mean and standard deviation were calculated. For qualitative variables such as gender, wound infection, bile leakage, and pneumonia, frequency and percentage were computed. To compare complications between the two groups, a chi-square test was used. A p-value of < 0.05 was considered statistically significant. Data were also stratified by age, gender, body mass index, and duration of cholelithiasis. Post-stratification, the two groups were compared for complications using chi-square tests for each stratum. A p-value of ≤ 0.05 was considered significant.

RESULTS

The mean age in Group A (laparoscopic cholecystectomy) was 44.60 ± 14.79 years, while in Group B (open surgery), it was 44.35 ± 14.55 years, with a range of 20-70 years for Group A and 21-69 years for Group B. The gender distribution was also comparable, with 43.8% males and 56.3% females in Group A, and 51.2% males and 48.8% females in Group B. Regarding body mass index (BMI), the majority of patients in both groups were either overweight or obese. The mean duration of disease was slightly higher in Group A (8.17 ± 2.61 years) compared to Group B (7.93 ± 2.42 years), but the duration range was the same for both groups (4-12 years).

In Group A (laparoscopic cholecystectomy), 7.5% of patients experienced wound infections, significantly lower than the 20% in Group B (open surgery), with a p-value of 0.017. For bile leakage, Group A had a slightly higher incidence (6.3%) compared to Group B (3.8%), but the difference was not statistically significant (p-value: 0.385). Pneumonia occurred in 3.8% of patients in Group A and 6.3% in Group B, with no significant difference observed (p-value: 0.222).

In the age group of 41-50 years, 5% of patients in Group A and 15% in Group B experienced complications, with a p-value of 0.044. In terms of

BMI, obese patients in Group A had a significantly lower complication rate (12%) compared to those in Group B (28%), with a p-value of 0.030. Moreover, patients with a disease duration of 4-8 years in Group A had fewer complications (10%) compared to Group B (25%), with a p-value of 0.044. No significant differences were found between gender and other BMI categories.

Table No.1: Demographic and Clinical Characteristics of Patients in Group A and Group B

Characteristic	Group A (n=80)	Group B (n=80)
Mean Age (±SD)	44.60 ± 14.79	44.35 ± 14.55
Age Range	20-70 years	21-69 years
Gender		
Male (%)	35 (43.8%)	41 (51.2%)
Female (%)	45 (56.3%)	39 (48.8%)
Body Mass Index (BMI)		
Normal BMI (%)	24 (30%)	25 (31.3%)
Overweight (%)	31 (38.8%)	32 (40%)
Obese (%)	25 (31.3%)	23 (28.7%)
Mean Duration of Disease (±SD)	8.17 ± 2.61	7.93 ± 2.42
Duration Range	4-12 years	4-12 years

Table No. 2: Postoperative Complications in Group A and Group B

Complication	Group A (n=80)	Group B (n=80)	p-value
Wound Infection (%)	6 (7.5%)	16 (20%)	0.017*
Bile Leakage (%)	5 (6.3%)	3 (3.8%)	0.385
Pneumonia (%)	3 (3.8%)	5 (6.3%)	0.222

The data indicates a significant difference in the complications between age groups in both groups, with patients over 50 years old showing a p-value of 0.034. However, there were no significant differences based on gender, with p-values of 0.517 for males and 0.594 for females. In terms of BMI categories, the incidence of complications was similar across the normal, overweight, and obese categories in both groups, with p-values ranging from 0.141 to 0.913, indicating no significant association. Additionally, disease duration did not show a significant impact on the rate of complications, with p-values of 0.74 for the 4-8 years group and 0.102 for the 9-12 years group.

Table No.3: Association of Wound Infection with Age, Gender, BMI, and Duration

Factor	Group A (n=80)	Group B (n=80)	p-value
Age Group			0.044*
20-30 years	0 (0%)	0 (0%)	
31-40 years	0 (0%)	0 (0%)	
41-50 years	2 (5%)	6 (15%)	
>50 years	4 (6%)	10 (13%)	0.202
Gender			
Male (%)	1 (2.9%)	10 (24.4%)	0.151
Female (%)	5 (11.1%)	6 (15.4%)	0.585
BMI Category			0.030*
Normal BMI (%)	1 (4.2%)	3 (12%)	0.171
Overweight (%)	2 (6.5%)	6 (18.8%)	0.478
Obese (%)	3 (12%)	7 (28%)	0.030*
Duration of Disease (years)			0.044*
4-8 years	2 (10%)	10 (25%)	0.044*
9-12 years	4 (6%)	6 (10%)	0.202

Table No.4: Association of Bile Leakage with Age, Gender, BMI, and Duration

Factor	Group A (n=80)	Group B (n=80)	p-value
Age Group			0.034*
20-30 years	0 (0%)	0 (0%)	0.41
31-40 years	1 (2.4%)	1 (2.4%)	0.17
41-50 years	2 (5%)	0 (0%)	0.34
>50 years	2 (6.3%)	2 (6.3%)	0.034*
Gender			0.517
Male (%)	3 (7.5%)	2 (5%)	
Female (%)	2 (5%)	1 (2.4%)	0.594
BMI Category			0.141
Normal BMI (%)	2 (8.3%)	0 (0%)	0.141
Overweight (%)	2 (6.3%)	2 (6.3%)	0.615
Obese (%)	1 (4%)	1 (4%)	0.913
Duration of Disease (years)			0.74
4-8 years	3 (7.5%)	0 (0%)	0.74
9-12 years	2 (5%)	3 (7.5%)	0.102

The p-value for the age group was 0.088, with no significant difference between 41-50 years and >50 years. Similarly, gender did not show a significant difference (p-value = 0.33 for males and 0.37 for females), and there were no significant findings for the BMI categories (p-value = 0.67 for normal BMI, 0.52

for overweight, and 0.257 for obese). Duration of disease also did not show a significant effect, with p-values of 0.098 for 4-8 years and 0.691 for 9-12 years.

Table No.5: Association of Pneumonia with Age, Gender, BMI, and Duration

Factor	Group A (n=80)	Group B (n=80)	p-value
Age Group			0.088
20-30 years	0 (0%)	0 (0%)	
31-40 years	0 (0%)	0 (0%)	
41-50 years	2 (5%)	3 (7.5%)	0.088
>50 years	1 (2.4%)	2 (4.8%)	0.613
Gender			0.33
Male (%)	1 (2.4%)	3 (7.3%)	
Female (%)	2 (4.7%)	2 (4.7%)	0.37
BMI Category			0.67
Normal BMI (%)	1 (4.2%)	2 (8.3%)	0.67
Overweight (%)	1 (3.2%)	3 (9.4%)	0.52
Obese (%)	1 (4%)	0 (0%)	0.257
Duration of Disease(years)			0.098
4-8 years	2 (5%)	2 (5%)	0.098
9-12 years	1 (2.5%)	3 (7.5%)	0.691

DISCUSSION

Life expectancy has been steadily increasing due to advancements in medical technology, prevention, and acute care. This increase in life expectancy has led to a higher proportion of elderly individuals undergoing surgeries, including cholecystectomies. According to another study, patients aged 75 years or older are considered the high-risk group for surgical procedures in developed countries. Similar findings were observed in our study, where the frequency of complications (wound infection, bile leakage, and pneumonia) was highest in patients over 50 years[9]. This reflects the increased risk with advancing age, corroborating the findings from Tang et al. In a study conducted by a researcher, the mean age of patients was 41.3 years, with a predominance of females (82%). Our study showed a similar mean age of 44.50 years, but the gender ratio was almost balanced. This aligns with findings of a research, where a majority of patients were females, though our study had a more even distribution of males and females[10]. Another study by Al-Otibi and Al-Junaid found the mean age to be 46.1 years, supporting the trend that most cholecystectomy patients are in their 40s and 50s, though this varies across studies. While the age group of 65 years and older is often a focal point in studies regarding surgical risk, our study specifically highlighted that complications were most common in patients older than 50[11]. This suggests that even in relatively younger elderly populations, such as those over 50, there is a higher incidence of complications. This finding underlines the importance of considering age as a significant factor in surgical risk assessments.

A study comparing laparoscopic and open cholecystectomy for acute cholecystitis found that laparoscopic cholecystectomy is generally considered advantageous due to quicker recovery and fewer complications[12]. However, elderly patients with acute cholecystitis have a lower likelihood of undergoing laparoscopic cholecystectomy compared to those with non-acute cholecystitis. For elderly patients in the US, the use of laparoscopic surgery varied widely (30.3% to 75.5%). Despite the higher co-morbidity in elderly patients, laparoscopic cholecystectomy remains a safe option, though it is associated with higher risks of conversion to open surgery, delayed recovery, and prolonged hospital stays when compared with younger patients. These factors should be considered in the surgical management of elderly patients in our study[13]. Our study's findings align with existing research showing that advancing age correlates with higher surgical risk and complication rates. However, the mean age of patients in our study was 44.50 years, which is significantly younger than those in many other studies, such as the study conducted by a researcher (41.3 years) and Al-Otibi and Al-Junaid (46.1 years). This suggests that the patient population in our study may represent a relatively younger demographic compared to some international studies, which may have focused on older populations[14-17]. Additionally, while the general advantage of laparoscopic cholecystectomy over open surgery is recognized, our study underlines that even within a younger elderly group, complications are common and should be carefully monitored[18]. This comparison helps reinforce the relevance of age in evaluating surgical risks, and our findings support the existing literature regarding the increased complication rates in older patients. Furthermore, while laparoscopic surgery remains the preferred approach, its use in elderly patients should be carefully evaluated based on their overall health and risk factors[19].

CONCLUSION

Laparoscopic cholecystectomy is a safer and more efficient procedure for patients with cholelithiasis compared to open cholecystectomy. It is easier to perform, less time-consuming, and associated with fewer complications. Our study supports the growing body of evidence that laparoscopic cholecystectomy is the preferred treatment option for symptomatic cholelithiasis due to its lower complication rates, particularly in terms of wound infection. Given its advantages, including faster recovery times and reduced hospital stay, laparoscopic cholecystectomy should be

prioritized in the management of cholelithiasis, wherever feasible.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hafiz Muhammad Khizar Nawaz Cheema, Muhammad Amin Warriach, Sobia Zafar
Drafting or Revising Critically:	Ansar Aslam, Uzair Ahmed Qureshi, Mubashir Iqbal
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Circulating MicroRNA-146a as a Biomarker Related to Oxidative Stress in Thalassemia Patients

Nawal Khinteel Jabbar and Heba Hani Hamzah

ABSTRACT

Objective: To examine the miRNA-146a expression in thalassemia patients with chronic anemia and its relationship to oxidative stress in these individuals.

Study Design: Case-control study

Place and Duration of Study: This study was conducted at the Diwaniyah Women and Children Teaching Hospital and the University of Al-Diwaniyah Al- Qadisiyah, College of Sciences, Iraq from October 2022 to February 2023.

Methods: A total of 80 thalassemia patients and 40 healthy controls, measuring serum ferritin levels with the Cobas e411 analyzer and interleukin-6 using sandwich immunodetection. It also assessed advanced oxidation protein products (AOPPs) colorimetrically, along with catalase (CAT), superoxide dismutase (SOD), and malondialdehyde (MDA) levels. Furthermore, serum miRNA-146a expression was analyzed through quantitative polymerase chain reaction.

Results: When comparing patients to controls, serum ferritin levels increased considerably ($P<0.05$), and patient groups had significantly higher activity levels of SOD, CAT, AOPP, and MAD. Patients also had higher levels of the gene miRNA-146a ($p< 0.05$).

Conclusion: There is a reciprocal relationship between increasing oxidative stress and the expression of the miRNA-146a gene, contributing to disease onset and enhancing antioxidant enzyme effectiveness. In thalassemia, the pathophysiology of oxidative stress drives the expression of miRNA-146a.

Key Words: Oxidative Stress, Thalassemia, MicroRNA

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INTRODUCTION

Thalassemia is a hereditary form of chronic anemia characterized by a reduction or absence of α- or β-globin chain synthesis, leading to hemolytic, hypochromic, microcytic anemia. Beta thalassemia is specifically caused by various point mutations on chromosome 11 affecting the β-globin gene. It is categorized into three primary categories depending upon their clinical presentation: major, intermedia, and minor.[1]

Oxidative stress occurs when the production of reactive oxygen species (ROS), like free radicals and ions, exceeds the ability of natural antioxidants to neutralize them, resulting in an excess of oxidants.[2]

[1.] Department of Chemistry, College of Sciences, Al Qadisiyah University, Iraq.

Correspondence: Heba Hani Hemzah, Department of Chemistry, College of Sciences, Al Qadisiyah University, Iraq.
Contact No: 0785 531 5583
Email: university/Iraqhibahani984@gmail.com

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Overproduction of ROS can be detrimental since it readily reacts with biological systems' lipids, proteins, and DNA.[3] Reactive oxygen species (ROS) are crucial for initiating signaling pathways that lead to cell damage and death, either through direct harm to biomolecules or by altering proteins and genes.[4] Antioxidant enzymes are crucial for detoxifying free radicals and reducing oxidative stress by facilitating the removal of reactive oxygen species (ROS).Superoxide Dismutase (SOD) is an antioxidant protein that converts superoxide anions into hydrogen peroxide (H_2O_2), which is subsequently detoxified into oxygen and water by catalase or glutathione peroxidise.[5]

AOPPs are oxidative indicators that can trigger inflammation by activating monocytes. MDA is a ketoaldehyde produced from the peroxidative breakdown of unsaturated lipids during arachidonate metabolism.[6]

MicroRNA (miRNA) is an endogenous gene that produces small RNA molecules that bind to specific target RNAs, leading to their decay or repression of translation.[7] significant roles in controlling gene expression as a number of human disorders develop. MiRNAs play a crucial role in maintaining erythroid homeostasis and regulate the expression of α-, β-, and γ-globin genes. It is important to examine how miRNAs influence globin expression in β-thalassemia.[8]

METHODS

The study involved 120 respondents divided into two groups: healthy controls and TM patients. Data collected included age, sex, splenectomy status, and other health issues, with the control group carefully selected to ensure no prior history of diabetes, hypertension, or other conditions. The study documented patients' age, gender, BMI, smoking status, family history, and any medications. It included laboratory test analyses from Nabu Scientific Foundation in Baghdad, the Thalassemia Center's Women and Children Teaching Hospital in Diwaniyah, and the Biochemistry Lab at Al-Qadisiyah University's College of Sciences. Patients with splenectomy, infections, chronic bone inflammation, liver failure, cardiac disease, and other blood conditions were excluded from this study.

Five milliliters of blood were collected from each subject, divided into two tubes, with four milliliters placed in a gel tube. The serum was extracted by centrifugation at 3600 rpm for 10-15 minutes and divided into four parts: one stored at -40°C for miRNA-146a analysis and the others at -20°C. Additionally, 1 mL of blood was collected in a K2EDTA tube for a complete blood count (CBC).

Spectrophotometry was used to determine the serum's activity (SOD). The calculation of (CAT) was done using UV spectrometry. Spectrophotometry was used to calculate the concentrations of (MDA).[9] AOPP's concentration was measured using UV spectroscopy.[10] Serum levels of miRNA-146a were measured using quantitative polymerase chain reaction (qPCR). RNA was extracted from 0.3 mL of serum using TRIzole™ reagent, and cDNA was generated using the Protoscript® first-strand cDNA synthesis kit from NEB, UK. The Polymerase Chain Reaction was conducted using Luna Universal qPCR Master Mix from NEB, UK. The complementary DNA produced was combined with forward and reverse universal primers for miR-146a and the cDNA Bright Green master mix. As an internal control, gene U6 was used. In order to determine the proportional levels of miR-146a and ($2^{-\Delta\Delta Ct}$), (2(-Ct)), A threshold cycle (Ct) by comparison was utilized, and A fold change in expression was observed in the results (Table 1).

SPSS version 26 was used for all analyses. A t-test assessed continuous data with a normal distribution. The chi-square test compared categorical variables, reporting data as frequency and percentage. The Pearson correlation test linked normally distributed quantitative data, examining the relationship between two continuous variables with a correlation coefficient (r) and a significance level of $P < 0.05$.

RESULTS

Patients with TM had slightly lower body mass index (BMI) values compared to controls. White blood cell (WBC) levels were significantly higher in the TM group, while hemoglobin (Hb) and red blood cell (RBC) levels were considerably lower. Additionally, the TM group exhibited higher random blood sugar (RBS) and packed cell volume (PCV) levels, but lower mean corpuscular volume (MCV) compared to controls. The mean corpuscular hemoglobin (MCH) was significantly higher in the control group, with a p-value greater than 0.05 (Table 2).

SOD activity was elevated in the TM group as compared to the control group (Fig. 1). CAT activity was elevated in TM as compared to the control group (Fig. 2). AOPP levels were significantly higher in the TM group compared to the control group, which also had elevated MDA levels (Figs. 3-4). Figure 5 presents a study comparing serum ferritin levels between patients and healthy controls. Additionally, qPCR miRNA analysis revealed that the TM group had significantly higher serum levels of miRNA-146a expression than the control group.

Tables 3 show the relationships between miRNA-146a and indicators of oxidative stress in patients with thalassemia (SOD, Catalase, MDA, and AOPP). The current findings indicate no significant relationship between miRNA-146a and any of the factors (Table 4).

Table No.1: Quantitative PCR analysis primers

Primers	Sequence	Product Size (bp)
miR-146_RT	GTCGTATCCAGTGCGTGTCGTGGAGTCGGCAATTGCACT GGATACGACAACCCA	
miR-146 For miR-146 Rev	GGGTGAGAACTGAATTCCA CAGTGCGTGTCGTGGAGT	
U6 For U6 Rev	CTCGTTCGGCAGCACA AACGCTTCACGAATTTGCGT	94

Table No.2: The demographics of thalassemia patients and healthy control participants

Characteristic	**Patients (*n* = 80)**	**Healthy control (*n* = 40)**	***P***
Age (years)			
Mean ±SD	12.47±6.42	14.60±6.49	0.092† (NS)
Range	2 – 33 years	4 – 30 years	

<12, *n* (%)	37 (46.3%)	14 (35.0%)	0. 498¥ (NS)
12-17, *n* (%)	27 (33.7%)	16 (40.0%)	
≥ 18, *n* (%)	16 (20.0%)	10 (25.0%)	
Sex (M/F)			
Male, *n* (%)	46 (57.5%)	18 (45%)	0.196¥ (NS)
Female, *n* (%)	34 (42.5%)	22 (55%)	
Body mass index (BMI) (Kg/m^2)			
Mean±SD	12.41±4.07	15.73±4.87	0.001† (S)
Range	4.72–22.70	6.7–25.8	
White blood cells count µL			
Mean±SD	14.74 ± 19.03	9.04±11.33	0.101† (NS)
Range	2.57 – 109.20	4.10- 78.00	
Red Blood Cells count µL			
Mean ±SD	3.12±0.49	4.70±0.49	< 0.001† (HS)
Range	1.68 – 4.94	3.89- 5.74	
Haemoglobin (Hb) g/dl			
Mean± SD	7.92±1.22	12.92±1.72	< 0.001† (HS)
Range	3.70 -11.10	10.01-16.70	
Packed cell volume (PCV) %			
Mean± SD	24.01±3.31	38.80±4.82	< 0.001† (HS)
Range	13.60 -30.60	30.10-49.10	
Mean Corpuscular Volume (MCV) fl			
Mean± SD	76.18±6.53	82.11±5.51	< 0.001† (HS)
Range	51.30 -88.50	67.10-91.30	
Mean corpuscular hemoglobin (MCH) pg			
Mean± SD	26.42 ± 5.99	27.57± 2.37	0.247†(NS)
Range	18.90 -75.50	20.80-31.10	

n: number of cases; SD: standard deviation; †: independent samples t-test; HS: Highly significant at P ≤ 0.001. NS: not significant at P > 0.05

Table No.3: Correlation between miRNA-146a and oxidative stress parameters (SOD, CAT, MDA and AOPP) in patients with thalassemia

Oxidative stress parameters	miRNA-146a	
	r	P
SOD	0.172	0.314
Catalase	0.161	0.407
MDA	0.017	0.917
AOPP	0.208	0.279

Table No.4: Correlation between serum ferritin, antioxidant enzyme and oxidative stress parameters (SOD, CAT, Catalase, MDA and AOPP) in patients with thalassemia

Oxidative stress parameters	Serum ferritin	
	R	P
SOD	0.198	0.078
Catalase	0.092	0.416
MDA	0.020	0.857
AOPP	0.297*	0.039

r: correlation coefficient.

Figure No. 1: SOD levels in healthy controls and patients

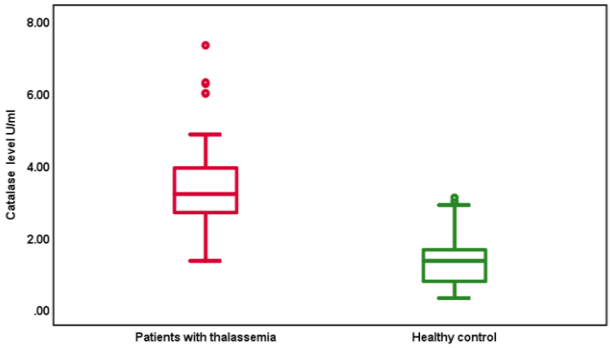

Figure No. 2: Catalase levels in healthy controls and patients

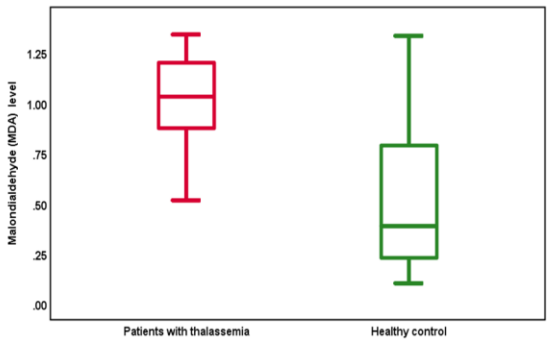

Figure No. 3: The levels of malondialdehyde (MDA) in patients and healthy controls

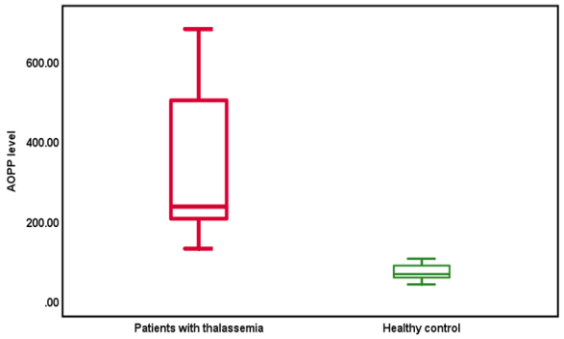

Figure No. 4: AOPP levels for both healthy controls and patients

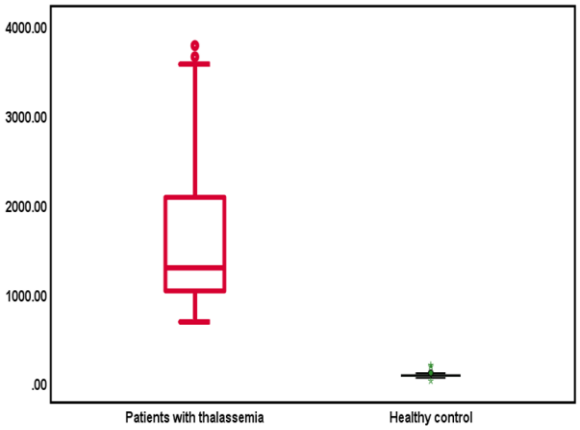

Figure No. 5: Serum ferritin levels in healthy controls and patients

DISCUSSION

In thalassemia disorders, oxidative stress is primarily caused by redox reactions of hemoglobin involving hydrogen peroxide (H_2O_2) and superoxide anion radicals (O2•). The Haber-Weiss process leads to the formation of molecular oxygen and hydroxyl radicals (•OH), with Fe3+ catalyzing this reaction and potentially generating •OH. Additionally, the absence of the β-globin chain causes unpaired α-chains to self-aggregate, further damaging oxidized membranes and affecting immature erythroblasts in the bone marrow. Thalassemia red cells exhibit in vivo oxidative damage and heightened susceptibility to external oxidant stress.[11] Thalassemic red blood cells (RBC) may experience biochemical and metabolic changes due to chronic oxidative stress, which is linked to the accumulation of excess alpha-globin chains, iron decompartmentalization, and the release of free iron.[12]

Patients with thalassemia were found to have elevated plasma malonyldialdehyde (MDA) levels, as determined by the spectrophotometry method. MDA indicates significant oxidative damage. A previous study found that thalassemia major patients receiving regular transfusions had higher levels of free and total MDA compared to thalassemia intermedia patients.[13] Another study showed lipid peroxidation products (such MDA) were more prevalent in thalassemia patients[14]. The research found elevated plasma MDA levels, suggesting that ongoing blood transfusions may lead to peroxidative tissue damage due to secondary iron overload in patients.

SOD is a protective antioxidant, Researchers previously discovered increased SOD activity in thalassemia patients.[15] In vivo lipid peroxidation is caused by thalassemia and the concomitant iron overload, and SOD and glutathione peroxidise (GPx) levels rise as a result of the compensatory rise in lipid peroxidation.[16] Compared to both healthy individuals and beta-thalassemic carriers, the catalytic activities of SOD and GPx were significantly greater in beta-thalassemic erythrocytes. Increased AOPP levels have been linked to monocyte activation, according to reports.[17] Previous studies have shown that elevated red cell SOD levels in thalassemic individuals are a response to or a compensatory mechanism for the elevated generation of superoxide radicals.[18] While the catalase result in β-thalassemia patients was much higher than in controls, this result was consistent.[19] A plausible explanation for the higher red cell catalase levels seen in the more severe genotype of β-thalassemia. Higher concentrations of hydrogen peroxide can directly damage catalase.

Ferritin 4-4 h and ferritin 4-24 h groups had significantly higher serum AOPP levels than the control group, supporting previous findings of elevated AOPP levels in thalassemia patients. It highlighted a correlation between serum ferritin and AOPP levels, as well as between blood transfusions and AOPP levels. Furthermore, ferritin and MDA levels were significantly higher in transfusion-dependent thalassemia (TDT) compared to non-transfusion-dependent thalassemia (NTDT). Furthermore, it was discovered that the concentrations of miRNAs in serum were constant, repeatable, and consistent between members of the same species showed that serum miR-146a levels were considerably higher in thalassemia patients.[20]

CONCLUSION

The globin gene expression could change the classification of thalassemia and alleviate its severe symptoms. Identifying miRNAs associated with the

disease's development is valuable for developing new diagnostic markers and treatment strategies for thalassemia.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Nawal Khinteel Jabbar, Heba Hani Hamzah
Drafting or Revising Critically:	Nawal Khinteel Jabbar, Heba Hani Hamzah
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Quality of Medical Care Provided in ICUs

Effectiveness of Medical Care Provided in ICUs According to Acute Physiology and Chronic Health Evaluation II (APACHE Ⅱ) Score Requirements

Hussein Jawad Kadhim[1], Zaman Sabah Mosleh[2], Ali Abdul Ameer Kareem[3], Moayad Mahmoud Dahir[3] and Azhar Sattar Ali[3]

ABSTRACT

Objective: The present study was conducted to assess the quality of medical care delivered in ICUs of IMAM Hussein Medical City, Karbala, Iraq, using the APACHE II scoring system.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Imam Al-Hussein Medical City in Karbala, Iraq from October–December 2023.

Methods: This study of 131 ICU patients (≥18 years) conducted at Imam Al-Hussein Medical City in Karbala, Iraq across emergency, medical, and surgical units. Demographic, clinical, and cardiovascular data were used to compute APACHE II scores and accurately predict mortality.

Results: Majority of the patients were males, 62.6%, and above 60 years of age, 38.2%. Pathological admission caused 61.8% into the ICU. The general mortality rate was 52.7% whereas 73.3% of patients were on mechanical ventilation. The statistical analysis done revealed that the APACHE II scores had a significant relation to the patient outcome mainly in the surgical and medical ICUs. Higher APACHE II scores were associated with an increased mortality and mainly so in the emergency ICU since the patients were admitted with more acute illnesses, with their mean APACHE II score standing at 21.77. The surgical ICU remarkably recorded an actual outcome significantly different from the APACHE II predicted mortality with a p-value less than 0.001.

Conclusion: APACHE II predicts ICU mortality, notably in surgical units (scores ≥30–34: 100% fatality; $p<0.001$). Age, comorbidities (DM/HTN), and pathological admissions elevate scores (medical: $r=0.553$; surgical: $r=0.384$; $p\leq0.002$). Males exhibit lower scores ($p\leq0.05$). Emergency ICUs show highest mortality (69.2%) despite comparable scores. Mechanical ventilation correlates with medical ICU scores ($p=0.009$). APACHE II's clinical/metabolic focus (no MAP/HR link) supports risk stratification. Future research needs biomarkers and gender-specific protocols.

Key Words: APACHE II, ICU's criteria, mortality, medical care &ICU.

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INTRODUCTION

[1.] Department of Anesthesia, Imam Hussein Medical City, Karbala Health Directorate, & Department Of Anesthesia Techniques In Alsafwa University College, Karbala, Iraq.
[2.] Health Professions Division, Technical Affairs Department, Karbala Health Directorate, Karbala, Iraq.
[3.] Department of Anesthesia, Imam Hussein Medical City, Karbala Health Directorate, Karbala, Iraq.

Correspondence: Dr. Hussein Jawad Kadhim, Member in Anesthesia Department, Imam Hussein Medical City, Karbala Health Directorate, & Department Of Anesthesia Techniques In Alsafwa University College, Karbala.
Contact No: +9647709416775
Email: anesthhush32@gmail.com

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The intensive care unit plays an essential role in managing critically ill patients, providing specialized medical care to those who have life-threatening conditions. Evaluating the effectiveness of care in these units is crucial for improving patient outcomes and ensuring consistent, high-quality treatment. One prominent tool for assessing the severity of illness and predicting patient outcomes in ICUs is the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system.[1]

APACHE II has been widely validated across various populations and medical conditions making it a reliable benchmark for monitoring ICU performance.[2] The score incorporates multiple physiological measurements and clinical data to estimate the risk of mortality. By comparing predicted outcomes with actual patient outcomes, medical practitioners can evaluate the performance of their ICUs and identify areas needing improvement.[3]

This study investigates the effectiveness of medical care provided in the ICUs of IMAM Hussein Medical City in Karbala, Iraq, by utilizing the APACHE II scoring system. Previous research has highlighted the importance of APACHE II in different settings, including surgical and medical ICUs, and has shown a strong correlation between high scores and increased mortality rates.[4] Furthermore, demographic factors such as age, gender, and cause of admission have also been shown to influence ICU outcomes.[5,6]

METHODS

This cross-sectional study evaluated the effectiveness of ICU care using APACHE II scores to predict mortality at Imam Al-Hussein Medical City in Karbala, Iraq -a tertiary referral center managing ~70% of the region's 641 annual ICU admissions (2021 data). The study enrolled 131 patients, ensuring generalizability to Karbala's urban population (1,066,900 residents; median age 36; 25% elderly). Participants included adults (≥20 years) admitted ≥24 hours to medical, surgical, or emergency ICUs between October–November 2023. Exclusion criteria comprised age <20, non-study ICU admissions, or incomplete records. Variables encompassed demographics (age, sex), clinical characteristics (admission cause, ICU type), physiological parameters (MAP, HR, mechanical ventilation), and outcomes (survival/death). APACHE II scores were calculated via MDApp, a validated mobile tool, using data from routine ICU monitoring (vital signs, arterial blood gas analyzers, and ventilators).

A simple random sampling method was applied to hospital records. Cases with incomplete data were excluded and replaced via identical randomization to maintain sample integrity. Non-pharmacological interventions (e.g. blood sampling) and pharmacological interventions (e.g. vasopressors: atropine, dopamine, adrenaline/noradrenaline) were documented. Ethical approval was obtained from the Karbala Health Directorate, adhering to WHO guidelines. Data were analyzed in SPSS-27. Normality was assessed via Kolmogorov-Smirnov tests; parametric (t-tests, ANOVA, Pearson correlation) or non-parametric (Mann-Whitney, Kruskal-Wallis, Spearman correlation) tests were applied as appropriate. Regression analyses identified predictors of mortality linked to APACHE II scores.

RESULTS

The study analyzed 131 ICU patients (62.6% male, mean age 50.2±22.8 years) across surgical (47.3%), emergency (42.7%), and medical (9.9%) units. Mortality was 52.7%, with higher rates in emergency ICU (69.2% vs. 50–51.8% elsewhere). APACHE II scores differed significantly by ICU type ($p<0.001$), highest in emergency (35.7±19.3 vs. 30.5±20.3 surgical, 32.4±19.5 medical). Mortality escalated with APACHE II thresholds: scores ≥30–34 predicted 100% mortality in all ICUs. Mechanical ventilation use (73.3% overall) correlated with higher APACHE II scores in medical ICU ($p=0.009$). Age strongly predicted APACHE II scores in medical ($r=0.553$, $p<0.001$) and surgical ($r=0.384$, $p=0.002$) units. APACHE II scores significantly associated with mortality in surgical ICU ($t=4.362$, $p<0.001$) but not medical/emergency units. Age and comorbidities (DM/HTN) influenced scores ($p<0.05$). Cardiovascular parameters (MAP, HR) showed weak/no correlation with APACHE II. Mortality rates aligned with APACHE-predicted risk strata ($p<0.001$): 34–66% risk groups had 24–25% mortality, rising to 100% in ≥67% strata. Gender impacted scores in surgical ($p=0.05$) and medical ($p=0.027$) ICUs, with males scoring lower. Trauma admissions had lower scores vs. pathological causes ($p\leq0.003$) [Tables 1-6).

Table No.1: Distribution of the patient's socio demographic data and clinical data characteristics (n=131)

Characteristics	No.	%
ICU wards		
Medical	13	9.9
Surgical	62	47.4
Emergency	56	42.7
Age (years)		
< 20	13	9.9
20 – 39	35	26.7
40 -59	33	25.2
> 60	50	38.2
Gender		
Male	82	62.6
Female	49	37.4
Cause of admission		
Traumatically	50	38.2
Pathological	81	61.8
Outcome		
Dead	69	52.7
Pass	62	47.3
Mechanical ventilation		
Yes	96	73.3
No	35	267
APACHE M. Rate		
0% - 33%	77	58.7
34% - 66%	42	32.1
67% - 100%	12	9.2

Table No.2: Distribution of the patients socio demographic data and clinical data characteristics according to ICU ward

Characteristics	Emergency (N=13)		Surgical (n=62)		Medical (n=56)	
	No.	%	No.	%	No.	%
Age (years)						
<20	-	-	6	9.7	7	12.5
20 – 39	1	7.7	23	37.1	11	19.6
40 – 59	1	7.7	15	24.2	17	30.4
> 60	11	84.6	18	29.0	21	37.5
Gender						
Male	8	61.5	40	64.5	34	60.7
Female	5	38.5	22	35.5	22	39.3
Cause of admission						
Traumatically	-	-	31	50.0	19	33.9
Pathological	13	100.0	31	50.0	37	36.1
Outcome						
Dead	9	69.2	31	50.0	29	51.8
Pass	4	30.8	31	50.0	27	48.2
Mechanical ventilation						
Yes	8	61.5	44	71.0	44	78.6
No	5	38.5	18	29.0	12	21.4
APACHE M. Rate						
0% - 33%	7	53.8	38	61.3	32	57.2
34% - 66%	5	38.5	18	29.0	19	33.9
67% - 100%	1	7.7	6	9.7	5	8.9

Table No.3: Comparing the APACHE II scores with the actual outcome for patients at surgical ICU, medical ICU and emergency ICU

APACHE II	Emergency ICU			Surgical ICU			Medical ICU		
	No.	Dead	%	No.	Dead	%	No.	Dead	%
0 – 4	-	-	-	2	2	-	-	-	-
5 – 9	1	-	-	7	3	42.0	4	2	50.0
10 – 14	-	-	-	8	5	62.5	13	8	61.1
15 – 19	5	3	60.0	16	10	62.5	14	12	85.7
20 – 24	3	2	66.6	15	13	86.6	11	10	90.9
25 - 29	3	2	66.6	7	4	57.1	10	8	80.0
30 - 34	1	1	100.0	5	5	100.0	4	4	100.0
≥ 35	-	-	-	2	2	100.0	-	-	-
Total	13	8	61.5	62	44	70.9	56	44	78.5

Table No.4: Comparing the APACHE II scores for the three groups with their socio demographic data and clinical data

Characteristics	Emergency				Surgical				Medical			
	Mean	SD	Analysis	Sig.	Mean	SD	Analysis	Sig.	Mean	SD	Analysis	Sig.
Age (years)												
<20			F=.418	.669	14.50	6.656	F=1.900	.140	12.57	3.645	F=11.23	.000
20 – 39	24.00	.			16.91	8.312			16.55	6.138		
40 – 59	16.00	.			20.67	5.653			16.53	6.135		
> 60	22.09	6.862			21.56	9.954			24.10	4.969		
Gender												
Male	24.00	6.024	t=1.673	.122	17.40	8.098	t=2.000	.050	17.26	6.694	t=2.280	.027
Female	18.20	6.181			21.73	8.253			21.36	6.374		
Cause of admission												
Traumatically	.	.	.	.	15.84	6.827	t=3.122	.003	15.21	5.360	t=3.100	.003

Patholo-gical	21.77	6.521			22.03	8.681			20.76	6.776		
Outcome												
Dead	23.67	5.500	t=.691	.119	23.00	8.386	t=4.362	.000	20.03	7.124	t=.684	.190
Pass	17.50	7.371			14.87	6.109			17.63	6.368		
Mechanical ventilation												
Yes	23.88	5.540	t=1.558	.148	20.07	8.793	t=1.695	.095	20.09	6.386	t=2.698	.009
No	18.40	7.127			16.17	6.573			14.42	6.735		
APACHE M. Rate												
0% - 33%	17.14	4.413	F=14.67	.001	14.58	5.889	F=45.72	.000	13.97	3.889	F=86.08	.000
34% - 66%	25.80	1.789			22.67	4.537			24.11	2.664		
67% - 100%	34.00	.			35.33	2.658			30.40	1.140		

M = Mean of APACHE score, S.D = Standard Deviation, P=probability value, NS: Non-Significant at P > 0.05, S: Significant at P < 0.05, HS: Highly Significant at P < 0.001

Table No.5: correlation of APACHE II scores for the three groups with their age, MAP, and HR

APACHE II	Emergency		Surgical		Medical	
	Cc.	Sig.	Cc.	Sig.	Cc.	Sig.
Age	-.021-	.944	.384	.002	.553	.000
MAP	-.307-	.308	-.018-	.887	.092	.498
H.R	.234	.424	.057	.660	-.007-	.958

Table No.6: Comparing between the actual outcome with APACHE mortality rate for patients at surgical ICU, medical ICU and emergency ICU

Ward	Dead		Pass		Statistical analysis		
	Mean	SD	Mean	SD	t	df	P value
Medical	39.22	19.136	27.75	19.670	.990	11	.343
Surgical	41.16	20.892	19.87	12.793	4.839	60	.000
Emergency	35.38	22.116	29.26	15.956	1.180	54	.243

DISCUSSION

A central observation is that APACHE II scores strongly correlate with patient outcomes, particularly within the surgical ICU. Notably, patients in the moderate-to-high APACHE II score categories (15–19, 20–24, and 25–29) experienced significantly higher mortality rates, with 96 deaths out of 131 cases - most of which occurred in the surgical ICU setting. These results contrast with other studies; for instance, Naved et al[7] reported that patients in the lowest APACHE II score category (3-10) had a 90% discharge rate, while those in higher score categories (31-40) faced substantially increased mortality rates. Similar evidence from (Lee et al[8] and Escarce et al[9] further validates that a higher APACHE II score reliably forecasts an increased risk of mortality, suggesting that the scoring system's calibration in our study is consistent with international benchmarks.[10]

The study found a predominance of male patients (62.6%), a trend supported by Garland et al[5], who postulated that men might present with more severe underlying conditions or be more inclined to accept aggressive ICU care compared to women. Furthermore, a significant proportion of patients (38.2%) were aged 60 years and above. These findings resonate with Boumendil et al[6], where the inclusion of older patients despite lower rates of certain co-morbid conditions was consistently linked to higher post-ICU mortality after adjusting for illness severity.

Pathological causes accounted for 61.8% of ICU admissions, a contrast to studies like Adenekan et al[11], which emphasize that ICU admissions resulting from internal medical conditions differ fundamentally from trauma cases. The high mortality rate (52.7%) observed in this study, particularly among patients requiring mechanical ventilation (73.3%), might be influenced by extrinsic factors such as frequent power outages, deficiencies in nursing training, medication shortages, inadequate nutrition, and complications associated with MV. In contrast, studies like those by Abate et al[12] noted that such factors contribute significantly to unstable vital signs - hypotension, sepsis, coma, and hypoxemia - all of which were prevalent and closely tied to 30-day ICU mortality in their cohort.

Age distribution analysis across ICU types revealed that the emergency and medical ICUs predominantly admitted older patients (60 years and above), whereas the surgical ICU had a greater proportion of younger patients (aged 20–39). This trend is supported by Chittawatanarat et al[13], suggesting that underlying disease profiles may differ markedly between elective surgical admissions and emergency cases. Despite reporting similar gender distributions across units,

outcomes varied significantly. The surgical ICU demonstrated relatively balanced outcomes (a 50-50 survival-to-mortality ratio) compared to the heightened mortality rates noted in both the emergency and medical ICUs.

Statistical analyses further underscored the efficacy of APACHE II scores in predicting outcomes. Table 6 demonstrated that the APACHE II score's predicted mortality closely aligned with observed mortality, particularly in the surgical ICU. This observation is in line with Asadzandi et al[14], where significant differences in APACHE II scores were noted between survivors and non-survivors, reinforcing the need for precise risk stratification in ICU settings. Moreover, the higher mean APACHE II score observed in the emergency ICU (Table 3) substantiates findings by Sungono et al[15] that non-operative and emergency surgical admissions are often burdened with prior organ insufficiencies, which intensify their overall risk profile.

Additional analysis (Table 5) indicated a strong positive correlation between APACHE II scores and patient age in the medical and surgical ICUs, although this relationship did not reach statistical significance in the emergency ICU. This pattern, consistent with Xu et al[16], signals that advancing age contributes to increased mortality risk as reflected in rising APACHE II scores. Furthermore, Table 4 revealed that the outcomes in the surgical ICU notably diverged based on the cause of admission, while in the medical ICU, factors such as gender, cause of admission, and mechanical ventilation usage influenced APACHE II scores and outcomes. These findings may be attributed to the differences in therapeutic aggressiveness and patient management strategies between ICU types. Surgical ICUs, for example, may benefit from more immediate and robust resuscitative measures compared to the more conservative approaches often adopted in medical ICUs.

CONCLUSION

The APACHE II-guided risk stratification in resource-limited ICUs to prioritize high-risk patients (e.g., elderly, comorbid) for targeted interventions. Emergency ICUs, despite comparable APACHE scores, exhibited the highest mortality (69.2%), suggesting unmeasured acuity factors. Future research should integrate dynamic biomarkers to refine prognostication, while clinical protocols must address gender and admission-specific vulnerabilities to optimize outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hussein Jawad Kadhim, Zaman Sabah Mosleh, Ali Abdul Ameer Kareem
Drafting or Revising Critically:	Moayad Mahmoud Dahir, Azhar Sattar Ali
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Validation of the Pashto Version of the Premature Ejaculation Diagnostic Tool (PEDT)

Hazratullah, Nasir Khan, Ishtiyaqurehman, Aminuddin and Ahsan Rafi

ABSTRACT

Objective: The research goal involved evaluating the validity of the Pashto version of the Premature Ejaculation Diagnostic Tool (PEDT) by assessing its relationship with clinical premature ejaculation (PE) diagnosis and intra-vaginal ejaculatory latency time (IELT).

Study Design: Prospective cross-sectional study

Place and Duration of Study: This study was conducted at the Urology Unit within the Surgery Department of Khyber Teaching Hospital in Peshawar from December 2020 to December 2021.

Methods: A total of 200 males within a 6-month minimum heterosexual relationship participated in the research. Participating subjects had to finish the PEDT questionnaire using the Pashto language.

Results: The study subdivided its population into two separate groups where 91 participants received clinical PE diagnoses while 71 participants did not have PE. Acquired PE was reported by 44 participants out of 60% (n = 44) who received PE diagnosis. Partakers in both groups engaged in sexual intercourse at the same pace achieving an average of two sessions weekly. Each demographic variable including mean age and relationship duration and education reached statistical parity between the two study groups. The participants with PE exhibited self-reported IELT times measuring 1.22 ± 0.52 minutes whereas other participants recorded IELT times measuring 3.73 ± 0.92 minutes. Self-reported IELT showed a negative relationship of 0.6 with results from the Pashto PEDT and the relationship achieved statistical significance at ($p < 0.05$). Patients scored 8 points or above on the PEDT tool were diagnosed with PE whereas scores of 8 points and below indicated no presence of PE. The diagnostic instrument produced nine false-positive outcomes in 73 participants while ten patients received incorrect negative results among 91 participants. The statistical measures calculated from the study demonstrated sensitivity of 89.01% (95% CI: 77.78% - 95.26%) alongside specificity at 87.32% (95% CI: 74.26% - 95.17%).

Conclusion: The Pashto-translated PEDT serves as both valid and reliable to identify PE in patients who speak Pashto. The tool achieved strong consistency between its items and produced statistical connections with medical PE evaluations and physical examinations.

Key Words: Premature Ejaculation Diagnostic Tool, Pashto, Validation, Psychometric, Reliability

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INTRODUCTION

Men experience premature ejaculation among the most common sexual dysfunctions based on reports from different populations.[1] Nevertheless the wide discrepancy of prevalence stems from people avoiding discussion of this condition and the absence of standard definitions and diagnostic tests.[2]

Department of Urology, Khyber Teaching Hospital in Peshawar.

Correspondence: Dr. Ahsan Rafi Trainee Ragistrar Urology Khyber Teaching Hospital in Peshawar.
Contact No: 03339227791
Email: ahsanrafi36@yahoo.com

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Various definitions in literature include ejaculatory latency with difficulty controlling ejaculation and psychologica DSM-IV-TR's previous definition of PE emerged from clinical assessment together with patient-observed symptoms.[3]

After some time, the International Society for Sexual Medicine (ISSM) came up with a standard, evidence-based description of PE.[4] This explanation says that the disease can be either lifelong or learned, and the differences between them are: (1) Ejaculation happening within one minute of vaginal penetration for lifelong PE or a clinically significant drop in latency to three minutes or less for acquired PE; (2) Not being able to delay ejaculation during almost all vaginal penetrations; and (3) Bad personal outcomes, such as upset, anger, or avoiding sexual intimacy.

The Arabic Index of Premature Ejaculation (AIPE) and the Premature Ejaculation Diagnostic Tool (PEDT) are two of the most often used questionnaires as part of the objective evaluation of premature ejaculation (PE).

Several diagnostic tools have been created to examine PE in an objective manner. Known as a tool that is generally acknowledged, the PEDT is a brief questionnaire consisting of five questions[5]. It has a basic scoring system: a score that is more than 11 indicates that a diagnosis of PE has been made, a score of 9 or 10 indicates that PE is likely to be present, and a score that is lower than 8 indicates that PE is not present. This instrument has been translated and verified in a variety of languages, and it has grown to become a standard for physical education evaluation. The Pashto version, on the other hand, had not yet been produced and established as reliable.

Pashto, a language spoken widely in Pakistan and Afghanistan, is an essential medium for effective communication in these regions. PE can have a profound impact on an individual's quality of life, extending beyond sexual health to psychological and emotional well-being. Despite these effects, only a small proportion of individuals seek treatment. Language barriers often pose a significant challenge for both patients and healthcare providers in diagnosing and managing PE.[6]

This study aims to translate and validate the PEDT for the Pashto-speaking population. Providing a version of the questionnaire in the native language facilitates a more comfortable environment for discussing the condition, allowing for accurate assessment, diagnosis, and follow-up care.

METHODS

The cross-sectional study received Ethical Review Committee approval for implementation within a twelve-month timeframe from December 2020 to December 2021 at the Urology Section of the Department of Surgery in Khyber Teaching Hospital Peshawar. The translation procedure followed the recommendation framework from the World Health Organization (WHO).

Two Pashto-speaking urologists administered the Premature Ejaculation Diagnostic Tool (PEDT) translation by reviewing a Pashto version of the questionnaire derived from their combined six or more years of clinical experience in PE management. The participating clinicians reached a mutual agreement to finalize one standardized version of the questionnaire in Pashto. The draft passage received linguistic assessment from experts at a respected Pashto department which led to small amendments to meet cultural standards. A bilingual linguist at that same institution provided the back-translation of the Pashto version into English. The final version of the Pashto PEDT resulted from comparing the original English text with its back-translated version to determine their precision levels.

Male participants between 20 and 60 years completed the study if they maintained one-year stable heterosexual partnerships while providing consent through writing and verbal communication. People were ineligible for recruitment when their medical history included erectile dysfunction and when they had major physical health conditions including angina or heart disease as well as kidney disease and liver conditions and psychological disorders and penile deformities such as Peyronie's disease and psychiatric medication usage.

A pilot study was conducted with 30 participants, comprising 15 individuals with PE and 15 without PE, to assess the diagnostic accuracy and user-friendliness of the Pashto version. The results demonstrated that the questionnaire was both effective and easy for participants to comprehend and complete.

Data collected included demographic information (age, marital status, relationship duration, and education level), comorbid conditions, intercourse frequency, self-reported intra-vaginal ejaculatory latency time (IELT), and PE type (lifelong or acquired). Participants completed the Pashto PEDT before and after consultation.

With the help of SPSSTM version 21.0, the data analysis was carried out. Cronbach's alpha was used to assess the psychometric qualities of the Pashto PEDT. An acceptable value of ≥ 0.70 was determined to be utilized for this evaluation. Both the association between self-reported IELT scores and PEDT scores, as well as the relationship between clinician-diagnosed PE scores and PEDT scores, was investigated with the use of Spearman correlation. A comparison was made using Pearson correlation to examine the PEDT scores obtained before and after consultation. A threshold of ≥ 0.70 was used to indicate that the reliability of the results was satisfactory.

RESULTS

Initially, 200 eligible participants completed the questionnaires during the first interview. However, 38 participants were lost to follow-up before the second interview. Consequently, the final analysis included 91(56.2%) individuals diagnosed with clinical PE and 71(43.8%) individuals without PE. Among those in the PE group, 44 (60%) were identified with acquired PE. The average ages of participants with and without PE were 36.05 ±8.65 years and 36.62 ±6.024 years, respectively. Both groups reported a similar frequency of sexual activity, approximately twice per week. The two groups were comparable in terms of mean age, frequency of intercourse, relationship duration, and educational background.

The mean self-reported IELT was significantly shorter in the PE group 1.22 ± 0.52 minutes compared to the non-PE group 3.73 ± 0.92 minutes (Table I). A strong negative correlation was observed between the Pashto PEDT scores and self-reported IELT $r = -0.6$, $p < 0.05$. Using a cutoff score of >8 for diagnosing PE and ≤8 for

ruling it out, the Pashto PEDT exhibited a false-positive rate of 9 (12.67%), where the tool indicated PE, but clinical evaluation confirmed no PE. Conversely, the false-negative rate was 10 (10.98%), where the tool failed to identify PE that was confirmed through clinical diagnosis.

It was determined that the Pashto PEDT had a sensitivity of 89.01% (95% confidence interval: 77.78% - 95.26%) and a specificity of 87.32% (95% confidence interval: 74.26% - 95.17%), respectively, as shown in Table 2. A score of 0.94 on the Cronbach's alpha test indicated that the Pashto PEDT had an outstanding level of internal consistency, with a 95% confidence interval ranging from 0.905 to 0.948. The reliability of the test-retest was found to be substantial across all five items, as shown by the Pearson correlation value of 0.944 for the overall PEDT score ($p < 0.001$), as presented in Table 3.

There was no significant difference in the mean PEDT scores between the two groups before and after the consultation. The scores for the Physical Education group consisted of 13.42 ± 2.57 and 13.23 ± 2.49, respectively. In a similar manner, the scores obtained by the non-physical education group before and after the consultation were 6.94 ± 3.43 and 6.45 ± 3.17, respectively.

Table No.I: Demographic Characteristics of Study Participants

	Total n=162	Clinical PE n= 91	No clinical PE n= 71	P value
Age (years)	36.31 ± 7.59	36.05 ± 8.652	36.62 ± 6.024	0.632
Frequency of Intercourse (weekly)	1.89± 0.88	1.75 ± 0.87	2.070± 0.867	0.25
Duration of Relationship	8.651 ± 6.16	8.923 ± 6.93	8.30 ± 5.03	0.52
Education [n (%)]				
Primary school	59 (36.4)	29 (17.90)	30 (18.5)	
High school	57 (35.2)	36 (22.2)	21 (12.96)	
Graduate	46 (28.4)	26 (16.0)	20 (12.34)	
Self-reported IELT (minutes)	2.32 ± 1.44	1.22 ± 0.52	3.73 ± 0.92	<0.001
PEDT score Pre-consultation	10.58 ± 4.3	13.42 ± 2.57	6.94 ± 3.43	<0.001
PEDT score Post-consultation	10.26 ± 4.38	13.23 ± 2.49	6.45 ± 3.17	<0.001

Table No.2: Sensitivity and Specificity of PEDT scores of greater/lesser than 8 with clinical diagnosis of PE

	Physician diagnosis PE % (n)	Physician diagnosis NO PE % (n)	Total
PEDT >8	89.01 % (81)	12.67% (9)	90
PEDT ≤ 8	10.98 % (10)	87.32% (62)	72
Total	n = 91	n= 71	

Table No.3: Test re-test reliability of each question and total PEDT score

	Question 1	Question 2	Question 3	Question 4	Question 5	Total
R	0.946	0.849	0.848	0.925	0.942	0.944
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

DISCUSSION

Premature ejaculation (PE) is commonly characterized by an intra-vaginal ejaculatory latency time (IELT) of less than one minute and can be evaluated using several diagnostic tools, including the widely accepted Premature Ejaculation Diagnostic Tool (PEDT).[8] Given its global prevalence, the PEDT has been translated and validated in numerous languages, such as Korean, Persian, French, Chinese, Russian, and, more recently, Urdu.[9-12] The prevalence of PE varies widely across regions, but data from Pakistan remains scarce. A study conducted in a tertiary care hospital in Khyber Pakhtunkhwa reported that PE affected approximately 13% of the male population, making it the second most common sexual dysfunction after erectile dysfunction.[13] Other studies have documented prevalence rates ranging between 24% and 27%, emphasizing the necessity for more localized research.[14]

Pashto, spoken by nearly 50 million people worldwide, is the native language for approximately 15% of Pakistan's population. It holds official status in Khyber Pakhtunkhwa and the northern districts of Balochistan and serves as Afghanistan's national language. Additionally, it is spoken in various parts of Pakistan, such as Punjab, Gilgit-Baltistan, Islamabad, and Karachi, as well as among Pashto-speaking communities in Iran, Tajikistan, the UAE, and the UK.[15]

Despite the fact that a number of diagnostic tools related to urology have been translated and validated in other languages, such as the PEDT and the International

Index of Erectile Function (IIEF).[16] This research represents the first time that an andrology-related diagnostic tool has been translated and verified into Pashto. The Pashto version of the PEDT addresses a critical need by enabling discussions about sexual health between clinicians and patients in Pashto-speaking communities. Despite the simplicity of the questionnaire, consisting of only five items, the translation process posed significant challenges. Finding culturally appropriate and comprehensible Pashto equivalents for specific terms, such as "ejaculation" and "penetration," was particularly difficult due to cultural sensitivities and the absence of commonly used, non-obscene terminology for these concepts in Pashto.

Premature ejaculation (PE) is a culturally sensitive topic, and open conversations about sexual health are uncommon, even between partners. As the PEDT is a self-administered questionnaire, using language that is clear and easy to understand was crucial. Our findings indicated that participants were able to comprehend the translated questionnaire effectively, likely due to the clinical setting in which it was provided, minimizing the need for assistance during completion.

The Pashto version of the PEDT was found to be both reliable and user-friendly for Pashto-speaking populations. It demonstrated strong internal consistency, with a Cronbach's alpha of 0.93, comparable to the Persian version ($\alpha = 0.89$).[10] The significant correlation between Pashto PEDT scores and self-reported IELT supports the tool's validity. However, since the diagnosis of PE involves more than just IELT, the moderate negative correlation ($r = -0.6$) between IELT and PEDT scores highlights the importance of considering situational PE and other contributing factors during clinical evaluations.

Test-retest reliability was evaluated by comparing PEDT scores before and after the clinical visit, showing strong consistency and correlation. However, the short interval between the two assessments may be a limitation, as a longer interval could introduce biases due to changes in symptoms or the effects of treatment.[17]

The present work serves as the initial attempt to translate and validate the PEDT in Pashto by following WHO-recommended validation procedures. The tool represents an objective system for PE diagnosis among Pashto-speaking people and provides needed research clarity for this population. The tool provides healthcare providers with a scientific methodology to assess treatment success rates while researchers obtain standards for evaluating different therapeutic approaches in this population.

This research demonstrates strength through its use of recognized translation and validation frameworks together with its pioneering work in studying an underprivileged cultural issue. The adoption of this diagnostic tool for PE makes new research and better service delivery possible for Pashto-speaking populations.

Limitations of the Study: The study happened in one center and this limits how much its findings apply to Pashto-speaking individuals beyond that location. Multiple research locations with varied participant demographics need to conduct additional studies to validate these current research findings.

CONCLUSION

The Pashto adaptation of the Premature Ejaculation Diagnostic Tool (PEDT) serves as a reliable and valid measurement tool for PE diagnosis among people who speak Pashto. The instrument showed outstanding reliability measurements and produced meaningful associations between its results and patient-reported IELT duration and PE clinical diagnoses. Additional population-based as well as multi-center studies need to happen to verify this tool's use as a standard diagnostic instrument for Pashto-speaking patients even though it works well in clinical environments.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hazratullah, Nasir Khan, Ishtiyaqurehman
Drafting or Revising Critically:	Aminuddin, Ahsan Rafi
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Evaluation of gal-9 Gene Expression and its Impact in some Apoptotic Proteins (Cas3,7) Levels in Patients with Beta Thalassemia Major

Abbas Abed Radam[1] and Sundus Kareem Hamzah[2]

ABSTRACT

Objective: To investigate the genetic relationship of affected samples with healthy controls.
Study Design: Case-control study
Place and Duration of Study: This study was conducted at the Al Kut Hospital for Women and Children, Iraq from 1st November 2023 to 29th February 2024.
Methods: There were 74 children in patient's group and 40 children in control group. Patients and the healthy control group were between the ages of 21 and 30. The hospital's consulting physician has made a clinical diagnosis of the illness. Five milliliters of blood were separated into two tubes: three milliliters in a plain tube for the ELISA test and three milliliters in EDTA tubes for molecular analysis. Molecular and serological analyses were carried out using quantitative real-time PCR and ELISA techniques, respectively.
Results: There were 38 (51.35%) males and the 36(48.65%) females in patients group while in control group, there were 25 males and 15 females. The largest group of patients between 10-20 years, 38 (51.35%), followed by those between 21-30 years, 15 (20.27%). The ELISA assay revealed there is no significant rise in cas-3 (976.93±55.58 pg/ml) and control group (945.87 ±92.57pg/ml). Whereas there was a significant decrease in levels of Cas-7(2267.90±315.56pg/ml) compared to healthy control group (2267.90±315.56pg/ml). The gal-9 gene expression was assessed by quantitative real-time PCR, which revealed a substantial ($P \leq 0.05$) drop in patient expression (0.0054 ±0.0004) as compared to the control, which recorded 1.00±0.00 fold.
Conclusion: The decreased level of galectin-9 production suggested there are many mutations in gal-9 gene this reflects in increased levels of Cas3 and Cas7 in patients with beta thalassemia major.

Key Words: Beta thalassemia major,Gal-9gene,Caspase,Quantitiverealtime PCR

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INTRODUCTION

Beta thalassemia major, a hereditary blood disorder, is characterized by reduced or nonexistent β-globin chain synthesis. This lowers RBC hemoglobin, RBC production, and anemia.[1] Old red blood cells' hemoglobin is broken down mostly by the spleen. In β-TM, hemopoiesis is accelerated to address anemia, leading to increased synthesis and removal of aberrant red blood cells. Additional changes include extramedullary hematopoiesis and splenomegaly. An increase in blood transfusions, red blood cell hemolysis, and iron deposition and buildup may cause splenomegaly.[2] Chronic hypoxia causes anemia and growth hormone deficiency (GHD) in thalassemia patients due to the liver's defective somatomedin production and rapid red blood cell destruction.[3] (Some gene expression is affected by promoter methylation.[4] Low Cas-8 levels and methylation may be diagnostic markers for certain malignancies.[5] owing to their intracellular and extracellular immune control mechanisms, galectin-mediated immune regulation is complicated owing to their extensive organ expression. Galectins regulate adaptive and innate immune responses via cellular and extracellular pathways. Galectins activate macrophages, attract immune cells, and facilitate phagocytosis to govern adaptive immunity via T cell activities and innate immunity through macrophage activation.[6,7] Nucleotide substitutions and frame shift mutations might impact β-globin gene transcription, splicing, and mRNA translation, resulting in β-globin chain absence or reduced synthesis.[8] Gal-9

[1.] Ministry of Education, General Directorate of Education of Wasit, Iraq.
[2.] Department of Chemistry, College of Education, University of Al-Qadisiyah, Al-Qadisiyah, Iraq.

Correspondence: Abbas Abed Radam, Senior Chemistry Educator, Ministry of Education, General Directorate of Education of Wasit, Iraq.
Contact No: +964 771 438 405
Email: chem.edu.post35@qu.edu.iq

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gene expression and caspase (3,7) levels in beta thalassemia major patients were the main focus of this study.

METHODS

The Iraqi Ministry of Health and the Ethics Committee of the Department of Biology, College of Education, University of Al Qadisiyah approved their participation in the research tests. All research participants obtained their fathers' written approval. A control group of 40 healthy individuals and 74 βTM patients hospitalized to Al Kut Hospital for Women and Children each had three milliliters of blood taken. The healthy control group and patients were 21–30. The hospital's consulting physician diagnosed the ailment. Three milliliters of blood were placed in EDTA tubes for molecular analysis and three in plain tubes for ELISA testing. Following manufacturer directions, the Enzyme Linked Immunosorbent Assay measured IL-37 and IL-35 levels in patients and controls. Human Caspase 7 and 3 ELISA Kits (SL3104Hu, SL2079Hu).This research uses TransGen Biotech-China.

The manufacturer's instructions were followed to extract total RNA from each sample using TRIzol®LS Reagent. Transcription of whole RNA to complementary DNA was done using the Easyscript® Kit. A 20µl reaction volume was employed for the technique. The reveres transcription phase was completed in one cycle using the following program: 25°C for 10 minutes, 42°C for 10 minutes, 85°C for 5 minutes, then 4°C until the run was ended. Using quantitative real-time PCR, gal-9 gene expression levels were determined. This expression was validated using TransStart® Top Green qPCR Super Mix (SYBR Green).The reference gene, glyceraldehyde 3-phosphaee dehydrogenase gene (gapdh), was amplified to standardize gal-9 mRNA levels.

Quantitative real-time PCR was done using specified primers. The reaction procedure was: Lyophilized primers were reconstituted in DNase/RNase-free water to a stock solution concentration of 100 pmol/µl. Reconstituted 10 pmol/µl primer in 90 µl deionized water provided a final concentration of 10µM in the working solution. Initial denaturation at 95°C for 5 minutes, denaturation at 95°C for 40 seconds, annealing at 58°C for gapdh and gal3 for 40 seconds, extension at 72°C for 1 minute, 35 cycles, and a hold at 4°C for 1 cycle. Gapdh and gal-9 gene primers were
F: 5′-AACTTTGGCATTGTGGAAGG-3′,
R: 5′-ACACATTGGGGGTAGAACA-3′ and
F: 5′-TCAGAGGTTCCACATCAA-3′,
R: 5′-CCACAGCATTCTCATCAA-3′, respectively.

Using the Livak and Schmittgen[9] equation, ΔCT and ΔΔCT were calculated. This research used SAS to analyze the effects of many characteristics. The least significant difference (LSD) test determined mean differences.

RESULTS

Gender-specific distribution results of β-thalassemic major (βTM) patients showed no significant differences, with 38 samples (51.35%) being male and 36 samples (48.65%) being female. In contrast, the control group had 25 samples (62.50%) males and 15 samples (37.50%) females (Table 1).

When the βTM patient samples were distributed by age, the results showed that the largest group of patients were between the ages of 10 and 20 (38, or 51.35%), followed by those between the ages of 21 and 30 (15, or 20.27%). These two groups form the higher attendance group of age when juxtaposed with the healthy control group (Table 2).

Caspase-3 and Caspase-7 were included in this study as proteins contribute in apoptotic processes. There were no significant changes in Caspase-3 protein in patients (976.93±55.58pg/ml) and healthy control group (945.87±92.57pg/ml) while there were a significant increase in Caspase-7 protein (2267.90 ±315.56pg/ml) compared to healthy control group (917.50± 162.07pg/ml) [Table 3].

Table No.1: Gender distribution among patients with β-thalassemia major and the control group

Gender	Patients	Control	P-value
Male	38 (51.35%)	25 (62.50%)	0.0419*
Female	36 (48.65%)	15 (37.50%)	
*P≤0.05			

Table No.2: Age distribution of β-thalassemia major patients and control group

Age (years)	Patients	Control	P-value
<10	12 (16.22%)	-	0.000**
10-20	38 (51.35%)	10 (25.00%)	
21-30	15 (20.27%)	24 (60.00%)	
>30	9 (12.16%)	6 (15.00%)	
**P≤0.01			

Table No.3: Comparison between patient and control groups in Cas-3 and Cas-7

Group	Caspase-3pg/ml	Caspase-7pg/ml
Patients	976.93 ±55.58	2267.90 ±315.56
Control	945.87 ±92.57	917.50 ±162.07
T-test	106.49 NS	878.72**
P-value	0.7661	0.0497
*P≤0.05,NS: Non-Significant		

No significant variations were seen in the Ct values of gapdh between individuals and the healthy control group (1±0.00). The average fold change of GAPDH

gene expression in the patient groups was (0.98 ± 0.08) [Table 4, Fig. 1]. Gene expression of gal-9was recorded significant decrease (P≤0.05) in patients (0.0054±0.0004) fold compared to control that recorded (1.00 ±0.00) fold (Table 5, Fig. 2).

Table No.4: Comparison of gapdh fold between study groups depending on 2- ΔCt Method

Group	Mean Ct of gapdh	2^-ct	Expression group/ control group	mean fold of gapdh expression
Patients	29.977	9.5 E10	9.5 E10/9.7 E10	0.98 ± 0.08
Control	29.946	9.7 E10	9.7 E10/9.7 E10	1 ± 0.00
LSD value	---	---	---	0.217 NS
NS: Non-Significant				

Table No.5: Comparison of gal-9 gene fold between study groups depending on $2^{-\Delta Ct}$Method

Group	Ct gal-9	Ct GAPDH	ΔCt	ΔΔ Ct	Fold change
Patients	20.15	20.94	-0.2121	-8.9973	0.0054 ±0.0004
Control	20.72	18.16	2.558	2.558	1.00 ±0.00
T-test	--	--	--	--	0.571*
P-value	--	--	--	--	0.03673
*P≤0.05					

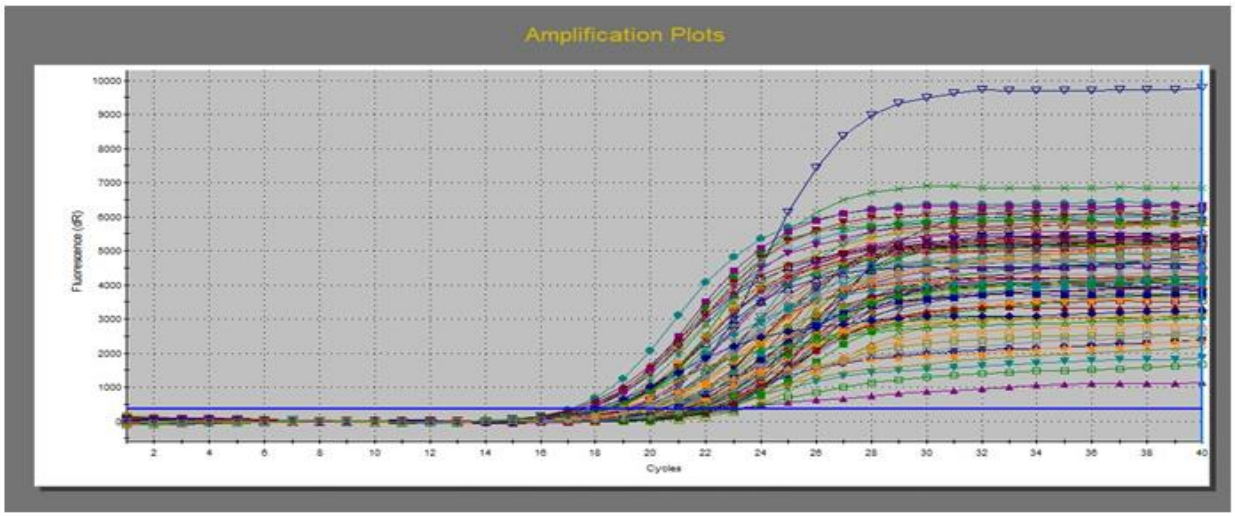

Figure No. 1: Gapdh genes amplification plots by qPCR. Ct values were ranged from 23.32 to 25.4. The photograph was taken directly from Qtower2.0/2.2

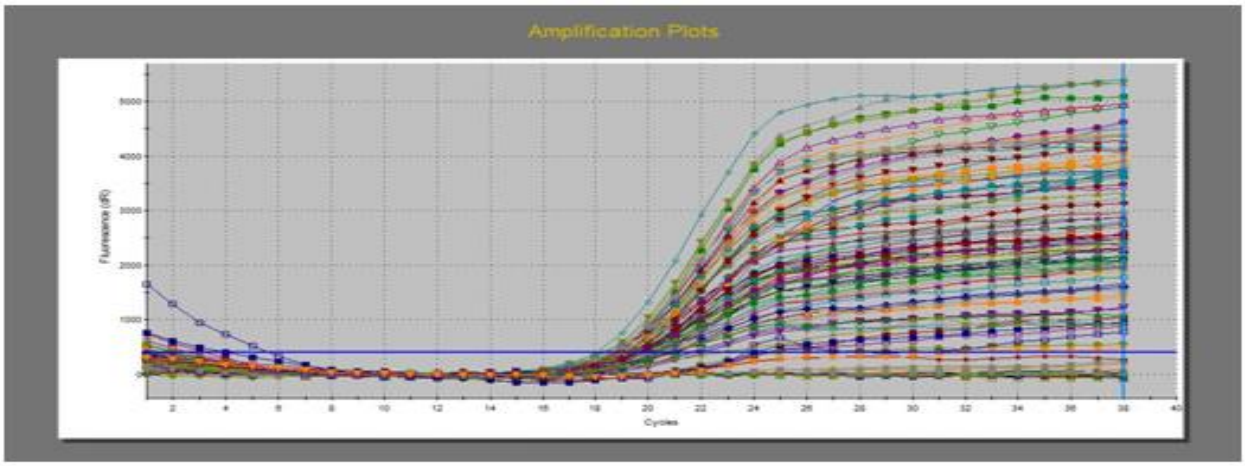

Figure No. 2: gal-9geneamplification plots by qPCR .Ct values was ranged from 27.11 to 31.18.The photograph was taken directly from Qtower2.0/2.2

DISCUSSION

Beta-thalassemia is an autosomal recessive illness that affects both sexes equally and is caused by defects in the β-globin gene on chromosome 11.[10,11] Researcher found similar results in his research of 1800 Iraqi βTM patients in Baghdad. In Saudi Arabia and Al-Bahrain, Al-Awamy[12] found 40% female cases and 60% male cases.

Regular blood transfusions may lengthen life, says one study. However, the strength varied, so some persons had just modest affects. In untreated βTM, hemolytic and severe anemia leads to marrow expansion and hyperplasia. In severe anemia, death might occur within five years. Long-term erythrocyte breakdown causes chronic bilirubin overproduction, which may lead to pigmentary gallstones and hemosiderosis from excess iron in the reticuloendothelial system, notably the liver, pancreas, and heart. Deaths from hemostasis may occur before 25.[13] Takeshita[14] also noted that high transfusion and chelating therapy enhanced survival beyond 30.

Apoptotic caspases kill many old or changed blood cells, which bone marrow, spleen, and liver macrophages remove. The last step of neutrophil and eosinophil lifespan is apoptosis.[15] The reticuloendothelial system eliminates erythrocytes after 100–120 days of senescence.[16] Even without mitochondria and the Apaf-1 adaptor protein, these cells may die via eryptosis, which may include caspases.[17] Platelets, ten-day-old anucleate cytoplasmic fragments, die by caspase-dependent apoptosis when Bcl-XL expression decreases.[18] After genetically modifying Caspase-3, which inhibited cell death in response to oxidative stress (OS), mitochondrial dysfunctions included a swollen morphology, disrupted cristae, decreased membrane potential, increased ROS concentrations, and deficits in mitochondrial oxidative phosphorylation (OXPHOS) enzymes. The fact that caspase-3 gene knockdown (KD) significantly lowered the expression of mitochondrial biogenesis transcriptional activators such Tfam and Nrf-1 suggests that procaspase-3 has a non-apoptotic role in mitochondrial biogenesis.

The idea behind the use of housekeeping genes in molecular research is that these genes are consistently expressed in cells.[19] Gapdh is one of the most often employed housekeeping genes, based on the gene expression data.[20] Robert et al[21] examined the expression of 1718 genes using qRT-PCR. They employed seventy-two distinct kinds of healthy human tissues, using the gapdh gene as a reference gene. They found that gapdh is a very reliable technique for qRT-PCR normalization when applied in clinical studies.

Galectins are the oldest mammalian glycan binding protein (GBP) family and the first to regulate the immune system. Vertebrates contain over 16 prototype galectins (galectin-1 to galectin-16) based on their structural properties.[22] Adipocytes express galectin-12, whereas gastrointestinal epithelial cells, the thymus, and endothelial cells express galectin-9.[23] Galectins in the extracellular environment may bind several glycoconjugates, including those on the cell surface and matrix.

Galectins may influence intracellular activities via glycan-dependent or glycan-independent interactions, unlike other GBPs.[24] Galectins are expressed in different organs and cross-act via several cellular and extracellular mechanisms to modulate immunology. Galectins regulate adaptive and innate immune responses in many ways. Explain galectins' basic properties to understand their regulatory roles in innate immunity, including immune cell migration, phagocytosis, and macrophage activation, and adaptive immunity control through T cell biology mechanisms.

CONCLUSION

The decreased level of galectin-9 production suggested there are many mutations in gal-9 gene this reflects in increased levels of Cas3 and Cas7 in patients with beta thalassemia major**.**

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Abbas Abed Radam, Sundus Kareem Hamzah
Drafting or Revising Critically:	Abbas Abed Radam, Sundus Kareem Hamzah
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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