

Vol. 36, No. 6 June, 2025

ISSN 1029 - 385 X (Print)

ISSN 2519 - 7134 (Online)



# MEDICAL FORUM MONTHLY

**RECOGNISED BY  
PMDC & HEC**

**APNS  
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**“Medical Forum” Monthly Recognised, Indexed and Abstracted by**

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- ☞ EMBASE SCOPUS Database Since 2000
- ☞ Registered with International Standard Serial Number of France bearing ISSN 1029-385X (Print), ISSN 2519-7134 (Online) Since 1992
- ☞ Registered with Press Registrar Govt. of Pak bearing No.1221-B Copr. Since 2009
- ☞ ABC Certification Since 1992
- ☞ On Central Media List Since 1995
- ☞ Medical Forum Affiliated with Medical Academic Foundation (MAF)
- ☞ On OJS, SCOPUS, Open Access, Online, Peer Reviewed Journal
- ☞ EScience Press (CrossRef DOI)
- ☞ Email: med\_forum@hotmail.com, medicalforum@gmail.com
- ☞ website: www.medicalforummonthly.com, www.medforum.pk

<b>MEDICAL FORUM MONTHLY</b>	ISSN 1029 - 385 X (Print)	ISSN 2519 - 7134 (Online)	
	APNS Member	CPNE Member	ABC Certified
	Online Journal	Published Since 1989	
	«Online» <a href="http://www.medicalforummonthly.com">www.medicalforummonthly.com</a>		

on <b>OJS</b>	<b>Scopus</b>	<b>Open Access</b>	<b>Peer Reviewed</b>	<b>Affiliation With:</b> <b>Medial Academic Foundation</b> (MAF) (Regd.)
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<b>Recognized, Indexed &amp; Abstracted by</b>	<b>PMD-IP-0048 (1998), HEC-Y-Category (2009), Excerpta Medica Netherlands (2000), EMBASE SCOPUS Database (2000), Index Medicus (IMEMR) WHO (1997), Cross Ref (DOI), SJR, HJRS, SCI Journal, Research Gate, Resurchify, Editage, Enago, Research Bib, Research Bite, Pastic and PSA, NLP, Pakmedinet &amp; CPSP</b>	<b>doi</b> Ease of Access in Article through doi in One Click doi:10.60110/medforum

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**Published By:** Prof. Nasreen Azhar, Gohawa Road, Link Defence / New Airport Road,  
Opposite Toyota Motors, Lahore Cantt. Lahore.  
Mobile Nos. 0331-6361436, 0300-4879016, 0345-4221303, 0345-4221323.  
E-mail: med\_forum@hotmail.com, medicalforum@gmail.com  
Website: www.medicalforummonthly.com

**Printed By:** Naqvi Brothers Printing Press, Darbar Market, Lahore.

**Affiliation With:** Medial Academic Foundation (MAF) (Regd.)

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**Rate per Copy:** Rs.3000.00

**Subscription Rates :** Pakistan (Rs.30000.00), USA & Canada (US\$ 500.00),  
(annually) China, Japan, UK &Middle East (US\$ 450.00)

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**Editorial**

# How to Maintain Bone Health with Age

**Prof. Dr. Azhar Masud Bhatti**

Editor-in-Chief

Human bone is calcified tissue composed of organic (30%), inorganic (60%) and water (10%). The primary organic material component is collagen a protein that provides flexibility and tensile strength. Then, the main inorganic component is hydroxyapatite, a mineral form of calcium phosphate, which gives bones their hardness and compressive strength. Other important composition of bone formation are bone marrow and different types of cells, like osteoblasts (bone forming cells), osteocytes (mature bone cells), Osteoclast (bone resorbing cells) and bone lining cells. Analysis of DNA often persists in Bones and Teeth. Bone doesn't contain DNA. They only have the breeding enzymes them.

## Key Points

- Vitamin D is important for good bone health because it aids in the absorption and utilization of calcium. There is a high prevalence of vitamin D insufficiency in nursing home residents, hospitalized patients, and adults with hip fractures.
- Calcium has been singled out as a major public health concern today because it is critically important to bone health.
- Genetic factors play a significant role in determining bone mass, controllable lifestyle factors such as diet and physical activity can mean the difference between a frail and strong skeleton.
- Physical activity is important for bone health throughout life. It helps to increase or preserve bone mass and to reduce the risk of falling. All types of physical activity can contribute to bone health.
- Maintaining a healthy body weight is important for bone health throughout life. Being underweight raises the risk of fracture and bone loss. Weight loss is associated with bone loss as well, although adequate diet and physical activity may reduce this loss.
- Reproductive issues can affect bone health. Pregnancy and lactation generally do not harm the skeleton of healthy adult women. Amenorrhea (cessation of menstrual periods) after the onset of puberty and before menopause is a very serious threat to bone health.
- Several medical conditions and prescription medications can affect bone health through various mechanisms, and health care professionals should treat the presence of such conditions and the use of such medications as a potential red flag that signals the need for further assessment of bone health and other risk factors for bone disease.

- Fractures are commonly caused by falls, and thus fall prevention offers another opportunity to protect bones, particularly in those over age 60.
- Smoking can reduce bone mass and increase fracture risk and should be avoided for a variety of health reasons. Heavy alcohol use has been associated with reduced bone mass and increased fracture risk.

A variety of studies indicate that genetic factors are responsible for determining 50–90 percent of bone mass and other qualitative aspects of bone (Recker and Deng 2002)<sup>1</sup>. Heredity not only sets limits on how much bone a person acquires, but also on bone structure, the rate of bone loss, and the skeleton's response to environmental stimuli like nutrients and physical activity. Normal bone mass and strength is controlled by many genetic elements working in concert. The tendency to develop bone diseases like osteoporosis and Paget's disease also appears to be due to genetic factors, although this tendency may also be influenced by environmental factors that are not yet completely understood.

## About Nutrition and Bone Health

- Research suggests that a well-balanced diet is important for bone health throughout life. Depending on age, it may help increase or preserve bone mass.
- Much of the research to date has focused on calcium and vitamin D. Calcium and vitamin D play crucial roles in bone health, although other nutrients are also important.
- The recommendation of calcium intake as children age, beginning with 210 mg per day in infants and rising to 1,300 mg per day in those age 9–18. Recommended levels drop to 1,000 mg per day in those age 19–50, and then increase to 1,200 mg per day for those over age 50. The same age-dependent recommendations for calcium apply to pregnant or nursing women. Recommended levels of vitamin D intake are 200 IU per day for those under age 50, 400 IU per day for those 50–70, and 600 IU per day for those over age 70.

## About Vitamin D and Calcium

The goal of this effort was to determine the level of nutrient intake for normal, healthy individuals that would prevent the development of a chronic condition associated with that nutrient. Some individuals lactose intolerance may play a role in not consuming adequate levels of calcium. Lactose intolerance is a condition in which individuals cannot metabolize lactose, the main sugar found in milk and other calcium-rich dairy products. An estimated 30–50 million Americans

(about 25 percent of the U.S. population) are affected by lactose intolerance, although to varying degrees. While least common among Whites (it affects about 15 percent of White adults), lactose intolerance is widespread among other ethnic groups. Among the adult population, an estimated 70 percent of African-Americans, 74 percent of Native Americans, 53 percent of Mexican-Americans, and 90 percent of Asian-Americans are affected (Jackson and Savaiano 2001)<sup>2</sup>.

Vitamin D is important for good bone health because it aids in the absorption and utilization of calcium. The main source of vitamin D is sunlight, and most people throughout the world get their supply of vitamin D by the conversion of precursors in the skin to active vitamin D, a process caused by exposure to sunlight.

Calcium eaten in the diet must first be absorbed into the body. In fact, much of the calcium consumed in the diet does not make its way to the skeleton; studies indicate that in adults only about 30 percent of calcium intake is actually absorbed by the body. Moreover, some calcium is excreted from the body into the intestine so that the actual net absorption is even lower (Heaney and Abrams 2004)<sup>3</sup>.

Several factors can affect the body's ability to absorb dietary calcium, including vitamin D and estrogen. Deficiencies in either can reduce calcium absorption. The problem of reduced calcium absorption is more acute in older persons, who absorb less dietary calcium because their intestines are no longer as responsive to the action of 1,25-dihydroxy vitamin D. Poor absorption of calcium can be overcome by increasing overall calcium intake and maintaining adequate levels of vitamin D.

#### **Effect of Calcium and Vitamin D on Bone**

Individuals who consume adequate amounts of calcium and vitamin D throughout life should enjoy better overall bone health for two reasons. First, they are more likely to achieve optimal skeletal mass early in life, and second, they are less likely to lose bone later in life. The net result should be higher bone mass and fewer fractures. Selected evidence to support the relationship between these nutrients and bone health during different stages of life.

#### **On Children and Adolescents**

The role of calcium and other minerals in achieving peak bone mass begins before birth. Premature infants tend to have lower bone mineral content later in life, although this may in part be due to their tendency to be light and short for their age. Low birth weight is also associated with low bone mass later in life (Antoniades et al. 2003)<sup>4</sup>.

Many observational studies make it clear that the role of calcium in achieving optimal peak bone mass continues into childhood and adolescence (Heaney et al. 2000)<sup>5</sup>.

Several randomized clinical trials have examined the effect of calcium supplements or calcium-rich foods in children and adolescents (Merrilees et al. 2000)<sup>6</sup>. These

studies have been combined and summarized in a meta-analysis (Wosje and Specker 2000)<sup>7</sup>, which concluded that higher calcium intake increases bone mineral density (BMD) in children and adolescents in certain circumstances. Increases in BMD were more likely in cortical bone sites and among populations with low baseline calcium intakes, and in most studies the increase did not persist beyond the calcium supplementation period. Adequate levels of calcium intake may also be important in maximizing the positive effect of physical activity on bone during the growth period.

#### **On Adults**

Eating adequate amounts of nutrients continues to be important during the young adult years when bone formation and bone resorption are balanced. Unfortunately, most studies of diet and supplement use and bone health have focused on either younger or older individuals. In a study did find that even young men may experience low vitamin D levels in the winter, and that these low levels were associated with lower BMD (Valimaki et al. 2004)<sup>8</sup>. More information is needed about the role of calcium, vitamin D, and other nutrients in maintaining bone in this age group of women and in men.

#### **On Older Adults**

Most randomized clinical trials examining the effect of calcium and vitamin D on bone health have focused on postmenopausal women and the elderly, so the role of these nutrients in promoting bone health is more clearly established for this age group.

Elderly individuals who are vitamin D deficient face an increased risk of falls (Flicker et al. 2004), studies have shown that vitamin D supplementation in these individuals may negate this effect (Dukas et al. 2004)<sup>9</sup>. It is important to note that the design of many of the randomized, controlled trials examining the effect of vitamin D supplements on bone loss or fracture incidence also called for participants to use a calcium supplement.

#### **Other Nutrients for Bone Health**

Other nutrients/dietary components that appear to play a positive role in bone health include vitamin K, vitamin C, copper, manganese, zinc, and iron. These micronutrients are essential to the function of enzymes and local regulators and therefore are important to forming the optimal bone matrix.

Potassium also appears to play an important role in bone health. Diets abundant in potassium-rich fruits and vegetables may reduce the need for calcium to be mobilized from the skeleton. Epidemiologic and short-term intervention studies suggest higher intakes of alkaline potassium salts reduce urine calcium excretion and markers of bone resorption and have been associated with increased bone density (New et al. 2004)<sup>10</sup>.

Many nutrients in addition to calcium and vitamin D play a role in bone health, it is important to consume a

well-balanced diet containing a variety of food, rather than just focusing on one or two bone-related nutrients. This approach can have positive effects on other aspects of health as well. For example, the DASH diet (Dietary Approach to Stop Hypertension), which encourages fruit and vegetable intake in addition to more calcium and less sodium intake, has been linked to lower bone turnover and better cardiovascular status (Lin et al. 2003)<sup>11</sup>. In a recent study of young girls a high intake of fruits and vegetables was associated with increased bone mineral content (Tylavsky et al. 2004)<sup>12</sup>. Fruit and vegetables also provide vitamins, minerals, and fiber, and should be encouraged for overall good nutrition. As alluded to above, abundant potassium intake via increased fruit and vegetable intake may be particularly beneficial for skeletal health. Specific suggestions for selecting a well-balanced diet.

### **Advise for Bone Health**

#### **Support your frame**

One of the best ways to shore up your skeleton is to choose a diet that includes plenty of calcium and vitamin D, two nutrients essential to strengthening bone tissue. The other crucial move: engaging in weight-bearing exercise – like walking, running, or strength training – a few times a week. These workouts exert a force on your bones that stimulates them to produce new cells. It's also important to get a bone-density test at some point, to check for weaknesses.

#### **Support with Physiotherapy**

If musculoskeletal pain crops up somewhere in your body and you end up in a doctor's office, you may be given a choice between drugs (such as painkillers or steroids), surgery, and physical therapy. Many orthopedists recommend trying the latter first: PT helps strengthen the area that's causing your discomfort and corrects any imbalances that may be contributing to the problem. The therapy may even build up your resilience. It could reeducate your central nervous system to be less sensitive to pain signals.

#### **Body Posture**

Many of us are spending even more time sitting at home. That could explain a lot about how your body feels. Sitting in one position or with poor posture tightens up many of your muscles, ligaments, and joints, which often leads to soreness and pain.

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# Role of M.R.I. in Evaluation of Traumatic Knee Joint Injuries

M.R.I. In  
Evaluation of Knee  
Joint Injuries

Ambareen Muhammad, Zeenat Adil, Abdul Majid, Aziz Zia and Rida Saleem

## ABSTRACT

**Objective:** To describe the MRI characteristics of traumatic lesions and to identify common knee joint lesions.

**Study Design:** Cross sectional study

**Place and Duration of Study:** This study was conducted at the Radiology Department of Kuwait Teaching Hospital between 1 July 2023 - 30<sup>st</sup> June 2024.

**Methods:** The study was performed on 160 consecutively registered patients. It is a cross sectional descriptive study. Patients 16 yrs. and above with traumatic knee injury were included in this study. Non cooperative patients, those who have undergone prior surgical procedures, periarticular tumors or infections and contraindications to MRI were excluded from the study.

**Results:** We analyzed MRI scans of total of 160 patients with knee joint injuries. The age of patient was grouped in clusters of 10 years. Majority of the patients (35%) were found in 26-35 years' age group. Out of total 160 patients; majority of them were male comprising 126 patients and 34 were female. They underwent MR imaging within 6 months of their injury. Right knee was involved in 55% and left knee in 45% cases. Among cruciate ligaments partial tear of ACL was most commonly seen. In one-third of our cases bone contusions were present.

**Conclusion:** Based on the current study's data, it can be said that MRI is the most effective method for evaluating internal knee joint derangement after injury. The most common findings were anterior cruciate ligament tears, medial meniscal tears, and joint effusions.

**Key Words:** Knee joint, MRI, ACL, PCL, MM, LM.

**Citation of article:** Muhammad A, Adil Z, Majid A, Zia A, Saleem R. Role of M.R.I. in Evaluation of Traumatic Knee Joint Injuries. Med Forum 2025;36(6):4-8. doi:10.60110/medforum.360601.

## INTRODUCTION

The knee joint is a hinge. It has a broad range of movement and is vulnerable to both acute and non-traumatic ligament damage<sup>1</sup>. Knee joint discomfort always affects the mobility of patient therefore early diagnosis of knee joint pathologies/injuries is very important. Osteoarthritis and meniscal tears are two common pathologies. Trauma or degeneration causes knee pain and meniscal tears are common findings. Meniscal tears should be treated on time, if not it will lead to osteoarthritis and will then require surgical treatment<sup>2</sup>. ACL tears are one of the most common and catastrophic sports injury in knee joint. After ACL injury, femur and tibia bone bruises can be seen on MRI which reveals hypo intense and hyper intense signals on T1 and T2 WI respectively.

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Received: December, 2024

Reviewed: January-February, 2025

Accepted: March, 2025

Patterns of bone bruises provides a clue to the mechanism of ACL injury and also provides information when the injury has occurred<sup>3</sup>. ACL injuries mainly affects young people which causes joint instability leading to reduced activity<sup>4</sup>.

Knee joint is an important and complex joint in human body characterized by presence of various ligaments and menisci. Human mobility is dependent upon stability of knee joint<sup>5,6</sup>. Knee pain can occur at any age. Knee discomfort can be caused by a number of things, including injuries and underlying conditions like arthritis. When determining the source of knee discomfort, radiology is crucial<sup>5</sup>. When it comes to identifying and evaluating both acute and chronic internal derangements of knee joint injuries, MRI is the preferred modality<sup>7</sup>.

Imaging techniques for knee pain include scintigraphy, arthrography, CT, MRI, and X-rays. Due to their accessibility and affordability, X-rays were the first imaging modality to be employed; nevertheless, their use was limited because they were unable to detect soft tissue pathology and exposed the patient to radiation<sup>8</sup>. According to the American College of Radiology Appropriateness Criteria, MRI should be the first radiological test performed in suspected cases of non-osseous knee injury. The gold standard for high-resolution evaluation of the musculoskeletal system is MRI<sup>9</sup>. MRI plays a vital role in diagnosing meniscal tears, helps in preoperative planning and post op rehabilitation<sup>10</sup>.



When evaluating traumatic knee injuries, MRI offers a considerable advantage over conventional imaging methods due to its multiplanarity and superior soft tissue contrast resolution. MRI should be performed often since it can reliably diagnose ligamentous injuries to the knee joint. Noninvasive MRI is capable of precisely assessing a variety of conditions, including fractures, arthritis, infections, trauma, torn tendons and ligaments, and damaged cartilage. Bony and soft tissue abnormalities can be accurately identified by MRI in terms of their nature and extent<sup>11</sup>. Multi ligament injuries are caused by high force and severe injury but are rare. Early detection is very important for prompt treatment of multi ligament injury. MRI is valuable in detection of isolated ligament injury however its role in assessment of multi ligament injury is not clear yet<sup>12</sup>. Although arthroscopy is the gold standard for diagnosing internal knee derangement, it is an intrusive treatment that has drawbacks, including surgical and anesthetic difficulties, hospital stays, and theater expenses, and it is user dependent<sup>13</sup>. When utilized properly, MRI has been shown to decrease the incidence of needless surgical arthroscopies and aid in pre-operative planning.

## METHODS

The study was performed in the Radiology Department of Kuwait Teaching Hospital between 1 July 2023 - 30<sup>st</sup> June 2024 on 160 consecutively registered patients. It is a cross-sectional descriptive study. Patients of either sex, 16 years or above referred for MRI knee with history of injury were included in the study. Non cooperative individuals, those who have undergone prior surgical procedures, periarticular tumors or infections and contraindications to MRI were excluded from the study.

Ethical approval was obtained from the hospital ethics committee. According to the inclusion criteria, patients with knee injuries who were sent to KTH's Radiology Department for knee MRIs were selected. A proper history was taken. Written informed permission was obtained after they were briefed on the study's significance and goal. Toshiba Japan's 0.3 Tesla MR machine was used to perform the knee MRI scan. To maximize the signal to noise ratio and enable full imaging of the ACL on a sagittal image, patients were positioned in a supine posture with their knee extended and slightly externally rotated (10–15 degrees) in an extremity coil. The following sequences were included in MRI protocols: fat suppressed T2, axial, coronal, and sagittal weighted sequences for T1, T2, and PD.

Two expert radiologists who were blinded evaluated four structures: the ACL, PCL, MM, and LM. PCL and ACL were categorized as either partial or total tears. Grade I, II, and III tears were assigned to MM and LM. The degree of joint effusion was rated as moderate and

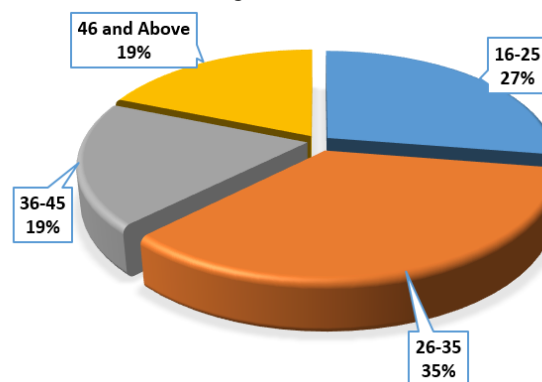
mild. Lastly, the existence or lack of bone bruising was evaluated as well.

**MR Image Evaluation:** Two skilled radiologists who were blinded to the damage pattern separately examined MR images to check for meniscus, ACL, PCL, MM, and LM injuries. The MRI results of each other were hidden from the two radiologists. The damaged ligaments were categorized as either a partial tear (the ligament was disturbed but continuous, Grade 1 or 2) or a total tear (interruption of ligament integrity, Grade 3), depending on the integrity of the ligaments. Grade 1 meniscal tears were defined as intra-substance abnormalities, grade 2 tears as lateral non-articular surface tears, and grade 3 tears as superior or inferior articular surface tears. Any discrepancies in the radiologists' assessments were settled by dialogue and agreement.

SPSS version 23.0 was used to gather, tabulate, and statistically analyze all of the data. The information was displayed in tables. Absolute frequencies (numbers) and relative frequencies (percentages) were used to express various variables. Age, gender, laterality, kind of injury, injured ligaments, injured menisci, presence or absence of bone bruising and joint effusions were the variables included in the study.

## RESULTS

We analyzed MRI scans of total of 160 patients with knee joint injuries. The age of patient was grouped in clusters of 10 years. Majority of the patients were found in 26-35 years' age group comprising 56 patients which make 35%. (Figure-1) Out of total 160 patients; majority of them were male comprising 126 patients and 34 were female. (Figure-2)



**Figure No.1: Age Group Distribution**

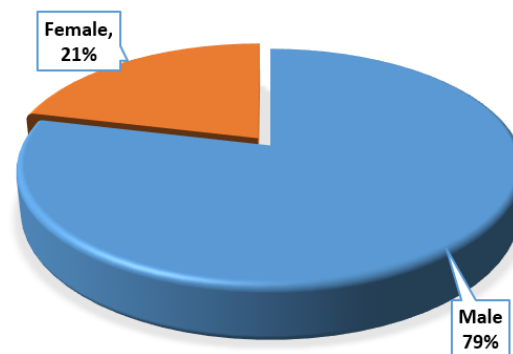
They underwent MR imaging within 6 months of their injury. When we analyzed the type of injury, it was found that majority of the patient had history of fall (30%), followed by sports trauma (18.8%) and road traffic accident (15%). 36.3% of patients had other type of trauma which did not fit in above categories. Right knee was affected in 55% cases and left knee in 45% cases.

**Table No. 1: Frequency of MRI Findings in Knee Injuries (n = 160)**

Parameter	Category	Number of Patients	%age
Affected Side	Right	88	55%
	Left	72	45%
Type of Injury	Sports	30	18.8%
	Fall	48	30%
	RTA	24	15%
	Other Trauma	68	36.3%
ACL	Intact	98	61.3%
	Partial Tear	42	26.3%
	Complete Tear	20	12.5%
PCL	Intact	158	98.8%
	Partial Tear	2	1.3%
	Complete Tear	0	0%
MM Anterior Horn	Intact	160	100%
	Grade 1	0	0%
	Grade 2	0	0%
	Grade 3	0	0%
MM Posterior Horn	Intact	40	25%
	Grade 1	20	12.5%
	Grade 2	28	17.5%
	Grade 3	72	45%
LM Anterior Horn	Intact	156	97.5%
	Grade 1	2	1.3%
	Grade 2	2	1.3%
	Grade 3	0	0%
LM Posterior Horn	Intact	118	73.8%
	Grade 1	20	12.5%
	Grade 2	10	6.3%
	Grade 3	12	7.5%
Joint Effusion	Normal	50	31.3%
	Mild/Small	90	65.3%
	Moderate	20	12.5%
Bone Contusion	Present	42	26.3%
	Absent	118	73.8%

When we assessed the injured structures after trauma to knee joint we found that ACL was intact in 98 cases, partial tear in 42 cases and complete tear in 20 cases. Similarly, PCL was intact in 158 cases, partial tear seen in 2 case and complete tear in 0 case. When we analyzed menisci, we noted that posterior horn of medial meniscus was most commonly injured. Grade 3 tears were most common comprising 72 patients which make 45%. Mild/small joint effusion was seen in 90

cases (65.3%) and moderate joint effusion was present in 20 cases (12.5%). Bone contusions were seen in 42 cases (26.3%). Table-1.

**Figure No.2: Gender Distribution**

## DISCUSSION

One of the biggest and most intricate joints in the body is the knee joint. Pathologies or injuries to the knee joint can significantly impair movement and result in disability. The most effective non-invasive imaging method for evaluating the knee's anatomical features is magnetic resonance imaging (MRI), however arthroscopy is the gold standard in evaluation of meniscal and cruciate ligament pathology<sup>14</sup>. Knee and shoulder are the most frequently requested examination in sports injury. With conventional and CT arthrography; it is very difficult to completely evaluate capsule, collateral ligament, menisci and tendons, however MRI provides excellent details of internal structures, soft tissue and bone bruises.

Males predominated among the patients in this study, with the majority being in the 26–35 age range. Our findings are consistent with those of Rana et al<sup>15</sup>, who showed that the majority of patients were male and in the 26–30 age range. Comparable to the Rana et al<sup>15</sup> study, in which the male population was 70.13% and the female population was 29.87%, our study had 78.8% males and 21.3% females. Men are more likely than women to be active and participate in outdoor activities, which puts their knees at higher risk of damage and injury. In our study we observed that right knee (55%) was affected more than the left knee (45%), these results are comparable with study of Wang et al<sup>16</sup> where right knee was involved in 58.44% and left knee in 41.56%<sup>5</sup>.

After assessment of injured structures in knee joint following various types of trauma we found that ACL partial rupture was present in 26.3% of cases and complete tear in 12.5%. These results are slightly different from the findings of Kucha et al<sup>17</sup> where partial tear was seen in 22.2% and complete tear in 77.78% cases. In meniscal injury we noted that posterior horn of medial meniscus was most commonly injured comprising 75% cases and in majority of the cases (45%), it was grade-3 tears. This is in line with

the study performed by Van et al<sup>18</sup> where posterior horn of medial meniscus was most commonly injured (51.9%). In our study majority (65.3%) of the cases either mild or small joint effusion is seen while moderate effusion was present in only 12.5% cases. The result corresponds well with study of Mattoo et al<sup>19</sup> where small joint effusion was seen in majority of patients while moderate effusion was seen in only 11.69%. In this study bony contusions involving either femur or tibia was seen in 42 patients which comprises 26.3%. This result is in concordance with the study of Mohabey et al<sup>20</sup> where bony contusions were present in 22.07 % cases<sup>5</sup>.

Many patients had normal MRI scans, which may be because patients with painful knees were included rather than those who had traumatic knee injuries. Joint effusion and meniscal damage were the most frequent soft tissue abnormalities found in our research. Most frequently observed was a grade 3 tear of the medial meniscus's posterior horn. Among cruciate ligaments partial tear of ACL was most commonly seen. In one-third of our cases bone contusions were present.

However, the study had its limitations as well. Patients with contraindications to MRI (e.g. cardiac pacemakers or cochlear implants or certain orthopedic prostheses) were excluded first to avoid selection bias. Second, although reclined and in the dark, having an MRI was still more difficult in claustrophobic or disoriented individuals, and these cases may have been excluded. Third, because the MRI was not closely accessible to non-ambulatory patients (for example, patients in wheelchairs or on hospital beds), these patients could not receive scans due to logistical limitations of the study. These factors potentially limited some cases of injury from being captured and may minimally impact the comprehensiveness of the study. Despite these limitations, this study sets a strong basis for future research and illustrates the important role of MRI in evaluating and managing knee injuries.

## CONCLUSION

Magnetic Resonance imaging (MRI) would be the best choice in assessment of internal derangement of knee joint following injury and most frequent findings include joint effusion, medial meniscal and anterior cruciate ligament tear. MRI provides rapid, accurate and non-invasive examination of knee joint following injury. It is also cost effective and reduces unnecessary surgical and arthroscopic procedures.

### Recommendations

Further randomized, multi-center studies with extended follow-up are recommended to validate and generalize these findings.

### Acknowledgement

First of all, I want to express my gratitude to Allah the Almighty for allowing me to finish this study. I am

appreciative of everyone who contributed their knowledge to assist me finish this project. I am also appreciative of my family's and parents' moral support during this research.

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

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

**Source of Funding:** None

**Ethical Approval:** No. 2023-929-1 Dated 27.06.2023

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# Perinatal Outcome of Baby Delivered Vaginally After Successful External Cephalic Version

Vaginal Delivery  
After Successful  
External  
Cephalic Version

Qurat ul Ain<sup>1</sup>, Saira Khan<sup>2</sup> and Basharat Ahmad<sup>2</sup>

## ABSTRACT

**Objective:** To assess the proportion of unfavorable birth-related events occurring after a successful fetal repositioning maneuver near expected delivery in pregnant individuals.

**Study Design:** Descriptive analytical evaluation study

**Place and Duration of Study:** This study was conducted at the Obstetrics and Women's Health Unit at Lady Reading Hospital, Peshawar, spanning from January through September of 2022.

**Methods:** The research encompassed 197 expectant participants who underwent effective manual fetal rotation to cephalic alignment. Postpartum evaluation involved identifying harmful neonatal indicators such as diminished Apgar performance—categorized as a score less than five at five minutes after birth (Annex II)—alongside the requirement for neonatal critical care admission. Criteria for neonatal intensive unit involvement included compromised breathing needing mechanical assistance, convulsive episodes, severe oxygen-deprivation-related encephalopathy, abnormal heart rhythms, or additional disorders needing specialized pediatric attention, including significant jaundice requiring blood-exchange treatment.

**Results:** Participants' ages ranged from 18 to 40 years, with an average age of  $28.629 \pm 2.53$  years, average pregnancy duration at  $38.421 \pm 0.98$  weeks, and mean childbirth count of  $1.416 \pm 1.23$ . Reduced Apgar levels occurred in 5.1% of subjects, while critical newborn unit referral was necessary in 2.5%.

**Conclusion:** To summarize, executing a cephalic repositioning procedure at full term does not correlate with heightened newborn health complications or death risk.

**Key Words:** Fetal turning maneuver, Spontaneous childbirth, Birth condition rating, Newborn intensive treatment

**Citation of article:** Qurat ul Ain, Khan S, Ahmad B. Perinatal Outcome of Baby Delivered Vaginally After Successful External Cephalic Version. Med Forum 2025;36(6):9-12. doi:10.60110/medforum.360602.

## INTRODUCTION

Manual fetal repositioning, often termed external cephalic version (ECV), represents a procedural technique where a fetus in breech alignment is guided into a vertex orientation through directed abdominal manipulation. Candidates who opt for this maneuver are commonly those who receive detailed procedural information, find reassurance in the documented safety profile, and are inclined toward experiencing vaginal parturition. In contrast, others may decline ECV due to apprehensions, insufficient medical briefing, or an inclination toward scheduled surgical birth.<sup>1</sup>

The central rationale for utilizing ECV is its capacity to elevate the occurrence of head-first fetal alignment at

labor onset, thereby diminishing reliance on operative delivery. Evidence from a comprehensive systematic review conducted in which synthesized data from eight randomized trials involving 1,308 subjects, supports this claim.<sup>2</sup> Findings indicated that ECV substantially decreased the incidence of breech labor presentations by nearly 60% (Relative Risk [RR] 0.42, 95% Confidence Interval [CI] 0.29–0.61) and resulted in approximately a 40% reduction in surgical birth rates (RR 0.57, 95% CI 0.40–0.82) compared with those not receiving the intervention.

Nonetheless, post-ECV cesarean rates remain disproportionately high relative to individuals who initially present in spontaneous cephalic position. A 2014 synthesis of observational datasets highlighted that women with successful ECV were nearly twice as likely to undergo cesarean delivery as those with naturally aligned fetuses (21% vs. 11%; RR 2.19, 95% CI 1.73–2.76).<sup>3</sup> This elevation was predominantly attributed to intrapartum challenges like obstructed labor and non-reassuring cardiotocography.

The precise factors underlying labor dystocia following effective ECV are not fully delineated. One prevailing hypothesis posits that structural or biomechanical elements associated with breech presentation—such as elevated fetal station or diminished pelvic capacity—may concurrently predispose to birth obstruction.

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Received: November, 2024

Reviewed: December-February, 2025

Accepted: April, 2025



Additionally, parity status plays a critical role in delivery outcomes, with multiparous individuals more frequently achieving vaginal delivery post-ECV compared to nulliparous counterparts.<sup>1</sup>

Empirical research supports varied neonatal outcomes. A clinical assessment led by Rosman AN identified that roughly 6.9% of infants exhibited reduced Apgar scores after successful ECV.<sup>4</sup> Conversely, El-Toukhy T and colleagues observed no such neonatal compromise in their cohort.<sup>5</sup> Furthermore, Son M and associates, in a 2018 study, documented a 3.3% rate of NICU admissions post-ECV<sup>6</sup>. Overall, ECV remains effective in minimizing breech births and reducing cesarean incidences. It also contributes positively to maternal well-being and lowers financial burdens on healthcare infrastructure. Recognizing these benefits, the Royal College of Obstetricians and Gynaecologists advises offering ECV to all patients with uncomplicated term breech gestations.<sup>7</sup>

Despite such endorsements internationally, outcome-specific data regarding ECV from the Pakistani demographic remain limited. Existing national studies have primarily emphasized maternal over neonatal metrics. Addressing this research gap, the current investigation seeks to quantify the rate of negative perinatal outcomes following a successful ECV procedure.

## METHODS

This analytical observational survey was implemented within the Obstetric and Gynecologic Division of Lady Reading Hospital, Peshawar, during the interval of January to September 2022. The sample included 197 expectant individuals whose pregnancies were managed with effective external head-turning procedures. After parturition, the neonates were assessed for undesirable clinical results, such as a reduced Apgar rating—characterized as a score under 5 at five minutes post-birth—and the necessity for intensive neonatal unit admission. NICU transfer criteria comprised respiratory compromise requiring mechanical breathing assistance, convulsions post-delivery, profound oxygen-deprivation-related brain injury, disturbances in cardiac rhythm, and other significant neonatal disorders, including acute jaundice needing blood exchange therapy, or any situation demanding evaluation and care by specialized newborn services.

## RESULTS

Participant ages ranged between 18 and 40 years, with an average age calculated at  $28.629 \pm 2.53$  years. The typical duration of pregnancy was measured at  $38.421 \pm 0.98$  weeks, while the mean number of previous births was found to be  $1.416 \pm 1.23$ , as detailed in Table 1. A decreased Apgar rating was identified in 5.1% of cases, as presented in Table 2. Admission into

the neonatal critical care unit occurred in 2.5% of neonates, according to Table 3.

**Table No.1: Distribution of Average Values for Age, Gestational Duration, and Birth History (n = 197)**

Parameter	Mean $\pm$ SD
Chronological Age (in years)	$28.629 \pm 2.53$
Weeks of Pregnancy at Delivery	$38.421 \pm 0.98$
Previous Deliveries (Parity)	$1.416 \pm 1.23$

**Table No.2: Occurrence and Percentage of Neonates Exhibiting Suboptimal Apgar Scores (n = 197)**

Low Vitality Rating	Count	Percentage
Confirmed	10	5.1%
Absent	187	94.9%
Aggregate	197	100%

**Table No.3: Proportion and Frequency of Newborns Transferred to Specialized Neonatal Units (n = 197)**

NICU Transfer Required	Total Cases	Proportion (%)
Yes	5	2.5%
No	192	97.5%
Overall	197	100%

**Table No.4: Breakdown of Low Apgar Scores According to Maternal Age Group**

Maternal Age (Years)	Reduced Apgar	Normal Apgar	p-value
18–30	10 (6.7%)	140 (93.3%)	0.069
>30	0 (0%)	47 (100%)	
Total	10 (5.1%)	187 (94.9%)	

**Table No.5: Association Between Gestational Length and Apgar Score**

Gestation Period (Weeks)	Low Apgar Count	Normal Apgar	p-value
37–38	6 (5.5%)	103 (94.5%)	0.760
39–40	4 (4.5%)	84 (95.5%)	
Combined Total	10 (5.1%)	187 (94.9%)	

**Table No.6: Relationship Between Previous Childbirths and Apgar Results**

Parity Level	Low Apgar Cases	Normal Apgar	p-value
0–2 Births	10 (6.9%)	134 (93.1%)	0.049
More than 2	0 (0%)	53 (100%)	
Total	10 (5.1%)	187 (94.9%)	

**Table No.7: Analysis of NICU Admissions by Age Bracket**

Maternal Age Group	NICU Needed	Not Needed	p-value
18–30	5 (3.3%)	145 (96.7%)	0.205
Above 30	0 (0%)	47 (100%)	
Aggregate	5 (2.5%)	192 (97.5%)	

Breakdown analysis of negative birth-related events based on maternal age, pregnancy duration, and delivery history is presented in Tables 4 through 8.

**Table No.8: Evaluation of NICU Requirement by Weeks of Gestation**

Gestational Window (Weeks)	NICU Yes	NICU No	p-value
37–38	2 (1.8%)	107 (98.2%)	0.485
39–40	3 (3.4%)	85 (96.6%)	
Total Cases	5 (2.5%)	192 (97.5%)	

## DISCUSSION

Within this investigation, 5.1% of newborns demonstrated diminished vitality scores at five minutes post-delivery, while 2.5% required transfer to specialized neonatal care facilities. In contrast, Rosman AN and collaborators reported a 6.9% occurrence of suboptimal Apgar indices after successful fetal rotation maneuvers.<sup>4</sup> Conversely, El-Toukhy T's team observed no instances of reduced Apgar performance in their findings.<sup>5</sup> A separate report by Son M in 2018 cited a 3.3% frequency of neonatal intensive care utilization.<sup>6</sup> Our observations closely reflect historical research outcomes. A comprehensive synthesis by Collaris and associates detailed a range of complications arising from fetal repositioning procedures, including fleeting irregular fetal heart tracings, maternal bleeding, premature placental detachment, umbilical cord complications, emergency operative births, and intrauterine deaths.<sup>7</sup> Nonetheless, the total frequency of such complications remained limited, with wide inconsistencies in case definitions and documentation across included sources. Notably, these adverse results pertained solely to individuals undergoing fetal turning, with no comparative data from non-intervention groups.<sup>8</sup>

Similarly, Grootscholten et al. aggregated data from multiple studies, identifying an overall post-procedure complication frequency of 6.1%, with severe events occurring in only 0.24% of instances<sup>9</sup>. However, this review emphasized outcomes between successful versus unsuccessful repositioning attempts, without fully addressing the broader question of whether the intervention should be attempted initially.

In contrast, our work adds depth to the existing literature by examining an expanded set of perinatal outcomes in a more diverse sample population. Hofmeyr et al., through a Cochrane database evaluation involving four randomized controlled studies encompassing 1,308 subjects, compared outcomes in individuals undergoing attempted fetal repositioning to those eligible but untreated. No meaningful statistical differences emerged regarding neonatal health

indicators, such as vitality scoring, venous blood acidity (pH < 7.20), NICU utilization, or perinatal loss. However, the majority of these parameters were secondary in nature, and only specific segments of the total cohort were evaluated for each outcome: 428 for Apgar scores, 368 for NICU transfer, and 52 for umbilical pH, with fetal death tracked universally.<sup>2</sup>

Though descriptive in methodology, our investigation enhances insight into ECV-associated neonatal implications by assessing a broader scope of clinically meaningful birth outcomes in a more comprehensive cohort.<sup>10</sup>

Several constraints affect interpretation of our data. First, the maneuver's success rate in our dataset stood at 40%, a figure on the lower side of existing published ranges, potentially limiting generalizability to environments with improved success metrics or differing procedural workflows. Second, although adverse infant outcomes were infrequent, their prevalence was still elevated relative to expectations, especially given the shortfall in targeted recruitment numbers. Third, the non-randomized nature of this analysis introduces intrinsic selection distortion.<sup>11,12</sup> Those seen as better suited for repositioning were more likely to be chosen, which may affect external validity. This is supported by noticeable demographic variances—individuals who underwent the procedure were more often previously pregnant and had reduced body mass index values at delivery than those excluded. While multivariate modeling was employed to adjust for observed disparities, residual bias due to unmeasured variables cannot be definitively ruled out.<sup>13</sup>

## CONCLUSION

To conclude, attempting external cephalic version (ECV) at term does not lead to a higher risk of complications for the newborn or mother. Although predicting the outcome of the procedure remains uncertain, performing ECV significantly lowers the likelihood of requiring a cesarean section compared to waiting for spontaneous correction. Therefore, current evidence continues to support the recommendation that ECV should be offered when a breech presentation is identified at term.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Qurat ul Ain, Saira Khan
Drafting or Revising Critically:	Qurat ul Ain, Basharat Ahmad
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No. 558/LRH/MTI Dated 11.08.2020

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# Prevalence of Bowel Dysfunction after Colorectal Surgery & its Impact on Quality of Life in Khyber Pakhtunkhwa (KPK), Pakistan

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## ABSTRACT

**Objective:** This study aimed to assess the prevalence of bowel dysfunction after colorectal surgery and evaluate its impact on health-related quality of life in patients treated at a tertiary care hospital in Khyber Pakhtunkhwa (KPK), Pakistan.

**Study Design:** Cross-sectional observational study

**Place and Duration of Study:** This study was conducted at the department of general surgery, Hayatabad Medical Complex, Peshawar, Pakistan between February 2020 and January 2024.

**Methods:** Total 240 patients were enrolled using consecutive non-probability sampling. Patients of any gender who were 18 years or older and who underwent emergency or elective surgery at our institute for a benign or malignant colorectal disease were included in the study.

**Results:** Surgical characteristics revealed that 62.5% of the patients were operated upon for colorectal cancer and 37.5% for benign disease. Resection at the rectum was performed in 45.8%. Right hemicolectomy was the most frequently performed colon surgery (25%), followed by left hemicolectomy (16.7%) and sigmoid colectomy (12.5%).

**Conclusion:** Postoperative bowel dysfunction is a frequent postoperative complication among colorectal surgery patients in KPK that affect their quality of life greatly. This underscores the need for functional outcome evaluation and multidisciplinary management in the routine follow-up of postoperative patients. Early identification and targeted interventions are necessary to enhance the long-term health of these patients.

**Key Words:** Bowel dysfunction, colorectal surgery, quality of life, LARS, stoma, rectal cancer

**Citation of article:** Shah FO, Raza TA, Imtiaz H, Mumtaz A. Prevalence of Bowel Dysfunction after Colorectal Surgery & its Impact on Quality of Life in Khyber Pakhtunkhwa (KPK), Pakistan. Med Forum 2025;36(6):13-17. doi:10.60110/medforum.360603.

## INTRODUCTION

Colorectal surgery is a cornerstone of treatment for many benign and malignant diseases such as colorectal cancer, diverticular disease, inflammatory bowel disease and benign anorectal diseases. Although the development of surgical procedures (such as laparoscopic and sphincter-preserving surgery) has resulted in enhanced oncological outcomes and decreased perioperative morbidity, a considerable proportion of patients still experience postoperative bowel dysfunction<sup>1</sup>.

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Received: January, 2025

Reviewed: February, 2025

Accepted: March, 2025

Bowel dysfunction include a spectrum of symptoms including fecal incontinence (FI), urgency, frequent bowel movements, clustering, and constipation that cumulatively lead to the long-term physical and psychosocial health of patients<sup>2,3</sup>.

Low Anterior Resection Syndrome (LARS), which occurs in around 80% of patients following low-anterior resection for rectal cancer, is a well-known example<sup>3</sup>. However, even after right or transversal colectomies, some patients continue to have postoperative changes in their bowel habits, such as increased frequency and urgency of stools, which are often overlooked in clinical practice<sup>4,5</sup>. The quality of life can be significantly impacted by these symptoms, which can significantly disrupt everyday activities, cause social isolation, and trigger anxiety and despair<sup>6</sup>.

In high income countries, standardized long-term follow up and validated tools such as the LARS score or the EORTC QLQ-CR29 questionnaire are routinely applied for assessment and management of these symptoms<sup>7,8</sup>. However, there is a dearth of information in underdeveloped nations like Pakistan, particularly when it comes to KPK, where initiatives are focused on problems related to the frequency and severity of bowel

dysfunction following colon surgery<sup>9</sup>. Additional factors contributing to under diagnosis and under treatment include a lack of patient and physician education, social stigma around bowel symptoms, and inadequate access to expert colorectal care<sup>10</sup>.

Given the rising incidence of colorectal diseases and the rise in surgical procedures in Pakistan, it is critical to assess the incidence and outcomes of postoperative bowel dysfunction in this population. This study aims to determine the prevalence of bowel dysfunction following colorectal surgeries in KPK and how it affects quality of life (QoL) by utilizing validated instruments.

## METHODS

This cross-sectional observational study was carried out in the department of general surgery, Hayatabad Medical Complex, Peshawar, from February 2020 to January 2024. Approval from the ethics committee was taken prior to study initiation under reference # 1109. Participants provided written informed consent following explanation of the study's aim, procedures, potential risks and benefits.

Total 240 patients were enrolled using consecutive non-probability sampling. Patients of any gender who were 18 years or older and who underwent emergency or elective surgery at our institute for a benign or malignant colorectal disease were included in the study. Eligible subjects were those who had been postoperatively followed for at least 6 months to ensure that bowel function had stabilized. Patients with insufficient medical records, metastatic or recurring disease, loss of bowel control due to a prior underlying neurological condition, and those who declined to participate were excluded.

Patients' information was derived from medical records and direct interviews with a structured questionnaire including demographic data of the patients (age, sex, address, and comorbidities), details of surgery (type of surgery, surgical indication, surgical technique, anastomotic level, and stoma), follow up information along and the use of neo-adjuvant and adjuvant therapy. Functional outcome was evaluated by matching LARS score for patients with a rectal resection with the validated LARS score and modified bowel function questionnaire for other types of colorectal transactions. The (LARS) score is a validated instrument that has been developed for the purpose of evaluating bowel function after rectal resection. It is an evaluation of five major symptoms incontinence for flatus, incontinence for liquid stool, frequency of evacuations, cluster of stools and urgency. The specific score is provided for each symptom, which add up to a total score of 42. A score between 0 and 20 denotes no LARS (normal bowel function). Major LARS (severe dysfunction) is indicated by numbers 30–42, whereas minor LARS (moderate dysfunction) is indicated by numbers 21–29.

The European Organization for Research and Treatment of Cancer (EORTC) QLQ-CR29, a colorectal-specific module that includes functional and symptom measures, was used to measure health-related quality of life. It primarily targets the problems of patients with colorectal cancer and is an add-on to the EORTC QLQ-C30 core questionnaire. It contains 29 entries that deal with:

Functional scales (such as sexual function, anxiety, and body image) and symptom scales/items (such as fecal incontinence, abdominal pain, bloating, and frequency of stools). All items are rated on a scale of 1 (not at all) to 4 (very much), and higher scores for functional scales are better, and for symptom scales they are worse. The final board scores are linearly translated to a 0–100 scale for analysis.

SPSS version 25 was used for statistical analysis. Descriptive statistics were used to summarize clinical factors and demographics. Continuous variables were represented by means and standard deviations, whereas categorical variables were displayed as numbers and percentages. To examine the relationships between bowel dysfunction and categorical factors, chi-square and Fisher's exact tests were used. Groups' quality-of-life values were compared using ANOVA and independent t tests. At  $p \leq 0.05$ , the results were deemed statistically significant.

## RESULTS

The cohort comprised 140 (58.3%) males and 100 (41.7%) female, with a mean age of  $52.4 \pm 11.3$  years. Urban residents constituted 54.2% of the sample, while 45.8% were from rural areas. Table 1 provides a summary of the demographic distribution.

**Table No. 1: Demographic profile of study participants**

Variable	N (%) / Mean $\pm$ SD
Total Patients	240 (100%)
Male	140 (58.3%)
Female	100 (41.7%)
Mean Age (years)	$52.4 \pm 11.3$
Urban Residents	130 (54.2%)
Rural Residents	110 (45.8%)

Surgical characteristics revealed that 62.5% of the patients were operated upon for colorectal cancer and 37.5% for benign disease. Resection at the rectum was performed in 45.8%. Right hemicolectomy was the most frequently performed colon surgery (25%), followed by left hemicolectomy (16.7%) and sigmoid colectomy (12.5%). Stomas were created, either temporary or permanent in 29.2% of patients. Neo-adjuvant therapy was received in 41.7% patients and adjuvant therapy by 50% of patients. Table-2



**Table No.2: Surgical and oncological details**

Variable	N (%)
Indication: Colorectal Cancer	150 (62.5%)
Indication: Benign Disease	90 (37.5%)
Rectal Resections	110 (45.8%)
Right Hemicolectomy	60 (25.0%)
Left Hemicolectomy	40 (16.7%)
Sigmoid Colectomy	30 (12.5%)
Stoma Creation (Temporary or Permanent)	70 (29.2%)
Neoadjuvant Therapy	100 (41.7%)
Adjuvant Therapy	120 (50.0%)

In 165 (68.8%) patients bowel dysfunction was identified. Based on the LARS score, 16.7% had mild LARS, 22.9% had moderate LARS, and 29.2% experienced severe LARS. The remaining 31.2% of patients had no postoperative bowel dysfunction. Table-3

**Table No. 3: Postoperative Bowel Dysfunction (LARS Score)**

Variable	N (%)
Patients with Bowel Dysfunction (Any)	165 (68.8%)
No Dysfunction	75 (31.2%)
Mild LARS	40 (16.7%)
Moderate LARS	55 (22.9%)
Severe LARS	70 (29.2%)

Body image ( $75.2 \pm 12.1$ ) and emotional function ( $62.3 \pm 15.4$ ) were also moderate in the quality of life questionnaire (EORTC QLQ-CR29). But the scores were much lower for social function ( $58.6 \pm 18.2$ ), stool frequency ( $42.1 \pm 17.6$ ), incontinence ( $38.4 \pm 20.3$ ) and pain ( $45.7 \pm 14.9$ ), indicating significant impact of bowel dysfunction on daily quality of life. Table-4

**Table No. 4: Quality of Life Scores (EORTC QLQ-CR29 Domains)**

Domain	Mean Score $\pm$ SD
Body Image	$75.2 \pm 12.1$
Emotional Function	$62.3 \pm 15.4$
Social Function	$58.6 \pm 18.2$
Stool Frequency	$42.1 \pm 17.6$
Incontinence	$38.4 \pm 20.3$
Pain	$45.7 \pm 14.9$

## DISCUSSION

In our study 68.8% of patients experienced some form of bowel dysfunction, which demonstrate the significant prevalence of postoperative functional problems in this patient population. This is similar to that of Berger et al<sup>11</sup>, who introduced Low Anterior Resection Syndrome (LARS) as a complication in nearly 70% of patients undergoing surgery for rectal cancer. Similarly, Sebastian et al<sup>12</sup> in their multicenter

assessment with the LARS score reported severe symptoms in approximately 30% of patients—almost exactly mirroring our severe LARS rate of 29.2%. The commonality of these findings indicates that despite regional differences in the level of health care services, the pathophysiology for post-surgical bowel dysfunction is similar throughout the world.

Among our cohort, a striking observation was the association between rectal resections and particularly high rates of dysfunction compared to colonic resections. This is substantiated by Ali et al<sup>13</sup> who reported low anastomosis, below 5 cm from the anal verge, as an independent risk factor for bowel symptoms, presumably due to constraint in rectal capacity and damage to pelvic nerves. The anatomical and neurophysiological basis to our findings is thus supported by our study.

Stoma diversion (n =31) was not related to protection against dysfunction (not significant), consistent with the findings of Raza et al<sup>14</sup> who mentioned that defunctioning stomas may slow down LARS but possibly do not prevent it. However, a discrepancy is present in comparison to the study by Rubio et al<sup>15</sup>, who argued that ileostomy diversion may alleviate early postoperative symptom. This discordance might be explained by differences in the time point of stoma closure and patient observation time.

Bhama et al<sup>16</sup> also noted in a study that patients with neoadjuvant therapy had more dysfunction, who connected preoperative chemoradiotherapy with worsening of bowel symptoms as the effect of radiation-induced pelvic fibrosis and nerve damage. Our findings support this conclusion and argue for considering oncological benefit balanced against functional preservation in treatment selection.

Regarding quality of life, domains such as body image and emotional function were less affected by reduction of QoL while social function and stool frequency, degree of incontinence scores were much lower. Daluvoy et al<sup>17</sup> also found that incontinence and urgency were the most distressing symptoms and caused social withdrawal. Goret et al<sup>18</sup> found a significant psychological burden in patients with moderate to severe LARS, which in line with our findings, (lower) emotional and social function scores.

Our mean age of 52.4 years is slightly younger than the typical Western cohort studied in colorectal research. This might be due to the pattern of demography in our region and earlier presentation of the disease in Pakistani Population as reported by Khan et al<sup>19</sup>. Younger age might also affect the recovery after surgery, but it did not seem to reduce the frequency of dysfunction.

Finally, cultural elements in KPK, including stigmatized conversation of bowel symptoms and lack of postoperative rehab access, may lead to underreporting and delay in recognition of dysfunction.

This is consistent with Rashid et al<sup>20</sup> highlighted the essential component of culturally sensitive patient education and structured follow-up in Pakistan to focus on postoperative QOL.

Despite its strengths, it is important to recognize the limitations of this study. Due to the cross-sectional character of the study, it is not possible to draw conclusions about the causes of bowel dysfunction and associated factors. The findings of a single-center study conducted at the Hayatabad Medical Complex might not be generalizable to other regions of the nation. There was no adjustment made for pertinent confounding factors such availability of rehabilitation, psychosocial support, and diet. Additionally, the power of our subgroup comparisons can be hampered by the absence of a formal sample estimation. To better understand postoperative bowel dysfunction, A multi-disciplinary approach is required for the best oncological and functional results in colorectal surgery patients in resource limited areas like Khyber Pakhtunkhwa, Pakistan.

## CONCLUSION

The significant prevalence of bowel dysfunction following colorectal surgery is highlighted in this study, and many of the patients in our sample experienced moderate to severe symptoms, which had a detrimental effect on their quality of life. The findings showed that the key operation-related risk factors for dysfunction were stoma development, neoadjuvant treatment, and rectal resection. The high prevalence and morbidity of these symptoms are described, despite geographical and demographic variations. These findings highlight the necessity of patient-centered therapies such early counselling, physical therapy, and long-term follow-up, as well as the use of functional outcome evaluation in early postoperative care.

### Acknowledgment:

The authors express their gratitude to the participants for their participation and time spent on this study.

### Recommendations:

Further randomized, multi-center studies with extended follow-up are recommended to validate and generalize these findings.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Farrukh Ozair Shah, Tilal Ahmed Raza
Drafting or Revising Critically:	Hajra Imtiaz, Asfa Mumtaz
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No. 1109 Dated 19.01.2020

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# Assessment of Public and High-Risk Group Awareness Regarding Colorectal Cancer Symptoms and Risk Factors in Peshawar, Pakistan

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## ABSTRACT

**Objective:** To assess the knowledge of colorectal cancer (CRC) symptoms and risk factors among the general population and at-risk groups attending the Surgical Department at Hayatabad Medical Complex, Peshawar.

**Study Design:** Descriptive cross-sectional study

**Place and Duration of Study:** This study was conducted at the Department of General Surgery, Hayatabad Medical Complex (HMC), Peshawar, from December 2023, to November 2024.

**Methods:** All adult patients who visited outpatient surgical clinics or accompanied patients admitted to surgical wards during the study period and were at least 18 years old were included in the study. Subjects were enrolled using convenience sampling.

**Results:** Total 64(35.6%) correctly identified rectal bleeding as a warning sign, while 51(28.3%) recognized persistent changes in bowel habits as a symptom. Other commonly known symptoms included abdominal pain (27.2%) and unexplained weight loss (23.9%). However, only 31(17.2%) could identify three or more CRC-related symptoms accurately.

**Conclusion:** Knowledge of colorectal cancer symptoms and risk factors is minimal in general as well as in at-risk population of Peshawar, substantial disparities are found due to education and residence. Targeted awareness programmes and increased physician involvement are crucial to increase early diagnosis and reduce CRC-load in this region.

**Key Words:** Colorectal cancer, Risk factors, Symptoms, Awareness, diagnosis

**Citation of article:** Raza TA, Shah FO, Imtiaz H. Assessment of Public and High-Risk Group Awareness Regarding Colorectal Cancer Symptoms and Risk Factors in Peshawar, Pakistan. Med Forum 2025;36(6): 18-22. doi:10.60110/medforum.360604.

## INTRODUCTION

With an expected 1.9 million new cases and 935,000 deaths in 2020, colorectal cancer (CRC) is the second most common cause of cancer-related deaths globally and the third most common type of cancer<sup>1</sup>. Although CRC was traditionally considered a disease of the western world, recent epidemiological patterns suggest an upsurge in the developing countries, including Pakistan<sup>2</sup>. These figures are largely the result of urbanization, changes in diet, lack of exercise and longer life expectancy<sup>3</sup>.

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Received: February, 2025

Reviewed: March, 2025

Accepted: April, 2025

However, the issue of public knowledge of CRC symptoms and signs in the country is alarming; hence, cases are diagnosed late with a resultant poor clinical outcome<sup>4</sup>.

Early detection, through the identification of symptoms, including rectal bleeding, continuous change in bowel habits, abdominal pain, and unexplained weight loss, is an important factor of CRC management<sup>5</sup>. Yet, several researches have demonstrated that the public commonly do not relate these symptoms to CRC, and typically consider them to be caused by benign conditions such as hemorrhoids or indigestion<sup>6</sup>. In addition, knowledge of established risk factors such as older age, family history, smoking, obesity, low dietary fiber intake, consumption of red/processed meats, and physical inactivity is also low, in both the general population and high-risk groups<sup>7</sup>. This gap in knowledge is striking, especially considering that CRC is highly preventable by life style changes and early screening<sup>8</sup>.

In Pakistan, lack of national CRC screening program, sociocultural barriers, low level of health literacy and poor accessibility to diagnostic facilities are few among the factors that have made patients present even in advanced stages of disease<sup>9</sup>. These higher risk groups including first degree relatives of patients with

colorectal neoplasia and patients with inflammatory bowel disease are also poorly served with respect to education and campaigns directed at them. Furthermore, the stigma surrounding GI symptoms and the embarrassment to enquire about bowel habit also cause delay in seeking help, especially in women and elderly population<sup>10</sup>.

This cross-sectional survey is conducted to assess the awareness level of CRC symptoms, risk factors and evaluation among the general population, and at-risk population in Pakistan. The results are expected to highlight specific areas for knowledge enhancement, associations with sociodemographic variables, and help guide the development of culturally tailored knowledge-translation approaches and policy changes to improve early detection and reduce CRC burden.

## METHODS

This was a descriptive cross-sectional study conducted at the Department of General Surgery, Hayatabad Medical Complex, Peshawar, KPK Pakistan. The period of data collection ranged from December 2023, to November 2024. The study comprised 180 adult patients who were at least 18 years old and who either accompanied patients admitted to surgical wards or visited the outpatient surgical department during the study period. Patients with previous colorectal carcinoma and those who were unable to comprehend the questionnaire due to cognitive and language differences were excluded in order to limit any bias and to ensure appropriate responses. Those at risk were defined as having a family history of colon cancer, being overweight, having diabetes, inflammatory bowel disease, smoking and older than 50 years.

A semi structured interviewer administered questionnaire was employed for data collection. The questionnaire was adapted to fit the local context and was based on previously used tools by international literature. It was translated in local languages (Pashto and Urdu) for understanding and included three parts, first, related to socio-demographic characteristics, second related to knowledge of CRC according to the most important warning signals, and third related to knowledge of associated risk factors. Each correct answer received a score of 1, whereas wrong or "don't know" answers received a score of 0. A total knowledge score was determined for overall awareness. Information was cumulated by trained research personnel under the supervision of senior surgical staff to achieve uniformity and minimize interviewer bias. All participants provided written informed consent before being enrolled in the study. Names and confidential data were coded to ensure no one was identifiable.

IBM SPSS version 25 was utilized for the collection and analysis of data. The data was described using frequency, percentage, mean  $\pm$  SD. To examine the

relationship between knowledge levels and sociodemographic factors, the chi-square test and the independent t-test were employed. A P value of  $\leq 0.05$  was deemed statistically significant. The study protocol was approved by the Institutional Review Board (reference # 1761).

## RESULTS

The mean age was  $41.3 \pm 13.2$  years, with participants ranging from 18 to 72 years. Of the total sample, 96(53.3%) were male and 84(46.7%) females. Majority of respondents were from urban areas (62.2%), and the remainder (37.8%) belonged to rural regions. Educational background varied with 21.1% having no formal education, 32.8% having completed secondary education, and 46.1% having a college-level or higher qualification. Among the participants, 77(42.8%) were categorized as being at risk for colorectal cancer due to factors such as age  $\geq 50$ , family history of CRC, diabetes, smoking, obesity, or inflammatory bowel disease. The remaining 103(57.2%) represented the general population without known risk factors. Table-1

**Table No.1: Sociodemographic Characteristics of Study Participants**

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	Mean $\pm$ SD	-	$41.3 \pm 13.2$
Gender	Male	96	53.3%
	Female	84	46.7%
Residence	Urban	112	62.2%
	Rural	68	37.8%
Education Level	No formal education	38	21.1%
	Secondary education	59	32.8%
	College or higher	83	46.1%
Risk Group	At-risk group	77	42.8%
	General population	103	57.2%

When asked about symptoms of colorectal cancer, 64(35.6%) correctly identified rectal bleeding as a warning sign, while 51(28.3%) recognized persistent changes in bowel habits as a symptom. Other commonly known symptoms included abdominal pain (27.2%) and unexplained weight loss (23.9%). However, only 31(17.2%) could identify three or more CRC-related symptoms accurately.

Knowledge of risk factors was also minimal with only 72(40%) were aware that increasing age is a risk factor, 61(33.9%) identified smoking, 58(32.2%) recognized a family history of CRC, and 53(29.4%) acknowledged obesity as a contributing factor. Limited participants



identified a low fiber diet (20%) or inflammatory bowel disease (12.2%) as risk factors. Only 47(26.1%) were able to correctly identify three or more risk factors. Table-2

**Table No.2: Knowledge of Colorectal Cancer Symptoms and Risk Factors**

Knowledge Area	Item	Frequency (n)	Percentage (%)
Symptoms	Rectal bleeding	64	35.6%
	Change in bowel habits	51	28.3%
	Abdominal pain	49	27.2%
	Unexplained weight loss	43	23.9%
	≥3 symptoms correctly identified	31	17.2%
Risk Factors	Increased age	72	40.0%
	Smoking	61	33.9%
	Family history of CRC	58	32.2%
	Obesity	53	29.4%
	Low fiber diet	36	20.0%
	Inflammatory bowel disease	22	12.2%
	≥3 risk factors correctly identified	47	26.1%

The mean knowledge score (out of 15) was  $4.8 \pm 2.6$ . Based on score categories, 26(14.4%) demonstrated good knowledge (score  $\geq 8$ ), 91(50.6%) had moderate knowledge (score 4–7), and 63 (35%) showed poor knowledge (score  $< 4$ ). Knowledge scores were significantly higher among participants from urban areas (mean score 5.2) than rural (4.1,  $p = 0.02$ ), and among those with higher education ( $p < 0.001$ ). The at-risk group had a slightly higher mean knowledge score ( $5.3 \pm 2.5$ ) compared to the general group ( $4.5 \pm 2.6$ ,  $p = 0.04$ ). Table-3.

**Table No.3: Knowledge score distribution among participants**

Knowledge Level	Score Range	Frequency (n)	%age
Good knowledge	$\geq 8$	26	14.4%
Moderate knowledge	4–7	91	50.6%
Poor knowledge	$< 4$	63	35%

Overall mean knowledge score  $4.8 \pm 2.6$

## DISCUSSION

The results of the present study suggested that knowledge of both groups were far below optimal, the awareness among the known risk factors was relatively better. These findings are in agreement with

conclusions from various national and international studies highlighting the formidability of low CRC awareness in the general population.

The average score of knowledge being 4.8 (out of 15) indicates poor to fair overall level of awareness, we are closely resemble this with the results of Khan et al<sup>11</sup> where the median score was 5.2 in an analogous Pakistani sample. Only 14.4% of participants showed good knowledge in our study which is significantly lower than the 28% reported by Imran et al<sup>12</sup> in a Saudi population. This discrepancy might be related to the divergence in the public healthcare system or national CRC screening program and public education program which are more commonly available in high income countries.

Symptom awareness in our study was poor; only 35.6% report rectal bleeding, then changes in bowel habits (28.3%) and abdominal pain (27.2%). These numbers are lower than the figures provided by Almadi et al<sup>13</sup>, there was a 48% reporting of rectal bleeding as a CRC symptom among Saudi participants. The discrepancy may be due to different levels of awareness and access to medical information in populations. Similarly, Bhurgri H et al<sup>14</sup> also indicated that more than 50% of the urban population of Lahore was aware of symptoms, indicating the positive effect that geographic and urban–rural disparities have on cancer awareness in Pakistan.

Risk factor awareness was also inadequate. Older age was identified as a risk factor by 40% of our respondent population and this is consistent with the reports of Abuadas et al<sup>15</sup> who also found age to be the most frequently identified risk factor in a sample in which the majority had poor oral hygiene. However, other modifiable risk factors like obesity (29.4%) and smoking (33.9%) were poorly known. These numbers are lower than those reported by Gong et al<sup>16</sup>, who found a recognition of over 50% of these risk factors among educated populations in Shingai, China. The low awareness in our cohort could be attributed to sociocultural taboos involving cancer discussions and the lack of appropriate educational campaigns in the area.

In this study 32.2% of respondents identified a family history of colorectal cancer (CRC) as a risk factor, which is marginally higher than the 25% reported by Pnadurangan et al<sup>17</sup> in India. However, this recognition is still below ideal given its significance in clinical practice. It can be a reflection of the overall undervaluation of genetic risk in Pakistani public health message. The extremely low awareness of inflammatory bowel disease (12.2%) as a risk factor is consistent with that of Schliemann et al<sup>18</sup>, who observed the same tendencies in rural Iran communities. These consistent global patterns imply a common requirement to incorporate this information into routine education of health.

There was a strong correlation between level of education and CRC knowledge in our study ( $p < 0.001$ ). This supports finding by May F et al<sup>19</sup> who highlighted the importance of formal education in enhancing health literacy and cancer awareness. Urban participants also had a significantly better knowledge score than rural participants (mean score 5.2 vs. 4.1,  $p = 0.02$ ) as found in previous studies, including the ones of Kamangar et al<sup>20</sup>, who revealed that urban place of residence was associated with cancer awareness among Iranian. This difference might be attributed to higher electronic media, health care, and school accessibility in urban areas.

Remarkably, the at-risk group in our population demonstrated slightly better knowledge than those in the general public (mean score 5.3, as compared to 4.5;  $p$ -value = 0.04) and may reflect some degree of exposure to the health care provider or personal concern for their health. This corroborates the findings of Parker et al<sup>21</sup> who observed that patients with chronic diseases or in a family history demonstrate slightly higher proactive attitude of health information seeking. But the difference was not much, suggesting that risk status alone cannot ensure adequate awareness especially in the absence of regular nursing patient's education.

There are some limitations to the current study, which needs to be acknowledged. First, the results may not be applicable to the entire population of Pakistan, particularly in rural or underdeveloped areas, because this study was conducted at a single centre. Second, the convenience sampling might lead to selection bias as persons visiting a surgical department might have different levels of health awareness and access to information as compared to the general population. Third, some participants may have over reported the information, and the use of self-reported data may have introduced recollection or social desirability bias. To validate and expand upon these findings, future research should involve larger, multi centre studies with diverse populations and preferably randomized controlled trials or longitudinal cohort designs to better assess the impact of educational interventions on colorectal cancer awareness and outcomes.

## CONCLUSION

This study found relatively low awareness of colorectal cancer symptoms and risk factors in both general population and at risk population in Peshawar, Pakistan. Individuals with identifiable risk factors had a slightly better knowledge, but a general low awareness of the disease was observed, particularly with regard to symptoms, such as rectal bleeding, and modifiable factors, such as obesity and smoking. Factors associated with better knowledge were higher education, urban residence as well as very few references to health professionals as a source of information.

## ACKNOWLEDGMENTS:

The authors express their gratitude to the participants for their participation and time spent on this study.

## RECOMMENDATIONS

Further randomized, multi-center studies with extended follow-up are recommended to validate and generalize these findings.

## Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Tilal Ahmed Raza, Farrukh Ozair Shah
Drafting or Revising Critically:	Tilal Ahmed Raza, Hajra Imtiaz
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No.1761 Dated 10.11.2023

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# Frequency of Hearing Loss in Children with Adenoid Hypertrophy

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Hearing Loss in  
Children with  
Adenoid  
Hypertrophy

## ABSTRACT

**Objective:** To determine the frequency of hearing loss in children with adenoid hypertrophy.

**Study Design:** Descriptive, cross sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Otorhinolaryngology, Sir Ganga Ram Hospital, Lahore from August 2, 2024, and February 1, 2025.

**Methods:** Total 95 patients with adenoid hypertrophy who are between the ages of 1 to 15 years were included, regardless of gender. cleft palate, bleeding disorders, sinonasal polyposis, choanal atresia, a significant deviated nasal septum, tumors of the nose and nasopharynx, ototoxic medication use, acoustic neurinoma, middle ear diseases, abnormal tympanometric curves, or barotrauma in their anamnesis were not included. A calibrated digital audiometer, the ALPS AD 2100, was used for the audiometric testing, which was conducted in a noise-free office setting. The hearing threshold for each ear was assessed between 250 and 8 kHz, and a threshold of more than 35 dB was considered to be suggestive of hearing loss.

**Results:** The mean age in this study was  $8.71 \pm 2.79$  years, with a range of 1 to 15 years. 51 patients, or 53.68% of the total, were between the ages of 9 and 15. With a male to female ratio of 1.7:1, 60 (63.16%) of the 95 patients were men and 35 (30.84%) were women. In our study, the average length of illness was  $6.47 \pm 1.74$  months. The average adenoid size was  $2.67 \pm 1.14$  cm. 45 patients (47.37%) in our study had hearing loss in children with adenoid hypertrophy.

**Conclusion:** The study's findings demonstrate the high frequency and wide range of hearing loss in kids with hypertrophic adenoids, with mild conductive hearing loss being particularly common.

**Key Words:** Adenoids hypertrophies, hearing loss, Audiometry

**Citation of article:** Asif M, Javaid W. Frequency of Hearing Loss in Children with Adenoid Hypertrophy. Med Forum 2025;36(6):23-26. doi:10.60110/medforum.360605.

## INTRODUCTION

The adenoid, also known as the pharyngeal tonsil, is a lymphatic tissue that produces antibodies and is situated in the superior region of the nasopharynx posteriorly, close to the choana and the eustachian tube entrance.<sup>1</sup> It increases in size during childhood, peaking in size in children aged 3 to 7 and then starting to decline during puberty.<sup>2</sup> Due to the comparatively lower volume of the nasopharynx and choanal aperture, children under the age of seven are more susceptible to the symptoms of an enlarged adenoid. The adenoid's physiologic growth and regression pattern is followed by the predominance of AH (pathologic enlargement).<sup>3</sup> These symptoms could include a nasal voice, trouble breathing through the nose, snoring at night, and irregular sleep patterns.

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Received: March, 2025

Reviewed: April, 2025

Accepted: May, 2025

These kids breathe through their mouths, therefore they keep their mouths open all the time.<sup>1</sup>

Adenoids, or enlarged pharyngeal tonsils, are one of the primary causes of eustachian tube dysfunction in children.<sup>4</sup> Blockage of the eustachian tube causes middle ear illness by causing negative pressure and inadequate ventilation of the middle ear. Chronic otitis media (COM) and otitis media with effusion (OME) have been identified as the most common causes of hearing loss in young infants.<sup>5</sup> The majority of research suggest worry, despite differing views regarding the degree of impact on the child's learning capacity. The issue is exacerbated in less-than-ideal listening environments where even a slight hearing loss might impede speech perception.<sup>6</sup> Hearing loss is a burden on both individuals and the country, negatively impacts learning capacity, and is mainly preventable.<sup>7</sup> According to one study, 56% of children with adenoid hypertrophy had hearing loss.<sup>8</sup>

The literature on the effect of adenoids on childhood hearing loss is insufficiently supported. Finding out how common hearing loss is in local children with adenoid hypertrophy is the goal of my research. Adenoidal hearing loss might go undiagnosed, although it is easily treated with medicinal and surgical techniques. An early diagnosis and course of treatment are necessary to avoid adenoidal consequences. Additionally, my research will contribute to the local literature.

## METHODS

The Department of Otorhinolaryngology at Sir Ganga Ram Hospital in Lahore conducted this descriptive cross-sectional study between August 2, 2024, and February 1, 2025. After the institutional ethical review committee gave its approval, non-probability sequential sampling was used to choose 95 patients who satisfied the inclusion criteria. The informed consent of each patient will be sought. A sample size of 95 cases has been established with a 56.0%<sup>8</sup> frequency of hearing loss, a 10% margin of error, and a 95% confidence level. All patients with adenoid hypertrophy who are between the ages of 1 to 15 years and who come with symptoms such as sore throat, difficulty swallowing, nasal blockage, plain radiographs of the postnasal area, and an adenoid nasopharyngeal ratio (ANR) >0.4 was considered positive. Based on the proportion of adenoid tissue that causes posterior choana obstruction, it will be divided into the following four grades: The following grades were included, regardless of gender: In Grade I, adenoid tissue blocks 0% to 25% of the posterior choana; in Grade II, it blocks 26% to 50%; in Grade III, it blocks 51% to 75%; and in Grade IV, it blocks 76% to 100% of the posterior choana. The following conditions were excluded: cleft palate, bleeding disorders, sinonasal polyposis, choanal atresia, a significant deviated nasal septum, tumors of the nose and nasopharynx, ototoxic medication use, acoustic neurinoma, middle ear diseases, abnormal tympanometric curves, or barotrauma in their anamnesis.

Age, gender, length of symptoms, adenoid size, adenoid grade, and residence were among the demographic characteristics recorded. Following this, a consultant surgeon performed audiometry on each patient to determine whether or not they had hearing loss. A calibrated digital audiometer, the ALPS AD 2100, was used for the audiometric testing, which was conducted in a noise-free office setting. The hearing threshold for each ear was assessed between 250 and 8 kHz, and a threshold of more than 35 dB was considered to be suggestive of hearing loss. The proforma had all of the data.

SPSS version 25 was used to enter and evaluate the data. The mean and SD for age, symptom duration, and adenoid size were displayed. Frequencies and

percentages for gender, adenoid grade (I/II/III/IV), place of residence (rural vs. urban), and hearing loss (present vs. absent) were displayed. Age, gender, length of symptoms, adenoid size, adenoid grade (I/II/III/IV), and place of residence (rural vs. urban) were all stratified. Additionally, the post-stratification chi-square test was used. A P-value of less than 0.05 was deemed significant.

## RESULTS

The mean age in this study was  $8.71 \pm 2.79$  years, with a range of 1 to 15 years. 51 patients, or 53.68% of the total, were between the ages of 9 and 15. With a male to female ratio of 1.7:1, 60 (63.16%) of the 95 patients were men and 35 (30.84%) were women. In our study, the average length of illness was  $6.47 \pm 1.74$  months. The average adenoid size was  $2.67 \pm 1.14$  cm. Table I displays the distribution of patients with additional confounding variables.

45 patients (47.37%) in our study had hearing loss in children with adenoid hypertrophy (Figure I). Table II displays the stratification of hearing loss by age, gender, duration of symptoms, adenoid size, adenoid grade, and place of residence.

**Table No.2: Distribution of patients with other confounding variables (n=95)**

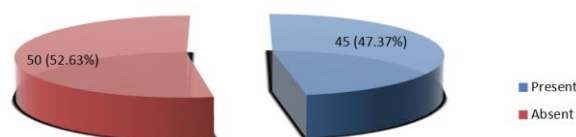
Confounding variables		Frequency	%age
Age (years)	1-8	44	46.32
	9-15	51	53.68
Gender	Male	60	63.16
	Female	35	36.84
Duration of disease (months)	≤6	53	55.79
	>6	42	44.21
Size of adenoid (cm)	≤3	73	76.84
	>3	22	23.16
Grade of adenoid	I	07	7.37
	II	35	36.84
	III	40	42.11
	IV	13	13.68
Place of residence	Rural	36	37.89
	Urban	59	62.11

**Table No.4: Stratification of hearing loss with respect to age, gender, duration of symptoms, size of adenoid, grade of adenoid and place of living.**

		Present (n=45)	Absent (n=50)	P-value
Age (years)	1-8	18 (40.91%)	26 (59.09%)	<b>0.241</b>
	9-15	27 (52.94%)	24 (47.06%)	
Gender	Male	33 (55.0%)	27 (45.0%)	<b>0.051</b>
	Female	12 (34.29%)	23 (65.71%)	
Duration of disease (months)	≤6	24 (45.28%)	29 (54.72%)	<b>0.647</b>
	>6	21 (50.0%)	21 (50.0%)	
Size of adenoid (cm)	≤3	34 (46.58%)	39 (53.42%)	<b>0.778</b>
	>3	11 (50.0%)	11 (50.0%)	
Grade of adenoid	I	03 (42.86%)	04 (57.14%)	<b>0.607</b>
	II	18 (51.43%)	17 (48.57%)	



Residence	III	20 (50.0%)	20 (50.0%)	0.982
	IV	04 (30.77%)	09 (69.23%)	
	Rural	17 (47.22%)	19 (52.78%)	
	Urban	28 (47.46%)	31 (52.54%)	



**Figure No.I: Frequency of hearing loss in children with adenoid hypertrophy (n=95).**

## DISCUSSION

Our study's demographic analysis showed that participants' ages ranged widely, with the largest group being those between the ages of 9 and 15 (53.68%). The study included a somewhat higher percentage of males (63.16%) than females (36.84%) in terms of gender distribution. The greater frequency of children from urban regions compared to those from rural areas was an intriguing finding that might point to a regional variation in the incidence of hypertrophic adenoids.

In contrast, Inoshita A et al.'s 2018 study shown that girls had greater OSA indices than boys, highlighting gender differences in craniofacial features and the severity of OSA in pre-adolescent groups.<sup>9</sup> Although our study did not directly look into this aspect, this may point to a possible association between the development of hypertrophic adenoids in different genders and changes in craniofacial anatomy.

A high prevalence of Type B tympanometry, especially in the left ear, was also discovered in a 2021 investigation by Hazem M. Abdel Tawab.<sup>10</sup> This resemblance emphasizes how important tympanometry is for identifying middle ear disorders in kids with hypertrophic adenoids. Regarding auditory outcomes, 45 patients (47.37%) had hearing loss in children with adenoid hypertrophy.

These results are supported by a 2018 study by Vadisha Bhat, which showed that individuals with chronic otitis media with effusion had a considerable rate of conductive hearing loss.<sup>11</sup> The World Health Organization said that the study's CHL ranged from mild to moderate, or 26 dB to 55 dB.<sup>12</sup> A hearing loss between 26 and 40 dB was present in 97.10% of case ears, while 2.89% of case ears had a hearing loss between 41 and 55 dB. The mean hearing loss was 31.69 decibels. This series' findings regarding hearing threshold were comparable to those of a research conducted by Sarwar et al.<sup>13</sup>

In 2022, Kishore Kumar Halder conducted research on how adenoidectomy affected hearing in kids with otitis media with effusion. A post-operative PTA and tympanometry were performed three months after the patients' sedated adenoidectomy surgeries. The study demonstrated adenoidectomy's function in lowering

middle ear effusion, enhancing hearing, and supporting speech and language development in children with enlarged adenoids by revealing notable improvements in hearing and alterations in tympanometric findings after surgery.<sup>14</sup>

Sultan Badar Munir and associates looked on the frequency of hearing loss in middle ear infection patients in 2021. According to their findings, most of the patients had hearing loss of some kind, from mild to severe.<sup>15</sup> In 2022, David E. Tunkel, MD, carried out a different study that looked at the prevalence of otolaryngologic surgery among people with achondroplasia. The study discovered that a sizable percentage of patients were having tympanostomy tube insertions and pharyngeal surgeries, such as adenoidectomies, underscoring the necessity of close observation and possible surgical procedures in this population.<sup>16</sup>

Adenoid hypertrophy was identified in this investigation as a potential contributing factor to the occurrence of OME and CHL. Additionally, it was discovered that when adenoids grew in size, the incidence of CHL increased. According to our research, the more adenoidal obstruction there was, the higher the degree of CHL. Children who had third- or fourth-degree adenoids at presentation had a five-fold increased risk of developing CHL. Therefore, symptoms that are caused by third- and fourth-degree adenoid might be regarded as one of the selection factors for surgical therapy.<sup>17,18</sup>

The thorough demographic, tympanometric, and audiometric data in this study are its strongest points; they offer important new information about the features of hearing loss in kids with hypertrophic adenoids. Limitations, however, include the absence of a thorough examination of plausible causes, such as genetic predispositions or environmental impacts, which would offer a more comprehensive explanation of the illness. Furthermore, the cross-sectional nature of the study makes it difficult to draw conclusions about causality or the evolution of hearing loss over time.

It is advised that a longitudinal strategy be used in future studies to gain a better understanding of how hearing loss develops in kids with hypertrophy adenoids. A more thorough understanding of the illness might also be obtained by looking into the effects of dietary practices, genetic predisposition, and environmental factors. Additionally, broadening the study's geographic focus to encompass a wider range of populations may aid in detecting possible regional variations in the frequency and intensity of hypertrophic adenoids and related hearing loss.

## CONCLUSION

The study's findings demonstrate the high frequency and wide range of hearing loss in kids with hypertrophic adenoids, with mild conductive hearing loss being particularly common. The demographic distribution showed a somewhat higher percentage of men and a higher representation of older children. The results highlight how crucial it is to regularly evaluate children with hypertrophic adenoids' hearing, especially in metropolitan environments. The study also suggests that in order to address and manage hearing loss in this population, focused interventions and awareness campaigns may be necessary.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Maria Asif, Waqas Javaid
Drafting or Revising Critically:	Maria Asif, Waqas Javaid
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No. 349-Synopsis/ERC Dated 12.01.2025

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# Physical, Mental, and Social Challenges Faced by Nurses during the Pandemic: Analysis of Demographic and Work-Related Factors in Al-Haweja Hospital, Iraq

Fadhel Abbas Ahmed and Salma K. Jihad

Physical, Mental,  
and Social  
Challenges Faced  
by Nurses during  
the Pandemic

## ABSTRACT

**Objective:** To address the inconsistencies by exploring the multidimensional challenges experienced by nurses during the pandemic, with a focus on how these factors contribute to their overall well-being.

**Study Design:** Cross-sectional study

**Place and Duration of Study:** This study was conducted at the Al-Haweja Hospital, Iraq from 15<sup>th</sup> December 2024, to 15<sup>th</sup> February 2025.

**Methods:** This study was conducted at Al-Haweja Hospital, Iraq among 100 nurse workers. Data were collected via a structured interview questionnaire.

**Results:** More than half of nurses (60%) reported infected by various viruses, indicating a significant health risk. In addition, 46% of nurses were unable to rest during the pandemic. However, there were no statistically significant differences found between nurses' demographic characteristics and their work related to pandemic challenges, especially a p-values for these comparisons were all greater than 0.05.

**Conclusion:** Nurses faced significant mental challenges, including fears of infection, isolation, and exhaustion, highlighting the critical need for psychological support. The study underscores the importance of screening nurses for both physical and mental health conditions, particularly in light of the ongoing demands of the pandemic.

**Key Words:** Physical challenges, Demographic factors, Pandemic stress, Work-related factors, Nurses

**Citation of article:** Ahmed FA, Jihad SK. Physical, Mental, and Social Challenges Faced by Nurses during the Pandemic: Analysis of Demographic and Work-Related Factors in Al-Haweja Hospital, Iraq. Med Forum 2025;36(6):27-32. doi:10.60110/medforum.360606.

## INTRODUCTION

The pandemic is a widespread outbreak of an infectious disease that significantly increases the likelihood of morbidity and mortality across a large geographic area. During the pandemic, nurses have been under increased pressure and responsibilities, and the demand for medical resources and supplies has increased.<sup>1</sup> One challenge has been the allocation of nursing staff to care for infected patients, especially professional nurses, who are considered essential to patient care.<sup>2</sup> Nurses are constantly engaging with the community and playing a vital role in both treating and preventing the spread of diseases.

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Received: March, 2025

Reviewed: April, 2025

Accepted: May, 2025

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Their responsibilities encompass a wide range of critical tasks, including clinical care, patient counselling, overseeing treatment protocols, educating patients, and promoting disease prevention strategies.

The pandemic has placed enormous strain on healthcare professionals, who have had to navigate significant risks to their own well-being and that of their families.<sup>3</sup> They have been responsible for handling a surge in patients, many of whom faced high mortality rates, all within a high-pressure, fast-paced environment. Therefore, understanding the physical and mental strain on healthcare workers is crucial, as long working hours, increased patient loads, and the prolonged use of personal protective equipment have significantly heightened their physical exhaustion.<sup>4</sup> The increase in musculoskeletal disorders, fatigue, and injuries linked to the prolonged use of personal protective equipment.<sup>5,6</sup> In addition, nurses also encountered significant social challenges during the pandemic. Isolation from family and friends due to concerns about spreading the virus, as well as the stigma associated with working in high-risk environments, has compounded feelings of loneliness and alienation.<sup>7</sup> Furthermore, the demands of their profession during the pandemic, including shift changes and the emotional burden of patient care, have disrupted family dynamics and social interactions.<sup>8</sup> These social factors have

contributed to nurses' stress and have affected their work-life balance. Moreover, to the physical challenges, nurses have faced considerable mental and emotional strain throughout the pandemic.<sup>9</sup> The mental health of nurses during the pandemic is an issue that requires urgent attention, as it impacts not only the well-being of the nurses themselves but also the quality of care they can provide to patients.

Fewer studies have attempted to holistically examine how these physical, mental, and social challenges are interrelated and how demographic and work-related factors such as age, gender, and role affect nurses' experiences. This study purposes to fill this gap by conducting a cross-sectional analysis in Al-Haweja Hospital Iraq that explores the multidimensional challenges faced by nurses during the pandemic.

## METHODS

This descriptive cross-sectional study was collected during the period from 15<sup>th</sup> December 2024 to 15<sup>th</sup> February 2025. The study was conducted at Al-Hawija General Hospital, which served as the designated site for data collection. Al-Hawija General Hospital provides a range of services similar to other hospitals in Kirkuk Governorate, including the pediatrics, medical, surgical, orthopedics, burns, maternal, laboratory, and various diagnostic and treatment departments. This convenience sample of 100 nurses working at Al-Hawija General Hospital during the study period was selected to achieve the study's objectives. The nurses were chosen from various hospital departments and had a minimum of two years of experience in nursing services. The total number of nurses at Al-Hawija General Hospital, both male and female, was 360. The present study was conducted through the following steps: A questionnaire was developed by the investigator after reviewing relevant literature on nurses' experiences with pandemic phenomena. The data for the questionnaire were collected through interviews, with each interview lasting between 20 to 30 minutes for every nurse. The questionnaire, which consisted of three main sections, was used to gather data: **Part One:** Demographic data, including general characteristics of the respondent such as sex, age, marital status, number of children, residence, and economic status. **Part Two:** Employment characteristics for nurses, including educational qualifications, years of experience, length of service in pandemic wards, participation in pandemic-related training courses, whether they had been infected during the COVID-19 pandemic, and whether they had a private nursing clinic during the pandemic. **Part Three:** Challenges faced by nurses during the pandemic. This section, which focused on the nurses' experiences, contained 41 items, divided into three dimensions: physical challenges: 9 items, mental challenges: 14 items, social challenges: 8 items

**Rating and Scoring of Instrument:** To measure the mean score, the items were rated using a three-point

Likert scale: extremely satisfied, satisfied, and unsatisfied. The scoring system was as follows: a response of "very satisfied" received a score of 3, "satisfied" received a score of 2, and "unsatisfied" received a score of 1.

**Validity of the Study Instruments:** The researcher used content validity to assess the accuracy of the study instrument, ensuring that the items effectively represented the content of the study. A panel of sixteen specialists from various colleges specializing in community and psychiatric nursing and medicine reviewed the questionnaire. They were asked to evaluate the content of the assessment instrument, providing feedback, comments, and suggestions, which were incorporated into the final version of the questionnaire.

**Reliability:** Reliability refers to the consistency and dependability of a testing tool in measuring a variable. To ensure the reliability of the questionnaire, the Cronbach's alpha statistical technique was employed.

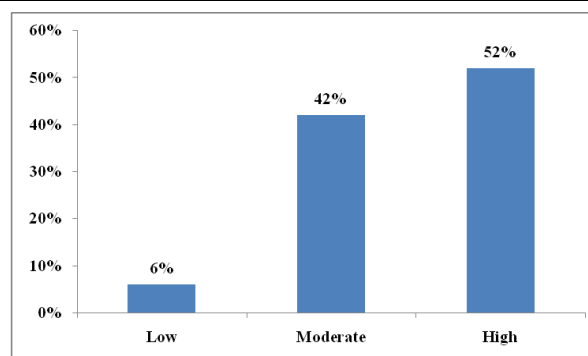
Data analysis was performed using SPSS-26. Inferential statistics were employed to make generalizations or draw conclusions about the larger population from the sample data. Various statistical tests were used depending on the nature of the variables. For comparisons between groups, t-tests or ANOVA were conducted for continuous data, and chi-square tests were used for categorical data. The significance level was set at  $p < 0.05$ .

## RESULTS

**Table No.1: Sociodemographical and employment data of nurses dealing with pandemic phenomena**

Socio demographics	No.	%
<b>Age (years)</b>		
20-29	52	52.0
30-39	36	36.0
40-49	12	12.0
<b>Gender</b>		
Male	60	60.0
Female	40	40.0
<b>Marital status</b>		
Single	36	36.0
Married	55	55.0
Divorced	4	4.0
Widow	5	5.0
<b>Number of children</b>		
0	53	53.0
1-2	16	16.0
3+	31	61.0
<b>Residence</b>		
Urban	47	47.0
Rural	53	53.0
<b>Economic status</b>		
Satisfied	35	35.0
Good	49	49.0
Not good	16	16.0

<b>Academic achievement</b>		
Diploma	59	59.0
Bachelor	41	41.0
<b>Years of service</b>		
1-5	61	61.0
6-10	19	19.0
11-15	11	11.0
16-20	9	9.0
<b>Duration of working in ward</b>		
1-5	51	51.0
6-10	31	31.0
11-15	14	14.0
16 and more	4	4.0
<b>Training program about pandemic disease</b>		
Yes	63	63.0
No	37	37.0
<b>Exposure to infection</b>		
Yes	60	60.0
No	40	40.0
<b>Do you own a nursing clinic during the pandemic</b>		
Yes	26	26.0
No	74	74.0



**Figure No. 1: Overall mean responses of nurses regarding mental challenges dimension.**

Socio-demographic trends among nurses, exposure to infection is common concern for 60% of nurses while only a small proportion own a nursing clinic during the pandemic (Table 1). The nurses' mental challenges were faced during the pandemic, including fears, stress, feelings of isolation, and concerns about their health and family (Table 2). In this table show that the maximum mean is 2.67 with the item (I'm afraid of transmitting the disease to my family/people around me), while the minimum mean is 1.98 with the items (I feel worthless in people's eyes in pandemic) [Fig. 1].

**Table No.2: Distribution of responses of nurses regarding physical and mental challenges dimension**

Variable		No.	%	Mean±SD
I'm afraid of getting infected	Disagree	13	13.0	2.47±0.71
	Partially agree	27	27.0	
	Agree	90	60.0	
I'm afraid of transmitting the disease to my family/people around me	Disagree	8	8.0	2.67±0.62
	Partially agree	17	17.0	
	Agree	75	75.0	
I'm afraid of dying	Disagree	27	27.0	2.18±0.83
	Partially agree	28	28.0	
	Agree	45	45.0	
I'm afraid of losing one of my family or the people I love because of the pandemic	Disagree	10	10.0	2.55±0.67
	Partially agree	25	25.0	
	Agree	65	65.0	
I can't enjoy life	Disagree	16	16.0	2.25±0.71
	Partially agree	43	43.0	
	Agree	41	41.0	
I feel sad because I have to live apart from my family/loved ones	Disagree	13	13.0	2.38±0.70
	Partially agree	36	36.0	
	Agree	51	51.0	
Uncertainty about the future worries me	Disagree	18	18.0	2.23±0.73
	Partially agree	41	41.0	
	Agree	41	41.0	
I'm experiencing increased stress	Disagree	16	16.0	2.28±0.72
	Partially agree	40	40.0	
	Agree	44	44.0	
My hygiene habits have turned into obsessions	Disagree	26	26.0	2.11±0.79
	Partially agree	37	37.0	
	Agree	37	37.0	
I feel worthless in people's eyes in the pandemic	Disagree	35	35.0	2.11±0.79

I have to live with my family because I don't have sufficient resources	Partially agree	32	32.0	1.98±0.82
	Agree	33	33.0	
	Disagree	16	16.0	
	Partially agree	37	37.0	
I feel my efforts are not appreciated by society	Agree	47	47.0	2.31±0.73
	Disagree	24	24.0	
	Partially agree	33	33.0	
	Agree	43	43.0	
I need psychological support	Disagree	17	17.0	2.19±0.80
	Partially agree	28	28.0	
	Agree	55	55.0	
	Disagree	11	11.0	
I feel exhausted	Partially agree	46	46.0	2.38±0.76
	Agree	43	43.0	
	Disagree	11	11.0	
	Partially agree	46	46.0	

**Table No.3: Relationship between the demographic characteristics and overall responses of the participants about experiences related to pandemic phenomena**

Socio-demographic characteristics		Physical challenges dimension	Mental challenges dimension	Social challenges dimension
Age	X <sup>2</sup>	.661	.702	.093
	Sig.	N.S	N.S	N.S
Sex	X <sup>2</sup>	.057	.493	.402
	Sig.	N.S	N.S	N.S
Marital status	X <sup>2</sup>	.126	.033	.362
	Sig.	N.S	Sig	N.S
Number of children	X <sup>2</sup>	.230	.001	.376
	Sig.	N.S	Sig	N.S
Residence	X <sup>2</sup>	.250	.300	.623
	Sig.	N.S	N.S	N.S
Economic situation	X <sup>2</sup>	.860	.249	.098
	Sig.	N.S	N.S	N.S
Academic achievement	X <sup>2</sup>	.394	.772	.920
	Sig.	N.S	N.S	N.S

\*Chi- square, N.S = no significant, Sig= significant, p-value=0.05

**Table No.4: Relationship between the work related data with and overall responses of the sample about experiences related to pandemic phenomena**

Work related data		Physical challenges dimension	Mental challenges dimension	Social challenges dimension
Years of service	X <sup>2</sup>	.310	.069	.820
	Sig.	N.S	N.S	N.S
Duration of working in ward	X <sup>2</sup>	.297	.537	.747
	Sig.	N.S	N.S	N.S
Training program about pandemic disease	X <sup>2</sup>	.807	.526	.198
	Sig.	N.S	N.S	N.S
Exposure to infection	X <sup>2</sup>	.462	.653	.704
	Sig.	N.S	N.S	N.S
Do you own a nursing clinic during the pandemic	X <sup>2</sup>	.335	.194	.949
	Sig.	N.S	N.S	N.S

\*Chi- square, N.S = no significant, Sig= significant, p-value=0.05

The table 3 presents the Chi-square test results for various socio-demographic characteristics and their relationships with the participants' responses to the physical, mental, and social challenges dimensions related to the pandemic phenomena.

The table 4 presents the Chi-square (X<sup>2</sup>) test results for the relationship between work-related data (such as years of service, training, and exposure to infection) and the participants' responses to the physical, mental,

and social challenges they experienced during the pandemic.

## DISCUSSION

In the present study, male nurses (60%) outnumbered female nurses, aligning with previous research conducted in the UK and China, which similarly reported a higher proportion of males compared to females in epidemic situations.<sup>10,11</sup> However, these results contrast with a recent study from Malaysia, which found a higher proportion of female nurses during the COVID-19 pandemic.<sup>12</sup>

This study indicates that a substantial proportion of nurses (46%) agreed that they were unable to rest during the pandemic, while an additional 33% partially agreed. Only a minority (21%) disagreed with this statement, underscoring the widespread nature of this issue. This finding was in the same line with a previous systematic review which found that the number of hours spent during duty epidemic situation may not equal social support, and rest.

This study revealed that participants experienced significant fears of contracting the virus and transmitting it to their families, feelings of isolation, exhaustion from prolonged separations, and the overall mental toll of the pandemic. Additionally, there was a notable need for psychological support, driven by the overwhelming emotional strain nurses faced. Overall, the data indicates moderate to strong agreement with the mental challenges identified, with nurses expressing substantial concerns regarding their psychological well-being throughout the development of the pandemic. Our findings are consistent with another studies<sup>13,14</sup> who reported that healthcare workers' ability to cope with the increased demands during the COVID-19 pandemic was accompanied by significant deterioration in mental health, particularly due to the fear of contracting the virus. Additionally, the extended working hours during the pandemic have been linked to several adverse physical, psychological, and safety outcomes among nurses. These include musculoskeletal pain<sup>15</sup>, fatigue and feelings of isolation<sup>16</sup>, as well as reduced opportunities to engage in social activities.<sup>17</sup> These factors likely contributed to the negative impact on nurses' psychological well-being.

This research is the first study conducted in Iraq, the correlation between nurses' demographic characteristics and their responses to experiences related to pandemic challenges revealed no significant associations. Specifically, factors such as age, gender, residence, economic status, and academic qualification showed no substantial impact on the physical, mental, or social dimensions of the challenges faced by nurses. The p-values for these comparisons were all greater than 0.05, indicating the absence of statistically significant relationships. On the other hand, previous studies found that are a strong link between nurses characteristics

with physical, mental, or social dimensions during COVID-19 infection.<sup>18,19</sup> The discrepancies between our findings and those of previous studies may be attributed to the timing of our study, which was conducted during the later stages of the COVID-19 pandemic.

This study has several limitations: as a cross-sectional design, it does not allow for the establishment of causal relationships between the variables. Additionally, due to the non-random sampling of participants, the potential for bias cannot be entirely ruled out. Moreover, other factors that may contribute to the challenges faced by nurses, such as environmental influences, workload, and psychological distress, were not addressed in this study. Future research could explore the impact of the physical environment on nurses during a pandemic.

## CONCLUSION

The multifaceted challenges faced by nurses during the pandemic. The mental challenges faced by nurses during the pandemic were substantial, with many experiencing fears of infection, isolation, and exhaustion. Nurses expressed a clear need for psychological support, which is essential to mitigate the emotional strain that significantly impacted their well-being. The implications are critical for healthcare authorities, as it emphasizes the need for effective screening of nurses for health and psychological conditions, especially considering the ongoing challenges posed by the pandemic.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Fadhel Abbas Ahmed, Salma K. Jihad
Drafting or Revising Critically:	Fadhel Abbas Ahmed, Salma K. Jihad
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No. 231 Dated 09.07.2024

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# Frequency of Admission with Hereditary Blood Diseases in Paediatric Wards of Basrah Hospitals Iraq

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## ABSTRACT

**Objective:** To Identify the Causes & Patient Characteristics of Hereditary Blood Diseases of Basrah City Iraq.

**Study Design:** Retrospective study

**Place and Duration of Study:** This study was conducted at the Basrah Medical College, Iraq from 1<sup>st</sup> July 2022 to 31<sup>st</sup> December 2023.

**Methods:** This retrospective study reviewed patient records from the hematology ward of a hospital and found that 1,799 inherited hemoglobin disorder patients.

**Results:** All patients were under 15 years of age, with the majority (34.5%) in the 6–10 years. Of the total patients, 55.48% were male, resulting in a male-to-female ratio of 1.24. Sick cell-related complications and morbidity were the predominant causes of admission, accounting for 64.48% of the cases. Outpatient referrals constituted the primary pathway for admission, with approximately half of the cases originating from the center and 97.44%. Most patients (88.6%) had a hospital stay of fewer than five days. Only 0.67% (12 patients) had prolonged stays (exceeding 15 days), primarily due to sickle cell-related morbidities. The average length of stay was 2.003 days, the range being 0–35 days.

**Conclusion:** Most of the admission trend was toward sickle cell and complications and recommendations were toward more preventive efforts toward vasoclosive pain and other complications in sickle cell patients

**Key Words:** Hemoglobinopathies, Sickle cell disease, Thalassemia, Inpatient, Admission

**Citation of article:** Jumaa DS, Al Hijaj BA, Ibrahim MA, Makki NA, Fadhil AA. Frequency of Admission with Hereditary Blood Diseases in Paediatric Wards of Basrah Hospitals Iraq. Med Forum 2025;36(6):33-37. doi:10.60110/medforum.360607.

## INTRODUCTION

Sickle cell disease and thalassemia stand as the principal well-known inherited blood abnormalities which affect broad regions of Mediterranean and Asian and African lands because of endemic malaria conditions.<sup>1</sup> Sigma 6 HBB point mutation causes sickle cell disease by creating beta-globin chain amino acid substitution at position 6. These mutations occur on autosomal recessive chromosomes. Sickle cell disease stands as one of the most common hemoglobin disorders found in Saudi Arabia and especially across its population.<sup>2</sup> Sickle cell disease happens with five unique beta-globin gene haplotypes which include the

patterns from Central African Republic, Cameroon, Benin, Senegal and Arab-Indian. HbF production is directly influenced by genetic factors which work to manage sickle cell disease severity because higher levels of HbF usually result in milder disease symptoms.<sup>3,4</sup>

The inherited hemoglobin disorders known as  $\beta$ -thalassemia causes significant health care challenges to Europe and worldwide because of their complicated nature and diverse characteristics. Genetic studies demonstrate that  $\beta$ -thalassaemic mutations exist in 1% to 5% of people worldwide.<sup>5,6</sup> Therapeutic and medical advancements significantly impacted the survival rates of patients with SCD particularly among young children because they increased the chances of surviving the diseases and outliving the original death prediction. A large majority (93.9%) of sickle cell anemia children and 98.4% of children with less severe SCD disease forms achieve adult life.<sup>7</sup> In Basrah, the prevalence of sickle Hemoglobin (Hb S) is 6.48%, with a carrier frequency of 0.0324%.<sup>8</sup>

Therapeutic and medical advancements significantly impacted the survival rates of patients with SCD particularly among young children because they increased the chances of surviving the diseases and outliving the original death prediction. A large majority (93.9%) of sickle cell anemia children and 98.4% of

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Received: January, 2025

Reviewed: February, 2025

Accepted: March, 2025

children with less severe SCD disease forms achieve adult life.<sup>9</sup> Therapeutic and medical advancements significantly impacted the survival rates of patients with SCD particularly among young children because they increased the chances of surviving the diseases and outliving the original death prediction. A large majority (93.9%) of sickle cell anemia children and 98.4% of children with less severe SCD disease forms achieve adult life.<sup>10</sup> The total number of people who had hemoglobinopathies amounted to 238 per 100,000 while the male population had 247 per 100,000 and the female population had 229 per 100,000. Most patients in the study belonged to the age group of 6 to 15 years and were male at 52.11% of the total sample. The number of sickle cell disease patients accounted for 68.58% of total cases. Sickle crisis appeared most frequently among reported complications which amounted to 14.21% of total cases while sickle crisis itself occurred in 26.83% of patients. Since 2012 the number of cases reached its maximum at 606 during 2019 then subsequently reduced to 349 in 2022.<sup>12</sup> The purpose was to determine how often children with various hemoglobinopathies and associated haematological disorders need hospital admission care along with identifying their respective causes in Basrah. Findings from this research will build a necessary understanding of thalassemia health problems in the country which will help create preventive measures for managing severe complications in affected individuals.

## METHODS

This observational study that depend on review of the patient records to collect certain demographic and clinical data, Demographic data for each patient include age (below 5 years, 5-10, 11-15), sex, locality (within Iraq, within Basrah), main disease category (sickle related, thalassemia related, bleeding disorders related and other haematological categories), and referral point (outpatient clinic, day care clinic, other hospital or emergency room). Clinical data include duration of admission, cause of admission and patient outcome (improved, discharge on responsibility, died or transferred to other hospital or centre). All the admitted haematological case inpatient of the BCHBD (the point at which the centre transferred to the current location within the Basrah paediatric speciality teaching hospital). The data was entered and analyzed through SPSS-22. P value by linear ANOVA had been calculated.

## RESULTS

Mostly of the patients 682 were 6-10 years, 55.48% were males with a male to female ratio of 1.24, sickle cell related complications and morbidity were the most predominant 64.48%, outpatient referral were the most path for admission, and about half of the cases were from the centre while 97.44% were from Basrah

governorate, 45.9% of the whole cohort study. Minimum 22 patients in August 2022, maximum 201 patients are in November 2023 with an average of 105 during the study period (Table 1).

The average duration of admission was 2.003 days. Most of the admitted cases were of a duration <5 days 1594 (88.60%) while only 12 (0.67%) were of prolonged admission stay (>15 days) in which most of them were of sickle cell related morbidities and average of the admission duration was 2.003 day (Table 2)

**Table No.1: Demographic characteristics of the admitted patients**

Variable	No.	%
<b>Age (years)</b>		
1-5	541	30.4
6-10	682	37.9
10-15	569	31.7
<b>Gender</b>		
Male	998	55.8
Female	797	44.2
<b>Main categories</b>		
sickle cell related	1160	64.4
Thalassemia related	258	14.5
bleeding disorder related	212	11.7
Others	169	9.4
<b>Referral</b>		
Outpatient	1017	56.5
Day clinic	543	30.3
Other hospital	34	1.8
Privates	205	11.4
<b>Locality</b>		
Basrah	1753	97.4
Other governorates	46	2.6
<b>Locality within Basrah</b>		
Centre	896	49.8
Abulkhasseb	238	13.2
Zubair	148	8.2
Fao	18	2.0
Safwan	7	0.4
Qurna	71	4.9
Mudynaah	65	4.6
Hartha	79	4.4
Shat Alarab	231	12.5
<b>Time trend of admission</b>		
<b>2022</b>		
July-September	46	2.6
November-December	263	14.6
<b>2023</b>		
Jan-March	406	22.6
April-June	420	23.4
July-September	416	23.3
November-December	247	13.7

The most common isolated cause for in patient admission in Basrah was sickle cell vaso-occlusive crises (40.19%) followed by transfusion emergencies and

bleeding in a patient with clotting disorders (20.68, 10.78%) respectively (Table 3). Patients being improved, discharged on responsibility, referred to

other hospital or died the patient distribution were 62.37%, 36.24%, 0.50% and 0.44% respectively (Table 4).

**Table No.2: Duration of admission categories**

Duration of admission			Sickle cell related		Thalassemia related		Bleeding disorder related		Others	
0-4 days	1594	88.60%	1022	88.10%	226	87.60%	201	94.81%	145	85.80%
5 - 9days	162	9.01%	107	9.22%	23	8.91%	10	4.72%	22	13.02%
10-14 days	31	1.72%	23	1.98%	6	2.33%	1	0.47%	1	0.59%
15 & above	12	0.67%	8	0.69%	3	1.16%	0	0.00%	1	0.59%
Total	1799	100%	1160	64.48%	258	14.34%	212	11.78%	169	9.39%

\*0 mean less 24 hours

**Table 3: Causes of admission categories**

Causes of admission		No.	%
Sickle related	Sequestration crises	114	6.34
	Acute chest syndrome	25	1.39
	Pulmonary infection	48	2.67
	Sickle painful crises	723	40.19
	Febrile sickle illness	61	3.39
	UTI	19	1.06
	Musculoskeletal infection	23	1.28
	Aplastic crises	3	0.17
	Stroke	5	0.28
	Other infectious diseases	69	3.84
	Sickle nephropathy	3	0.17
Thalassemia related	Blood transfusion emergency	372	20.68
	Hormonal disturbance and complication	9	0.50
Bone marrow failure related		42	2.33
Bleeding disorders related	Clotting	194	10.78
	Platelets	37	2.06
HLH		13	0.72
Preparation to surgery		8	0.44
Other causes		31	1.72

**Table No. 4: Fate of the admitted cases**

Fate of the patients	No.	%
Improved	1122	62.37
Discharged on responsibility	652	36.24
Referred to other hospital	9	0.50
Death	8	0.44

## DISCUSSION

The sex distribution and sickle cell reasons for hospital stay were found to be comparable between this study and another Saudi research design. Researchers studied 103 SCD patients through an age range of 18–62 years. The majority of sickle cell disease patients at the facility were males who belonged to the ≤30 year old age group. Most admissions for sickle cell patients were associated with a painful crises (n=94, 91.3%) followed by cases of hemolytic crisis (27 of the cases; 26.2%) and acute chest syndrome (n=32, 31.1%) exams.<sup>13</sup>

The Lebanese series investigation demonstrated thalassemia patients needed transfusions in fifty-four

percent of cases while fewer patients received treatment for infectious conditions. The hospital stay duration exceeded five days within this cohort. The different age range of patients between studies partly explains this finding since elderly adults made up most of the Lebanese data.<sup>14</sup>

The research conducted by Karemi et al during 2011 in Iran demonstrated that males accounted for (59.75%) of the total patient population while females made up (40.25%). Among admitted patients the most common reasons for admission involved splenectomy (21.8%) and infections aetiology (19.9%) and diabetes mellitus (13.4%) and congestive heart failure (19.0%) and Liver biopsy (11.5%); those patients had an average age of 11.28 years.<sup>15</sup>

Sickle cell related morbidity and complications served as the most common hospitalization diagnosis (64.48%) according to this study while a large USA dataset showed 19,250 sickle cell patients had sickle cell-related admissions throughout 2016 to 2020. The annual rate of vasoclosive cause of pain admissions rose from 10.2 per 100,000 individuals in 2016 to 14.7

in 2019 followed by a decrease to 13.9 in 2020. The complications of acute kidney injury presented were 4.9% of admissions. During 2017 the number of bacteraemia illnesses rose to 0.9% while priapism maintained steady growth of 2.3% in 2016 but admissions complicated by pneumonia reached 6% in 2016. Less than one percent of total admissions involved complications of osteomyelitis, heart failure exacerbation, stroke, splenic sequestration, acute chest syndrome, or sepsis and statistical analysis did not show any relevant findings. This cohort demonstrates a female predominance over males. The opposite results stem primarily from two factors: the different genotypic categories of SCD and population differences between patients.<sup>16</sup>

A study in Thailand showed high hospital admission rate among paediatric patients with thalassemia under the NHC scheme in Thailand from 2015 to 2019. The admission rate, ranging from 416 to 559 per 100,000, within this cohort, main age category was 11-16 years and minimal was in below 1 year. Most hospitalized patients had  $\beta$ -thalassemia, with iron overload and infections as prominent co-diagnoses. This study identified a significant presence of cardiovascular complications and diabetes mellitus among patients. Respiratory tract infections constituted approximately 63% of all infections.<sup>17</sup> Beazrkar et al<sup>18</sup> in Iran described the causes of hospital admission in 555 patients with beta-thalassemia major at a referral university hospital in Iran from 2000 to 2005. The most common causes of hospital admission were splenectomy, heart failure, liver biopsy, uncontrolled diabetes mellitus, and arrhythmia. Origa et al<sup>19</sup> in Sardinia described 690 hospital admissions in 276 paediatric and adult patients with thalassemia major in a tertiary care centre. The most common causes for hospital admission were heart failure/arrhythmias, infections, mesenteric lymphadenitis in patients treated with subcutaneous desferrioxamine, digestive tract diseases, and liver diseases.

Outpatient referral were the most path for admission, and about half of the cases were from the centre while 97.44% were from Basrah governorate, 45.9 % of the whole cohort study with a monthly admission. A similar trend found in a study in USA in which Hospital admission rate rose steadily from 106 per 100,000 AA populations in 2004 to 137 in 2012. Seasonal and trend decomposition revealed the highest hospitalization rate in January. Hospital LOS decreased from 7.1, 7.65 days in 2004 to 6.23 6.42 days in 2012.<sup>20</sup> While in a large study in UK showed also a 74.9% of admitted were from the capital and 57.9% of patients admitted are discharged within 24 hours referral from ER (79.6) and being from the centre (92.8) area (metro covered areas) was found in a study done by Kathryn et al also the vaso-occlusive pain (78.3%) in this study was the predominant cause in sickle cell patients.

Whether being improved, discharged on responsibility, referred to other hospital or died the patient distribution was 62.37%, 36.24%, 0.50%, 0.44% respectively a similar results were seen in other studies like in US series.<sup>21,22</sup>

## CONCLUSION

Most of paediatric admitted patients were from age group 6-10, males referred from outpatients live in the centre of the Governorate. The most disease category was the sickle related type and the most common cause for admission was the vaso-occlusive crises. Average of the admission duration was 2.003 day and most of the long admission duration was sickle cell category. Death was a minority while cure was the most of the admitted patient fate.

### Recommendations

1. More interest should concentrate on the sickle cell preventive program to minimize admission rate like vaccinations, antibiotic prophylaxis and regular outpatient visits.
2. More interest should be directed toward the prevention of vaso-occlusive crises like offering hydroxycarbamide and erythrocytapheresis.
3. A more analytic study to be done on the same sample in regards to the risk factor for in patient admission and death fate, and ICU referral

### Author's Contribution:

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

**Source of Funding:** None

**Ethical Approval:** No.78989/QM/APPROVAL/09028nh Dated 02.06.2022

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# Retinol Binding Protein-4 and Procollagen III N-Terminal Peptide as Indicators of Nephropathy in Type 2 Diabetic Patients

Procollagen III  
N-Terminal  
Peptide and  
Retinol Binding  
Protein- 4 Levels  
in Diabetic  
Nephropathy

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## ABSTRACT

**Objective:** To investigate the correlation between the parameter levels (Retinol Binding Protein-4 and Procollagen III N-Terminal Peptide) and multiple risk factors including resistant to insulin, HbA1c, overweight, obesity, eGFR and Urine albumin to creatinine ratio with linking these results with those of individuals in good health.

**Study Design:** Case control study

**Place and Duration of Study:** This study was conducted at the College of Medicine, Al-Nahrain University, Baghdad-Iraq from 1st March 2024 to 31st October 2024.

**Methods:** One hundred and thirty five 135 individuals were enrolled. The study population consisted of 45 healthy persons serving as a control group, 40 persons type-2 diabetes mellitus with normoalbuminuria, and 50 persons with T2DM nephropathy presenting microalbuminuria and macroalbuminuria.

**Results:** Both procollagen III n-terminal peptide and retinol binding protein- 4 levels were markedly increased in diabetic nephropathy. The levels in the blood of retinol binding protein-4 among patients along with type-2 diabetic nephropathy was markedly elevated compared to healthy individuals and type 2 diabetes patients without nephropathy. ( $p < 0.001$ ). Moreover, those with type-2 diabetes that shows nephropathy demonstrated a significantly elevated serum procollagen III N-terminal peptide value compared to those without nephropathy, individuals with control subjects ( $p < 0.001$ ).

**Conclusion:** Procollagen III N-terminal peptide and Retinol binding protein- 4 levels in diabetic nephropathy increase in proportion to the disease's progression. Moreover, individuals with elevated Retinol binding protein-4 levels and type-2 diabetes are at a higher risk of suffering from nephropathy previous in their illness course

**Key Words:** Retinol binding protein-4 (RBP-4), Procollagen III amino terminal peptide (PIIINP), Urine albumin to creatinine ratio (UACR), Type 2 diabetes mellitus, Diabetic nephropathy

**Citation of article:** Hasan AZ, Hamza MI, Khudhair MS. Retinol Binding Protein-4 and Procollagen III N-Terminal Peptide as Indicators of Nephropathy in Type 2 Diabetic Patients. Med Forum 2025;36(6):38-43. doi:10.60110/medforum.360608.

## INTRODUCTION

Type two diabetes mellitus is a long-term, multisystem condition and a considerable global worldwide health risk that regularly decreases the value of life. Diabetes-associated kidney disease (DKD) is characterized as a specific category of ongoing kidney damage resulting from type-2 diabetes, and these two terms are utilized simultaneously through this article.

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Received: January, 2025

Reviewed: February, 2025

Accepted: March, 2025

An integrated approach encompassing education, self-management, changes in lifestyle, medical intervention, cardiovascular disease early detection, and emotional assistance has become essential for reducing the rate of and development of diabetes-related kidney disease (DKD).<sup>1</sup> Hyperglycemia and hypertension are major factors contributing to the beginning of diabetic kidney damage ; therefore, optimizing the regulation of glucose levels and lowering blood pressure levels are essential for preventing the initial development of DKD (primary prevention) and/or mitigating its progression and associated complications (secondary prevention).<sup>2</sup> Retinol binding protein 4, considered to be the key retinol transporter in bloodstream, appears primarily in the liver cells and is found in comparatively lower concentrations in the fat cells and muscular myocytes, RBP-4 enhances the migration of retinol from hepatic cells to peripheral target organs.<sup>3</sup> The correlation between heart disease, metabolic syndrome, diabetes, specifically type-2 and sensitivity to insulin, elevated RBP-4 levels, as well as inflammation.<sup>4</sup> A major need in this research area is the creation of quantitative

indicators for insulin resistance and complication of nephropathy, including biochemical biomarkers. Recent research indicates that circulating PIIINP may be linked to inflammations<sup>5</sup>, the risk of cardiovascular mortality<sup>6</sup> and patients with hypertension.<sup>7</sup> The important component of collagen synthesis is PIIINP, particularly the aminoterminal peptides, it is partially cleaved by a specific enzyme procollagen proteinase during collagen maturation. Consequently, it is released into the bloodstream during the decomposition of collagen fibers<sup>8</sup> and inflammatory conditions, including pulmonary fibrosis, acromegaly, and rheumatoid arthritis.<sup>9</sup> Many research indicates that PIIINP levels elevate in persistent liver illnesses, pulmonary disorders, and heart conditions such as heart disease, stroke, and coronary artery disease<sup>10</sup> and are additionally linked with skeletal muscle repair and growth, associated with collagen production, which is critical for muscle regeneration and remodeling following injury or prolonged physical activity. Therapies using both growth hormone and testosterone could stimulate collagen synthesis, resulting in elevated levels of PIIINP.<sup>11</sup>

## METHODS

This case-control study was comprised 135 individual and conducted at College of Medicine, Al-Nahrain University, Baghdad-Iraq from 1st March 2024 to 31st October 2024. The study population consisted of 45 healthy persons serving as a control group, 40 persons type-2 diabetes mellitus with normoalbuminuria and 50 persons with T2DM nephropathy presenting microalbuminuria and macroalbuminuria. In the present investigation, involved overall 95 patients diagnosed with type-2 diabetes mellitus, with and without nephropathy, and individuals who did not have diabetes mellitus were included. The renal disease in the end stage (ESRD), heart disease, cancer, thyroid, pregnancy, disorders, and liver disease. Furthermore, patients diagnosed with diabetes with type 1 mellitus have been accepted for the study excluded.

Everyone in the group underwent surveys that gathered demographic and baseline information, encompassing their sex, age, medical history, smoking status, hypertension, BMI, height, and tests for blood, all of which were then submitted for audit. The evaluation is advised for both the patients and the experimental cohort, and consent has been obtained. The venous fasting samples of blood, about between six and eight milliliters, were drawn from each subject in the morning during a 12-hour fast using a syringe that was disposable and promptly stored at  $-20^{\circ}\text{C}$ . All of the blood samples were divided into two distinct portions. Initially, two ml of human blood were obtained in tubes containing EDTA for HbA1c measure. Furthermore, six ml of whole blood specimens were obtained in a gel tube and permitted to remain stationary for 20 minutes

at ambient temperature. After coagulation, isolate the clot using centrifugal force at 2,000-3,000 revolutions per minute for 20 minutes. Urine samples were promptly collected from both patients and controls and will be packed into sterile containers. The current investigation incorporates assays to quantify the levels of albuminuria and creatinine in urine. The study participants were assessed using the urine albumin-to-creatinine ratio (ACR), a physiological indicator for kidney disease, classified as being normal ( $<30\text{ mg/g}$ ), microalbuminuria ( $30\text{ to }299\text{ mg/g}$ ), and macroalbuminuria ( $\geq 300\text{ mg/g}$ ). Serum levels of glucose, urea, creatinine, and lipid parameters were immediately evaluated using the Cobas Roche 311. Serum levels of insulin and indicators of disease, especially RBP-4 (SunLong Biotech, China) and PIIINP (SunLong Biotech, China), were determined in serum samples kept at  $-20^{\circ}\text{C}$  using ELISA technique.

The statistical assessment was carried out using SPSS-26.0. To assess the degree of association between two numerical variables, the Pearson correlation coefficient was calculated. The statistically significant level was determined at an appropriate p-value threshold of  $p < 0.05$ . The diagnostic importance of the indicators was determined by calculating the area under curve the Receiving operating characteristic curve studies.<sup>12</sup>

## RESULTS

The study population's characteristics showed in table 1. Table 2 provides an illustration of the clinical features of the research population. Subjects were divided into a total of three categories: normoglycemic, type-2 diabetes mellitus with albumin in the urine and type-2 diabetes mellitus without albuminuria. There were no statistically significant variations in age were seen across the research groups in relation to those in the control group. Individuals with type-2 diabetes mellitus, either with or without albuminuria, have increased levels of the body's mass index, FBS, HbA1c, HOMA-IR, LM, PIIINP, and UACR, as demonstrated in Tables 2, 3 and 4 and Figures 1 and 2. Decreased levels of eGFR, a significantly significant difference was observed in RBP-4, PIIINP, FBS, and HbA1C, among the four groups ( $p < 0.001$ )

The correlation between medical and laboratory elements along with serum levels of each indicator RBP-4 and PIIINP. The next stage of this research involves evaluating the association between blood levels of PIIINP, RBP-4 and other parameters across all demographic categories by Pearson correlation coefficients analysis (Table 5). Serum PIIINP had a substantial positive connection with RBP-4 ( $p=0.016$ ,  $r=0.53$ ), FBS ( $p=0.004$ ,  $r=0.275$ ), HbA1C ( $p=0.019$ ,  $r=0.185$ ), HOMA ( $p=0.0027$ ,  $r=0.283$ ), and UACR ( $p<0.001$ ,  $r=0.551$ ). and shown a substantial negative connection with eGFR ( $p = 0.009$ ,  $r = -0.302$ ). Serum RBP-4 demonstrated a positive and

statistically significant correlation with age ( $p=0.037$ ,  $r=0.31$ ), duration of diabetes ( $p=0.011$ ,  $r=0.47$ ), and

UACR ( $p<0.018$ ,  $r=0.52$ ). and shown a significant negative connection with eGFR ( $p<0.012$ ,  $r=-0.66$ ).

**Table No.1: Details about the socioeconomic background of the research group**

Variables	Control (n=45)	T2DMW.A.(n=40)	T2DM.Mi (n=25)	T2DM.Ma (n=25)	p –value
Ages (years) (Range)	51.63±5.46 (44 – 65)	53.09±7.18 (48-65)	56.31±6.38 (52-67)	57.98±3.66 (48-70)	0.255
BMI (k/m <sup>2</sup> ) (Range)	24.4±1.93 (18.8-26.1)	27.6±3.84 (20.5-28.6)	30.6±2.86 (25-33)	34.28±3.8 (30-37)	<0.01
Duration years (Range)	-----	-----	14.2±3.91 (8.0-21)	17.18±3.70 (11.0-23)	<0.05
<b>Hypertension</b>					
Yes	45 (100%)	34 (75.5%)	7 (28%)	2 (8%)	<0.001
No	-	11 (24.5%)	18 (72%)	23(92%)	

**Table No.2: Comparison of the research groups' biochemical parameters**

Variable	Group 1 (n=45)	Group 2 (n=40)	Group-3 (n=50)	P value
FBS (mg/dl)	96.9±6.98	200±50.16	259±41.43	<0.01
HbA1C (%)	5.18±0.28	7.7±1.42	9.22±1.01	<0.001
TC (mg/dl)	169.00±11.5	205.4±25.5	208.70±28.0	<0.001
TG (mg/dl)	114.00±11.1	162.6±32.96	191.2±41.84	<0.001
HDL (mg/dl)	49.70±8.03	41.00±7.05	33.16±4.00	<0.01
LDL (mg/dl)	91.07±7.00	109.30±18.81	124.1±13.39	<0.01
VLDL (mg/dl)	22.79±2.23	31.75±7.22	38.24±8.39	<0.01
HOMA-IR (μU/ml)	2.03±0.27	8.80±2.36	15.77±3.38	<0.001
eGFR ml/min/1.73m <sup>2</sup>	122.0±28.71	102.90±18.72	48.81±10.96	<0.001
UACR (mg/g)	15.24±7.524	19.37±5.163	355.6±34.06	<0.001

n: the quantity of encounters; data presented as mean & standard deviation; One-way ANOVA; Post hoc Tukey's test; Highly significant at  $P < 0.001$  or 0.01; significant at  $P \leq 0.05$

**Table No. 3: The result for procollagen III N-terminal peptide in all study groups**

Indicator/Groups	G1 (n=45)		G2 (=40)		G3 (50)	
	No.	%	No.	%	No.	%
<b>PIIINP (pg/ml) FR (%)</b>						
Below N (<13)	-	-	-	-	-	-
Normal (13-800)	43	95.5	29	72.5	14	28.0
Above N (>800)	2	5.5	11	27.5	16	72.0
Mean ± SD	360.3±57.5		721.6±80.0		860.9±47.67	
p-value	G1/G2: <0.01		G1/G3:<0.001		G2/G3: p<0.05	

n: the number of experiences; data provided as mean and standard - deviation; One-way ANOVA; Post hoc Tukey's test; very significant at  $P < 0.001$  or 0.01; significant at  $P \leq 0.05$

**Table No.4: Retinol binding protein-4 outcome for every investigation groups**

Indicator/Groups	G1 (n=45)		G2 (=40)		G3 (50)	
	No.	%	No.	%	No.	%
<b>RBP-4 (ng/ml) FR(%)</b>						
Below-Normal (<0.1)	4	8.9				
Normal (0.1-8)	40	88.9	32	80.0	13	26.0
Above - Normal (>8)	1	2.2	8	20.0	37	74.0
Mean ± SD	6.20±0.04		7.99±0.28		10.08±0.33	
p-value	G1/G2: <0.05		G1/G3: <0.01		G2/G3<0.05	

n: the quantity of encounters; data presented as mean & standard deviation; One-way ANOVA; Post hoc Tukey's test; Highly significant at  $p<0.001$  or 0.01; significant at  $P \leq 0.05$



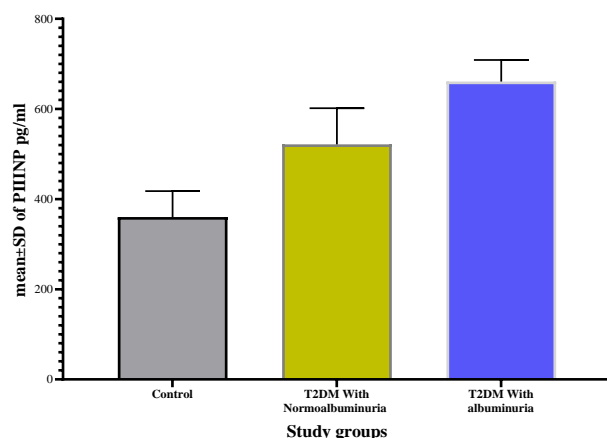
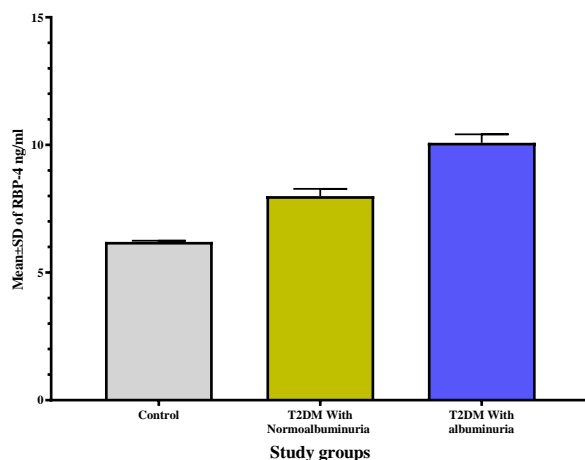
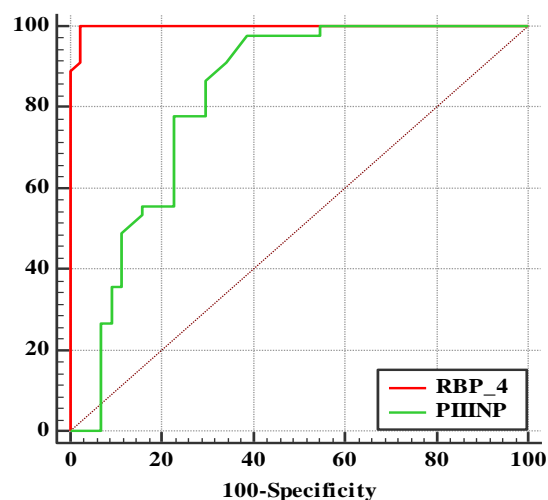
**Table No. 5: The relationship between PIINP, RBP-4, and the laboratory and clinical indicators**

Parameters	PIINP		RBP-4	
	P	r	P	r
Age (years)	0.848	0.015	0.037	0.310
Duration of disease			0.011	0.47
PIINP			0.016	0.530
RBP-4	0.016	0.530		
FBS (mg/dl)	0.004	0.275	0.6	0.10
HbA1C (%)	0.019	0.185	0.02	0.17
HOMA-IR ( $\mu$ U/ml)	0.0027	0.283	0.0027	0.283
eGFR ml/min/1.73m <sup>2</sup>	0.0097	-0.302	0.009	-0.302
UACR (mg/g)	<0.001	0.551	0.018	0.52

Significant difference  $P < 0.05$

**Table No.6: Shows the ROC and cutoff values for RBP-4 and PIINP in the groups under study**

Marker	AUC	SE	95%CI	Cutoff	Sensitivity	Specificity
RBP-4	0.998	0.002	0.955 to 1.000	>3.29	100.00	97.70
PIINP	0.970	0.023	0.910 to 0.994	>587.00	100.00	97.52

**Figure No. 1: Serum levels of procollagen III N-terminal peptide in each study groups****Figure No. 2: Serum levels of Retinol binding protein-4 in each study groups****Figure No. 3: ROC curve and cutoff values for RBP-4 and PIINP in the study groups**

A receiver operating characteristic (ROC) curve analysis was performed due to the significant difference in RBP-4 and PIINP amounts between individuals with Type 2 diabetes groups, both with and without albuminuria. The findings revealed excellent discriminatory power is demonstrated by RBP-4 AUC of 0.998, sensitivity of 100% and a specificity of 97.7%. The area under the curve 0.970 for PIINP indicates high discriminating power. The cutoff is >587, with a specificity of 97.52% and a sensitivity of 100% (Fig. 3, Table 6)

## DISCUSSION

This case-control study revealed that the combination of RBP-4 levels and PIINP values can be utilized to

diagnose diabetic nephropathy, identifying RBP-4 + PIIINP as a unique independent marker for nephropathy. The principal conclusions of this study are as follows: Initially, ROC curve analysis revealed that the AUC of the RBP-4 group surpassed that of the individual PIIINP groups, indicating that the diagnostic accuracy for diabetic nephropathy utilizing combined RBP-4 and PIIINP data was superior to that of RBP-4 or PIIINP alone. In this Iraqi cohort, we identified an excellent dependent on concentration correlation between elevated plasma RBP-4 and PIIINP levels and a simulated complication of type 2-diabetes such as nephropathy. In the past few years, the adipokine RBP-4 was being investigated as a possible indicator of type 2-diabetic mellitus.<sup>13</sup> It has performed a series of tests to elucidate the relationship between RBP-4, T2DM, and diabetic nephropathy, particularly its influence on resistance to insulin and pancreatic  $\beta$ -cell functionality. The findings of these researches demonstrate that RBP-4 significantly impacts T2DM, with nephropathy identified as a potential biomarker for T2DM sequelae, particularly diabetic nephropathy. Nonetheless, debates have arisen regarding the association between RBP-4 levels and type 2 diabetes mellitus with nephropathy. There exists a clinical requirement for detecting humans at risk of complications from type 2 diabetes mellitus using simple, accessible, and cost-effective techniques. This study investigated the association of the type III collagen production marker PIIINP with risk variables for diabetic nephropathy and its potential to predict future occurrences of the condition. A relationship was identified between higher plasma PIIINP levels in individuals with type 2 diabetes mellitus, both with and without nephropathy. Individuals with type-2 Diabetes (T2DM) frequently demonstrate resistance to insulin (IR), reduced tolerance for glucose, lipid disorders, and hypertension.<sup>1</sup> The results correspond with the present investigation, which demonstrated increased levels of triglyceride, total cholesterol, HOMA-IR, low density lipoprotein, and VLDL in both T2DM and diabetic nephropathy (DN) groups (Table 1). Hyperglycemia and high HbA1c amounts adversely affect profiles of lipid and heighten the development of type 2 diabetic and diabetic nephropathy.

Lipid profiles elevate the probability of developing type 2 diabetes mellitus and lipid disorders. Rise levels of free fatty acid (FFA) enhance triglycerides (TG) synthesis, which results in heightened production of apolipoprotein B, also known as (ApoB) and low-density lipoprotein. The hormone insulin generally facilitates the degradation of ApoB through the activation of phosphatidylinositol-3 kinase; however, this mechanism is compromised in insulin-resistant circumstances, thereby elucidating the increased triglyceride levels observed in such states.<sup>14</sup>

In this study, we identified an excellent dependent on concentration correlation between elevated plasma RBP-4 and PIIINP levels and a simulated complication of type 2-diabetes such as nephropathy. Our study is primarily constrained by rather tiny numbers of participants and the lack of the longitudinal follow-up. This study is, to our knowledge, the first to incorporate levels of PIIINP and UACR in patients with diabetic nephropathy. Higher PIIINP and RBP-4 concentration than in the control group, the diabetic nephropathy has changed both RBP-4 and PIIINP.

To highlight the great relevance of this indicator in diabetes nephropathy, more cohort research on bigger groups among individuals with type-2 diabetes nephropathy and determination of the kidneys activity in subgroups of individuals with different type 2 diabetic stages is necessary.

## CONCLUSION

For immediately detection and follow-up of nephropathy across people who have type-2 diabetes, PIIINP and RBP-4 are useful biomarkers. Their complementing capacity to reflect renal fibrosis and tubular dysfunction respectively helps to control DN. Their extensive usage will be made possible by further investigation and clinical validation, hence possibly changing the field of diabetic nephropathy diagnosis and management.

### Author's Contribution:

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

**Source of Funding:** None

**Ethical Approval:** No.5 Dated 03.05.2022

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# Sarcopenia in Dialysis Patients: Correlation with Haemoglobin and Creatinine Levels

Natalia Hariyanti, Ahmad Syauqy and Etika Ratna Noer

## ABSTRACT

**Objective:** To analyse association among sarcopenia also haemoglobin as well as creatinine levels at patients undergoing haemodialysis.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** This study was conducted at the KRT Setjonegoro Wonosobo Hospital for 7 months in December 2023 to July 2024.

**Methods:** Research used a cross-sectional design, conducted at KRT Setjonegoro Wonosobo Hospital in December 2023. Sample of 83 respondents was selected utilizing consecutive sampling technique. Instruments used were BIA, handgrip strength dynamometer, and stopwatch to determine sarcopenia parameters and biochemical results before haemodialysis to see haemoglobin and creatinine levels. Data collected were tested using the Mann Whitney test.

**Results:** There were 19 out of 83 respondents experienced sarcopenia (22.9%), there was a correlation of sarcopenia in haemodialysis patients in terms of haemoglobin levels ( $p=0.024$ ), and there was a correlation of sarcopenia in haemodialysis patients in terms of creatinine levels ( $p=0.043$ ).

**Conclusion:** There is big correlation among haemoglobin also creatinine levels as well as the incidence sarcopenia at patients undergoing haemodialysis.

**Key Words:** Chronic Kidney Disease, Creatinine, Haemodialysis, Haemoglobin, Sarcopenia

**Citation of article:** Hariyanti N, Syauqy A, Noer ER. Sarcopenia in Dialysis Patients: Correlation with Haemoglobin and Creatinine Levels. Med Forum 2025;36(6):44-48. doi:10.60110/medforum.360609.

## INTRODUCTION

Chronic Kidney Disease (CKD) remains a condition characterized by chronic kidney disease that lasts three months or longer. CKD is characterized by a gradual and irreversible loss of kidney tissue, with or without kidney damage, and is characterized by a Glomerular Filtration Rate (GFR) below 60 mL/min/1.73 m<sup>2</sup> for more than three months<sup>1</sup>. End Stage Renal Disease (ESRD) is the last stage of CKD also is characterized by extremely poor renal function; patients at this stage require permanent renal replacement therapy, such as dialysis or kidney transplantation<sup>2</sup>. ESRD patients require renal replacement therapy to support their quality of life. This is because the failure of kidney function in the final stage can result in abnormalities in the body's electrolytes and can form toxins in the bloodstream. Kidney replacement therapy that can be done is by kidney transplantation or by dialysis.

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Received: January, 2025

Reviewed: February, 2025

Accepted: March, 2025

There are two types of dialysis that are often used, namely peritoneal dialysis and haemodialysis (HD)<sup>3</sup>.

Sarcopenia is common in ESRD patients undergoing dialysis<sup>4</sup>. Declining muscular strength and/or physical performance accompanied by a gradual decrease of skeletal muscle mass is known as sarcopenia, and it is a common age-related clinical disease<sup>5</sup>. Sarcopenia caused by many factors, mainly physical inactivity and ageing. Other factors include low calorie and protein intake, decreased anabolic hormones (testosterone, IGF-1, DHEA, GH), increased inflammatory cytokines, and reduced blood flow to the muscles<sup>6</sup>. Sarcopenia occurs with advancing age, but can also develop in young adults<sup>7</sup>. Sarcopenia is categorised into primary sarcopenia (caused by the ageing process), secondary sarcopenia (associated with bed rest, sedentary life style, zero-gravity conditions, and organ failure diseases such as heart, liver, kidney), and nutrient intake-related sarcopenia (caused by inadequate energy and protein intake due to malabsorption, gastrointestinal disorders, and use of drugs that cause anorexia)<sup>8</sup>. The prevalence of sarcopenia in non-dialysis CKD patients ranges from 5.9-9.8% also in dialysis patients is reported to be higher at 20-42.2%.<sup>9</sup> Other studies mentioned from 25.9-34.6%<sup>4</sup>. Meanwhile, the prevalence of sarcopenia using the SARC-F assessment was 30% also prevalence of severe sarcopenia ranged by 18% till 35%<sup>10</sup>. Variations in the prevalence of sarcopenia in CKD depend on the method

also cut-off applied as well as the diagnosis criteria used<sup>9</sup>.

Haemoglobin is a significant biomarker for sarcopenia, with diagnostic and prognostic uses<sup>11</sup>. There seems to be a correlation between haemoglobin and physical performance, strength of muscles, and muscle mass in chronic kidney disease patients, according to research. A loss of hunger, anaemia, metabolic acidosis, and other systemic symptoms are all part of chronic renal failure. A loss of muscle mass also an overall decline at physical performance may be attributed to all of these disorders<sup>12</sup>. Creatinine is another potential biomarker of sarcopenia characteristics in dialysis patients that may be seen in test results. A dependable predictor of a person's muscle mass and function, serum creatinine levels are frequently evaluated at ESRD patients on dialysis<sup>13</sup>. A lower blood creatinine level suggests muscle atrophy and an elevated risk of death, while a higher creatinine level is related with a lower risk of death<sup>14</sup>.

According previous studies on correlation among haemoglobin also creatinine to incidence sarcopenia in haemodialysis patients, researchers consider this study important to understand how haemoglobin and creatinine levels can make risk of sarcopenia at dialysis patients so that it can be the basis for better prevention and management efforts to improve patients life quality.

## METHODS

Model of research was analytical observational by a cross-sectional model. Ethical Clearance of study has been approved by KEPK of the Faculty of Medicine, Diponegoro University Semarang with ethical code number: 567/EC/KEPK/FK-UNDIP/XI/2023. The collection of independent variables and dependent variables was carried out on the day the patient arrived, during dialysis, until the patient was discharged. The study was conducted in the haemodialysis unit of KRT.

Setjonegoro Wonosobo Hospital. The inclusion criteria in this study were male and female outpatient haemodialysis patients who had a minimum age of 20 years, a length of haemodialysis  $\geq 3$  months, agreed to be a research subject by filling in and signing the informed consent that had been provided, and the patient was still doing daily activities. A total of eighty-three patients were sampled. We used a sequential sampling method, which entails selecting a sample from all participants who fulfilled the study's inclusion criteria up to a certain time point, and then screening them if necessary.

The research instruments used were a stepped weight scale and microtoa from TANITA WB-380, LLA tape from OneMed, BIA (Bioelectrical Impedance Analysis) from Omron HBF-375, hand grip strength dynamometer from Camry EH-101, informed consent, and stopwatch from Q&Q MF01J. The collected data were then analysed univariate and bivariate using statistical tests. Data analysis utilizing IBM SPSS Statistic 27.0.1.0 64-bit edition software. Data normality test and characteristic test were conducted before data analysis. The data normality test used Kolmogorov Smirnov. Univariate analysis utilized for describing the frequency of each variable. Bivariate analysis used Chi Square statistical test for categorical data also Mann Whitney statistical test by numerical data that were not normally distributed.

## RESULTS

Table 1 shows the results of the socio-demographic data, which includes the frequency of variables of gender, age, length of haemodialysis, and sarcopenia. Table 2 shows the results of the analysis of the relationship between sarcopenia and the independent variables in the study, namely haemoglobin and creatinine levels.

**Table No.1: Socio-demographic data of respondents (N = 83)**

Variables	Not Sarcopenia	Sarcopenia	P value	Amount
<b>Gender</b>				
Male	31	11	0.469	42 (50.6)
Female	33	8		41 (49.4)
<b>Age Category</b>				
Late adolescence (17-25 years old)	3	2	0.789	5 (6)
Early adulthood (26-35 years old)	7	2		9 (10.8)
Late adulthood (36-45 years)	16	4		20 (24.1)
Early elderly (46-55 years)	18	3		21 (25.3)
Late elderly (56-65 years)	16	6		22 (26.5)
Elderly ( $\geq 66$ years)	4	2		6 (7.2)
<b>Length of HD Category</b>				
New (< 12 months)	28	6	0.542	34 (41)
Fair (12-24 months)	19	8		27 (32.5)
Old (>24 months)	17	6		23 (26.5)
<b>Sarcopenia</b>	64 (77.1)	19 (22.9)		

**Table No.2: Relationship between Haemoglobin and Creatinine with the Incidence of Sarcopenia**

Variables	Not Sarcopenia	Sarcopenia	P value
Haemoglobin (g/dL)	8.1 (4.3 – 11.5)	8.9 (7.2 – 11.3)	0.024
Creatinine (mg/dL)	11.71 (4.96 – 18.87)	13.12 (5.9 – 17.39)	0.043

## DISCUSSION

In this research, commonly of participant were male with total 42 (50.6%), while female respondents totalled 41 people (49.4%). Factors that may influence this are unhealthy living habits that men often have, such as smoking, consuming coffee, alcohol, and certain supplements that can reduce kidney function<sup>15</sup>. On the other side, women have a lower risk of developing chronic kidney disease than men because sexual hormones play a role in protecting kidney function. Oestrogen in women has a protective effect on the development of kidney disease, especially on the nephron component, glomerulosclerosis, and fibrosis<sup>16</sup>. In this study, Late Elderly age group 56-65 years was the largest respondent with a total of 22 people (26.5%). Ageing has a significant impact on the decline in glomerular filtration rate (GFR). Research shows that GFR in healthy adults at the age of 20 years ranges from 100-110 ml/min/1.73m<sup>2</sup>, but can decrease by 5-25% when reaching the age of 50 years<sup>16</sup>.

The most respondents in this study were those who had been on haemodialysis for less than 12 months with 34 people (41%). The duration of haemodialysis can affect nutritional status through the catabolism that occurs during the procedure. This catabolism leads to the loss of essential nutrients such as amino acids, vitamins, protein, and glucose. The longer the patient is on haemodialysis, the longer the catabolism process takes place. If not balanced with adequate nutritional therapy, the risk of malnutrition will increase<sup>17</sup>. From a total of 86 respondents, 66 people (76.7%) did not experience sarcopenia, while 20 people (23.3%) were detected to have sarcopenia. As we become older, our skeletal muscles naturally lose bulk and strength, a disease known as sarcopenia. This may lead to a decrease in our ability to do physical activities<sup>5</sup>. The three primary criteria that were defined by (EWGSOP) also (AWGS) for the diagnosis of sarcopenia<sup>18</sup>.

**Relationship between Haemoglobin and the Incidence of Sarcopenia:** According findings of analysis at table 1, as we can see the Mann Whitney test of haemoglobin with the incidence of sarcopenia obtained a result of  $p=0.024$  ( $p<0.05$ ). Those findings assume indicate that there is a correlation between sarcopenia in haemodialysis patients in terms of haemoglobin levels. As line with study from of Tseng et al (2021) which tells low haemoglobin levels are significantly associated with a decrease in walking speed ( $p=0.01$ ), weak hand grip strength ( $p=0.025$ ), and the occurrence of sarcopenia ( $p=0.028$ ) in patients undergoing haemodialysis<sup>11</sup>. A study in the Netherlands

also suggested that lower haemoglobin levels correlated decreased muscle mass and strength ( $p<0.001$ ) in kidney transplant patients who had previously undergone dialysis. These results were consistent after researchers measured muscle mass also muscle strength using two different methods, namely through creatinine and BIA levels as well as hand grip strength also (FTSTS) test<sup>19</sup>.

Haemoglobin has a major role in binding also transporting oxygen to various tissues of human bodies. When haemoglobin levels decrease, the supply of oxygen to cells or tissues decreases leading to hypoxia in skeletal muscles thus affecting muscle strength also function. Low haemoglobin levels also reflect inadequate nutritional intake, inhibit protein synthesis, and result in decreased muscle mass, muscle strength, also may accelerate development sarcopenia. Low haemoglobin is often associated with anaemia, where anaemic patients tend to experience fatigue that lessens the need for physical exercise also motor control. Anaemic individuals' mitochondrial metabolism as well as myoglobin production are both impacted by iron shortage, which in turn hinders muscular function<sup>20</sup>. Anaemia is often experienced by patients undergoing haemodialysis and can exacerbate symptoms correlated decreased kidney function, such as fatigue, dyspnoea, oxidative stress, as well as decreased tolerance to physical activity. These conditions can negatively affect development strength also muscle hypertrophy<sup>21</sup>.

**Relationship between Creatinine and the Incidence of Sarcopenia:** According on the results of the analysis in table 1 above, it can be seen that the Mann Whitney test of creatinine with the incidence of sarcopenia obtained the result of  $p=0.043$  ( $p<0.05$ ). those findings assume that there is correlation between sarcopenia in haemodialysis patients in terms of creatinine levels. This is in line with study of Kakita et al (2022) who said that has a strong correlation among creatinine levels also its derivatives with sarcopenia ( $p<0.001$ ) in patients undergoing haemodialysis. These results remained consistent even after adjustments were made for factors such as demographics, physical condition, primary kidney disease, comorbidities, nutritional status, remaining kidney function, and treatment centre<sup>13</sup>. A Brazilian study suggested that increasing creatinine levels could reduce the prevalence of sarcopenia ratio by 21.2%<sup>22</sup>. Another study in Eastern Taiwan also stated that creatinine levels correlate with walking speed ( $p=0.003$ ), and can be used as a marker to detect sarcopenia and assist in the screening process of sarcopenia in advanced CKD patients<sup>23</sup>.

Creatinine is a substance produced from the metabolism creatine phosphate at skeletal muscle and total creatinine the body produces depends on skeletal muscle mass when kidney function is stable. Creatinine is easily filtered by the kidneys and not much reabsorbed so it can be a marker to estimate skeletal muscle mass in different groups of people<sup>23</sup>. Kidneys account for among 20% of production guanidinoacetic acid which is the direct precursor for creatine formation at human body. When kidney function gradually declines and animal protein intake is also low in haemodialysis patients with CKD, the creatine balance in the body may be disturbed. This may increase the risk of sarcopenia, fatigue, decreased cognitive ability, worsened life qualities, also improving mortality at patients CKD<sup>22</sup>.

## CONCLUSION

There is a big corelation among haemoglobin and creatinine levels also incidence sarcopenia in haemodialysis patients. Low haemoglobin ( $p=0.024$ ) also creatinine ( $p=0.043$ ) contributed to the increased risk of sarcopenia. Those results emphasise urgency monitoring both parameters to prevent and optimally treat sarcopenia.

**Acknowledgements:** The authors much obliged to people in the haemodialysis room of KRT. Setjonegoro Hospital for their support and permission to carry out data collection in the haemodialysis room.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Natalia Hariyanti Ahmad Syauqy
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No. 567/EC/KEPK/FK-UNDIP/XI/2023 Dated 24.11.2023

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# A Study to Determine the Correlation between the Intercondylar and Interdental Widths in the Pakistani Asian Population

Correlation  
between the  
Intercondylar  
and Interdental  
Widths

Muhammad Hadee Aziz, Muhammad Aamir Ghafoor Chaudhary, Hira Riaz, Ayesha Batool, Gohar Ali and Parivash Anwar

## ABSTRACT

**Objective:** To investigate the correlation between intercondylar distance (ICD) and occlusal vertical dimension (OVD) in a segment of the Pakistani Asian population, and assess whether ICD can serve as a reliable anatomical landmark for determining OVD in dentate individuals.

**Study Design:** Cross-sectional analytical study

**Place and Duration of Study:** This study was conducted at the Islamic International Dental Hospital, Islamabad, from January 2024 to December 2024.

**Methods:** A total of 160 dentate individuals (80 males, 80 females) aged 18–30 years with Class I occlusion were selected through randomized sampling. ICD was measured using the Denar reference point and a modified digital vernier caliper. OVD was assessed using a Willis Gauge. The Shapiro-Wilk test was applied to evaluate data normality. Gender-based differences were assessed using the Mann-Whitney U test, while the relationship between ICD and OVD was evaluated using Spearman's correlation.

**Results:** The mean ICD was 132.1 mm in males and 123.7 mm in females, revealing a statistically significant difference ( $p = 0.001$ ). The mean OVD was 49.3 mm in males and 50.4 mm in females, with no significant gender difference ( $p = 0.29$ ). Spearman's correlation showed a weak, non-significant association between ICD and OVD ( $\rho = 0.18$ ,  $p = 0.25$ ).

**Conclusion:** ICD significantly differs by gender, while OVD does not. No statistically significant correlation was found between ICD and OVD, indicating ICD alone may not be a reliable predictor for determining OVD.

**Key Words:** Intercondylar distance, occlusal vertical dimension, anatomical landmarks, complete denture

**Citation of article:** Aziz MH, Chaudhary MAG, Riaz H, Batool A, Ali G, Anwar P. A Study to Determine the Correlation between the Intercondylar and Interdental Widths in the Pakistani Asian Population. Med Forum 2025;36(6):49-53. doi:10.60110/medforum.360610.

## INTRODUCTION

Advancements in healthcare, medicine and technology have exponentially increased life expectancy; giving rise to an increasing geriatric population<sup>1</sup>. According to WHO, between 2015 and 2050, the proportion of the world's population over 60 years will nearly double.

Aging individuals have to deal with many age-related diseases and conditions, with edentulism being a common and major concern<sup>2</sup>.

Edentulism, or the complete loss of natural teeth, may arise from various factors including limited access to healthcare, low socioeconomic status, and general neglect of oral hygiene. Edentulism is a significant health concern as it is an irreversible condition affecting day to day activities<sup>3</sup>. It can affect the oral health, masticatory function, facial aesthetics and phonetics of the individual which may lead to malnutrition and a diminished quality of life<sup>4</sup>.

Restoring lost dentition through prosthetic means should aim not only to recover masticatory efficiency but also to support oral tissues, improve appearance, and facilitate clear speech. The effectiveness of a prosthesis is largely dependent on its ability to meet these functional and aesthetic demands<sup>5</sup>. Researcher proposed that denture fabrication constitutes multiple steps and every step leading to the delivery of prosthesis should be done following proper guidelines and recommendations<sup>6</sup>. Lapses in judgement, mishandling of steps or reliance on assumptions can adversely affect the final quality of the denture.

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Received: February, 2025  
Reviewed: March, 2025  
Accepted: April, 2025

A critical component of complete denture fabrication is determining the correct vertical dimension of occlusion (OVD). The loss of natural teeth makes it difficult to determine the appropriate OVD. There have been numerous reported methods to determine OVD with no universally accepted method<sup>6</sup>. As stated by Shen et al, almost every method has its own set of short comings<sup>7</sup>. Incorrect measurements can cause an increased or decreased OVD which can lead to a strained appearance, clicking, temporomandibular discomfort, or angular cheilitis, poor aesthetics, cheek biting respectively<sup>8</sup>.

There are certain anatomical parameters that remain constant throughout an individual's life which are not prone to resorption or time related changes. Jassim et al reported that the inter condylar distance (ICD) is one such landmark, which is 'the distance between the rotational centres or two condyles or their analogues'<sup>10</sup>. Various parts of the human body are proportionate to each other, and theoretically the ICD may be used to estimate the OVD.

The purpose of pursuing this study is to determine whether the ICD can be utilised to serve as a reliable landmark for determining the OVD in a cross section of the Pakistani subpopulation. Although previous studies have reported positive results, there is a dearth of data of a study of this nature targeting a segment of Pakistani population. These results may help future clinicians in fabricating a more accurate prosthesis.

## METHODS

The ethical review board of Islamic International Dental Hospital approved this study, Ref. No. IIDC/IRC/2023/11/056, without restrictions and an informed consent was taken from all participants. This was a cross-sectional study based on a randomized sampling technique on participants visiting Islamic International Dental Hospital from January 2024 to December 2024. A sample size of 160 was calculated according to a confidence level of 95%, margin of error 5% with a population proportion of 50% based on a population size of 258<sup>5</sup>.

All participants were selected on the basis of the following criteria; male and female participants, who are completely dentate (excluding third molars), are within the age group of 18-30 years with a Class I occlusal relationship. Participants with any significant oral pathology, gross malocclusion, facial asymmetry, temporomandibular disorder, excessive parafunctional habits or fixed dental prostheses were excluded from the study. Uncooperative participants and/or patients with neurological disorders or under any sort of intoxication were excluded as well.

The intercondylar distance was measured using the Denar reference point<sup>11</sup> bilaterally to approximate the location of the condyles. This arbitrary point is located 12 mm anterior and 5 mm inferior to an imaginary line

joining the superior border of the tragus and the outer canthus of the eye. To help in locating this point easily, a large plastic ruler was modified<sup>5</sup> with a 0.5 mm hole 12 mm anterior and 5 mm inferior starting from the zero reading on the ruler. Using this modified ruler, the Denar point was marked bilaterally with an indelible pencil with the participants sitting relaxed in the dental chair, in an upright position, whilst looking straight forward. (Figure 1).

A digital vernier caliper was modified to extend its arms in order to measure the marked points easily. With the extended arms contacting the marked points, the ICD of the participant was recorded in millimeters. (Figure 2).

Next, the occlusal vertical dimension of the participants was recorded with the help of a Willis Gauge, which uses the sub-nasale and Menton as reference points. Participants were asked to inter-cuspalte their teeth and relax their lips beforehand. Readings were taken twice for each participant to reduce error, and values were recorded nearest to 0.1 mm. (Figure 3).

Data accumulated was tabulated and analyzed statistically by means of SPSS software (version 23). Descriptive statistics were calculated for qualitative and quantitative variables. Quantitative variables like ICD and OVD were calculated in terms of mean. Shapiro-Wilk test was applied to check the normality of data. As data was not normal, non-parametric tests and median were reported. Mann-Whitney U test was applied to compare OVD and ICD in male and female patients. A Spearman's correlation analysis was conducted to assess the relationship between ICD and OVD.

## RESULTS

The Intercondylar Distance (ICD) and Occlusal Vertical Distance (OVD) of a total of 160 participants were recorded which comprised of 80 males and 80 females. The general mean of ICD was 127.9 mm and OVD was 49.8 mm. For males the mean ICD was 132.1 mm and the mean OVD was 49.3 mm. The mean ICD in female participants was 123.7 mm and the mean OVD was 50.4 mm. (Figure 4).

**Table No.1: Shapiro-Wilk test**

		Test Statistic (W)	p-value
Intercondylar Distance (ICD)	Male	0.949	0.003
	Female	0.957	0.008
Average		0.95	0.005
Occlusal Vertical Distance (OVD)	Male	0.899	0.001
	Female	0.909	0.001
Average		0.90	0.01

A Shapiro-Wilk test was conducted to assess the normality of ICD and OVD measurements. The results indicated that ICD was not normally distributed,  $W = 0.95$ ,  $p = 0.005$ , and OVD was also not normally

distributed,  $W = 0.90$ ,  $p = 0.001$ . Since  $p$ -values were less than 0.05, the assumption of normality was violated, and non-parametric tests were used for further analysis. (Table 1).



Figure No.1: whilst looking

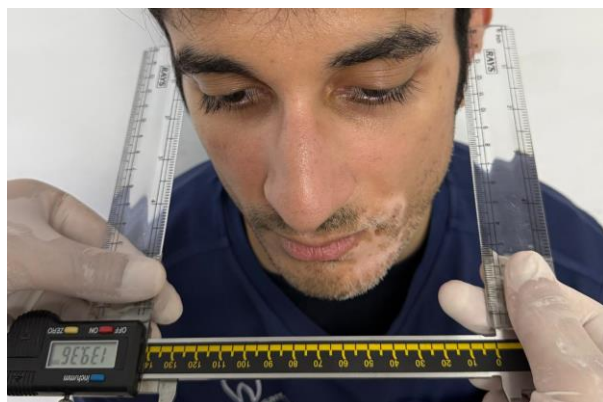


Figure No.2: A digital vernier caliper to measure the marked points



Figure No.3: Occlusal vertical dimension

A Mann-Whitney U test was performed to examine the differences in ICD between male and female patients. The results showed a significant difference,  $U = 1899.5$ ,  $p = 0.001$ . The median ICD for males was 134.0 mm, while for females, it was 123.9 mm. Since  $p < 0.05$ , we conclude that males have a significantly higher ICD as compared to females.

When comparing OVD between genders, the Mann-Whitney U test revealed no statistically significant difference,  $U = 2888$ ,  $p = 0.29$ . The median OVD for males was 48 mm, while for females, it was 50 mm. Since  $p > 0.05$ , it was concluded that gender does not significantly affect OVD.

A Spearman's correlation analysis was conducted to assess the relationship between ICD and OVD. The results indicated a weak and non-significant correlation,  $\rho = 0.18$ ,  $p = 0.25$ . Since  $p > 0.05$ , there was no statistically significant association between ICD and OVD.

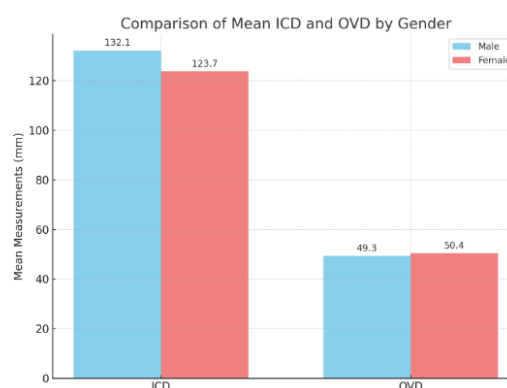


Figure No.4: ICD and OVD comparison

## DISCUSSION

The OVD in edentulous patients is arguably one of the most important parameters that needs to be calculated precisely for an accurate prosthesis. As discussed earlier, various methods can be used, albeit their shortcomings<sup>8</sup>. In this study, we aimed to find the correlation between the OVD and ICD to assess if the ICD could be used as a landmark to predict the OVD accurately.

Correct determination of the condylar position is essential for determining the ICD. Different researchers employed different methods to determine the ICD. In this study, the Denar reference point was used to determine the location of condyles and a vernier caliper was used afterwards. In a similar fashion, Jassim utilized the Beyron point and then a caliper for measuring the intercondylar distance<sup>10</sup>. These methods have been proven to be very accurate in determining OVD as discussed by Baretto<sup>12</sup>. CBCT allows for accurate evaluation of craniofacial structures and was used to effectively measure ICD.

Oremosu et al stated that craniometric and facial measurements are usually greater in men than women<sup>13</sup>. A similar observation was made noting that the intercondylar distance is within the range of 101-119 mm for males and 91-100 mm for females. Patil et al. also noticed a significant difference of with a p-value of  $< 0.05$  in males and females' condylar length amongst other factors<sup>14</sup>. A study done by Debnath et al in a South Indian population, measured the average ICD in males and females to be 112 mm and 108 mm respectively<sup>15</sup>. This is in line with our findings, with a mean ICD of male participants of 132.1 mm and 123.7 mm for females. Thus, deducing that males have a higher ICD in comparison to females.

Comparison of OVD between male and female patients revealed that the mean OVD was 49.3 mm for males and 50.4 mm for females. On the contrary, a study carried out in a Tunisian population revealed the mean OVD in male subjects to be higher,  $67.60 \pm 4.49$  mm, as compared to females,  $60.72 \pm 3.84$  mm<sup>8</sup>. This finding was also supported by Morata et al<sup>16</sup>. Based on our results, there is no significant evidence indicating the impact of gender on OVD in this population group, which is a stark contrast to previous studies<sup>8,16</sup> and to the findings of Bajracharya<sup>17</sup>. Although, a small difference between the median values of OVD between the two variables is noticeable yet this difference is not statistically significant owing to the lack of a significant p value. This makes the probability of natural variation much higher in comparison to a difference that could be attributed to gender. This outcome indicates that clinicians do not necessarily need to take into account gender while determining OVD in comparison to other factors that might impact OVD significantly more like age, ethnicity or anatomical variations.

Spearman's rank correlation analysis was conducted to evaluate the relationship between ICD and OVD. A p-value of 0.18 suggested a weak positive correlation between ICD and OVD. Thus, theoretically, as the intercondylar distance will increase, the occlusal vertical dimension will also tend to increase, but this relationship is very weak. Since this p-value is greater than 0.05, it indicates that the correlation is not statistically significant, providing no strong evidence to suggest that ICD and OVD are meaningfully related. This contradicts previous studies carried out by Bhat<sup>5</sup>, Debnath<sup>15</sup> and Awotile<sup>18</sup>.

Bhat et al reported a statistically significant positive correlation between ICD and OVD, with a Pearson correlation coefficient of  $R = 0.619$  ( $P < 0.001$ ). He emphasized the potential to predict OVD using ICD through regression analysis, reducing dependency on subjective methods of measuring OVD<sup>5</sup>.

Meanwhile, Debnath et al. analysed the relationship between inter-condylar distance and occlusal vertical dimension in 120 dentate South Indian individuals, divided into two groups and further subdivided into

four subgroups based on their facial form. These results were less definitive due to variability in the OVD/ICD ratio across face forms, suggesting that ICD may not consistently predict OVD as its relation with OVD is less consistent and influenced by other factors such as facial morphology<sup>15</sup>.

In Awotile's study, Spearman's correlation coefficient analysis revealed a positive correlation of intercondylar distance with occlusal vertical dimension ( $R^2 = 0.911$ ) among other factors. Thus, the value of inter condylar distance can be calculated from known or measured OVD, and with the help of regression equations but he further argued that the mathematical method be used in combination of other techniques<sup>18</sup>.

This has important implication as this suggests clinicians should not rely only on one to predict the other parameter and changes or measurements in one of these variables (such as ICD) may not reliably predict or be associated with changes in the other (OVD), contrary to the correlation exhibited in previously done studies. Thus, a multifaceted approach should be taken into consideration.

Several limitations should be noted. The study's sample size, although adequate for preliminary analysis, was limited to a specific age group and geographic population. These constraints may restrict the generalizability of the findings. Furthermore, being a single-center study, variability due to ethnic diversity and broader anatomical differences was not captured. Differences in study protocols, measurement tools, and patient characteristics across published literature may also explain the conflicting results. Additionally, potential uncontrolled confounding variables could have impacted the observed associations.

To strengthen future conclusions, studies with larger and more diverse samples across multiple regions are recommended. Incorporating imaging-based techniques such as CBCT may also enhance accuracy in identifying anatomical landmarks.

## CONCLUSION

Based on the results of this study, the following conclusions can be drawn:

- A statistically significant difference was observed in the intercondylar distance (ICD) between male and female participants, with males exhibiting greater values.
- No significant difference was found in occlusal vertical dimension (OVD) between genders, indicating that gender does not play a notable role in determining OVD.
- The correlation between ICD and OVD was weak and statistically non-significant, suggesting that ICD cannot be reliably used as a sole predictor of OVD.

These findings highlight the importance of using a comprehensive and individualized approach when determining OVD, rather than relying on a single anatomical reference.

#### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Hadee Aziz, Muhammad Aamir Ghafoor Chaudhary, Hira Riaz
Drafting or Revising Critically:	Ayesha Batool, Gohar Ali, Parivash Anwar
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No. IIDC/IRC/2023/11/056 Dated 11.11.2023.

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# Comparative study for the Result of Using Different Topical Agents in Management of Second Degree Burn

Ahmed Miri Saadoon

Using Different Topical Agents in Management of Second Degree Burn

## ABSTRACT

**Objective:** To determine the best method for second degree burn treatment that provide rapid healing, prevent infection, comfortability, cost and returning the patient to full productivity during treatment period.

**Study Design:** Comparative study

**Place and Duration of Study:** This study was conducted at the outpatient private clinic from 20<sup>th</sup> January 2025 to 31<sup>st</sup> March 2025.

**Methods:** This comparative study was done in outpatient private clinic for patients were complaining from burn. Sixty patients were enrolled. These patients were randomly divided into three groups, each group consist of 20 patients. 1<sup>st</sup> group was managed by topical antibiotic (silver sulfadiazine), 2<sup>nd</sup> group by oil based herbal paste (MEBO) and 3<sup>rd</sup> group by hydrocolloid dressing. The outcome measures we investigated in early follow-up for number of dressing changes, conformability and time from treatment until wound healing. In late follow-up we assessed, scar quality after 4 to 6 months from time of burn and cost of treatment.

**Results:** The mean of time healing regarding patients treated with silver sulfadiazine and MEBO was 8 days, while it was 5 days for patients treated with hydrocolloid. Treatment with hydrocolloid was comfortable in 15 patients (75%), 5 patients (25%) for patients treated with silver sulfadiazine and in 4 patients (20%) treated with MEBO. Three patients used silver sulfadiazine developed hyperpigmentation.

**Conclusion:** Hydrocolloid has superior early outcomes as compared with other agents in management of second degree burn.

**Key Words:** Topical agent, Management, Second degree burn, Treatment

**Citation of article:** Saadoon AM. Comparative study for the Result of Using Different Topical Agents in Management of Second Degree Burn. Med Forum 2025;36(6):54-57. doi:10.60110/medforum.360611.

## INTRODUCTION

Heat has a significant morbidity and mortality rate when it comes to tissue damage or loss. Burns can result in complex issues that need for specialized care and severe forms of trauma with several variations. Burn injuries are one of the major global health issues. At the United States, there are about 1.2 million burn cases annually, the most of which are mild and handled at an outpatient clinic.<sup>1</sup>

Numerous factors influence how burns are evaluated and treated. The burn type - such as thermal, chemical, electrical, or radiation - comes first.

The second factor is the burn's extent, which is typically represented as a percentage of the total body

surface area (%TBSA) affected. Next, the burn's depth is classified as full thickness (third degree), partial thickness (second degree), or superficial (first degree). Lastly, additional factors include the patient's age (less than 10 years old or more than 50 years old), any other medical conditions, whether the burn is in a specific location (the face, eyes, ears, nose, hands, feet, or perineum), and whether there are any other injuries, especially traumatic ones or those related to smoke inhalation.<sup>2-5</sup>

The goals of local burn wound care are to minimize the patient's discomfort while preserving the burn site's surface protection, fostering healing, and limiting the wound's progression.<sup>6</sup>

The common dressings used to cover burn wounds are non-adherent films or fine mesh gauze (in conjunction with topical antimicrobials). However, films, foams, alginates, hydrocolloids, and hydrogels can also be used, depending on the unique requirements of the burn wound and the specific qualities of the dressing (e.g., silver containing). These can be administered directly to the site or over a burn that has been treated with a topical medication.<sup>7</sup> Various wound management have been developed for the treatment of superficial burn.<sup>8</sup>

In addition to having strong biocompatibility and maintaining a moist wound environment, proper wound management also speeds up the healing process.<sup>9</sup>

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Received: April, 2025

Reviewed: April, 2025

Accepted: May, 2025

Additionally, minimizing pain throughout the healing process and reducing the creation of scars are crucial factors to consider when choosing the best wound dressing.<sup>10</sup> The selection of an appropriate wound treatment product is heavily influenced by cost effectiveness as well.<sup>11</sup>

Most burn injuries can be treated as outpatient cases; topical applications of lotions, honey, aloe vera, or antibiotic ointment can be used to heal superficial burns. Topical antibiotics or occlusive dressings can help reduce pain, enhance healing, and minimize wound desiccation when treating partial thickness burns.<sup>12</sup> However, there is no consensus on which local agents is optimal for burn wound management to prevent or control infection or enhance wound healing.<sup>13</sup> These modalities of treatment have different effectiveness in treatment of partial thickness burn injuries, healing time, pain during dressing, patient comfort, post burn scar and also have different price.

## METHODS

This comparative study was done in outpatient private clinic from 20<sup>th</sup> January 2025 to 31<sup>st</sup> March 2025 for patients were complaining from burn. Despite the fact that burns are the source of many mishaps at home and at work, there are still no widely accepted guidelines for how to treat them. New goods hit the market every day, all vying to be the most successful. All the patients signed an informed consent form and the patients were studied clinically and evaluated before treatment according to age, cause of burn, site of burn and total body surface area of burn (TBSA). Facial burn, 3<sup>rd</sup> degree burn wounds and extensive burn patients with more than 20 percent body surface burn area were excluded from this study.

Sixty patients were meeting the eligibility criteria were enrolled. These patients were randomly divided into three groups, each group consist of 20 patients. 1<sup>st</sup> group was managed by topical antibiotic (silver sulfadiazine), 2<sup>nd</sup> group by oil based herbal paste (MEBO) and 3<sup>rd</sup> group by hydrocolloid dressing.

Dressing was done daily in case of silver sulfadiazine and MEBO while every five days in case of hydrocolloid. The change dressing was performed until the wound be healed. The wounds were deemed cured when they became a vibrant pink color, ceased exuding, and showed no signs of healing. The outcome measures we investigated in early follow up for number of dressing changes, conformability and time from treatment until wound healing. In late follow-up we assessed, scar quality after 4 to 6 months from time of burn and cost of treatment.

## RESULTS

There were 24 (40%) females and 36 (60%) males (Fig. 1). The age range of those presenting was 1 year to 60 years, with a mean age of  $30.3 \pm 10.2$  years. The cause of burn was scalds (70%) and flame was (30%). The most common site affected by burn was upper limb (50%) followed by lower limb (33%). The average total body surface area was 8%. The main of time healing regarding patients treated with silver sulfadiazine and MEBO was 8 days, while it was 5 days for patients treated with hydrocolloid. Treatment with hydrocolloid was comfortable in 15 patients (75%), 5 patients (25%) for patients treated with silver sulfadiazine and in 4 patients (20%) treated with MEBO. All burn area treated with the three types of treatment return to same normal skin features (color, firmness, hair distribution, except few patients developed hyperpigmentation (Tables 1-3, Figs.1-2.).

**Table No.1: Comparison of burn areas among three groups**

Burn area	Silver sulfadiazine		MEBO		Hydrocolloid dressing		P value
	No.	%	No.	%	No.	%	
Upper limbs	12	43	10	59	8	53	0.8
Lower limbs	10	36	5	29	5	33	
Trunk	6	21	2	12	2	14	
Total	28	100	17	100	15	100	

**Table No.2: Comparison of genders between the three groups**

Gender	Silver sulfadiazine		MEBO		Hydrocolloid dressing		P value
	No.	%	No.	%	No.	%	
Male	18	64	12	71	5	40	0.1
Female	10	36	5	29	9	60	
Total	28	100	17	100	15	100	

**Table No.3: Frequency distribution of comfortability and its comparison between the three groups**

Variable	Silver sulfadiazine	MEBO	Hydrocolloid dressing	P value
Time of healing	9.1±1.3	8.01±1.4	5.1±2.1	0.001
<b>Comfortability</b>				
Yes	7	4	11	0.003
No	21	13	4	
Total	28	17	15	



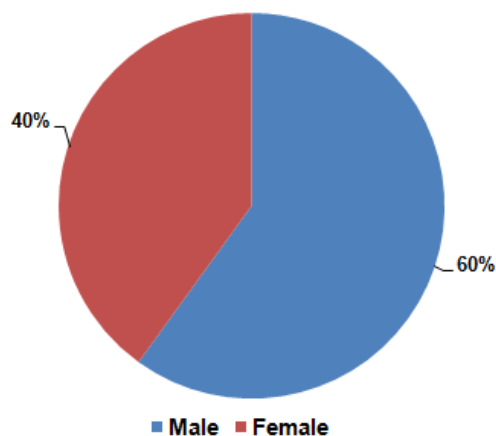


Figure No. 1: Distribution of genders

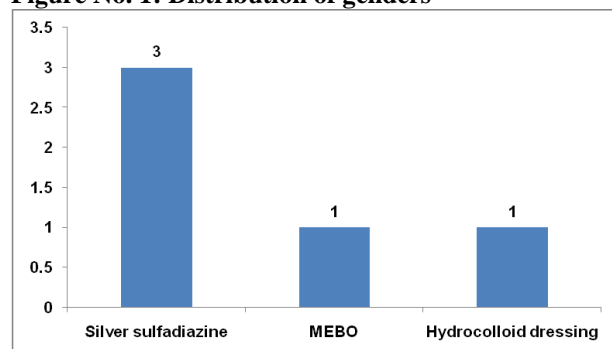


Figure No. 2: Frequency of hyperpigmentation in the three groups

## DISCUSSION

According to our study, burn was more common in female (60%) this due to most women spend many hours a day preparing food so there is more chance to get burn and upper limb is the most common site affected by burn although our results regarding gender and site of burn are statically not significant. A study was done by Daryabeigi<sup>14</sup> show that burn was more prevalent in men due to their work and contact with burning substances.

To determine the best method for burn treatment, we must consider the goals of burn treatment, like rapid healing, prevent infection, comfortability, cost and returning the patient to full productivity during treatment period.<sup>15</sup>

Hydrocolloid are wildly used because of it is like in structure to extracellular matrix, it contains many pore so can retain a moist healing environment for angiogenesis that help in healing.<sup>15-16</sup>

Researcher found hydrocolloid had statically significant better wound healing, pigmentation fewer dressing changes and less cost and this go with our study. Researcher found that MEBO is a great burn wound dressing alternative because it reduces bacterial colonization, shortens the wound healing duration, reduces the need for analgesics and antibiotics, and produces better-looking wound healing.<sup>17</sup> While in our

study there is no difference in time period of healing between MEBO and silver sulfadiazine.

In the present study, we found that hydrocolloid is more comfortable for patients as other many studies found the same results due to using hydrocolloid improve quality of life by decreasing the pain because of infrequent change dressing.

We found few patients 3 developed hyper pigmentation of skin when using silver sulfadiazine cream and this is due to a side effect of drug or delay in wound healing and secondary skin reaction with hyperpigmentation when using this cream.

## CONCLUSION

Hydrocolloid has superior early outcomes as compared with other agent there is no difference in time period no difference in healing period between MEBO and silver sulfadiazine.

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

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

**Source of Funding:** None

**Ethical Approval:** No.35401 Dated 16.01.2025

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# Exposing Subclinical Cardiac Dysfunction in Shift Workers Using Speckle Tracking Echocardiography

Subclinical  
Cardiac  
Dysfunction in  
Shift Workers

Asaad Hasan Noaman<sup>1</sup>, Ali Ismail Qasim<sup>1</sup> and Shaymaa AH Jasim<sup>2</sup>

## ABSTRACT

**Objective:** To assess subclinical myocardial disorders in shift workers using Speckle tracking echocardiography, compare shift workers and day employees' left ventricular global longitudinal strain and right ventricular free wall longitudinal strain and investigate the relationship between myocardial stress and sleep quality.

**Study Design:** Cross-sectional study

**Place and Duration of Study:** This study was conducted at the Department of Physiology, Faculty of Medicine, University of Kufa from 1<sup>st</sup> October 2024 to 28<sup>th</sup> February 2025.

**Methods:** A total of 120 healthy adults were recruited for this cross-sectional study, 60 of whom were shift workers (including those who work nights) and 60 of whom were day workers, matched for age and sex. Every subject received a thorough echocardiographic evaluation, which included Speckle tracking echocardiography to assess the right ventricular free wall longitudinal strain and left ventricular global longitudinal strain. Standard echocardiographic measurements and surveys on work schedules and sleep quality were safeguarded by further tests.

**Results:** The left ventricular global longitudinal strain was significantly lower for shift workers ( $-18.4 \pm 2.3\%$ ) than for day workers ( $-20.3 \pm 1.5\%$ ,  $p < 0.001$ ). Likewise, shift workers had a decline in right ventricular free wall longitudinal strain ( $-22.1 \pm 2.7\%$ ) compared to day workers ( $-24.5 \pm 2.4\%$ ,  $p < 0.001$ ). The ejection fraction and chamber diameters, two common echocardiographic metrics, did not differ significantly between study groups. In shift workers, poor sleep was most closely associated with lower strain levels.

**Conclusion:** Even in the absence of overt cardiac illness, shift workers are linked to subclinical myocardial impairment that can be identified by Speckle Tracking Echocardiography. These results highlight the importance of early cardiac monitoring for shift workers in order to impose preventive measures.

**Key Words:** Shift work, Speckle tracking echocardiography, Subclinical cardiac dysfunction, Circadian rhythm, Myocardial strain

**Citation of article:** Noaman AH, Qasim AI, Jasim SAH. Exposing Subclinical Cardiac Dysfunction in Shift Workers Using Speckle Tracking Echocardiography. Med Forum 2025;36(6):58-61. doi:10.60110/medforum.360612.

## INTRODUCTION

A growing portion of today's workforce relies on shift labor to maintain continuous operations across a wide range of industries. Shift occupations, especially those involving night shifts, provide significant health risks even yet they are essential for economic productivity. Irregular working hours have been linked to a number of harmful health effects, most notably cardiovascular

diseases (CVD), by upsetting the body's natural circadian rhythm.<sup>1</sup> Circadian rhythms alter cardiovascular characteristics as well as a number of physiological processes. As shift workers demonstrate, a misalignment between endogenous circadian cycles and external environmental cues can lead to autonomic imbalance, metabolic disruptions, and inflammatory reactions, all of which increase the risk of cardiovascular disease.<sup>2</sup> Shift workers have been associated in epidemiological research with increased rates of stroke, coronary artery disease, and hypertension.<sup>3</sup> Conventional cardiovascular imaging diagnostics are unable to detect myocardial alterations before symptoms appear. A sensitive imaging technique that can identify distributed myocardial deformation and provide information on subclinical cardiac dysfunction is Speckle tracking echocardiography (STE).<sup>4</sup>

Speckle tracking echocardiography derived metrics, such as global longitudinal strain, can serve as early indicators of myocardial damage in asymptomatic individuals and have prognostic value in a variety of

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Received: March, 2025

Reviewed: April, 2025

Accepted: May, 2025

cardiac scenarios.<sup>5</sup>Few studies have examined the effectiveness of Speckle tracking echocardiography in identifying early cardiac alterations in shift workers. Early measures to reduce long-term cardiovascular outcomes could be made easier with an understanding of subclinical myocardial changes in those individuals. This study examines efforts to evaluate myocardial characteristics in shift workers using Speckle Tracking Echocardiography, comparing results with those of day workers in order to identify potential subclinical heart disorders.

## METHODS

This cross-sectional study was conducted on 120 healthy adults. Participants were split into two groups: 60 shift workers (who had worked night shifts and other rotating shifts for at least a year) and 60 day workers (who worked regular daylight hours). Excessive blood pressure, diabetes mellitus, established cardiovascular disease, and several chronic conditions were excluded. In order to use the Pittsburgh Sleep Quality Index (PSQI), participants filled out questionnaires on their demographics, work schedules routines, lifestyle choices, and sleep quality.

Transthoracic echocardiography was performed on each person using a standard protocol. Ejection fraction (EF), wall thickness, and chamber dimensions were all covered by standard measurements. Using specialized software, Speckle tracking echocardiography is performed to evaluate left ventricular global longitudinal strain (LVGLS) and right ventricular free wall longitudinal strain (RVFWLS) using strain measurements averaged over three cardiac cycles.

Statistical Package for Social Sciences version 25 has been used to analyze the data. Unbiased t-tests were used to compare continuous variables, which were

represented as indicate  $\pm$  fashionable deviation. Chi-square assessments have been used to compare categorical variables. Relationships between strain levels and assessments of sleep quality were evaluated using Pearson correlation analysis. A p-value below zero was considered  $P < 0.05$  statistically significant.

## RESULTS

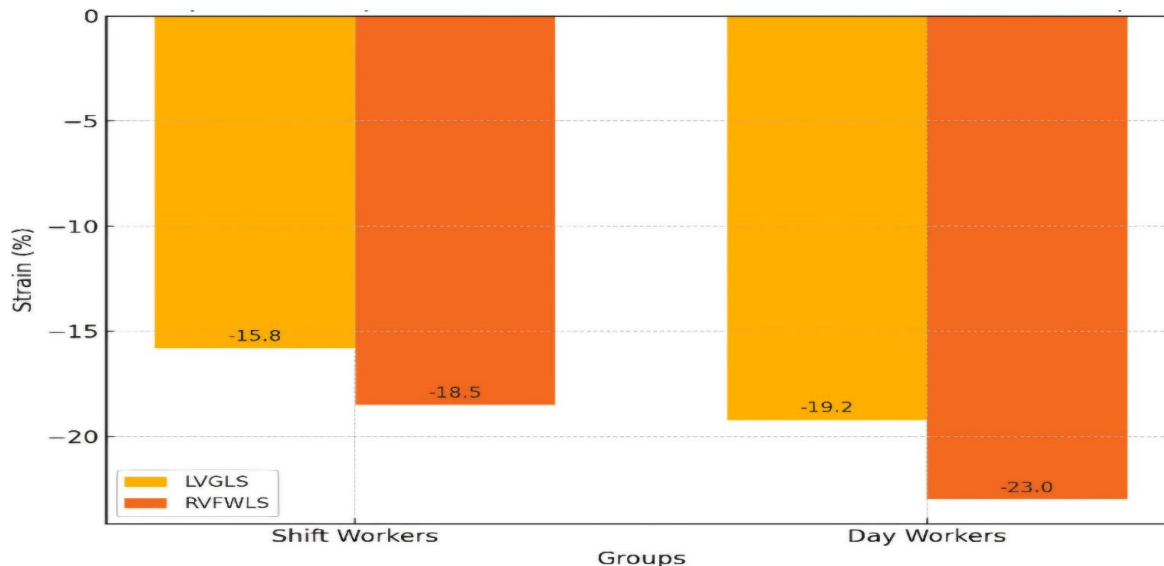
**Participant Characteristics:** Age and sex were matched among the groups. Compared to day workers, shift workers reported significantly lower levels of sleep satisfaction with  $8 \pm 2.2$  with high Pittsburgh Sleep Quality Index  $5.3 \pm 1.9$  ( $p < 0.001$ ) [Table 1].

**Table No. 1: Demographic and clinical characteristics**

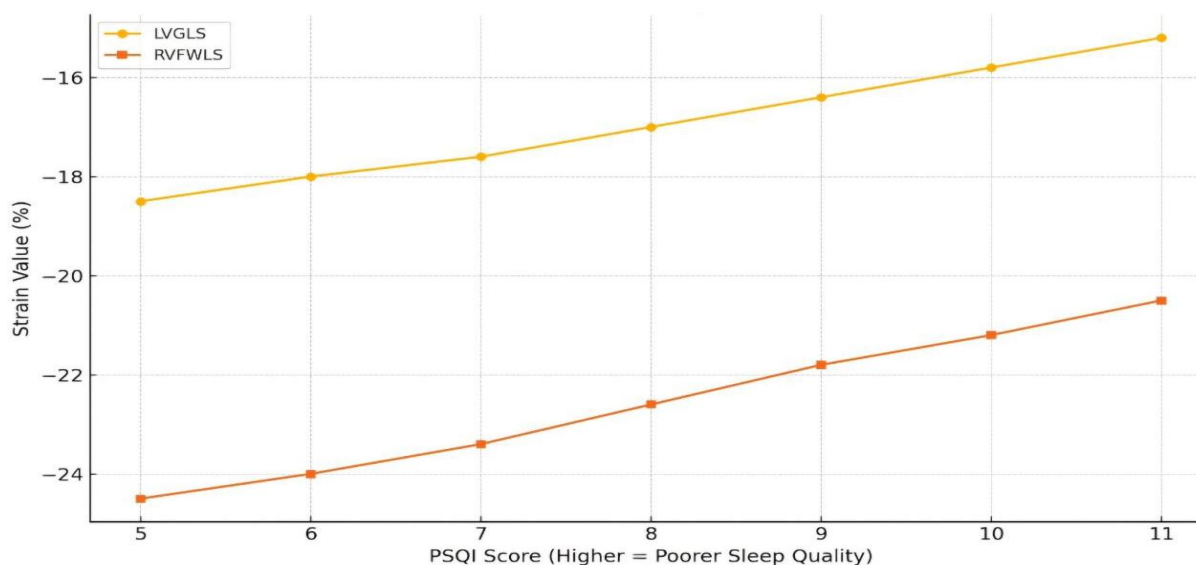
Variable	Shift worker (n=60)	Day worker (n=60)	p-value
Age (years)	$38.8 \pm 5.5$	$39 \pm 5.9$	0.6
Male	59%	59%	0.8
BMI (kg/m <sup>2</sup> )	$26 \pm 2.6$	$25.7 \pm 3$	0.5
PSQI score	$8 \pm 2.2$	$5.3 \pm 1.9$	$< 0.001$
Smoking	28.2%	24.9%	0.7

**Table No.2: Echocardiographic and Speckle tracking echocardiography (STE) parameters**

Parameter	Shift worker (n=60)	Day worker (n=60)	p-value
LVEF (%)	$61 \pm 3.7$	$62 \pm 3$	0.3
LVGLS (%)	$-18.4 \pm 2.3$	$-20.3 \pm 1.5$	$< 0.001$
RVFWLS (%)	$-22.1 \pm 2.7$	$-24.5 \pm 2.4$	$< 0.001$



**Figure No. 1: Comparison of left ventricular global longitudinal strain (LVGLS) and right ventricular free wall longitudinal strain (RVFWLS) between groups**



**Figure No. 2: Correlation between Pittsburgh Sleep Quality Index(PSQI) and myocardial strain in shift workers**

**Echocardiographic findings:** Standard echocardiogram parameters showed no significant change in chamber size and ejection fraction values but Speckle tracking echocardiography discovered significant differences (Table 2). Figure 1 Clearly indicating lower strain values in shift workers.

**Correlation with Sleep Quality:** Higher Pittsburgh Sleep Quality Index scores, which indicate poorer sleep quality, have been significantly linked to lower left ventricular global longitudinal strain ( $r = 0.40$ ,  $p = 0.002$ ) and right ventricular free wall longitudinal strain ( $r = 0.4$ ,  $p = 0.004$ ) in shift workers, indicating that sleep disturbances may also worsen myocardial strain abnormalities even when there is no overt scientific illness (Fig. 2)

## DISCUSSION

By showing that shift workers exhibit lower global longitudinal strain values detectable by Speckle tracking echocardiography (STE), even in the absence of overt cardiovascular disease, this observation offers new insight into the subclinical effects of shift work on myocardial function. These results are consistent with growing evidence that cardiovascular risk is influenced by disrupted circadian rhythms.<sup>6</sup> Despite the conserved ejection fraction, the observed decreases in left ventricular global longitudinal strain and right ventricular free wall longitudinal strain among shift workers support early myocardial deformation and contractile dysfunction. This highlights how Speckle tracking echocardiography is more sensitive than traditional echocardiographic measures at identifying myocardial disorders early on.<sup>7</sup>

This phenomena may also be caused by a number of processes, such as endothelial disorders linked to circadian disturbance, systemic inflammation, and chronic autonomic imbalance.<sup>8,9</sup> An indication of shift

employment, circadian misalignment, can cause prolonged cardiac stress by impairing sympathetic-parasympathetic stability, increasing nocturnal blood pressure, and reducing night-time dipping.<sup>10</sup> The biological plausibility of our findings is enhanced by the evidence from animal studies that circadian gene disruption causes cardiac remodeling, fibrosis, and decreased contractility.<sup>11</sup>

Additionally, poor sleep is strongly associated with strain impairment and is much worse in the shift workgroup. Lack of sleep is linked to oxidative stress and prolonged inflammatory indicators (such as IL-6 and C-reactive protein), all of which have a detrimental influence on cardiac mechanics.<sup>12,13</sup> The complex character of cardiovascular stress in shift workers is affected by these facts. Our analysis emphasizes the subclinical spectrum of heart disorders, supporting early detection methods, whereas previous research has mostly focused on medical endpoints like hypertension or coronary events. Additionally, the application of Speckle tracking echocardiography (STE) in occupational health examinations may provide valuable predictive data and direct prompt actions.<sup>14,15</sup> To the best of our knowledge, this is among the first studies to confirm right ventricular (RV) and left ventricular (LV) strain in healthy shift workers, adding original data to the field. Even in the absence of structural abnormalities, the significant variation in strain readings highlights the hidden cardiovascular load on this population.

## CONCLUSION

Early indicators of subclinical cardiac impairment as identified by Speckle tracking echocardiography (STE) are linked to shift workers, which mostly involve circadian disturbance and poor sleep quality. These findings undoubtedly enable preventative

cardiovascular methods by assisting with the integration of myocardial strain analysis into routine health opinions for shift workers.

**Limitations:** This examination has a number of challenges. First, causal inference is not possible because to its cross-sectional design. Second, the sample size restricts generalizability even though it is sufficient for first comparisons. Lastly, using single imaging modality (speckle Tracking Echocardiography) can miss useful information that could be gleaned via biomarkers or cardiac magnetic resonance imaging.

#### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Asaad Hasan Noaman, Ali Ismail Qasim
Drafting or Revising Critically:	Asaad Hasan Noaman, Shaymaa AH Jasim
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No.MEC-143 Dated 20.09.2024

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# The Relationship between Asthma Severity and Blood Biomarkers: Serum Periostin and IgE Levels in Iraqi Population

Relationship  
between Asthma  
Severity and  
Blood  
Biomarkers

Aula Hamod and Zahraa Abdulaali Al-Mudhafar

## ABSTRACT

**Objective:** To investigate the relationship between asthma severity and two blood biomarkers, serum periostin and IgE levels in Iraqi patients with asthma.

**Study Design:** Cross-sectional study

**Place and Duration of Study:** This study was conducted at the Department of Physiology, College of Medicine, University of Kufa from 1st January 2024 to 31st December 2024.

**Methods:** One hundred and fifty three asthmatic patients were enrolled. Individuals diagnosed with asthma, according to GINA criteria patients should meet the criteria; history of respiratory symptoms, such as wheeze, persistent dry cough or dyspnea at rest or on exertion that fluctuate in terms of duration and severity and low respiratory indices. Asthma severity was classified based on predicted FEV1 values: mild (>80%), moderate (60-80%), and severe (<60%). Serum periostin and IgE levels were measured. Statistical analysis included ANOVA and Chi-square tests.

**Results:** A significant association was found between asthma severity and IgE levels ( $p = 0.046$ ), with higher IgE levels in severe cases. Although serum periostin levels increased with asthma severity, the difference was not statistically significant ( $p = 0.051$ ). Mild cases had the lowest mean periostin levels, while severe cases had the highest.

**Conclusion:** Serum IgE levels showed a significant correlation with asthma severity, supporting its role in identifying allergic phenotypes. Serum periostin levels increased with severity, suggesting a potential role in airway remodeling, although statistical significance was not achieved. The combined use of these biomarkers may enhance asthma characterization and support personalized management strategies.

**Key Words:** Asthma, Serum periostin, IgE, Biomarkers, Airway remodeling, Asthma severity

**Citation of article:** Hamod A, Al-Mudhafar ZA. The Relationship between Asthma Severity and Blood Biomarkers: Serum Periostin and IgE Levels in Iraqi Population. Med Forum 2025;36(6):62-66. doi:10.60110/medforum.360613.

## INTRODUCTION

Asthma affects millions worldwide and poses significant health, social and economic burdens. Its heterogenous nature means that clinical presentations and responses to standard treatments vary considerably among patients. A better understanding of the underlying immunological and inflammatory processes has led to the identification of specific biomarkers, such as serum IgE and Periostin, that are associated with allergic inflammation and airway remodeling.<sup>1,2</sup>

Periostin, an extracellular matrix protein its production enhanced by interleukin-13 (IL-13), has emerged as an

indicator for type 2 (Th2-high) hypersensitivity reaction in asthma.<sup>3</sup> The higher levels of serum periostin are produced in patients with severe asthma, particularly in eosinophilic asthma. Matsusaka and colleagues<sup>4</sup> discovered that patients with severe asthma had considerably elevated serum periostin levels, which were also found to be connected with specific phenotypic characteristics though they were not consistently linked to total IgE concentrations.

Immunoglobulin E plays the main antibody that is involved allergic sensitization and pathogenesis of allergic asthma of atopic asthma. It is synthesized by B lymphocytes in response to allergens and is pivotal in stimulation of mast cells and basophils to release pro-inflammatory mediators. However, the association between total serum IgE and asthma severity is less robust than for periostin. Some studies indicate a weak or inconsistent relationship. For instance, in the study by Scichilone et al<sup>5</sup>, higher IgE levels were observed in severe cases, but periostin had a stronger correlation with eosinophilic inflammation and disease control.

Interestingly, Tajiri et al<sup>6</sup> demonstrated that both serum periostin and immunoglobulin E could be a useful

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Received: January, 2025

Reviewed: February, 2025

Accepted: March, 2025

biomarkers to monitor treatment response to anti-IgE monoclonal antibody; omalizumab, particularly in cases of severe asthma, suggesting that combined biomarker strategies may offer more nuanced insights into disease monitoring.

Periostin is extensively researched as a biomarker for eosinophilic asthma. It is secreted by airway epithelial cells following Interleukin-4 and Interleukin-13 stimulation. Elevated periostin levels in asthmatic patients are indicative of chronic subepithelial fibrosis, a process that contributes to airway remodeling and fixed airflow limitation. Clinical studies have further linked high periostin levels to asthma exacerbations and a decline in lung function over time.<sup>7,8</sup>

Reviewed literature indicates that periostin serves as both a predictive and prognostic biomarker. In asthma, patients with high baseline periostin levels show a better response to anti-IL-13 therapies, suggesting that periostin could guide personalized treatment strategies.<sup>2</sup> Moreover, studies have demonstrated that periostin levels correlate with lung function decline in both asthma and IPF, reinforcing its value as a marker of disease progression.<sup>9</sup>

The elevated synthesis of IgE in response to allergen exposure is mediated by the activation of type 2 T-helper cells and the release of IL-4 and IL-13. The binding of IgE to high-affinity receptors on effect or cells stimulate the secretion of inflammatory mediators such as histamine, leukotrienes, and prostaglandins. These mediators induce bronchoconstriction, mucus production, and airway edema - all hallmarks of an asthma attack. Several studies have referred to the relations between asthma severity and blood IgE level where increasing IgE levels suggest a robust allergic inflammatory response that parallels clinical worsening.<sup>10,11</sup>

In parallel, periostin contributes to the structural changes observed in chronic asthma. Under the influence of IL-13 and IL-4, airway epithelial cells up-regulate periostin production. This protein then facilitates subepithelial fibrosis by interacting with extracellular matrix (ECM) components and promoting collagen cross-linking<sup>2</sup>. Through its effects on fibroblast differentiation into myofibroblasts and modulation of collagen deposition, periostin fundamentally drives the remodeling process that leads to persistent airway narrowing.<sup>12,13</sup>

IgE is predominantly responsible for the initiation and enhancement of allergic reaction, periostin predominantly reflects the downstream consequences of chronic inflammation - namely, tissue remodeling and fibrosis. Both biomarkers, however, are up-regulated in response to a type 2 inflammatory environment. This shared immunological pathway suggests that an integrative assessment of serum IgE and periostin levels may provide complementary information. Whereas IgE levels indicate the extent of active allergic

inflammation, periostin levels provide insights into long-term structural changes in the airways. Such a dual biomarker approach could potentially enhance the clinician's ability to both tailor treatment strategies and predict disease progression.<sup>14</sup>

While periostin and IgE may not correlate directly with each other, both serve important but distinct roles in asthma characterization. Periostin is more directly associated with airway remodeling and Th2-driven eosinophilic inflammation, while IgE reflects systemic atopic status. In the Swedish GA<sup>2</sup>LEN cohort, James et al<sup>15</sup> found that periostin related more closely to type 2 inflammation and lung function than total IgE, reinforcing the differential diagnostic utility of these markers.

## METHODS

This cross-sectional study includes 153 patients from Alhilla Pulmonology outpatient clinic recruited from 1st January 2024 to 31st December 2024. This research is authorized by Ethical Approval Committee at Kufa College of Medicine. Individuals diagnosed with asthma, according to GINA criteria patients should meet the following criteria: i) a history of respiratory symptoms, such as wheeze, persistent dry cough or dyspnea at rest or on exertion that fluctuate in terms of duration and severity, and ii) low respiratory indices were included. Respiratory diseases other than asthma, malignancy, and heavy smokers were excluded. Statistical analysis has been performed utilizing SPSS-27. Independent test was used to compare means between two groups we used t-test. ANOVA test was used to compare means among three groups. Pearson Chi-Square test has been used to find the relationship between categorical variables. P value  $\leq 0.05$  was considered as significant.

## RESULTS

**Table No.1: Distribution of Asthmatic patients according to socio-demographic characteristics (N=153)**

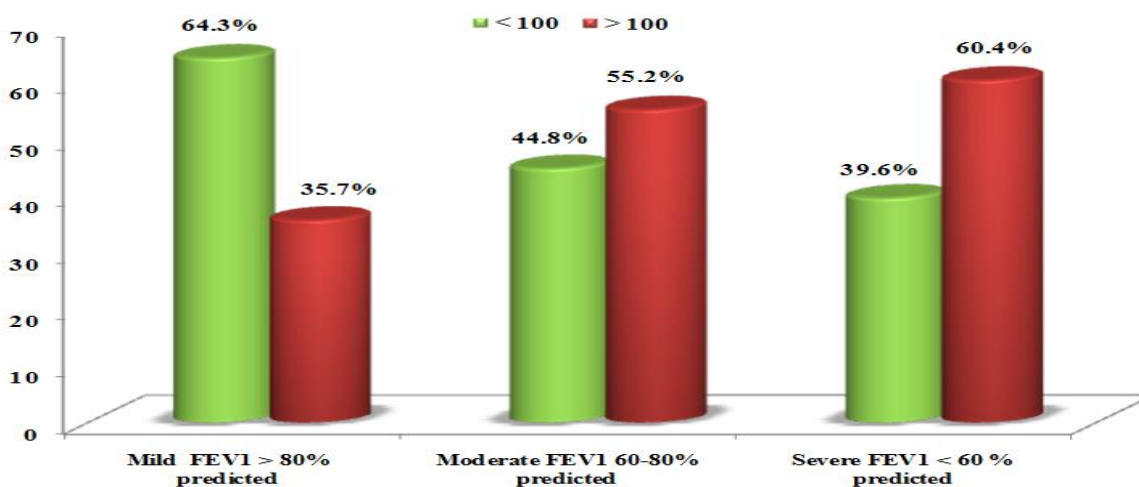
Variable	No.	%
<b>Age (years)</b>		
15-25	34	22.2
26-45	52	34.0
46-65	49	32.0
$\geq 65$	18	11.8
<b>Gender</b>		
Male	59	38.6
Female	94	61.4
<b>Body mass index (Kg/m<sup>2</sup>)</b>		
Underweight (18.5)	1	0.7
Normal (18.5-24.9)	36	23.5
Overweight (25-29.9)	59	38.6
Obese ( $\geq 30$ )	57	37.3

**Table No.2: The association between GINA severity grades and IgE (kU/l) level (N=153)**

IgE (kU/l)	GINA severity grades			Total	P value
	Mild (>80%) (N=42)	Moderate (60-80%) (N=58)	Severe (< 60 %) (N=53)		
< 100	27 (64.3%)	26 (44.8%)	21 (39.6%)	74 (48.4%)	0.046
> 100	15 (35.7%)	32 (55.2%)	32 (60.4%)	79 (51.6%)	
Total	42 (100%)	58 (100%)	53 (100%)	153 (100%)	

**Table No.3: The comparison among Asthma severity according to serum periostin (ng/ml) (N=153)**

Asthma Severity	S. Periostin ng/ml	P value
Mild (PRED.FEV1 > 80) [N=42]	58.81±7.61	0.051
Moderate (PRED.FEV1 60 ≤ FEV1 ≤ 80) [N=58]	62.50±6.31	
Severe (PRED FEV1 < 60) [N=53]	67.99±10.05	

**Figure No. 1: The association between asthma severity and IgE (kU/l) level****Figure No. 2: The comparison among GINA severity grades according to serum periostin (ng/ml)**

Mean age of patients was 40.99±17.51 years, older patient was 83.0 years and younger patient was 15.0 years. More than one third of patients (N=52, 34.0%) presented with age group (25-45 years). Less than two third of patients were females (N=94, 61.4%). Mean

body mass index was 28.61±5.38 Kg/m<sup>2</sup>, with maximum value was 46.87 Kg/m<sup>2</sup> and minimum value was 15.21 Kg/m<sup>2</sup>. Obese patients represent 57 patients (37.3%) [Table 1].



The association between Asthma severity including (Mild FEV1 predicted > 80%, Moderate FEV1 predicted (60-80%) and Severe FEV1 < 60 % predicted) and IgE (kU/l) level including (< 100 and > 100). There is significant relation between Asthma severity and IgE (kU/l) level. Majority of patients with Mild grade (N=27, 64.3%) presented with IgE (< 100 kU/l), while majority of patients with severe grade (N=32, 60.4%) presented with IgE (> 100 kU/l) [Table 2].

The comparison among Asthma severity including (Mild FEV1 predicted > 80%, Moderate FEV1 predicted (60-80%) and Severe FEV1 predicted (< 60 %) according to serum periostin (ng/ml). There was no significant mean difference of serum periostin (ng/ml) according to Asthma severity (Table 3). These values emphasize that serum IgE serves as a reliable laboratory parameter to distinguish between varying degrees of asthma severity. The increasing mean serum IgE levels support the notion that as the degree of chronic inflammation and allergic sensitization intensifies, so does the production of IgE (Fig. 2).

## DISCUSSION

Clinically, serum IgE levels have been utilized to confirm an allergic phenotype in asthmatic patients. Elevated levels indicate that allergic mechanisms are contributing to the disease process, thereby guiding the clinician's choice of therapy, including the use of biologic therapies targeting IgE. Such targeted therapies, like omalizumab, act by neutralizing circulating IgE, thereby reducing airway inflammation.<sup>16,17</sup>

Although most studies on serum IgE and asthma severity have been conducted in populations outside Iraq, these findings offer a significant foundation for hypothesis development. In Iraq, environmental allergens such as dust and other pollutants may modulate IgE responses differently due to regional differences in exposure. Therefore, a similar study conducted in the Iraqi population could verify whether the same correlations hold true and might reveal unique patterns pertinent to this specific group.<sup>18-20</sup>

The Iraqi population presents unique challenges such as: Environmental Factors: High levels of dust and industrial pollutants may influence baseline levels of inflammatory biomarkers. Genetic Variability: Ethnic and genetic factors might affect IgE and periostin expression and should be accounted for by including a diverse sample representative of different Iraqi regions. Resource Limitations: Assay costs and laboratory infrastructure may vary; therefore, it is essential to collaborate with regional medical centers and, if possible, integrate cost-effective yet reliable biomarker assessment techniques.

## CONCLUSION

Serum periostin has proven to be a more specific and dynamic biomarker for assessing asthma severity, particularly in Th2-high and eosinophilic subtypes. In contrast, IgE remains valuable in identifying atopy but lacks consistent correlation with severity metrics. Integrating both biomarkers, possibly alongside others such as FeNO and eosinophil counts, could enhance asthma phenotyping and guide biologic therapy selection in clinical practice.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Aula Hamod, Zahraa Abdulaali Al-Mudhafar
Drafting or Revising Critically:	Aula Hamod, Zahraa Abdulaali Al-Mudhafar
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No.MEC-15 Dated 14.01.2024

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# Job Stress among Night-Shift Nurses in Critical Care Units

Job Stress among  
Night-Shift  
Nurses in CCU

Yamen Chaban Ahmad and Shatha Saadi Mohammed

## ABSTRACT

**Objective:** To assess job stress among night-shift critical care nurses under the working hour's system in effect.

**Study Design:** Quantitative cross-sectional study

**Place and Duration of Study:** This study was conducted at the College of Nursing, Adult Nursing, University of Babylon from 12<sup>th</sup> September 2024 to 29<sup>th</sup> October 2024.

**Methods:** 178 night-shift critical care nurses working in three randomly selected governmental hospitals were enrolled. Nurses were selected by the availability sampling method. Data were collected by demographic characteristics and The Expanded Nurses Stress Scale (ENSS).

**Results:** Females those working overtime in the private sector were significantly more likely to experience high stress.

**Conclusion:** Most of the females have high level of job stress and there are significant relationships between job stress and gender, level of income, level of education, years of experience, and type of unit.

**Key Words:** Job stress, Night Shift, Critical Care Units

**Citation of article:** Ahmad YC, Mohammed SS. Job Stress among Night-Shift Nurses in Critical Care Units. Med Forum 2025;36(6):67-71. doi:10.60110/medforum.360614.

## INTRODUCTION

Stress is a well-known topic, and people's lives are filled with demands that cause it to rise steadily. It also is somewhat individualized, depending on character, social support, coping abilities, and other aspects. According to the Effort-Recovery theory, workplace effort expenditure is inevitable, and this results in load response, or physiological changes brought in by stress. Effort must be balanced by enough recovery. Nevertheless, in some situations, such as extended exposure to high workload without sufficient recovery, short-term load reactions can build up and eventually result in the emergence of health issues, such as fatigue, or manifest illness.<sup>1</sup> Based on data from the International Council of Nurses, it is estimated that job stress costs the US economy \$200-300 million a year, and over 90% of medical issues among employees are linked to job stress.<sup>2</sup> In the workplace, in addition to specific risks that cause occupational diseases, job-related stress could be one of the most common causes of occupational disorders, including cancer.<sup>3</sup> Because of their line of work, nurses are subjected to various stressors and obstacles that can lead to job stress and burnout.

These include long hours, conflict with medical teams, conflict among co-workers and issues with job shifts.<sup>4</sup>

Because nursing is such a dangerous job, nurses are more likely to suffer potentially fatal illnesses and injuries, particularly in critical care units. They provide intensive care, deal with emergencies, and see dying patients.<sup>5</sup> These causes nurses to experience high job stress, which has negative impacts like forgetfulness, and fatigue all of which result in low performance.<sup>6</sup> This study seeks to assess job stress among critical care nurses working night shifts which might contribute to illuminating an essential aspect of their well-being and professional performance.

## METHODS

This descriptive quantitative cross-sectional study was conducted to assess job stress among night-shift nurses in critical care units. The study was conducted in three governmental facilities located in the Holy City of Karbala vide letter No.35 dated 23-6-2024. First, there is AL-Imam Alhussain Medical City, second, Imam Al-Hassan Al-Mujtaba Teaching Hospitals, and the Karbala Center for Cardiac Disease and Surgery. To select the hospitals for the study, a simple random method was employed. The names of all six hospitals were written on separate pieces of paper, which were then placed in a small box and mixed thoroughly. Three random draws were conducted from this box. The hospitals chosen are some of the largest and busiest facilities serving a significant number of patients. The target population consisted of 277 night-shift critical care nurses. This number was determined during a pre-data collection visit, where the researcher interviewed nursing directors at the three selected

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Received: January, 2025  
Reviewed: February, 2025  
Accepted: March, 2025

hospitals to determine the number of night-shift critical care nurses. Using the Finite Population Collection formula and at a 95% confidence level and a margin of error of 0.05, the minimum sample size required was 161. The final sample size was estimated at 178, taking into account a 10% dropout rate. Nurses of both genders from the selected hospital, who expressed have willingness to participate and had at least one year of experience in critical care units, were included in this study. Nurses in administrative positions were excluded as they were not directly involved in patient care.

The demographics including age, gender, marital status, level of education, level of income, years of experience in critical care units, department, workplace, and working as a nurse in the private sector were noted. The specific questionnaire English version of the Expanded Nursing Stress Scale (ENSS) was used. It was developed by French<sup>7</sup> in 2000, to identify sources and frequency of stress experienced by nurses. Permission to use this scale was obtained from the original author by email. The ENSS was reliable and valid in the original study since the alpha coefficients of the subscales were 0.70 or higher and the ENSS, which initially comprised 57 items. The researcher adapted this scale by removing 6 items incompatible with the traditions of the local country. The Remaining 51 items contain eight sub-scales: death and dying stressors (7 items), conflict with physician (4 items), emotional preparation (3 items), problems with peers (6 items), supervision stressors (7 items), workload stressors (9 items), uncertainty concerning treatment stressors (9 items), and patient/ family stressors (6 items). The adapted ENSS scale is reliable ( $\alpha=0.983$ ) and a valid tool. A five-point semantic scale was used (never stressful, occasionally stressful, frequently stressful, extremely stressful, does not apply) to assess job stress. Items have been rated and scored as (1) never stressful, (2) occasionally stressful, (3) frequently stressful, (4) extremely stressful, and (0) does not apply. The mean of scale = 2,  $W=0.99$ , no job stress = 0-0.99, low job stress = 1-1.99, moderate job stress = 2-2.99, and high job stress = 3-4. The data was entered analyzed through SPSS-26.

## RESULTS

There were 52.2% females, most held diploma (41.0%), with insufficient income (45.5%), most of them had 1–5 years of experience (62.4%), were in the General ICU (38.8%). Additionally, (55.6%) of participants had a job in private sector (Table 1).

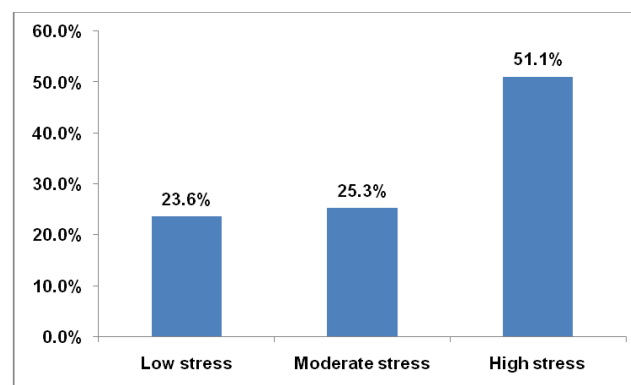
Figure 1 illustrates the distribution of job stress levels among the participants. A significant proportion of participants (51.1%) reported high stress levels, and no participants reported no stress.

Among the subscales, workload stressors had the highest mean ( $3.40\pm0.78$ ), followed by patients and family stressors ( $3.12\pm0.81$ ). In contrast, conflict with

physician stressors had the lowest mean score ( $1.87\pm0.75$ ). The overall job stress mean score was  $2.83\pm0.83$ , indicating variability in stress levels across the participants (Table 2).

**Table No.1: Participant demographics and characteristics (n=178)**

Variable	No.	%
<b>Gender</b>		
Male	85	47.80
Female	93	52.20
<b>Marital Status</b>		
Single	47	26.40
Married	126	70.80
Other	5	2.80
<b>Education</b>		
Nursing Secondary School	26	14.60
Diploma	73	41.00
Bachelor Degree	67	37.60
Higher Education	12	6.70
<b>Income</b>		
Sufficient	42	23.60
Somewhat Sufficient	55	30.90
Insufficient	81	45.50
<b>Experience</b>		
1–5 years	111	62.40
6–10 years	45	25.30
More than 10 years	22	12.40
<b>Unit</b>		
General ICU	69	38.80
CCU	51	28.70
Emergency Unit	40	22.50
Open Heart ICU	18	10.10
<b>Private Sector</b>		
Yes	99	55.60
No	79	44.40



**Figure No. 1: Stress level distribution among participants**

A significant association between job stress categories and various participant characteristics. Female nurses were significantly more likely to experience high job stress (73.1%). Similarly, nurses with insufficient income (77.8%), nurses with diplomas (60.3%), 1-5

years of experience (76.6%), emergency nurses (62.5%), and those work overtime in private sector (71.7%) all reported high levels of job stress. In

contrast, nurses working in the OH unit reported low stress (55.6%) [Table 3].

**Table No. 2: Descriptive statistics for job stress and subscales**

Variable	Minimum	Maximum	Mean	Standard Deviation
Death and Dying Stressors	1.29	4.00	2.86	.76
Conflict with Physician Stressors	.25	3.00	1.87	.75
Emotional Preparation Stressors	.67	4.00	2.79	1.11
Problems with Peer Stressors	.67	4.00	2.75	1.10
Supervision Stressors	.14	4.00	2.77	1.21
Workload Stressors	.89	4.00	3.40	.78
Uncertainty Concerning Treatment Stressors	.67	3.67	2.58	.89
Patient or Family Stressors	.83	4.00	3.12	.81
Overall Job Stress	1	3.86	2.83	.83

**Table No.3: Association between job stress and nurses' characteristics (n=178)**

Variable	Category	Low Stress	Moderate Stress	High Stress	p-value
Gender	Male	31 (36.5%)	31 (36.5%)	23 (27.1%)	< 0.001
	Female	11 (11.8%)	14 (15.1%)	68 (73.1%)	
Marital Status	Single	1 (2.1%)	19 (40.4%)	27 (57.4%)	< 0.001
	Married	41 (32.5%)	23 (18.3%)	62 (49.2%)	
	Other	-	3 (60.0%)	2 (40.0%)	
Education	Nursing Secondary School	5 (19.2%)	12 (46.2%)	9 (34.6%)	< 0.001
	Diploma	14 (19.2%)	15 (20.5%)	44 (60.3%)	
	Bachelor Degree	12 (17.9%)	17 (25.4%)	38 (56.7%)	
	Higher Education	11 (91.7%)	1 (8.3%)	-	
Income	Sufficient	31 (73.8%)	11 (26.2%)	-	< 0.001
	Somewhat Sufficient	11 (20.0%)	16 (29.1%)	28 (50.9%)	
	Insufficient	-	18 (22.2%)	63 (77.8%)	
ICU experience	1–5 years	-	26 (23.4%)	85 (76.6%)	< 0.001
	6–10 years	39 (86.7%)	2 (4.4%)	4 (8.9%)	
	More than 10 years	3 (13.6%)	17 (77.3%)	2 (9.1%)	
Unit	General ICU	17 (24.6%)	17 (24.6%)	35 (50.7%)	< 0.001
	CCU	9 (17.6%)	14 (27.5%)	28 (54.9%)	
	Emergency Unit	6 (15.0%)	9 (22.5%)	25 (62.5%)	
	Open Heart ICU	10 (55.6%)	5 (27.8%)	3 (16.7%)	
Private Sector	Yes	11 (11.1%)	17 (17.2%)	71 (71.7%)	< 0.001
	No	31 (39.2%)	28 (35.4%)	20 (25.3%)	

## DISCUSSION

A large percentage of nurses in our study experienced levels of job stress ranged from moderate to high, which is supported by several studies.<sup>8,9</sup> Critical care nurses frequently report high job stress levels, with studies indicating prevalence rates of 68.29% in India<sup>10</sup>, 82.8% in Iran.<sup>8</sup> A study conducted in Saudi noted that ICU nurses experienced moderate stress, with higher levels reported in cardiac care units compared to open-heart units.<sup>11</sup> Additionally, Kibria<sup>12</sup> reported that 90% of critical care nurses in a Bangladeshi hospital experienced such stress. Night shift work disrupts the body's natural circadian rhythms which lead to sleep disturbances, as shift workers are forced to sleep when

their body's internal clock signals wakefulness.<sup>13,14</sup> Such sleep disturbances are strongly linked to psychological issues, including stress.<sup>15,16</sup> Workload stressors, death and dying stressors were considered causes of stress among night shift nurses. This is supported by the findings of several studies, which showed that workload and long shifts are primary factors of stress among nurses.<sup>13,17</sup> Bolado et al<sup>13</sup> also found that nurses who witnessed death and dying at critical care units were 2.34 times more likely to report high stress compared to those who hadn't been exposed to such situations. On the other hand, conflict with physician stressors was found to be the least factor affecting stress in this study. This could be attributed to the strong inter-professional teamwork observed in

Iraq's healthcare settings.<sup>18</sup> This finding aligns with recent studies suggesting that while conflicts with physicians occur, they are often overshadowed by more pressing challenges, such as high patient acuity or emotional demands.<sup>17</sup>

The results of this study reveal significant associations between job stress and various demographics such as gender, income, education level, units, and private sector. Female nurses were significantly more likely to experience high stress. This aligns with several studies, which suggest that female often face additional stressors, such as balancing household responsibilities and work-family conflicts, which can amplify stress levels.<sup>19</sup> Income level significantly influenced stress. Nurses with insufficient income were more likely to report high job stress compared to those with sufficient income. Financial stress is a well-documented stressor, and its impact on mental health is particularly pronounced in high-pressure professions like nursing. This finding is consistent with previous research, which highlighted the role of financial instability in exacerbating stress levels among healthcare workers.<sup>20</sup> Education level also played a significant role, with nurses holding diplomas and bachelor's degrees reporting higher stress levels compared to those with higher education. The result aligns with Khodadadi et al<sup>21</sup> who reported that nurses with a higher educational level (Master of Science in Nursing) had a lower level of stress compared to those with a Bachelor of Science in Nursing (BScN). This could be attributed to high performance among nurses with high education degrees, as well as their enhanced problem-solving and coping skills that may help them manage stress more effectively.<sup>19</sup> The current study showed that nurses with less experience reported the highest levels stress compared to those with more experience. This finding aligns with previous researches.<sup>22,23</sup> Less experienced nurses often face higher stress due to high working hours, adaptation to the environment, meeting professional anticipations, and team cooperation.<sup>23</sup> The type of unit significantly influenced stress levels. Nurses in general ICUs and CCUs reported moderate to high stress, while those in emergency units experienced even higher stress levels. In contrast, nurses working in OH units predominantly reported low stress. This variation may reflect differences in patient acuity and the specific challenges associated with each unit type. Also, Nurses with additional job in the private sector reported higher stress than those without one. This could be due to factors such as longer working hours, higher workloads, and potentially less supportive work environments in private workplace.<sup>24</sup>

## CONCLUSION

Most of participants have high level of job stress. In addition, there are significant relationships between job stress and gender, level of income, level of education,

years of experience, and type of unit. Healthcare administrators should consider implementing comprehensive mental health programs that include stress management training, psychological support services, and strategies to reduce workplace stressors. Additionally, further research is needed to identify other factors that may better mitigate the effects of job stress.

### Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Yamen Chaban Ahmad, Shatha Saadi Mohammed
Drafting or Revising Critically:	Yamen Chaban Ahmad, Shatha Saadi Mohammed
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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

**Source of Funding:** None

**Ethical Approval:** No.35 Dated 23.06.2024

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# Investigated the Link between Some Cytokines and Gene Expression of Gastritis in Type 2 Diabetic Patients in Iraq

Some Cytokines  
and Gene  
Expression of  
Gastritis in  
Diabetic Iraq

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Issam Abdul-Karim Selman<sup>4</sup>

## ABSTRACT

**Objective:** To investigate immunological and molecular features of gastritis in individuals with diabetes mellitus.

**Study Design:** Comparative study

**Place and Duration of Study:** This study was conducted at the Gastroenterology & Hepatology Teaching Hospital, Medical City, Baqubah Teaching Hospital, and Al-Kazemi Teaching Hospital, Department of Gastroenterology, from 1<sup>st</sup> January 2024 to 30<sup>th</sup> April 2024.

**Methods:** A total of 138 participants including 67 H. pylori gastritis with type 2 diabetic (GHP+ve DM) group, 21 with gastritis without diabetes mellitus (G group), and 50 control group.

**Results:** The GHP+ve, diabetes mellitus had reduced levels. Regarding IL-10 in comparison to G and control, IL-18 levels increased in GHP+ve. In addition, discovered GHP+ve diabetes mellitus had lower levels of IL-10 than G ( $p<0.05$ ). Moreover, found IL-18 more highly expressed in GHP+ve DM than in gastritis ( $p<0.05$ ).

**Conclusion:** The gastritis by H. pylori infection to type 2 diabetes and shows IL-10 levels reduced in GHP +ve diabetes mellitus contrast with gastritis group and healthy controls and inversely correlated with high-sensitivity C-reactive protein, IL-18 levels raised in GHP +ve.

**Key Words:** Gastritis, Gene expression of IL-10 and IL-18, Helicobacter Pylori, RT-qPCR, Type 2 diabetic

**Citation of article:** Abdul-Sahib ZM, Mohammad NA, Nema AR, Selman IAK. Investigated the Link between Some Cytokines and Gene Expression of Gastritis in Type 2 Diabetic Patients in Iraq. Med Forum 2025;36(6):72-77. doi:10.60110/medforum.360615.

## INTRODUCTION

Gastritis mean inflammation mucosal lining of stomach. Major etiological agent's Helicobacter pylori infection and nonsteroidal anti-inflammatory medications.<sup>1</sup> Helical bacteria (Helicobacter pylori) common causes of gastritis has many feature which is gram-negative, microaerophilic and S-shaped bacteria.

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Received: January, 2025

Reviewed: February, 2025

Accepted: March, 2025

The organism's exceptional motility attributed to a solitary cluster of enclosed flagella located at one end.<sup>2</sup> Due to inhabit mucosal layer of stomach's surface epithelium, stimulating persistent gastritis that may progress to cancer of stomach.<sup>3,4</sup> The interaction between H. pylori and superficial mucosa releasing of pro- and anti-inflammatory cytokines. These cytokines subsequently recruit polymorph nuclear cells and initiate inflammatory response.<sup>5</sup>

Type 2 diabetic is chronic metabolic disorder characterized by persistently elevated blood glucose levels. T2DM caused by defect in insulin function, either due to insulin resistance, inadequate insulin secretion, or due to a combination of both factors.<sup>6,7</sup> Infection with H. pylori can cause inflammation and production of inflammatory cytokines, leading to onset of diabetes.<sup>8</sup> Because chronic inflammatory response of H. pylori infection the neutrophils, T-cell and B-lymphocytes, macrophages, and plasma cells recruitment to gastric mucosa which promote continuous and localized inflammation.<sup>9</sup>

Activation and migration these inflammatory cells to stomach mucosa linked to an increased release proinflammatory cytokines and a reduction in anti-inflammatory cytokines, such as IL-10 and IL-18, subsequent to H. pylori infection.<sup>10</sup> IL-10, an



inflammatory mediator, secreted and generated by stomach epithelial cells in response to infection caused by *H. pylori*.<sup>11</sup> It plays a crucial role as an immunosuppressive cytokine with immune regulatory and antigenic effects.<sup>12</sup> IL-10 synthesized by a range of cell types, including innate lymphocytes, T cells, dendritic cells (DC), macrophages, and B cells.<sup>13</sup> As IL-10 gene affects inflammation, any change in IL-10 gene leads to increased production proinflammatory cytokines, which affects insulin action and causes type 2 diabetes.<sup>14</sup> The IL-18, belonging to IL-1 superfamily of cytokines, has a function in controlling both adaptive and innate immune responses. More precisely, it plays a role in stimulating synthesis IFN- $\gamma$  in natural killer cells and CD4 T helper 1 lymphocytes.<sup>15</sup> Furthermore, IL-18 inhibits activity of Th2 and Th17 cells and regulates function of CD8 cytotoxic cells.<sup>16</sup> The evidence links genetic variations in IL-18 gene to increased susceptibility to *H. pylori* infection. This study examined serum concentration IL-18 and IL-10 in patients with type 2 diabetes and *H. pylori*-associated gastritis compared to those with gastritis and a healthy control. Blood glucose, HbA1c, BMI, *H. pylori* IgG, and hs-CRP that act as systemic inflammatory marker estimated in all three groups. Additionally, expression both IL-18 and IL-10 genes quantified using RT-qPCR.<sup>17,18</sup>

## METHODS

The study involved 138 Iraqi participants, including 88 patients with gastritis (62 males, 26 females aged 16-77 years) and 50 healthy controls matched for age and sex, with no symptoms gastritis or diabetes and not on medications. Diagnosis gastritis in patients confirmed by doctors based on clinical symptoms and result gastric biopsy reports patients who underwent gastroscopy in one of hospitals: Gastroenterology and Hepatology Teaching Hospital, Medical City, Baqubah Teaching Hospital, and Al-Kazemi Teaching Hospital, Department of Gastroenterology, from January 2024 to April 2024. Diabetes was diagnosed based on fasting blood sugar (FBS)  $\geq 120$  mg/dl and HbA1c  $\geq 6.5\%$ . Subjects with neoplastic, autoimmune, inflammatory bowel, type 1 diabetes, or severe kidney and liver diseases were excluded.

Blood samples of 3 ml were collected in gel tubes, allowed to clot at room temperature, and then centrifuged at 3000 rpm for 10 minutes to obtain serum, which was stored at  $-20^{\circ}\text{C}$  until analysis. Serum samples were used to quantitatively measure *H. pylori* IgG levels using a specific ELISA kit (Elabscience). Additionally, levels of hs-CRP, IL-10, and IL-18 were also measured using ELISA kits following the manufacturer's instructions. The results were read using a semi-automated human reader. All serological and biochemical assessments were performed on both patients and healthy controls.

Diabetes screened by estimating FBS  $\geq 120$ mg/dl and HbA1c  $\geq 6.5\%$ , immediately after sample collection by Roche kit using a fully automated analyzer "INTEGRA-400 plus" and determine body mass index (BMI)kg/m<sup>2</sup>normal range (18.5–24.9).

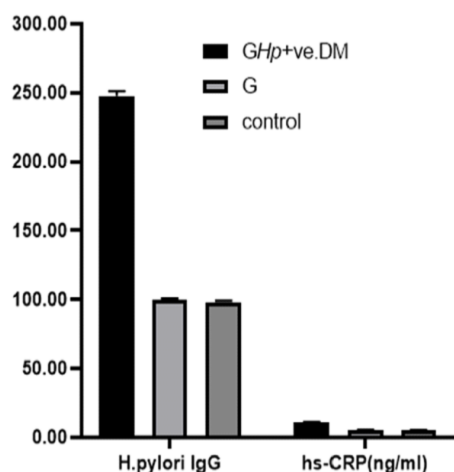
Gene expression analysis for IL-10 and IL-18 involved extracting RNA from blood samples of 38 participants - comprising 12 with *H. pylori* gastritis and type 2 diabetes mellitus, 13 with gastritis only, and 13 healthy individuals. Blood (2 ml) was collected in EDTA tubes, transferred into Eppendorf tubes with Trizol reagent, and stored at  $-20^{\circ}\text{C}$ . RNA was isolated using the TransZol up plus RNA kit, and its concentration and purity were measured with a nanodrop device, ensuring acceptable purity ranges specific to each group. The extracted RNA was reverse transcribed into cDNA using the EasyScript® SuperMix kit. RT-PCR was performed to assess gene expression levels of IL-10, IL-18, and GAPDH (internal control) using SYBR Green dye. Primer sequences in Table 1 were designed accordingly, and qPCR reactions were conducted at an optimal annealing temperature of  $64^{\circ}\text{C}$ . The relative gene expression was analyzed using the  $2^{-\Delta\Delta\text{CT}}$  method to determine changes in IL-10 and IL-18 expression levels among the groups. Statistical analysis performed using IBM SPSS statistics software (version 26.0) with Graph Pad Prism (8.4.3).

## RESULTS

There were 89 male participants (64.5%) and 49 female subjects (35.5%) out of total 138 subjects. Percentage Ghp+ve. DM was (48.6%), percentage G was (15.2%), and Control was (36.2%). *H. pylori* IgG and hs-CRP levels: The IgG levels highly elevated at  $247.74 \pm 3.38$  in GHP+ve. DM compared to G and control ( $P < 0.05$ ). Control found to be  $98.33 \pm .96$  and a slight elevation could be seen in G group at  $99.44 \pm 1.48$  suggesting non-significant in gastritis contrasting to control ( $P > 0.05$ ). In addition to IgG, levels of hs-CRP exhibit a substantial increase in average ( $10.87 \pm 0.27$ ) for GHP+ve.DM participants ( $p < 0.05$ ), compared to average level of hs-CRP ( $5.46 \pm 0.29$ ) for G subjects and control ( $5.31 \pm 0.14$ ) [Fig. 1]

Level of HbA1c shown significantly elevated among patients in GHP +ve and DM from  $4.58 \pm .04$  (control) to  $10.11 \pm .24$  ( $p < 0.05$ ). On other hand, gastritis patients showed a slight increase ( $4.82 \pm .07$ ) compared to control. This likely confirms relationship between diabetes and gastritis. A similar trend was observed with FBS levels, where their levels were abnormally high among GHP+ve.DM patients by  $172.70 \pm 4.01$  ( $P < 0.05$ ) compared to group G  $79.57 \pm 1.32$  and control  $82.12 \pm 0.99$ . As compared to mean level BMI(kg/m<sup>2</sup>) ( $22.56 \pm 0.23$ ) for control, no significant changes seen among subjects.GHP+ve.DM  $24.21 \pm 0.27$  and G  $24.64 \pm 0.33$  ( $P > 0.05$ ). This same level was seen among

gastritis subjects also which clearly states that BMI is not influenced in study ( $p>0.05$ ) [Fig. 2].

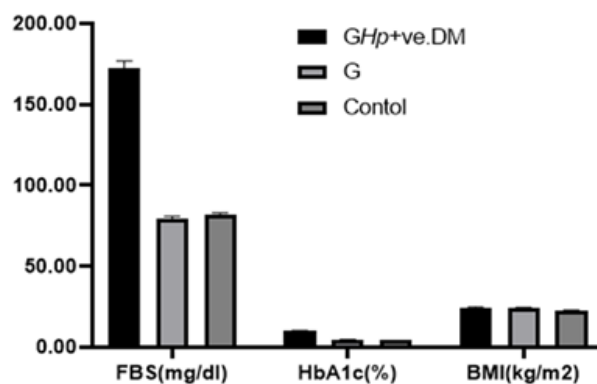


**Figure No. 1: Comparative mean levels of H .pylori IgG level and hs-CRP between studied groups**

After measuring levels IL-10 and IL-18 by ELISA and comparing levels of interleukins between GHp+ve.DM, G, and control, IL-10 found abnormally lowered to  $9.16\pm0.14$  and  $24.36\pm2.48$  for GHp+ve.DM and G groups respectively ( $P<0.05$ ) from  $44.73\pm2.39$ . On the other hand, IL-18 was found to be elevated to  $327.30\pm12.58$  and  $124.41\pm3.54$  respectively for GHp+ve.DM and G from  $81.33\pm1.72$  (control) result of

ANOVA P-values ( $P<0.05$  for both IL-10 and IL-18) [Fig. 3].

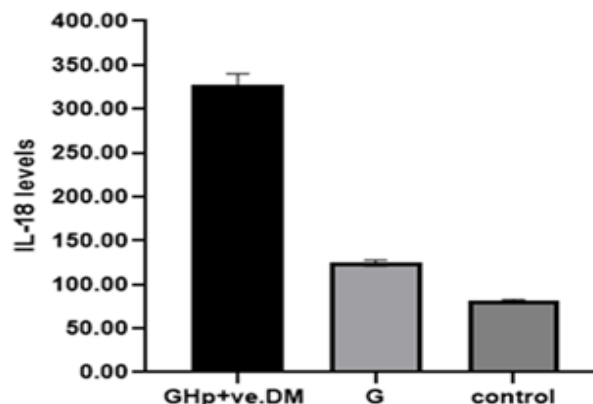
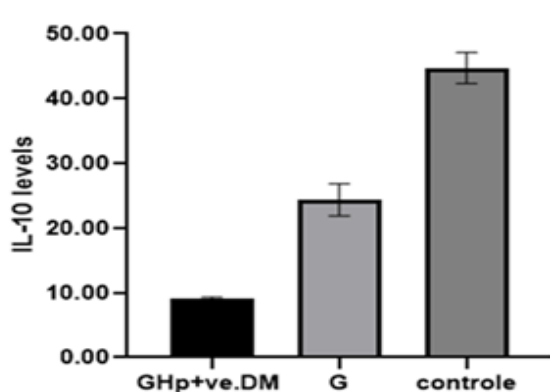
Result gene expression IL-10 and IL-18 between studies groups performed by using RT-qPCR and quantitative  $2^{-\Delta\Delta CT}$ . Relative expression ratio of each gene member to control gene used to show expression. Relative expression of IL-10 was found to be down regulated in subjects when compared to control ( $p<0.01$ ). The GHp+ve.DM was found to be down regulated to 0.63 fold when compared to 1.00 control ( $P<0.05$ ) [Fig. 4 & 5]. Similarly, in case of G, level found to be down regulated to 0.75 from 1.00 (control).



**Figure No. 2: Comparative mean levels of FBS, HbA1c and BMI between studied groups**

**Table No.1: Real time PCR Primers sequence for IL-10 and IL-18 Gene**

Gene	Primer sequence (5'-3')	Base pairs	References
IL-10	TCTCCGAGATGCCTTCAGCAGA	22	19
	TCAGACAAGGCTTGGCAACCCA	22	
IL-18	GATAGCCAGCCTAGAGGTATGG	22	20
	CCTTGATGTTATCAGGAGGATTCA	24	
GAPDH	GTCTCCTCTGACTTCAACAGCG	22	21
	ACCACCCTGTTGCTGTAGCCAA	22	



**Figure No. 3: Comparative mean levels of IL-10 pg/ml (left) and IL-18 pg/ml (right) between studied groups**

A similar trend was seen with cytokine level expression by ELISA method ( $P<0.05$ ). Conversely, it was found participants' GHp+ve.DM relative expression IL-18

(2.6432) was increased in comparison to control (1.0025) ( $p<0.01$ ). A similar trend seen among G group also demonstrating an increase IL-18 levels (1.245)

from 1.0025 (control) were shown in Figures 4 and 5. Association between T2DM and cytokine expression: Appeared important link between GHp +ve. DM and G group about cytokines ( $r=0.5515$ ,  $P=0.014$ ). Nevertheless, no statistically significant difference was seen between male and female participants ( $p<0.01$ ). Spearman rank correlation analysis showed that T2DM

was directly proportional to Cytokine levels within the plasma ( $r = 0.6132743$ ,  $P < 0.001$ ). We found IL-10 levels to be down regulated in H. pylori-associated gastritis than gastritis ( $p<0.01$ ). At the same, found IL-18 to be upregulated in H. pylori-associated gastritis than gastritis ( $p<0.01$ ).

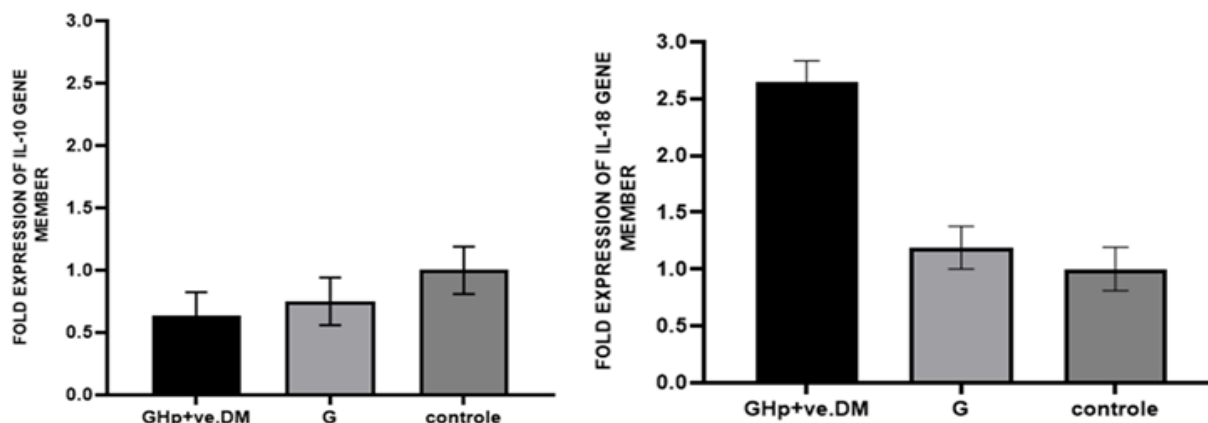


Figure No. 4: Graph showing relative fold expression of cytokine gene members (IL-10 and IL-18) of both subjects and control

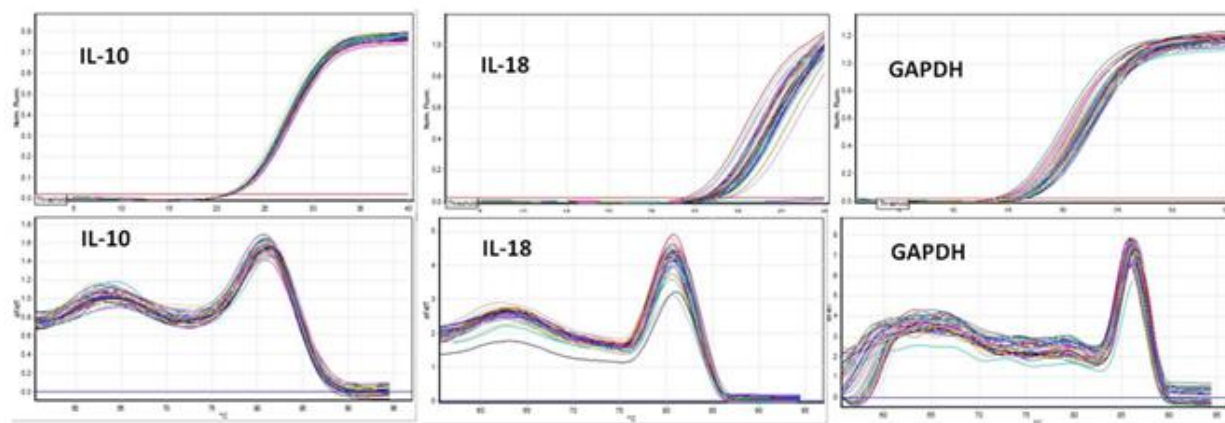


Figure No. 5: qPCR Ct and melt curves. Top: Ct curve; Bottom: Melt curves of respective gene members

## DISCUSSION

Correlation between gastritis, specifically in H. pylori infection, and diabetes is intricate and diverse. Research has been conducted found individuals diagnosed with diabetes type 2, are more likely to have H. pylori infection. One study showed that 71.4% of diabetic patients tested positive for IgG antibodies against bacterium, indicating a strong bond between H. pylori infection and diabetes.<sup>19</sup> This study revealed link between IL-10 and IL-18 within GHp+ve.DM, which shows IL-10, a cytokine recognized for its anti-inflammatory characteristics, plays essential function in inflammatory response, associated with diabetes. Furthermore levels decreased in GHp+ve.DM, In agreement with research conducted by Novianti and others<sup>20</sup>, a study revealed reduced level in individuals with diabetes, in particular patients with oral problems,

in comparison to healthy controls. This suggests that inflammation may inhibit IL-10 production, indicating an insufficient anti-inflammatory response and explaining development of inflammation in these patients.<sup>21</sup> Interleukin-18 is a pro-inflammatory protein released by stimulated macrophages, epithelial cells, bone marrow cells keratinocytes, and malignant cells. It is one of cytokines involved in inflammation.<sup>22</sup> Through this research, elevated IL-18 levels were observed in both gastritis and diabetes., which is consistent with Abdel-Moneim et al<sup>23</sup> that indicating a heightened inflammatory response. Multiple investigations have demonstrated a distinct association between H. pylori infection with both type 2 diabetes mellitus (T2DM) and insulin resistance.<sup>24</sup> Root cause of insulin resistance and type 2 diabetes is chronic, mild inflammation that persists over time. Aggregation of active innate immune cells in metabolic organs

ultimately results in secretion of pro-inflammatory cytokines, including IL-10 and IL-18. Subsequently, these cytokines cause harm to  $\beta$ -cells and lead to emergence of insulin resistance.<sup>25</sup> *H. pylori* intestinal lipopolysaccharides found to be associated with activation of Toll-like receptors. This activation, in turn, leads to fat precipitation, energy harvesting, and stimulation of innate immunity. These factors all contribute to insulin resistance.<sup>26</sup> For level of *H. pylori* IgG, results of investigation indicated a significant elevated in GHp+ve.DM ( $247.74 \pm 3.38$ ) which aggregated with Al-Mamari et al<sup>27</sup>, while no statistical significance between G ( $99.44 \pm 1.48$ ) and control ( $98.33 \pm .96$ ). The C-reactive protein: main source of human CRP is hepatocytes, and its production is controlled by inflammatory cytokines TNF- $\alpha$  and IL-10. Previous studies have mostly examined correlation between risks of diabetes with quantity of high-sensitivity CRP (hs-CRP), in our study noticed significant increase ( $10.87 \pm 0.27$ ) in GHp+ve.DM participants. Compared to G participants ( $5.46 \pm 0.29$ ) and control ( $5.31 \pm 0.14$ ) related with study of Li et al<sup>28</sup>, that found 65.28% of diabetic patients *H. pylori* positive, with mild increases hs-CRP levels noted.

Regarding present study, direct association observed between *H. Pylori* infection in diabetes patients with HbA1c% levels, which is a measure of their glycemic status. The GHp+ve.DM had significantly elevated HbA1c levels compared to control ( $4.58 \pm .04$  vs.  $10.11 \pm .24$ ,  $p < 0.05$ ). Nevertheless, individuals who only had gastritis experienced a slight rise ( $4.82 \pm .07$ ) compared to control. This is likely to confirm connection between diabetes and gastritis. The FBS readings exhibited a comparable pattern.<sup>21</sup> While BMI among three groups non-significant ( $p > 0.05$ ) due to anorexia, difficulty swallowing, and chronic gastritis.<sup>29</sup> Expression levels of both cytokines (IL-10 and IL-18) measured using serum samples obtained from both participant and control by a real-time PCR technique. When compared to control, participants' relative expression of IL-10 found to be downregulated ( $p < 0.01$ ). Compared to 1 (control), GHp+ve.DM shown to be downregulated by 0.63 fold ( $P < 0.05$ ) enhanced by Mitra et al.<sup>30</sup> Comparably, in instance of G, level was seen to have been downregulated from 1 (control) to 0.75. By using ELISA approach, a similar trend in cytokine level expression was observed ( $P < 0.05$ ). On reverse, when evaluating to control (1.0025) ( $p < 0.01$ ), participants' (GHp+ve.DM) relative expression of IL-18 (2.6432) was shown to be higher (Fig. 4). A similar pattern was observed in G group, which similarly showed an increase IL-18 levels from (1.0025) control to (1.245).

## CONCLUSION

The gastritis by *H. pylori* infection to type 2 diabetes and shows IL-10 levels reduced in GHp+ve. DM contrast with gastritis group and healthy controls and inversely correlated with high-sensitivity C-reactive protein, IL-18 levels raised in GHp+ve. IL-10

significantly downregulation in GHp+veDM, in contrast, IL-18 expression significantly upregulated for GHp +ve diabetes mellitus confirming gene's influence on *H. pylori* and diabetes.

### Author's Contribution:

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

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

**Source of Funding:** None

**Ethical Approval:** No.7739 Dated 13.01.2023

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