RECOGNIZED BY:

Higher Education Commission of Pakistan in "Y" Category

Pakistan Medical & Dental Council

College of Physicians and Surgeons Pakistan

INDEXING


CAS
A division of the
American Chemical Society


IMEMR
INDEX MEDICIUS
FOR THE EASTERN MEDITERRANEAN REGION


Scilit


Crossref


Google
Scholar


LOCKSS


ResearchGate


Dimensions


ICMJE
INTERNATIONAL COMMITTEE of
MEDICAL JOURNAL EDITORS


ASIAN
Research Index


EuroPub
Directory of Academic and Scientific Journals


BASE


OPEN ARCHIVES


OCLC
WorldCat®


ASCI
Asian Science Citation Index

Pakistan Journal of Health Sciences (Lahore) (PJHSL) is a monthly, double blinded peer-reviewed open access Journal. It is affiliated with Lahore Medical Research Center and publishes high-quality original research and reviews.

Aims and Scope

PJHSL aims to advance scientific knowledge, promote evidence-based research, and facilitate the practical application of findings to improve health outcomes.

The Pakistan Journal of Health Sciences (Lahore) covers all areas of health sciences, clinical medicine, biomedical sciences, health systems and policy, nursing and allied health sciences, public health, including preventive measures and community-level health initiatives.

This journal is open to all the research professionals whose work fall within our scope. Submissions are welcome and may be submitted here:

editor@thejas.com.pk
www.thejas.com.pk

Title
The title of the paper should provide a concise statement of the contents of the paper. A good title is very important and will attract readers and facilitate retrieval by online searches, thereby helping to maximize citations. The title should include topical keywords and allude to the interesting conclusions of the paper. A title that emphasizes the main conclusions, or poses a question, has more impact than one that just describes the nature of the study.

Running Head
Running head should be added in the header along with the page numbers.

Type of Article
Research Article/ Case Report/ Review Article/ Opinion/ Short Communication/ Mini Review.
Running Title: A short version of the paper title.

Keywords: The major keywords used in the article have to be mentioned.

Authors
List here all author names Author[1], Author[2] and Author[3]
[1]Author department, University, Country
[2]Author department, University, Country
[3]Author department, University, Country

*Corresponding Author
Author Name, Affiliation, Department Name, University Name, Address, City, State, Country, E-mail.

ABSTRACT
Abstract should include a brief content of the article. It should be structured and not more than 250 words. It should include following sub headings: Objective, Methods, Results and Conclusions.

Abbreviations
If there are any abbreviations in the article they have to be mentioned.

INTRODUCTION
Provide a context or background for the study (i.e., the nature of the problem and its significance). State the specific purpose or research objective, or hypothesis tested the study or observation; the research objective is often more sharply focused when stated as a question. Both the main and secondary objectives should be made clear and any pre-specified subgroup analysis should be described. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

METHODS
The methods section should include only information that was available at the time or plan of the protocol. All information gathered during the conduct of study should be included in the methods section.
Study Design, Inclusion / Exclusion Criteria, Data collection Procedure and Statistical analysis.

RESULTS

Present your results in logical sequence in the text, tables and illustrations, giving the main or most important findings first.

Do not repeat the data in text and in the tables or illustrations; emphasize or summarize only important observations. When data are summarized in the results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them. Table font should be 10 and caption should be above table and below the figure.

Data should not be duplicated in both figures and tables. There is no limit to tables and figures. Mention the findings of the study in paragraph, while mentioning figure and table number in text in sequential order.

TABLE

Table should not be copy pasted or in picture form.

DISCUSSION

Discuss your findings by comparing your results with other literature.

REFERENCES

References should not be less than 20.
In text references should be in number style. For Example [1]
Follow the Pubmed Referencing style.
Provide the DOI link.

Example

Here is an example for a journal article: Sharmin SN. Prognostic Value of Serum D-dimer in Predicting Outcomes in COVID-19 Positive Pregnant Women. Scholars International Journal of Obstetrics and Gynecology. 2024; 7(11): 554-9. doi: 10.36348/sijog.2024.v07i11.004.

If there are more than six authors, write *et al*. after the first six names.

CONCLUSION(S)

Conclusion should elucidate how the results communicate to the theory presented as the basis of the study and provide a concise explanation of the allegation of the findings.

ACKNOWLEDGEMENT

Provide the list of individuals who contributed in the work and grant details where applicable.

Plagiarism policy

Similarity index should be less than 19%, and less than 5% from individual sources.

Authorship Letter

Signed authorship letter by all authors including there current Department, University, City, Country, Email.

Declaration Form

Signed declaration form submit by corresponding author.

The submission of article should include: manuscript according to journal guidelines, authorship letter and declaration form. It should be submitted to the following email id: editor@thejas.com.pk

ISSN (E) 2790-9352
ISSN (P) 2790-9344

PJHS
Pakistan Journal of Health Sciences
Lahore

VOLUME 07 ISSUE 02

Editorial Team

CrossLinks International Publishers
Missouri Harrisonville, United States
www.clipllc.us
isni 000000052402317 5

VOLUME 07 ISSUE 02

PJHS
Pakistan Journal of Health Sciences
Lahore

ISSN (E) 2790-9352
ISSN (P) 2790-9344

Editorial Team

CrossLinks International Publishers
Missouri Harrisonville, United States
www.clipllc.us
isni0000000524023175

ISSN (E) 2790-9352
ISSN (P) 2790-9344

PJHS
Pakistan Journal of Health Sciences
Lahore

TABLE OF CONTENTS

VOLUME 07 ISSUE 02

CrossLinks International Publishers
Missouri Harrisonville, United States
www.clipllc.us
isni 0000000524023175

VOLUME 07 ISSUE 02

TABLE OF CONTENTS

PJHS
Pakistan Journal of Health Sciences
Lahore

ISSN (E) 2790-9352
ISSN (P) 2790-9344

CrossLinks International Publishers
Missouri Harrisonville, United States
www.clipllc.us
isni0000000524023175

ISSN (E) 2790-9352
ISSN (P) 2790-9344

PJHS
Pakistan Journal of Health Sciences
Lahore

TABLE OF CONTENTS

VOLUME 07 ISSUE 02

CrossLinks International Publishers
Missouri Harrisonville, United States
www.clipllc.us
isni 0000000524023175

VOLUME 07 ISSUE 02

TABLE OF CONTENTS

PJHS
Pakistan Journal of Health Sciences
Lahore

ISSN (E) 2790-9352
ISSN (P) 2790-9344

CrossLinks International Publishers
Missouri Harrisonville, United States
www.clipllc.us
isni0000000524023175

DOI: https://doi.org/10.54393/pjhs.v7i2.3974

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Angiotensin-Converting Enzyme Inhibitors Increase Substance P, Which Is Involved in Coughing, Inflammation, and Lung Cancer

OPEN ACCESS

Miguel Muñoz[1*] and Riffat Mehboob[2,3]

[1]Research Laboratory on Neuropeptides, Institute of Biomedicine Sevilla (IBIS), Sevilla, Spain
[2]Rotogen Biotech LLC, United States of America
[3]Lahore Medical Research Center, Lahore, Pakistan
miguel.mmunoz@gmail.com

ARTICLE INFO

How to Cite:
Munoz, M., & Mehboob, R. (2026). Angiotensin-Converting Enzyme Inhibitors Increase Substance P, Which Is Involved in Coughing, Inflammation, and Lung Cancer: ACE Inhibitors and Lung Inflammation. Pakistan Journal of Health Sciences, 7(2), 01-02. https://doi.org/10.54393/pjhs.v7i2.3974

Angiotensin-converting enzyme inhibitors (ACEIs) are effective and safe drugs that have been used for many years to control high blood pressure. However, a systematic review and meta-analysis have reported the association between long-term (more than five years) use of ACEIs and the risk of lung cancer (LC). Of the 2,400 records reviewed, 13,061,226 patients met the inclusion criteria [1]. In line with this, it is known that the substance P (SP) peptide, after binding to the neurokinin-1 receptor (NK-1R), is involved in coughing [2], neurogenic inflammation (inflammation SP mediated) [3], and LC [4] and, therefore, could be considered mechanistically responsible for the risk of LC mediated by prolonged ACEIs use for the following reasons: ACE hydrolyze SP [5], while ACEIs can prevent the degradation of SP by blocking ACE [5], ACEIs increases SP levels and induces cough, in fact, ACEIs to cause coughing in 5-10% of patients [2]. SP also induces neurogenic inflammation [3] and LC [4]. ACE or kininase II is a peptidyl dipeptidase that splits C-terminal dipeptides of a large range of substrates, including angiotensin I, bradykinin, neurotensin, and SP [5]. It is a fact that ACE transforms the dormant decapeptide angiotensin I to the octapeptide angiotensin II. However, an important, lesser-known fact is that ECA also hydrolyzes SP, increasing its levels. In contrast, SP hydrolysis was completely blocked by the ACEI, captopril, in a concentration-dependent manner [5]. Thus, ACEI therapy increases SP levels and induces cough [2]. SP plasma levels are higher in subjects with cough [3] (including patients with ACEI treatment) and in patients with cancer compared to healthy subjects [3]. Previous studies indicate that long-term use of ACEIs may increase SP levels in lung tissue and mediate chronic neurogenic inflammation via SP [3, 6]. In addition, it is well known that chronic inflammation is the hallmark of cancer promotion. In fact, chronic inflammatory diseases are known to cause cancer (chronic pancreatitis can promote pancreatic cancer, chronic hepatitis can promote hepatocellular carcinoma, and inflammatory bowel disease can promote colon cancer) [6]. Similarly, persistent neurogenic inflammation mediated by SP can promote LC [3, 6]. Moreover, LC cells overexpress SP and NK-1R, and SP is a mitogen in LC cells [4]. In contrast, the drug aprepitant, a specific NK-1R antagonist, has an antitussive effect in patients with LC and refractory cough [7], as well as anti-inflammatory effects [3], and inhibits LC cell proliferation and induces apoptosis in LC cells [4]. In conclusion, ACEIs block ACE and increase SP levels, which, after binding to NK-1R, can cause coughing and neurogenic inflammation. Persistently elevated SP levels would cause chronic neurogenic inflammation, which, in the long term, could lead to the promotion of LC. Conversely, the use of the specific NK-1R antagonist drug, aprepitant, counteracts coughing, inflammation, and LC.

DOI: https://doi.org/10.54393/pjhs.v7i2.3974

REFERENCES

[1] Wu Z, Yao T, Wang Z, Liu B, Wu N, Lu M *et al.* Association Between Angiotensin-Converting Enzyme Inhibitors and the Risk of Lung Cancer: A Systematic Review and Meta-Analysis. British Journal of Cancer. 2023 Jan; 128(2): 168-76. doi: 10.1038/s41416-022-02029-5.

[2] Tomaki M, Ichinose M, Miura M, Hirayama Y, Kageyama N, Yamauchi H *et al.* Angiotensin Converting Enzyme (ACE) Inhibitor-Induced Cough and Substance P. Thorax. 1996 Feb; 51(2): 199-201. doi: 10.1136/thx.51.2.199.

[3] Sáez MM and Delgado AP. Long-Term Use of Angiotensin-Converting Enzyme Inhibitors Increases Substance P Levels, Which Is Involved in The Risk of Lung Cancer. Archivos de Bronconeumología: Official Journal of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) and the Latin American Thoracic Association. 2023; 59(12): 848-9. doi: 10.1016/j.arbres.2023.09.017.

[4] Muñoz M, González-Ortega A, Rosso M, Robles-Frias MJ, Carranza A, Salinas-Martín MV *et al.* The Substance P/Neurokinin-1 Receptor System in Lung Cancer: Focus on the Antitumor Action of Neurokinin-1 Receptor Antagonists. Peptides. 2012 Dec; 38(2): 318-25. doi: 10.1016/j.peptides.2012.09.024.

[5] Skidgel RA, Engelbrecht S, Johnson AR, Erdös EG. Hydrolysis of Substance P and Neurotensin by Converting Enzyme and Neutral Endopeptidase. Peptides. 1984 Jul; 5(4): 769-76. doi: 10.1016/0196-9781(84)90020-2.

[6] Esteban F, Ramos-Garcia P, Munoz M, González-Moles MA. Substance P and Neurokinin 1 Receptor in Chronic Inflammation and Cancer of the Head And Neck: A Review of the Literature. International Journal of Environmental Research and Public Health. 2021 Dec; 19(1): 375. doi: 10.3390/ijerph19010375.

[7] Smith JA, Harle A, Dockry R, Holt K, Russell P, Molassiotis A *et al.* Aprepitant for Cough in Lung Cancer. A Randomized Placebo-Controlled Trial and Mechanistic Insights. American Journal of Respiratory and Critical Care Medicine. 2021 Mar; 203(6): 737-45. doi: 10.1164/rccm.202006-2359OC.

DOI: https://doi.org/10.54393/pjhs.v7i2.3635

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Outcomes of One Point versus Two Point Fixation in Zygomatic Bone Fracture

Maria Jabbar[1*], Uzair Bin Akhtar[1], Komal Akram[1], Shoaib Younas[2], Mustafa Ayub Khawaja[1] and Muhammad Khalil[1]

[1]Department of Oral and Maxillofacial Surgery, Sharif Medical and Dental Hospital, Lahore, Pakistan
[2]Department of Oral and Maxillofacial Surgery, Combined Military Hospital, Lahore, Pakistan

ARTICLE INFO

Keywords:
Zygomatic Bone Fracture, Malar Height, One-Point Fixation, Two-Point Fixation

How to Cite:
Jabbar, M., Akhtar, U. B., Akram, K., Younas, S., Khawaja, M. A., & Khalil, M. (2026). Outcomes of One Point versus Two Point Fixation in Zygomatic Bone Fracture: One Point versus Two Point Fixation in Zygomatic Bone Fracture. Pakistan Journal of Health Sciences, 7(2), 03-07. https://doi.org/10.54393/pjhs.v7i2.3635

Corresponding Author:
Maria Jabbar
Department of Oral and Maxillofacial Surgery, Sharif Medical and Dental Hospital, Lahore, Pakistan
drmariajabbar@gmail.com

Received Date: 25th October, 2025
Revised Date: 9th December, 2025
Acceptance Date: 1st January, 2026
Published Date: 28th February, 2026

ABSTRACT

Fractures of the zygomatic bones are quite common injuries. There are several different surgical methods for fixing zygomatic bone fractures, and there is no universally accepted one. **Objective:** To compare the outcomes of one-point and two-point fixation in zygomatic bone fractures. **Methods:** This prospective comparative study was carried out on 60 patients admitted to the Department of Oral and Maxillofacial Surgery at Sharif Medical and Dental Hospital, Lahore, from September 2023 to August 2024. The patients were divided into two groups (A/B). Thirty consecutive patients in group A received one-point fixation, and thirty consecutive patients in group B received two-point fixation for their zygomatic fracture repair. The outcomes of procedures were evaluated by assessment of the bone diastasis at the inferior orbital margin and frontozygomatic suture on postoperative CT scan, and evaluation of malar height clinically. **Results:** There was a non-significant association between bone reduction in the Frontozygomatic suture and method of fixation (p=0.237). The association between bone reduction in the infraorbital margin and method of fixation was significant (p=0.005). For malar height, a statistically non-significant difference in the post-operative malar height among the groups that had undergone one and two-point fixation (p=0.067). **Conclusion:** The majority of individuals who had two-point fixation exhibited appropriate reduction at the infra-orbital margin and frontozygomatic suture. Those who had one-point fixation treatment exhibited higher post-operative malar height.

INTRODUCTION

Facial bone fractures have been known for a very long period, and attempts to cure them efficiently continue to date. Fractures involving the zygomatic complex are the most common occurrence in the maxillofacial region. Trauma from attacks, falls, and injuries related to sports, road traffic accidents, and civilian combat are some of the types of injuries [1]. Direct trauma can cause damage to the zygomatic arch, a laterally placed portion of the skull that is made up of the zygoma as well as the temporal bone. Approximately 10% of all zygomatic fractures result in isolated zygomatic arch fractures, which produce a pronounced depression over the arch fracture area. A fractured arch tends to apply pressure on the coronoid process, which impedes mouth opening [2]. Nevertheless, the prevalence of facial bone fractures is also highly dependent upon sociodemographic and environmental factors [3]. ZMC fractures are typically diagnosed clinically. A CT scan aids in the diagnosis of these fractures significantly by providing three-dimensional reconstruction films, axial and coronal planes, which confirm the diagnosis [4]. ZMC fractures that have no or very little displacement are managed conservatively without surgical procedures, whereas fractures that have functional or aesthetically problematic issues like diplopia, a limited range of movement in the mouth, or a depression of the malar eminence need to be managed surgically [5]. To get excellent results, a variety of surgical procedures have been used, including the Gillies' temporal procedure,

DOI: https://doi.org/10.54393/pjhs.v7i2.3635

upper eyelid, lateral brow, subciliary, transconjunctival, and intraoral routes [6]. Restricted mouth opening, major arch flattening, as well as diplopia are some of the important aesthetic as well as functional issues associated with displaced zygomatic bone fractures [7]. Stable and appropriate reduction needs to be accomplished to reestablish function, along with the appearance of the face. Since the zygoma can get fractured within a range of patterns, an extensive range of therapy suggestions have developed: compared to the minimum reduction procedures conducted without fixation, to complex kinds of open reduction. The zygomatic bone can be fixed by using different types of fixations [8]. The type of post-fixation segment stability is determined by the fixation technique, which is dependent on the impact of trauma [9]. Several studies have examined the results based on the variety of fixations, despite earlier research reporting that one-point fixation using the oral technique is adequate [10]. On the other hand, two-point and three-point fixation have been compared in numerous studies. According to one study that used X-rays to assess one-point and two-point fixation, two-point fixation was better for bone stability than one-point fixation [11]. Although three-point fixation has historically been considered the traditional method for managing displaced ZMC fractures, recent literature indicates that comparable stability can often be achieved with fewer fixation points, especially in non-comminuted unilateral fractures [7]. Three-point fixation also requires additional surgical exposure, greater operative time, and a higher risk of visible scarring, which makes it less favorable in cases where adequate reduction can be achieved with fewer fixation points [12].

Despite the widespread use of one-point and two-point fixation techniques for isolated unilateral ZMC fractures, there remains inconsistency in clinical decision-making regarding the optimal approach to achieve adequate stability with minimal morbidity. There is a lack of robust comparative evidence, particularly in similar clinical settings, evaluating functional and aesthetic outcomes between one-point and two-point fixation, underscoring the need for further focused investigation. This study aimed to focus specifically on comparing one-point and two-point fixation, as these represent the most commonly used contemporary approaches for isolated unilateral ZMC fractures while balancing surgical access, stability, and aesthetic outcomes.

METHODS

This prospective comparative study was conducted after attaining ethical approval from the Sharif Medical Research Center (SMRC) (Ref. no SMDC/SMRC/311-23). The sample size was calculated using the WHO sample size formula, taking malar symmetry in one point fixation group as 94.1% with 95 % confidence level at 0.06 precision [3]. A total of 60 patients having zygomatic complex fractures, visiting the Oral and Maxillofacial OPD at Sharif Medical and Dental Hospital, Lahore, from September 2023 to August 2024, were included. After informed consent, using a non-probability convenience sampling technique, patients were allocated into two groups of 30 patients each: group A and group B. All patients aged > 18 years diagnosed with isolated unilateral zygomatic bone fracture, diagnosed on CT scan, were included. Patients with comminuted zygomatic bone fracture, or having other facial fractures associated with zygomatic bone fracture, bilateral fractures, old fractures (>2 weeks), or medically unfit patients were excluded from this study. Under General Anesthesia, thirty consecutive patients in Group A underwent one-point fixation at the zygomaticomaxillary buttress, and 30 consecutive patients in Group B underwent two-point fixation at the zygomaticomaxillary and the frontozygomatic region. Oral and maxillofacial surgeons carried out a standard procedure for fracture repair. In the maxillary vestibular region, above the mucogingival junction, an incision was made; zygomaticomaxillary and nasomaxillary buttresses were exposed. The frontozygomatic junction and infraorbital ridge were palpated to assess correct reduction. The zygomatic complex fracture was stabilized with a miniplate and screws at the zygomaticomaxillary buttress in group A. The frontozygomatic junction was exposed for a second fixation point through the lateral eyebrow incision, which was then stabilized by miniplates in group B. The sulcus and the lateral eyebrow incisions were closed using sutures (Vicryl 3-0) and (Prolene 5-0), respectively. The follow-up was done on the 7th day and after one month of the procedure. Clinically, malar height was measured using two reference points: point A at the intersection of the mid-sagittal line with the intercanthal line, and point B at the maximum prominence of the malar region, viewed from the vertex perspective. The distance between the two points was measured with a vernier caliper, and all postoperative results depended on this measurement. All measurements were performed by a single calibrated maxillofacial surgeon to minimize inter-observer variability. Radiologically, post-operative stability of the zygomatic segments was evaluated using maxillofacial CT scans (1–1.25 mm slices). Assessment included alignment of the frontozygomatic suture, infraorbital rim, zygomaticomaxillary buttress, and lateral orbital wall compared with the contralateral side. Displacement was measured in axial, coronal, and sagittal views (less than 3mm is adequate, and more than 3 mm is inadequate) [13]. Malar projection symmetry and orbital floor continuity were also reviewed. All radiological measurements were

DOI: https://doi.org/10.54393/pjhs.v7i2.3635

performed independently by two surgeons, with discrepancies resolved by consensus. All data were analyzed using SPSS version 23.0. Nominal data were presented as frequencies and percentages, and numeric data as mean ± standard deviation. The Shapiro–Wilk test was used to assess the normality of continuous variables, and Levene's test assessed equality of variances. The independent t-test was used for normally distributed continuous variables with equal variances, while the Chi-square test and Fisher's exact test were applied to categorical variables. No formal adjustment was made for multiple comparisons due to the limited number of primary outcomes; p-values were interpreted cautiously, with $p<0.05$ considered statistically significant.

RESULTS

Among all 60 included patients, the mean age was 30.75 ± 11.12 years. A total of 95% were males and 5% were females. Half of the patients underwent one-point fixation, while the remaining half received two-point fixation. A statistically non-significant association was found between bone reduction at the frontozygomatic (FZ) suture and the fixation method (p=0.237). Among patients with adequate bone reduction, a higher proportion belonged to the two-point fixation group (Table 1).

Table 1: Association Between Bone Reduction at the Frontozygomatic Suture and Method of Fixation

Radiological Assessment of the FZ suture	One-Point Fixation	Two-Point Fixation	Total	p-value
Adequate Bone Reduction (≤3 mm)	27 (47.4%)	30 (52.6%)	57	0.237
Inadequate Bone Reduction (>3 mm)	3 (100%)	0 (0%)	3	

A statistically significant association was identified between bone reduction at the infra-orbital margin and the fixation method (p=0.005). Patients with adequate reduction were predominantly from the two-point fixation group (Table 2).

Table 2: Association Between Bone Reduction at the Infra-Orbital Margin and Method of Fixation

Radiological Assessment of Infra-Orbital Margin	One-Point Fixation	Two-Point Fixation	Total	p-value
Adequate Bone Reduction (≤3 mm)	19 (40.4%)	28 (59.6%)	47	0.005*
Inadequate Bone Reduction (>3 mm)	11 (84.6%)	2 (15.4%)	13	

There was a non-significant difference in postoperative malar height between the two groups (p=0.067). Although not statistically significant, patients treated with one-point fixation showed slightly higher postoperative malar height (Table 3).

Table 3: Post-Operative Malar Height Comparison Between One-Point and Two-Point Fixation

Group	n	Mean ± SD	p-value
One-Point Fixation	30	63.27 ± 2.26	0.067
Two-Point Fixation	30	62.30 ± 1.73	

DISCUSSION

Zygomatic bone fractures are difficult to treat because of their intricate three-dimensional dynamic structure. Fixation must be carried out with the right technique and precise reduction in order to produce good surgical outcomes, both aesthetically as well as functionally. Although three-point fixation with the three-point approaches technique has been the historically recommended method for zygomatic bone surgery, research has found that one-point as well as two-point fixation could produce stability comparable to that of three-point stabilization [14]. According to one study, one-point fixation over the zygomatico-frontal suture can help achieve both functional as well as aesthetic goals [15]. According to other research, one-point fixation by the oral technique could produce good surgical outcomes. However, there is still disagreement over how many plates are necessary for proper fixing [16]. With parameters taken at precisely the same fixation points as in our investigation, a prior study compared the surgical outcomes of one-point versus two-point fixation in zygomatic bone fractures using X-ray images. According to that study, two-point fixation produced better bone stabilization outcomes [11]. CT is a better way to assess whether sufficient postoperative outcomes have been obtained in the facial bone because it is the gold-standard method for assessing postoperative outcomes and taking anatomical assessments of facial bone fractures that constitute a complicated three-dimensional framework [17]. In current study, bone loss in the Frontozygomatic suture and fixing technique was not significantly correlated (p=0.237). Among those with sufficient bone reduction, it was observed that a larger proportion belonged to the two-point fixation group. These results are consistent with a study that found that one-point fixation of fractures of the zygomatic bone could yield adequate stability as well as aesthetic outcomes in 94.1% of instances. Its benefits include preventing external scarring and plate palpability, lowering the risk of infection of the wound, and increasing the overall satisfaction of patients about the procedure (94.1%) [18]. On the other hand, it has drawbacks, such as the failure to produce satisfactory outcomes in cases where the zygomatic buttress was crushed, which happened in 5.9% of cases. Nonetheless, in 97% of cases, two-point fixation of the zygomatic bone may result in acceptable stability alongside aesthetically pleasing outcomes. Nevertheless, it has drawbacks, including the possibility of unsightly scarring in 41.2% of cases, palpable plate in 35.3% of cases, a higher risk of infection from the wound in 17.6% of cases, and less favorable satisfaction rates (58.8%) [19]. As far as the malar height is concerned, according to our study a difference between both groups

DOI: https://doi.org/10.54393/pjhs.v7i2.3635

that went through one-point and two-point fixation in terms of post-operative malar prominence that was statistically insignificant (p=0.067) [20]. Those that received one-point fixation had a higher post-operative malar height than those who had two-point fixation, even though the disparity was not statistically significant, these results are contrary to a study stated that they concluded that the malar height, which demonstrated that two-point fixation produced better correction outcomes than one-point fixation. Disparities between these two operative techniques were statistically significant (p<0.001) [9]. Although two-point fixation provided better radiological reduction, one-point fixation remains a viable option in specific clinical scenarios. Patients with isolated, non-comminuted fractures, minimal displacement, and an intact zygomaticomaxillary buttress may benefit from one-point fixation due to reduced surgical exposure, lower risk of scarring, and shorter operative time. Additionally, one-point fixation may be preferred in patients with great cosmetic concerns or in settings where additional surgical sites increase morbidity. Present study supports that with careful patient selection, one-point fixation can achieve satisfactory functional and aesthetic outcomes.

A limitation of our study is the relatively short follow-up period of 1 month, which may not fully reflect long-term radiologic stability and bone healing. Previous studies suggest that postoperative assessment of zygomatic fracture alignment and malar prominence is ideally conducted at 3–6 months to account for remodeling and late changes. Future studies with extended follow-up are warranted to confirm the durability of one-point versus two-point fixation outcomes.

CONCLUSIONS

Fixation using two points showed better radiologic results, with the percentage of patients with sufficient reduction in both the frontozygomatic suture and the infra-orbital margin being greater. On the contrary, one-point fixation led to a very minor increase in postoperative malar height, which was not statistically significant. Generally, although two-point fixation was the best in terms of anatomy, one-point fixation was still acceptable, which suggests that both methods could be used in case of fracture pattern and clinical needs.

Authors' Contribution

Conceptualization: MJ
Methodology: MJ, UBA, KA, SY, MK
Formal analysis: MAK
Writing and drafting: MJ, UBA, SY, MAK, MK
Review and writing: MJ, UBA, KA, SY, MK, MAK

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Lee KS, Do GC, Shin JB, Kim MH, Kim JS, Kim NG. One-Point Versus Two-Point Fixation in the Management of Zygoma Complex Fractures. Archives of Craniofacial Surgery. 2022 Aug; 23(4): 171. doi: 10.7181/acfs.2022.00164.

[2] Shahine MS, El-Dein Gaber Shaltout S, Osman MH, Thabet MG, Abdel-Tawab M, Abbas HS. One-Point Versus Two-Point Fixation of Tripodal Zygomatic Fractures. The Egyptian Journal of Surgery. 2022 Oct; 41(1).

[3] MCPS M. One Point Fixation Versus Two Point Fixation in Zygomaticomaxillary Complex Fractures. Journal of the Pakistan Dental Association. 2021 Apr; 30(02). doi: 10.25301/JPDA.302.74.

[4] Mittal G, Garg R, Sharma S, Rathi VC, Ranjan R, Khare G. Efficacy of Two-Point Fixation in the Management of Zygomatic Complex Fractures-A Prospective Clinical Study. National Journal of Maxillofacial Surgery. 2019 Jul; 10(2): 223-7. doi: 10.4103/njms.NJMS_49_18.

[5] Gawande MJ, Lambade PN, Bande C, Gupta MK, Mahajan M, Dehankar T. Two-Point Versus Three-Point Fixation in the Management of Zygomaticomaxillary Complex Fractures: A Comparative Study. Annals of Maxillofacial Surgery. 2021 Jul; 11(2): 229-35. doi: 10.4103/ams.ams_75_20.

[6] Degala S, Radhakrishna S, Dharmarajan S. Zygomaticomaxillary Fracture Fixation: A Prospective Comparative Evaluation of Two-Point Versus Three-Point Fixation. Oral and Maxillofacial Surgery. 2021 Mar; 25(1): 41-8. doi: 10.1007/s10006-020-00881-4.

[7] Kumar CS, Singh KP, Sorokhaibam T, Pillai KS, Lokesh V. Radiological Assessment of Two-Point Versus Three-Point Fixation in Unilateral Zygomatic Tripod Fractures: A Comparative Study. International Surgery Journal. 2025; 12(8): 1275-1281. doi: 10.18203/2349-2902.isj20252276.

[8] Altimmimi HM, Alhussainy YA, Al Mualla HD. Minimal Invasive Treatment of Displaced Zygomatic Bone Fracture. Al-Rafidain Journal of Medical Sciences (ISSN 2789-3219). 2025 Apr; 8(2): 42-6. doi: 10.54133/ajms.v8i2.1744.

[9] El-Gisr MM, Naggar AA, Khalifa MA, Amer MA. Single Versus Multiple Point Fixation of

DOI: https://doi.org/10.54393/pjhs.v7i2.3635

Zygomaticomaxillary Complex Fracture. Pan Arab Journal of Rhinology. 2024; 14(1): 4. doi: 10.58595/2090-7559.1232.

[10] Vaddamanu SK, Khalid I, Binduhayyim RI, Alsaeed AY, Alshahrani SS, Salih AS *et al.* Impact of Zygomaticomaxillary Complex Fracture on Masticatory Muscle Dysfunction and Pain: Systematic Review and Observational Meta-Analysis. Journal of Oral and Facial Pain and Headache. 2025 Sep; 39(3): 38.

[11] Nasr WF, ElSheikh E, El-Anwar MW, Sweed AH, Bessar A, Ezzeldin N. Two-Versus Three-Point Internal Fixation of Displaced Zygomaticomaxillary Complex Fractures. Craniomaxillofacial Trauma and Reconstruction. 2018 Dec; 11(4): 256-64. doi: 10.1055/s-0037-1604199.

[12] Shanmugam D, Thanasekaran V, Biradar N, Purushothaman A, Sridhar D, Shanmugam D. Management of Zygomaticomaxillary Complex Fractures with Two-Point Fixation Retrospective Study for 5 Years. Asian Journal of Medical Sciences. 2021 Jan; 12(1): 100-5. doi: 10.3126/ajms.v12i2.31114.

[13] Starch-Jensen T, Linnebjerg LB, Jensen JD. Treatment of Zygomatic Complex Fractures with Surgical or Nonsurgical Intervention: A Retrospective Study. The Open Dentistry Journal. 2018 May; 12: 377. doi: 10.2174/1874210601812010377.

[14] Guo L, Cheng T, Feng L, Feng J, Li X. Comparison of Two-Point Versus Three-Point Fixation in Treatment of Zygomaticomaxillary Complex Fractures: An Updated Meta-Analysis. Journal of Oral and Maxillofacial Surgery. 2025 Apr; 83(4): 448-55. doi: 10.1016/j.joms.2024.12.006.

[15] Raghoebar II, Rozema FR, Langue JD, Dubois L. Surgical Treatment of Fractures of Zygomaticomaxillary Complex: Effect of Fixation on Reposition and Stability. A Systematic Review. British Journal of Oral and Maxillofacial Surgery. 2021 Jul; 60(1). doi: 10.1016/j.bjoms.2021.07.006.

[16] Jazayeri HE, Khavanin N, Jason WY, Lopez J, Shamliyan T, Peacock ZS *et al.* Fixation Points in the Treatment of Traumatic Zygomaticomaxillary Complex Fractures: A Systematic Review and Meta-Analysis. Journal of Oral and Maxillofacial Surgery. 2019 Oct; 77(10): 2064-73. doi: 10.1016/j.joms.2019.04.025.

[17] Zaman G, Khan MA, Hyder MZ, Hassan TU, Zafar A, Ashraf W. Three-Point Fixation Is Superior to Two-Point Fixation Technique for Zygomatic Complex Fracture. International Journal of Clinical Trials. 2019 Oct; 6(4): 61-. doi: 10.18203/2349-3259.ijct20193618.

[18] Chaitanya G, Sushma B, Dubey S, Chaturvedi M, Gupta S, Shah SJ *et al.* Efficacy of Two-Point Rigid Internal Fixation of Fronto-Zygomatic Suture and Zygomatic Buttress: An Original Research. Journal of Pharmacy and Bioallied Sciences. 2025 Sep; 17(Suppl 3): S2338-40. doi: 10.4103/jpbs.jpbs_1413_24.

[19] Yousri N, Sadakah AE, Khalifa M, Essa E. Evaluation of Intraoral Two-point Fixation in Monobloc Zygomatic Complex Fractures. Egyptian Journal of Oral and Maxillofacial Surgery. 2021 Jul; 12(3): 197-204. doi: 10.21608/omx.2021.82856.1123.

[20] Shabana MA, Hamed MS, Elsayed AK, Anter O, El Naga AM. Facial Asymmetry After Management of Unilateral Zygomaticomaxillary Complex Fractures Using Two-Point Fixation Technique. Egyptian Journal of Hospital Medicine. 2024 Jul; 95(1): 2071-7. doi: 10.21608/ejhm.2024.357947.

DOI: https://doi.org/10.54393/pjhs.v7i2.3610

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Anatomical Study: Anatomical Variations of Dorsalis Pedis Artery and Its Correlation with Clinical Assessment

Shehla Khatoon[1], Faizan Shah[1*], Rahmat Ullah Jan[2], Munila Shabnum[3], Asif Kamal[2] and Syed Mohammad Tahir Shah[4]

[1]Department of Anatomy, Khyber Medical College, Peshawar, Pakistan
[2]Department of Anatomy, Muhammad College of Medicine, Peshawar, Pakistan
[3]Department of Trauma and Orthopedics, Hayatabad Medical Complex, Peshawar, Pakistan
[4]Department of Anatomy, College of Medicine and Dentistry at the Hills, Abbottabad, Pakistan

ARTICLE INFO

Keywords:
Dorsalis Pedis Artery, Anatomical Variation, Doppler Ultrasonography, Pedal Pulse, Anterior Tibial Artery

How to Cite:
Khatoon, S., Shah, F., Jan, R. U., Shabnum, M., Kamal, A., & Shah, . S. M. T. (2026). Anatomical Study: Anatomical Variations of Dorsalis Pedis Artery and Its Correlation with Clinical Assessment: Anatomical Variations of Dorsalis Pedis Artery and Clinical Assessment. Pakistan Journal of Health Sciences, 7(2), 08-13. https://doi.org/10.54393/pjhs.v7i2.3610

***Corresponding Author:**
Faizan Shah
Department of Anatomy, Khyber Medical College, Peshawar, Pakistan
faizan.roghani2021@gmail.com

Received Date: 24th October, 2025
Revised Date: 9th December, 2025
Acceptance Date: 18th December, 2025
Published Date: 28th February, 2026

ABSTRACT

The dorsalis pedis artery, the distal continuation of the anterior tibial artery, is a key landmark for pulse assessment, vascular access, and reconstructive procedures of the foot. Its anatomical variability, however, may complicate clinical examination and contribute to diagnostic uncertainty. **Objectives:** To describe the anatomical configurations and morphometric features of the DPA and to determine how these variations influence clinical pulse palpability. **Methods:** A descriptive cross-sectional study was conducted at Khyber Medical College, Peshawar, from March 2024 to August 2025, in collaboration with the Radiology Department at Khyber Teaching Hospital. A total of 103 lower limbs were examined through standardized palpation followed by colour Doppler ultrasonography using a 7.5–10 MHz linear transducer. The artery's origin, course, termination, diameter, and length were documented and classified. Associations between anatomical type and pulse palpability were assessed using Chi-square tests and Cramer's V. **Results:** The DPA was present in all limbs. Type I was the most common pattern (80.6%). Variant origins (Types II, IV, V) accounted for roughly one-fifth of cases. A palpable pulse was detected in 88.3% of limbs, with significantly higher palpability in Type I compared with variant types ($p<0.001$). Pulse palpability did not differ by sex or limb side. **Conclusions:** Although the DPA generally follows a predictable anatomical course, variations are not uncommon and may reduce clinical pulse detectability. Recognition of these variants is important for accurate vascular assessment, imaging interpretation, and surgical planning.

INTRODUCTION

The dorsalis pedis artery (DPA), the distal continuation of the anterior tibial artery, is an essential vascular landmark for bedside assessment of peripheral perfusion and remains one of the routinely examined pedal pulses in clinical practice [1]. Its superficial position on the dorsum of the foot makes it easily accessible for pulse palpation, Doppler assessment, and a range of diagnostic and surgical procedures. Beyond routine vascular examination, the DPA is frequently used for flap planning, grafting, and distal access in complex limb revascularization. Anatomical reliability is therefore assumed in daily practice, yet normal variants may complicate pulse detection or lead to misinterpretation of vascular status [2, 3]. Although the Type I configuration direct continuation of the anterior tibial artery, is the most frequently reported pattern, multiple studies have described high-origin anterior tibial divisions, double-origin vessels, and collateral replacements arising from the peroneal system [4]. These deviations may produce absent or weak palpable pulses despite normal perfusion, contributing to diagnostic uncertainty or unnecessary investigations [5]. Understanding these variations is especially important in

DOI: https://doi.org/10.54393/pjhs.v7i2.3610

settings where palpation remains the primary initial assessment tool [5]. Recent advances in noninvasive vascular imaging, particularly high-resolution Doppler ultrasonography and angiographic techniques, have increased the need for precise anatomical mapping of pedal arteries. Accurate identification of the DPA supports safer interventional radiology procedures, optimizes flap donor-site selection, and assists surgeons in planning reconstructive, orthopedic, and vascular interventions [6, 7]. Despite the clinical importance of this artery, regional data documenting its anatomical patterns and their effect on pulse detectability remain limited, especially in populations where vascular assessments are frequently performed by palpation alone. Accordingly, the present study investigates the anatomical configurations and morphometric characteristics of the DPA in a local adult population and examines how these structural variations influence clinical pulse palpability. Using combined physical examination and colour Doppler ultrasonography, the study compares classical and variant arterial patterns to clarify their clinical implications.

In routine clinical practice, absent or diminished dorsalis pedis pulses are often interpreted as indicators of peripheral vascular compromise, despite the possibility of underlying anatomical variations in an otherwise well-perfused limb. There is limited locally generated, imaging-correlated evidence assessing dorsalis pedis artery anatomical variants and their direct impact on clinical pulse palpability, highlighting the need for population-specific evaluation.This study aimed to enhance anatomical understanding, reduce misinterpretation of absent pedal pulses, and improve accuracy in vascular assessment and surgical planning.

METHODS

This descriptive cross-sectional study was conducted from March 2024 to August 2025 at the Department of Anatomy, Khyber Medical College, Peshawar, in collaboration with the Department of Radiology at Khyber Teaching Hospital. The Institutional Research and Ethical Review Board (IREB) of Khyber Medical College/Khyber Teaching Hospital approved the protocol (Certificate No. 167/DME/KMC). The study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision), and written informed consent was obtained from all participants before examination. Participant anonymity and confidentiality were ensured, and participation was voluntary with the option to withdraw at any time without affecting clinical care. Adult volunteers and patients temporarily attached to the Anatomy Department and Radiology Unit for teaching ultrasound or minor musculoskeletal assessments were invited to participate. A non-probability consecutive sampling approach was used, enrolling all eligible adults during the study period. Individuals aged 18 years or older with no history of peripheral vascular disease, major trauma, deformity, or previous foot surgery, and with normal skin colour and temperature of the feet, were included. Exclusion criteria were diabetes mellitus, known vascular disorders, visible surgical scars over the dorsum of the foot, active infection, significant oedema, or pregnancy. The sample size was calculated using the formula for estimating a single population proportion: $n = Z^2 \times p \times (1 - p) / d^2$, where Z is the value corresponding to a 95% confidence level (1.96), p is the expected proportion of anatomical variation, and d is the allowable error. Previous reports suggested dorsalis pedis artery (DPA) variations in approximately 20–25% of individuals, and p was set at 0.22 with d at 0.09 [8], yielding a minimum sample of 95 limbs. To increase precision and compensate for potential data loss, 103 limbs were finally included. All examinations were performed in a quiet room with ambient temperature maintained at approximately 22–24°C. Participants were examined in the supine position with the ankle slightly dorsiflexed and the feet at heart level, and were allowed to rest for at least 10 minutes before assessment. The DPA pulse was first sought by palpation lateral to the tendon of extensor hallucis longus and recorded as palpable or not palpable. The same examiner used light fingertip pressure in a standardized manner to avoid artificially occluding the artery. When the feet felt cold, they were gently covered until the skin temperature normalized before palpation. Following clinical examination, colour Doppler ultrasonography was performed using a 7.5–10 MHz linear-array transducer to confirm the presence and course of the DPA. Because the DPA is a superficial vessel on the dorsum of the foot, this frequency range provided sufficient resolution and depth penetration to delineate its origin, course, and branching pattern. For participants with greater soft-tissue thickness, depth, and gain settings were adjusted, and the probe was gently angled until a clear colour and spectral Doppler signal was obtained; no limb was excluded because of inadequate visualization. The origin, course, termination, external diameter, and total length of the DPA were documented. Anatomical variations of the DPA were categorized using the modified classification which recognizes Types I (continuation of the anterior tibial artery), II (high origin), IV (double origin), and V (collateral replacement). Each morphometric measurement was taken three times by the same examiner, and the mean value was used for analysis to minimize intra-observer variability. Independent reviewers confirmed the palpation findings, and an experienced radiologist performed all Doppler examinations. A pilot evaluation of ten limbs showed complete inter-observer agreement for pulse

DOI: https://doi.org/10.54393/pjhs.v7i2.3610

palpability (κ = 1.0). All data were analyzed using IBM SPSS Statistics version 26.0. Continuous variables such as age, height, weight, and arterial measurements were summarized as means and standard deviations. Categorical variables, including sex, side, DPA type, and pulse palpability, were described as frequencies and percentages. Because these variables are categorical, χ^2 tests with Cramer's V were used to examine associations and effect sizes between DPA type and pulse palpability, as well as between palpability and demographic factors (sex and side). A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study evaluated 103 limbs from adult participants with a mean age of 43.27 ± 11.36 years. Most participants were male (66.0%), with average anthropometric measures of 165.52 cm in height, 66.23 kg in weight, and a BMI of 24.24 ± 3.42 kg/m^2. Right limbs accounted for 37.9% of assessments and left limbs for 62.1%, indicating a well-distributed sample (Table 1).

Table 1: Demographic Characteristics of the Study Population (n=103)

Variables	Category	n (%) / Mean ± SD
Age (Years)	–	43.27 ± 11.36
Sex	Male	68 (66.0%)
	Female	35 (34.0%)
Height (cm)	–	165.52 ± 6.90
Weight (kg)	–	66.23 ± 8.68
BMI (kg/m^2)	–	24.24 ± 3.42
Side Examined	Right	39 (37.9%)
	Left	64 (62.1%)

Among the 103 limbs assessed, most DPAs (87.4%) followed a normal superficial course, with smaller proportions showing a deep (6.8%) or tortuous (5.8%) trajectory. The artery most frequently continued as the first dorsal metatarsal artery (59.2%), followed by the arcuate (23.3%) and lateral tarsal arteries (17.5%). Mean dimensions were 3.05 ± 0.53 mm in diameter and 8.48 ± 1.05 cm in length, indicating generally uniform anatomy with a minority of morphological variations (Table 2).

Table 2: Anatomical and Morphometric Findings of the Dorsalis Pedis Artery (n=103)

Variables	Category	n (%) / Mean ± SD
Presence of DPA	Present	103 (100.0%)
Origin of DPA	Type I – Continuation of Anterior Tibial Artery	83 (80.6%)
	Type II – High Origin from ATA	15 (14.6%)
	Type IV – Double Origin	3 (2.9%)
	Type V – Collateral Replacement	2 (1.9%)
Course of DPA	Normal (Superficial)	90 (87.4%)
	Deep Course	7 (6.8 %)
	Tortuous	6 (5.8 %)
Termination Pattern	First Dorsal Metatarsal Artery	61 (59.2%)
	Arcuate Artery	24 (23.3%)
	Lateral Tarsal Artery	18 (17.5%)
External Diameter (mm)	–	3.05 ± 0.53 (2.02–4.32)
Length (cm)	–	8.48 ± 1.05 (6.27–11.25)

The DPA pulse was palpable in 88.3% of limbs, with only 11.7% showing an absent pulse. A strong association was found between arterial origin and palpability (χ^2 = 28.6, p<0.001), as Type I arteries had the highest detection rate (96.4%) while variant types more frequently lacked a palpable pulse. This moderately strong correlation (Cramer's V = 0.527) indicates that anatomical variation significantly affects clinical pulse detection (Table 3).

Table 3: Association Between Anatomical Variation of the Dorsalis Pedis Artery and Pulse Palpability (n=103)

DPA Types	Palpable, n (%)	Not Palpable, n (%)	Total, n (%)	χ^2 (df)	p-value	Cramer's V
Type I – Continuation of the anterior Tibial Artery	80 (96.4%)	3 (3.6%)	83 (80.6 %)	–	–	–
Type II – High Origin from the Ata	9 (60.0%)	6 (40.0%)	15 (14.6 %)	–	–	–
Type IV – Double Origin	1 (33.3%)	2 (66.7%)	3 (2.9 %)	–	–	–
Type V – Collateral Replacement	1 (50.0%)	1 (50.0%)	2 (1.9 %)	–	–	–
Total	91 (88.3%)	12 (11.7%)	103 (100 %)	28.6 (3)	<0.001*	0.527

* Pearson Chi-square = 28.599, df = 3, p < 0.001 (significant). Cramer's V = 0.527 → moderately strong association between DPA type and pulse palpability

Pulse palpability did not differ significantly by sex or limb side, with both variables showing non-significant χ^2 values. This demonstrates that demographic and laterality factors do not affect the detectability of the dorsalis pedis artery pulse (Table 4).

Table 4: Association Between Pulse Palpability, Sex, and Side (n=103)

Variables	Category	Palpable, n (%)	Not Palpable, n (%)	Total, n (%)	χ^2 (df)	p-value	Cramer's V
Sex	Male	60 (88.2%)	8 (11.8%)	68 (66.0%)	0.003 (1)	0.960	0.005
	Female	31 (88.6%)	4 (11.4%)	35 (34.0%)			

DOI: https://doi.org/10.54393/pjhs.v7i2.3610

Side Examined	Right	35 (89.7%)	4 (10.3%)	39 (37.9%)	0.12 (1)	0.731	0.034
	Left	56 (87.5%)	8 (12.5%)	64 (62.1%)			

* All tests are Pearson Chi-square (2 × 2 tables); Fisher's exact p > 0.05 in both comparisons.

This study demonstrates that the DPA most commonly originates as a Type I vessel with a superficial and consistent course, explaining the high palpability observed in most limbs. In contrast, variant origins were associated with reduced pulse detection, as reflected in markedly lower palpability rates compared with Type I (96.4% vs. 60%, 33.3%, and 50%). This pattern aligns with the significant association between origin type and palpability (χ^2 = 28.6, p<0.001; Cramer's V = 0.527), underscoring the clinical relevance of anatomical variation for vascular assessment and surgical planning. The X-axis shows the four anatomical patterns (Types I, II, IV, and V), while the Y-axis depicts the percentage of limbs with palpable or non-palpable pulses. The clustered bars highlight the markedly higher palpability in Type I arteries compared with the variant types (Figure 1).

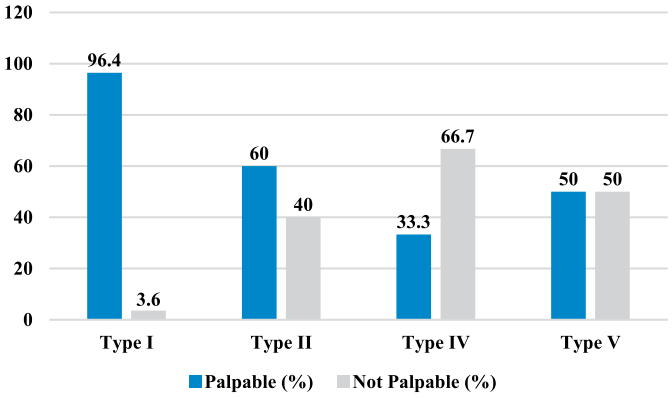

Figure 1: Distribution of DPA Origin Types and Their Corresponding Pulse Palpability in 103 Limbs

DISCUSSION

In this investigation, the most common type was the DPA, which continued from the anterior tibial artery (Type I), accounting for 80.6% of the limbs, while variants (Types II, IV, V) made up about 1 in 5 limbs. This distribution is consistent with recent anatomical studies, which report predominance of the classic pattern while also acknowledging, albeit a smaller minority, variants. In a cadaver-based population-level study, Hemamalini and Manjunatha *et al.* noted alternative sources and courses, with origins from 'textbook' locations, which also carry important implications in the hands of the surgeon [8]. At the case level, vascular imaging continues to reveal DPA arising from the peroneal artery and other unusual configurations, indicating variant anatomy is by no means rare and also complicates surface examination or planning access [9]. Clinical implications from your cohort were the associations in origin type with palpable pulse (χ^2 = 28.6; Cramer's V = 0.527). This aligns with modern teachings that the absence of a DPA pulse does not equate to pathology; clinical appreciation involves both the anatomical and physiological. DPA is identified as a peripheral pulse, and variation in anatomy and technique is warranted [10]. Additionally, Doppler sonography is one of the most palpation-equivalent techniques and is increasingly recommended as a first-line, non-invasive test for vascular assessment of the foot and ankle [11]. Current morphometric values align with established imaging ranges for the distal anterior tibial/DPA segment, confirming suitability for Doppler assessment and distal access procedures. These findings are consistent with modern CT angiography and Doppler criteria used for evaluating pedal vessel caliber and hemodynamics [12, 13]. From a revascularization standpoint, the DPA continues to serve as an important distal target or access point, even as therapeutic strategies evolve. Recent multicenter studies have reported favourable outcomes for popliteal-to-distal and pedal bypasses, as well as newer conduit options that support limb salvage in critical ischemia. Ultrasound-guided pedal access, including via the DPA, is now widely used when antegrade routes are not feasible, with evidence supporting its safety and expanding indications [14]. The angiosome concept further highlights that restoring flow to the DPA and first dorsal metatarsal region can meaningfully affect wound healing, as shown in contemporary perfusion-imaging studies [15, 16]. Current finding that sex and side did not affect palpability fits with current bedside guidance: examination reliability hinges on consistent technique and awareness of anatomic course, with Doppler as a rapid adjunct when edema, obesity, or variant paths obscure signals [10]. In diabetes and foot ulcer care settings where DPA assessment is routine, recent international guidelines emphasize a combined strategy of clinical pulses, Doppler/duplex, and, when needed, advanced imaging to direct revascularization and gauge healing potential [17]. The anatomically based, reconstructively related conclusions can be strengthened further. Modern literature continues to validate the adaptability of the FDMA-based flaps originating from the DPA system to repair the hallux and dorsal foot defects. More recent reviews have also pointed out the utility of briefly described, flow-through, perforator flaps, which take advantage of the pneumatically flow-continuous state of the DPA [18, 19]. These multiple, interconnected strands of anatomy, noninvasive testing, imaging, endovascular/bypass tactics, and flap design justify the need and importance of clinical documentation

DOI: https://doi.org/10.54393/pjhs.v7i2.3610

of DPA variations and their impact on the palpability demonstrated in this study [20]. The dataset includes clinical palpation and Doppler confirmation, exceeding the calculated minimum sample size and improving internal validity; however, the single-center design and lack of universal angiographic mapping may be limitations in generalizability. Future multicenter studies using standardized duplex ultrasound, CT angiography (CTA), or dual-energy CT (DECT) protocols may improve estimates of prevalence and also clarify the hemodynamic and clinical implications of each anatomical variant. Additionally, the use of consecutive participants from the Anatomy and Radiology Departments introduces an element of convenience sampling, which may limit the representativeness of the study population. This study confirms that while the DPA typically continues from the anterior tibial artery, clinically relevant variants occur in about one-fifth of limbs and are associated with reduced pulse palpability. These anatomical differences help explain instances of absent pedal pulses despite otherwise normal perfusion. The findings support current recommendations to integrate palpation with Doppler or advanced imaging when needed, and they provide useful anatomical guidance for decisions involving pedal access, distal bypass, and flap planning.

The single-center design and use of convenience sampling from Anatomy and Radiology departments may limit the representativeness of DPA variant prevalence. Additionally, the absence of routine angiographic mapping restricted detailed hemodynamic correlation for each anatomical variant. Multicenter studies using standardized duplex ultrasound and CT angiography protocols are recommended to better define the prevalence and clinical impact of dorsalis pedis artery variants.

CONCLUSIONS

This study confirms that the DPA most commonly arises as a direct continuation of the anterior tibial artery, with about one-fifth of limbs showing anatomical variants. These variants were strongly linked to reduced pulse palpability, while sex and limb laterality had no meaningful influence. Recognizing such variations is essential for accurate vascular examination and for interpreting Doppler or imaging findings. A clear understanding of DPA anatomy can help avoid misinterpreting absent pulses and support safer planning in reconstructive and vascular procedures of the foot and ankle.

Authors' Contribution

Conceptualization: SK
Methodology: RUJ, MS, AK, MTS
Formal analysis: FS, MS
Writing and drafting: SK, FS, RUJ, AK, SMTS
Review and editing: SK, RUJ, MS, AK, SMTS, FS

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Boman R, Penkala S, Chan RH, Joshua F, Cheung RT. Reliability of Ultrasound Imaging in Examining Integrity and Inflammation in the Dorsalis Pedis Artery. Ultrasound in Medicine and Biology. 2023 Sep; 49(9): 2199-202. doi: 10.1016/j.ultrasmedbio.2023.06.017.

[2] Yavuz U, Celayir A, Karaismailoglu B. Clinical Anatomy of the Foot and Ankle. In Clinical and Radiological Examination of the Foot and Ankle: The Path to Definitive Diagnosis. Singapore: Springer Nature Singapore. 2024 Aug: 33-51. doi: 10.1007/978-981-97-4202-8_3.

[3] Tonogai I, Tsuruo Y, Sairyo K. Implications of Dorsalis Pedis Artery Anatomical Variants for Dorsal Midfoot Surgery. Foot and Ankle International. 2022 Jul; 43(7): 942-7. doi: 10.1177/10711007221081527.

[4] Chalise U, Pradhan A, Dhungel S. Variation in the Branching Pattern of the Dorsalis Pedis Artery: A Cadaveric Study. Nepal Medical College Journal. 2025 Apr; 27(1): 29-33. doi: 10.3126/nmcj.v27i1.77539.

[5] Olonade AA and Tiryakioglu M. Vascular Anomalies in the Course and Branching Pattern of the Dorsalis Pedis Artery: A Case Report. National Journal of Clinical Anatomy. 2023 Apr; 12(2): 115-7. doi: 10.4103/NJCA.NJCA_33_23.

[6] Kaur A. Assessment of Variation in Branching Pattern of Dorsalis Pedis Artery. International Journal of Life Sciences, Biotechnology and Pharma Research. 2023; 12(3).

[7] Modisane O, Naicker J, Myburgh J, Tshabalala Z, Mogale N. Anatomical Study on the Branching Pattern of the Dorsalis Pedis Artery and its Exact Position on the Ankle Joint. 2025 Aug. doi: 10.2139/ssrn.5393555.

[8] Hemamalini and Manjunatha HN. Variations in the Origin, Course and Branching Pattern of Dorsalis

DOI: https://doi.org/10.54393/pjhs.v7i2.3610

Pedis Artery with Clinical Significance. Scientific Reports. 2021 Jan; 11(1): 1448. doi: 10.1038/s41598-020-80555-z.

[9] Johnson M, Lavanga EA, Aziz F, Johnson ML. Unilateral Anomalous Origin of Dorsalis Pedis Artery from Peroneal Artery in a Cadaver. Cureus. 2023 Aug; 15(8). doi: 10.7759/cureus.43414.

[10] Zimmerman B and Williams D. Peripheral pulse. In-Stat Pearls [Internet]. Stat Pearls Publishing. 2023 Apr.

[11] Tehan P, Sommerset J, Rounsley R, Fox M. Commentary: Demystifying Doppler–Revisiting A Vital Diagnostic Tool. Journal of Foot and Ankle Research. 2022 Mar; 15(1): 24. doi: 10.1186/s13047-022-00530-x.

[12] Keddie D, Abdulrehman Y, Shiau G. Reporting Lower Extremity CT Angiography for Treatment Planning. Diagnostic and Interventional Imaging. 2022 Sep; 103(9): 387-93. doi: 10.1016/j.diii.2022.06.010.

[13] Liang HL. Doppler Flow Measurement of Lower Extremity Arteries Adjusted by Pulsatility Index. American Journal of Roentgenology. 2020 Jan; 214(1): 10-7. doi: 10.2214/AJR.19.21280.

[14] Abdul-Malak OM, Semaan DB, Madigan MC, Sridharan ND, Chaer RA, Siracuse JJ *et al.* Midterm Outcomes and Predictors of Failure of Lower Extremity Bypass to Para-Malleolar and Pedal Targets. Annals of Vascular Surgery. 2024 Sep; 106: 227-37. doi: 10.1016/j.avsg.2024.04.002.

[15] Kuroki MT, Parikh UM, Chandra V. How I Do It: Pedal Access and Pedal Loop Revascularization for Patients with Chronic Limb-Threatening Ischemia. Journal of Vascular Surgery Cases, Innovations and Techniques. 2023 Sep; 9(3): 101236. doi: 10.1016/j.jvscit.2023.101236.

[16] Shao J, Ma J, Lai Z, Yu X, Li K, Xu L *et al.* Impaired Pedal Arch Affects the Treatment Effect in Patients with Single Tibial Artery Revascularization Demonstrated by Intraoperative Perfusion. Quantitative Imaging in Medicine and Surgery. 2022 Jun; 12(6): 3204. doi: 10.21037/qims-21-801.

[17] Schaper NC, Netten JJV, Apelqvist J, Bus SA, Fitridge R *et al.* IWGDF Guidelines on the Prevention and Management of Diabetes-Related Foot Disease. 2023. doi: 10.1002/dmrr.3657.

[18] Saboye M, Majchrzak A, d'Andréa G, Bronsard N, Camuzard O, Lupon E. The First Dorsal Metatarsal Artery Perforator Flap: A Description and Anatomical Study. Journal of Clinical Medicine. 2025 Jun; 14(12): 4136. doi: 10.3390/jcm14124136.

[19] Mei W, Tang Q, Li C, Wang S, Zhou Q, Xu L *et al.* Improving Lower-Extremity Artery Depiction and Diagnostic Confidence Using Dual-Energy Technique and Popliteal Artery Monitoring in Dual-Low Dose CT Angiography. Scientific Reports. 2025 May; 15(1): 16143. doi: 10.1038/s41598-025-97868-6.

[20] Ren BW, Boman R, Chan RH, Cheung RT, Penkala S, Joshua F *et al.* Identification and Quantification of Precursory Changes of Rheumatoid Vasculitis in the Dorsalis Pedis Artery. Ultrasound in Medicine and Biology. 2024 Nov; 50(11): 1661-8. doi: 10.1016/j.ultrasmedbio.2024.06.012.

DOI: https://doi.org/10.54393/pjhs.v7i2.3348

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Platelet Rich Plasma Dressing Versus Normal Saline Dressing in the Management of Chronic Diabetic Wounds

Muhammad Qasim[1], Khalil Ahmad[1], Mudassar Malik[1], Zain Himayoun[1], Muhammad Saleem[1], Muhammad Irfan Jamil[2*] and Adeel Ahmed[2]

[1]Department of General Surgery, Gulab Devi Hospital, Lahore, Pakistan
[2]Department of General Medicine, Lahore General Hospital, Lahore, Pakistan

ARTICLE INFO

Keywords:
Chronic Diabetic Wounds, Platelet-Rich Plasma, Wound Healing, Randomized Controlled Trial

How to Cite:
Qasim, M., Ahmad, K., Malik, M., Himayoun, Z., Saleem, M., Jamil, M. I., & Ahmed, A. (2026). Platelet Rich Plasma Dressing Versus Normal Saline Dressing in the Management of Chronic Diabetic Wounds: PRP Versus Saline Dressing in Chronic Diabetic Wounds. Pakistan Journal of Health Sciences, 7(2), 14-19. https://doi.org/10.54393/pjhs.v7i2.3348

***Corresponding Author:**
Muhammad Irfan Jamil
Department of General Medicine, Lahore General Hospital, Lahore, Pakistan
irfanravian51@gmail.com

Received Date: 16th July, 2025
Revised Date: 11th October, 2025
Acceptance Date: 1st January, 2026
Published Date: 28th February, 2026

ABSTRACT

Platelet-rich plasma (PRP) has emerged as a promising modality in wound healing due to its concentration of platelets and growth factors that stimulate tissue repair, angiogenesis, and epithelialization. **Objectives:** To compare the efficacy of PRP dressings with normal saline dressings in the management of chronic diabetic ulcers. **Methods:** This randomized controlled trial was conducted at the Department of Surgery, Gulab Devi Hospital, Lahore, from January 2025 to June 2025. After ethical approval, 156 patients with chronic diabetic wounds were recruited using consecutive sampling and randomly allocated into PRP and NS dressing groups (1:1). Interventions were administered over six weeks. Baseline and weekly wound area and healing status were assessed. Data were analyzed using SPSS version 26. A confidence level of 95% was used for all statistical analyses. Results were considered statistically significant at a p-value ≤0.05. **Results:** A total of 156 patients were enrolled, with a mean age of 39.05 ± 9.75 years and mean BMI of 25.85 ± 2.30 kg/m^2. Males comprised 63.5% of the participants, and 53.2% were aged 41–60 years. Complete healing was achieved in 92.3% of PRP patients compared to 61.5% in the NS group (p<0.001). PRP significantly reduced healing time (3.62 ± 1.25 vs. 4.85 ± 1.27 weeks; p<0.001) and post-treatment infections (7.7% vs. 23.1%; p=0.008), with no amputations in the PRP group. **Conclusions:** PRP dressing offers a more effective and safer alternative to conventional care in managing chronic diabetic wounds, promoting timely healing and supporting its inclusion in clinical wound care strategies.

INTRODUCTION

Chronic diabetic wounds, particularly diabetic foot ulcers, are an important and growing global health problem, with especially high prevalence in countries like Pakistan [1]. Globally, approximately 15% of diabetic individuals will develop foot ulcers in their life, and up to 25% of these cases may progress to lower limb amputation if not effectively managed [2]. The prevalence of diabetic foot ulcers in Pakistan is 12.16%, rising to 19.54% in studies from 2011–2022 [3]. In Punjab, the prevalence is 16.83%, higher in urban (17.96%) than rural (13.91%) areas, and peaks at 66.67% in individuals aged 75 and above [4]. These wounds are featured by impaired healing due to presence of neuropathy, ischemia, and immune dysfunction, leading to persistent inflammation and deficient tissue regeneration [5]. Standard wound care in DFUs generally comprises debridement, infection control, pressure offloading, and moisture-retaining dressings, with normal saline (NS) being one of the most commonly used solutions. Although NS is safe, affordable, and facilitates autolytic debridement, it lacks intrinsic biological activity and does not directly contribute to the wound healing cascade. This limitation often results in delayed granulation and epithelialization, particularly in patients with extensive or ischemic wounds. In recent years, autologous platelet-rich

DOI: https://doi.org/10.54393/pjhs.v7i2.3348

plasma (PRP) has originated as an adjunctive treatment in wound management. PRP is a plasma fraction enriched with platelets and their associated growth factors [6, 7]. These molecules play an important role in wound healing by promoting angiogenesis, fibroblast migration, matrix remodeling, and epithelial regeneration. In addition, PRP may exert antimicrobial and anti-inflammatory effects, which further enhance its therapeutic utility [8, 9]. Multiple randomized controlled trials and systematic reviews have reported favorable outcomes with PRP application in chronic wound settings. Healing rates, time to epithelialization, and wound contraction have all shown statistically significant improvements with PRP compared to NS dressing. For instance, Elsaid *et al.* demonstrated a mean healing time of 10.9 ± 3.4 weeks in the PRP group versus 13.5 ± 3.4 weeks in the saline group (p=0.01), and Narayanan *et al.* noted that the PRP group demonstrated an average healing duration of 3.17 weeks versus 4.56 weeks in the NS group ($p < 0.001$) [10, 11]. A study by Afzal Ali *et al.* documented a decrease in wound area and faster granulation tissue formation in PRP-treated ulcers compared to saline dressings [12]. Furthermore, a meta-analysis by Li *et al.* noted that PRP was linked with higher odds of complete healing at 8 and 12 weeks, without increasing the incidence of adverse events [13]. Pakistan carries one of the highest global burdens of diabetes, with foot ulcers. Patients frequently present with poorly controlled disease, recurrent infections, and high amputation risk, while access to advanced wound care remains limited [14, 15].

Although PRP has shown favorable outcomes in international studies, evidence from South Asia is scarce and not readily generalizable due to differences in healthcare systems and patient profiles. This trial was therefore designed to provide region-specific data to support cost-effective management of chronic diabetic wounds. This research seeks to contribute robust evidence to support optimized and individualized wound care strategies for diabetic patients.This study aims to compare the wound healing efficacy of PRP dressing versus NS dressing in patients with chronic diabetic wounds and to assess time to complete healing and evaluate complication rates(infection, amputation, failed healing).

METHODS

A randomized controlled trial (ID: NCT06867328) was carried out at the Department of Surgery, Gulab Devi Hospital, Lahore, from January 2025 to June 2025. Ethical approval was taken from the Institutional Ethical Review Board of Gulab Devi Hospital, Lahore (Ref. No. AAMC/IRB/EA/18/2025). A non-probability consecutive sampling technique was used to enroll eligible patients presenting with chronic diabetic wounds. The sample size was measured by assuming a 5% level of significance, 90% power, an anticipated wound healing rate of 86.11% in the PRP group and 63.89% in the normal saline group [16]. A total of 170 patients were initially recruited. Fourteen patients did not complete the study due to withdrawal of consent or missed follow-up visits and were excluded from analysis. Thus, 156 patients who completed all planned follow-up visits were included in the final analysis. Patients aged 18 to 60 years of either gender with DM and a chronic diabetic foot ulcer of at least 6 weeks' duration, measuring 2–10 cm^2 post-debridement and classified as Wagner grade II to IV, were included. Patients with ulcer-site infection or gangrene, prior PRP or grafting on the same ulcer, uncontrolled comorbidities (heart failure, dialysis-dependent renal disease, hepatic dysfunction), recent immunosuppressive use, bleeding disorders, tendon or bone involvement, malignancy, or autoimmune disease were excluded. After obtaining informed consent, all participants were assigned to one of two groups using a computer-generated simple randomization technique: the PRP dressing group or the normal saline (NS) dressing group. Allocation concealment was ensured using sealed, opaque envelopes opened at the time of intervention. Baseline demographic and clinical variables, including age, gender, duration of diabetes, HbA1c, BMI, ulcer type, co-morbidities, wound duration, wound area, and Wagner grade, were documented before initiating treatment. In the PRP group, autologous PRP was prepared using a standardized two-step centrifugation technique to reduce variability observed in previous studies. Venous blood (20 mL) was drawn from each patient into tubes containing acid citrate dextrose anticoagulant in a 9:1 ratio. The first centrifugation was performed at 1,500 rpm for 10 minutes to separate the plasma from red cells. The supernatant plasma was then subjected to a second centrifugation at 3,500 rpm for 15 minutes to concentrate the platelets. The upper platelet-poor fraction was discarded, and the lower one-third containing the platelet-rich plasma was collected. The obtained PRP was applied without the use of exogenous activators: approximately half was infiltrated around the wound margins, while the remainder was spread evenly over the wound bed, followed by sterile gauze placement. This double-spin protocol was consistently applied for all PRP-treated patients to ensure standardization and reproducibility. The PRP dressing was repeated twice weekly for a total of six weeks, provided there was no sign of infection or adverse reaction. In the NS group, sterile gauze soaked in normal saline was applied to the wound, ensuring full coverage of the wound bed. Dressings were changed daily or as needed based on wound exudate. In both groups, wounds were cleaned and debrided under aseptic technique before dressing

DOI: https://doi.org/10.54393/pjhs.v7i2.3348

application. All patients received standard offloading measures appropriate to their ulcer location and regular monitoring of glycemic control as part of routine care. Wound healing progress was monitored weekly for six consecutive weeks. At each follow-up visit, the wound was cleaned, assessed, and the area was measured using a sterile disposable ruler. Healing status was documented as either "Healed" (formation of pinkish granulation tissue completely over the wound, declared by the consultant surgeon through visual inspection) or "Not Healed". The duration required to achieve complete healing and complications, including signs of local infection (increased discharge, redness, foul odor), need for amputation, and failure to heal (no significant reduction in wound area by week six), were also monitored. Statistical analysis was conducted using SPSS 26.0. Continuous variables were expressed as mean and standard deviation and compared using an independent samples t-test, while categorical variables were summarized as frequencies and percentages and analyzed by chi-square test. Effect sizes were reported as mean differences for continuous data and odds ratios (OR) with 95% confidence intervals (CI) for categorical outcomes. Healing status and wound area over six weeks were analyzed using repeated measures ANOVA and chi-square tests. A p-value ≤0.05 was considered significant (Figure 1).

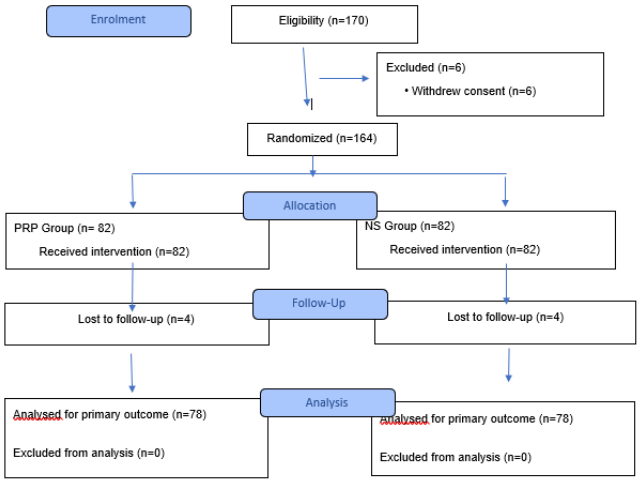

Figure 1: CONSORT-Style Flow Diagram

RESULTS

In this study, 156 patients were included with an average age of 38.55 ± 10.74 years in the PRP group and 39.56 ± 8.60 years in the NS group (p=0.517). A greater proportion of participants in the NS group were aged 18–40 years (65.4% vs. 46.2%, p = 0.016), whereas the PRP group had more individuals aged 41–60 years (53.8% vs. 34.6%). The average duration of diabetes was lower in the PRP group (8.27 ± 2.06 years) compared to the NS group (9.50±2.65 years; p=0.001), and the PRP group also demonstrated better glycemic control with a lower mean HbA1c (7.84 ± 0.41 vs. 8.03 ± 0.45; p=0.006). Wound duration was significantly shorter in the PRP group (7.44 ± 1.59 weeks) compared to the NS group (8.33 ± 1.76 weeks; p=0.001) (Table 1).

Table 1: Comparison of Baseline Characteristics Between PRP and Normal Saline Groups

Variables	Subgroup	PRP Group	NS Group	Test Statistic (χ^2 / t)	Effect Size (OR / Mean Diff. [95% CI])	p-value
Age Group (years)	18–40	36 (46.2%)	51 (65.4%)	χ^2=5.847	OR=0.454 [0.238–0.865]	0.016
	41–60	42 (53.8%)	27 (34.6%)			
Gender	Male	48 (61.5%)	51 (65.4%)	χ^2=0.249	OR=0.847 [0.441–1.627]	0.618
	Female	30 (38.5%)	27 (34.6%)			
Type of Ulcer	Neuropathic	54 (69.2%)	57 (73.1%)	χ^2=0.281	OR=0.829 [0.414–1.659]	0.596
	Non-neuropathic	24 (30.8%)	21 (26.9%)			
Hypertension	Yes	33 (42.3%)	27 (34.6%)	χ^2=0.975	OR=1.385 [0.725–2.647]	0.323
Ischemic Heart Disease	Yes	24 (30.8%)	15 (19.2%)	χ^2=2.769	OR=1.867 [0.890–3.914]	0.096
Smoking	Yes	21 (26.9%)	26 (33.3%)	χ^2=0.761	OR=0.737 [0.371–1.465]	0.383
Wagner Grade	II	45 (57.7%)	48 (61.5%)	χ^2= 1.430	–	0.489
	III	21 (26.9%)	15 (19.2%)			
	IV	12 (15.4%)	15 (19.2%)			
Age (years)	–	38.55 ± 10.74	39.56 ± 8.60	t = -0.650	-1.013 [-4.090–2.064]	0.517
Duration of Diabetes (years)	–	8.27 ± 2.06	9.50 ± 2.65	t = -3.236	-1.231 [-1.982–-0.479]	0.001
BMI (kg/m^2)	–	25.89 ± 2.16	25.81 ± 2.43	t = 0.192	0.071 [-0.656–0.797]	0.848
HbA1c (%)	–	7.84 ± 0.41	8.03 ± 0.45	t = -2.801	-0.191 [-0.325–-0.056]	0.006
Wound Duration (weeks)	–	7.44 ± 1.59	8.33 ± 1.76	t = -3.337	-0.897 [-1.429–-0.366]	0.001
Wound Area (cm^2)	–	6.67 ± 2.52	7.09 ± 2.57	t = -1.038	-0.423 [-1.228–0.382]	0.301

Chi-square test was used for dichotomous variables, and the Independent Samples t-test was applied for continuous variables. A p-value <0.05 was considered statistically significant

Repeated measures ANOVA showed a significant effect of time on wound area reduction (F4.003, 616.529 = 364.275, p<0.001,

DOI: https://doi.org/10.54393/pjhs.v7i2.3348

η^2=0.703), indicating progressive healing in both groups. A significant group effect (F1,1541=14.734, p<0.001, η^2=0.087) and a group × time interaction (F4.003,616.529=6.621, p<0.001, η^2=0.041) confirmed that PRP-treated wounds healed faster than NS-treated wounds (Table 2).

Table 2: Results of Repeated Measures ANOVA for Wound Area Over Six Weeks

Effects	DF	F	p-value	Partial η^2	Interpretation
Time (Week effect)	4.003, 616.529	364.275	<0.001	0.703	Wound area decreased significantly across weeks
Group (PRP vs NS)	1, 154	14.734	<0.001	0.087	PRP wounds were consistently smaller than NS wounds
Time × Group	4.003, 616.529	6.621	<0.001	0.041	PRP showed a faster healing trajectory compared with NS

The PRP group consistently demonstrated higher healing rates across all weeks, with statistically significant differences emerging from Week 3 onward. In Week 1, healing was observed in 7.7% (PRP) versus 3.8% (NS) (p=0.303). Week 2 showed a non-significant trend favoring PRP (23.1% vs. 11.5%, p=0.057). From Week 3, healing was higher in PRP group: 46.2% vs. 23.1% (p=0.002), 69.2% vs. 38.5% in Week 4 (p<0.001), 84.6% vs. 53.8% in Week 5 (p<0.001), and 92.3% vs. 61.5% in Week 6 (p<0.001), confirming superior efficacy of PRP (Figure 2).

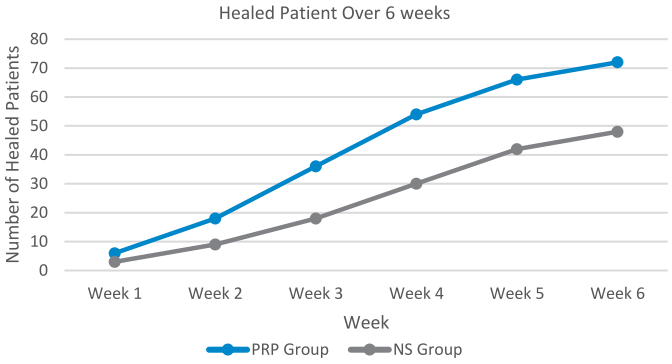

Figure 2: Comparison of Healing Status (Healed/Not Healed) Between PRP and NS Groups Over 6 Weeks

At final follow-up, complete healing was achieved in 92.3% of patients in the PRP group versus 61.5% in the NS group (χ^2=20.800, OR=7.500 [95% CI: 2.902–19.384], p<0.001). The average time to wound healing was shorter in the PRP group at 3.62 ±1.25 weeks compared to 4.85 ±1.27 weeks in the NS group (t=–6.099, MD=–1.231 [95% CI: –1.629 to –0.832], p<0.001) (Table 3).

Table 3: Comparison of Final Healing Status and Duration to Wound Healing Between PRP and NS Groups

Variables	PRP Group	NS Group	χ^2 / t-value	Effect Size [95% CI]	p-value
Complete healing, n (%)(yes)	72 (92.3%)	48 (61.5%)	χ^2= 20.800	OR=7.500 [2.902 –19.384]	<0.001
Mean healing duration (weeks)	3.62 ± 1.25	4.85 ± 1.27	t= -6.099	MD =-1.231 [-1.629 to -0.832]	<0.001

Chi-square test was used for dichotomous variables, and the Independent Samples t-test was applied for continuous variables. A p-value < 0.05 was considered statistically significant

Post-treatment complications were lower in the PRP group than in the NS group. Infection occurred in 6 (7.7%) PRP-treated patients versus 18 (23.1%) in the NS group (p=0.008). Amputations were reported in 6 (7.7%) patients from the NS group, with no cases observed in the PRP group (p=0.012). Failed healing was markedly more prevalent in the NS group (30; 38.5%) than in the PRP group (6; 7.7%) (p<0.001) (Figure 3).

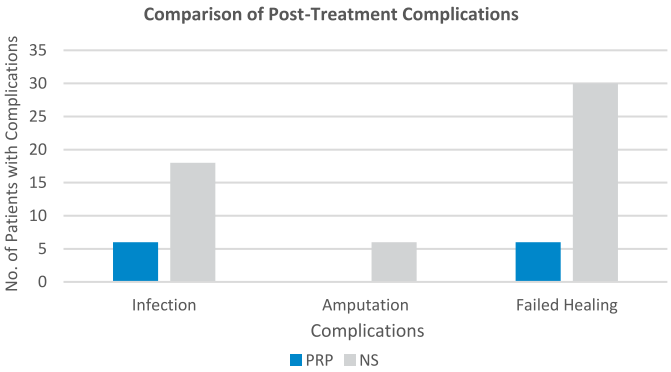

Figure 3: Comparison of Post-Treatment Complications Between PRP and Normal Saline Groups

DISCUSSION

This study of 156 patients demonstrates a significantly higher rate and earlier onset of wound healing, reduced complications, and shorter healing time associated with PRP dressing, reinforcing its therapeutic superiority. Age distribution differed significantly (p=0.016), with more younger patients in the NS group, aligning with previous studies [10]. Gender distribution was balanced (p=0.618), consistent with earlier reports [17]. In terms of wound progression, PRP demonstrated a consistent and significantly greater reduction in wound area beginning from Week 4 onwards, culminating in a mean wound size of 0.85 ± 0.67 cm^2 at Week 6 compared to 1.65 ± 0.88 cm^2 in the NS group. This progressive decline in wound dimensions parallels findings from previous studies [12, 18, 19]. Complete healing by Week 6 was observed in 92.3% of PRP-treated participants versus 61.5% in the NS group, with an odds ratio of 7.5 (p<0.001). These outcomes align with meta-analytical data reporting higher odds of complete healing with PRP [13, 20]. The mean healing duration was significantly shorter in the PRP group (3.62 ± 1.25 weeks) compared to 4.85 ± 1.27 weeks in the NS group [11, 21]. Post-treatment complications were markedly lower in the PRP group. Infections occurred in only 7.7% of PRP patients versus 23.1% in the NS group (p=0.008), with zero amputations in PRP versus 7.7% in NS (p=0.012). Failed healing was significantly more frequent in NS (38.5%) than PRP (7.7%), indicating a protective role of PRP not only in

DOI: https://doi.org/10.54393/pjhs.v7i2.3348

promoting healing but also in preventing adverse outcomes [12, 20]. The trajectory of weekly healing rate and cumulative healed cases throughout the 6-week follow-up further supports the superior regenerative effect of PRP. Healing rates were significantly higher from Week 3 onwards, with statistically significant odds ratios ranging from 2.857 to 7.500 [19]. This study's strengths include its randomized controlled design, adequate sample size, and weekly follow-up assessments, enabling precise evaluation of wound healing progression.

Limitations include the single-center setting, restricting generalizability, and a lack of blinding, which may introduce observer bias. Additionally, histological assessment of wound tissue and long-term follow-up were not performed. Future studies should incorporate multicenter designs, larger populations, and explore cellular mechanisms of PRP. Comparative evaluations with other advanced dressings and extended outcome tracking would further substantiate the clinical utility and cost-effectiveness of PRP therapy.

CONCLUSIONS

In conclusion, platelet-rich plasma (PRP) dressings were more effective than normal saline (NS) dressings in the management of chronic diabetic wounds. PRP accelerated wound area reduction, shortened healing time, and lowered complication rates compared with NS. These findings support the clinical utility of PRP as a superior dressing method for chronic diabetic ulcers and highlight its potential integration into standard wound care protocols.

Authors' Contribution

Conceptualization: MQ, KA, MM, ZH
Methodology: MQ, KA, MM, ZH, MS
Formal analysis: MQ, KA, MM, ZH, MS, MIJ, AA
Writing and drafting: MQ, KA, MM, ZH, MS, MIJ, AA
Review and editing: MQ, KA, MM, ZH, MS, MIJ, AA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Ahmed M, Reffat SA, Hassan A, Eskander F. Platelet-Rich Plasma for the Treatment of Clean Diabetic Foot Ulcers. Ann Vascular Surgery. 2017 Aug; 38: 206-11. doi: 10.1016/j.avsg.2016.04.023.

[2] Sidhu AS, Harbuzova V. Emerging Technologies for the Management of Diabetic Foot Ulceration: A Review. Frontiers in Clinical Diabetes and Healthcare. 2024 May; 5: 1440209. doi: 10.3389/fcdhc.2024.1440209.

[3] Akhtar S, Ali A, Ahmad S, Khan MI, Shah S, Hassan F, *et al.* The Prevalence of Foot Ulcers in Diabetic Patients in Pakistan: A Systematic Review and Meta-Analysis. Frontiers in Public Health. 2022 Oct; 10: 1017201. doi: 10.3389/fpubh.2022.1017201.

[4] Akhtar S, Latif M, Ahmed OS, Sarwar A, Alina A, Khan MI, *et al.* Prevalence of Foot Ulcers in Diabetic Patients in Punjab, Pakistan. Frontiers in Public Health. 2022 Aug; 10: 967733. doi: 10.3389/fpubh.2022.967733.

[5] Menke NB, Ward KR, Witten TM, Bonchev DG, Diegelmann RF. Impaired Wound Healing. Clinical Dermatology. 2007 Jan-Feb; 25(1): 19-25. doi: 10.1016/j.clindermatol.2006.12.005.

[6] Everett E, Mathioudakis N. Update on Management of Diabetic Foot Ulcers. Annals of the New York Academy of Sciences. 2018 Jan; 1411(1): 153-65. doi: 10.1111/nyas.13569.

[7] Chicharro-Alcántara D, Rubio-Zaragoza M, Damiá-Giménez E, Carrillo-Poveda JM, Cuervo-Serrato B, Peláez-Gorrea P, *et al.* Platelet Rich Plasma: New Insights for Cutaneous Wound Healing Management. Journal of Functional Biomaterials. 2018 Jan; 9(1): 10. doi: 10.3390/jfb9010010.

[8] Xiao H, Chen X, Liu X, Wen G, Yu Y. Recent Advances in Decellularized Biomaterials for Wound Healing. Materials Today Bio. 2023 Apr; 19: 100589. doi: 10.1016/j.mtbio.2023.100589.

[9] Veith AP, Henderson K, Spencer A, Sligar AD, Baker AB. Therapeutic Strategies for Enhancing Angiogenesis in Wound Healing. Advanced Drug Delivery Reviews. 2019 Jun; 146: 97-125. doi: 10.1016/j.addr.2018.09.010.

[10] Elsaid A, El-Said M, Emile S, Youssef M, Khafagy W, Elshobaky A, *et al.* Randomized Controlled Trial on Autologous Platelet-Rich Plasma Versus Saline Dressing in Treatment of Non-Healing Diabetic Foot Ulcers. World Journal of Surgery. 2020 Apr; 44(4): 1294-301. doi: 10.1007/s00268-019-05316-0.

[11] Narayanan L, K K, T JV. Autologous Platelet Rich Plasma Dressing Versus Normal Saline Dressing in Diabetic Foot Management. International Journal of Pharmaceutical and Clinical Research. 2023; 15(4): 237-42.

[12] Afzal Ali MF, Palaniappan NK, Chellappa PM. Effectiveness of Autologous Platelet-Rich Plasma Dressing in Healing Chronic Diabetic Foot Ulcers in Comparison with Saline Dressing: A Randomized Controlled Study. Journal of Current Research in

DOI: https://doi.org/10.54393/pjhs.v7i2.3348

Science and Medicine. 2023; 9(2): 61-6. doi: 10.4103/jcrsm.jcrsm_69_22.

[13] Li S, Xing F, Yan T, Zhang S, Chen F. The Efficiency and Safety of Platelet-Rich Plasma Dressing in the Treatment of Chronic Wounds: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Journal of Personalized Medicine. 2023 Feb; 13(3): 430. doi: 10.3390/jpm13030430.

[14] Khan TM, Asghar O, Sadiqa A, Ishaq Z, Tahir MJ, Ullah I, *et al*. Predisposing Factors of Diabetic Foot Amputation among the Diabetic Patients in a Tertiary Care Hospital. International Surgery Journal. 2022 May; 9(5): 794-800. doi: 10.18203/2349-2902.isj20220937.

[15] Arif A, Malik NM, Bhatti AM, Sohail A, Riaz B, Imtiaz MS, *et al.* The Impact of Knowledge, Perception on the Major Amputation in People with Diabetic Foot Ulcers. Pakistan Armed Forces Medical Journal. 2022 Dec; 72(6): 2126-9. doi: 10.51253/pafmj.v72i6.7398.

[16] Orban YA, Soliman MAE, Hegab YH, Alkilany MM. Autologous Platelet-Rich Plasma vs Conventional Dressing in the Management of Chronic Diabetic Foot Ulcers. Wounds. 2022 Jan; 34(1): 36-42. doi: 10.25270/wnds/2022.3642.

[17] Rajendran S, Thiyagarajan M, Balaji Singh K, Navrathan N. A Comparative Study on the Effect of Platelet Rich Plasma vs Conventional Dressing in Healing Rate of Chronic Diabetic Ulcers. Biomedicine. 2021 Dec; 41(4): 849-54. doi: 10.51248/.v41i4.121.

[18] Devesvar MV, Shetty SK, Ramesh KS. Comparative Study between Platelet-Rich Plasma, Platelet-Derived Growth Factor Gel, and Normal Saline Dressing in Chronic Ulcer Healing. Annals of African Medicine. 2025; 24(4): 406-14. doi: 10.4103/aam.aam_235_24.

[19] Das S, Kumar S, Pandey SK, Kumar A, Kumar N, *et al.* Comparison between Topical Platelet Rich Plasma and Normal Saline Dressing, in Conjunction with Total Contact Casting in Treatment of Diabetic Foot Ulcer: A Randomized Controlled Trial. Annals of Medicine and Health Sciences Research. 2024; 14: 995-1000. doi: 10.4103/ijpmr.ijpmr_43_24.

[20] El-Mabood ESAA, Ali HE. Platelet-Rich Plasma Versus Conventional Dressing: Does This Really Affect Diabetic Foot Wound-Healing Outcomes? Egyptian Journal of Surgery. 2018; 37(4): 920-5. doi: 10.4103/ejs.ejs_83_17.

[21] Gade RR, VR M, Inamdar P, *et al.* A Comparative Study between Platelet Rich Plasma and Conventional Dressing in Chronic Non-Healing Leg Ulcers. International Surgery Journal. 2020 Mar; 7(3): 751-5. doi: 10.18203/2349-2902.isj20200817.

DOI: https://doi.org/10.54393/pjhs.v7i2.3651

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Role of Intravenous Dexmedetomidine for Attenuation of Hemodynamic Response to Laryngoscopy and Intubation in Controlled Hypertensive Patients: A Prospective Cohort Study

Areej Saeed[1*], Syed Muhammad Abbas[1], Muhammad Qamar Abbas[1], Shakeel Malik[1], Vijai Kumar[1] and Sagar Khurana[1]

[1]Department of Anesthesia and Pain Management, Sindh Institute of Urology and Transplantation, Karachi, Pakistan

ARTICLE INFO

Keywords:
Dexmedetomidine, Hemodynamics, Laryngoscopy, Intubation, Intratracheal, Hypertension

How to Cite:
Saeed, A., Abbas, S. M., Abbas, M. Q., Malik, S., Kumar, V., & Khurana, S. (2026). Role of Intravenous Dexmedetomidine for Attenuation of Hemodynamic Response to Laryngoscopy and Intubation in Controlled Hypertensive Patients: A Prospective Cohort Study: Intravenous Dexmedetomidine: Laryngoscopy and Intubation in Controlled Hypertensive Patients. Pakistan Journal of Health Sciences, 7(2), 20-25. https://doi.org/10.54393/pjhs.v7i2.3651

***Corresponding Author:**
Areej Saeed
Department of Anesthesia and Pain Management, Sindh Institute of Urology and Transplantation, Karachi, Pakistan
areejsk20@gmail.com

Received Date: 14th November, 2025
Revised Date: 23rd December, 2025
Acceptance Date: 8th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Due to sympathetic stimulation, laryngoscopy and endotracheal intubation are known to cause brief but noticeable elevations in blood pressure and heart rate, which can be dangerous for hypertensive individuals. It has been demonstrated that the specific α2-adrenergic agonist dexmedetomidine reduces these reactions. **Objectives:** To evaluate whether intravenous dexmedetomidine could effectively reduce hemodynamic reactions to laryngoscopy and intubation in patients with controlled hypertension. **Methods:** This prospective cohort study was carried out at Sindh Institute of Urology and Transplantation (SIUT) and used a non-probability consecutive sampling technique for six months from January 1, 2025, to June 30, 2025. Eligible were ASA II patients with high blood pressure who had been planned for elective surgery while under the influence of general anesthesia. Individuals were randomly assigned to receive either a placebo (20 mL normal saline) or dexmedetomidine (0.5 µg/kg diluted to 20 mL in saline) ten minutes before induction. Repeated-measures ANOVA and the Student's t-test were used to examine the data; $p \leq 0.05$ was deemed significant. **Results:** The groups' baseline characteristics were similar. When compared to control, dexmedetomidine significantly reduced the increase in HR and SBP following laryngoscopy and intubation ($p < 0.001$ at all post-intubation intervals). Bradycardia (5.7%) and hypotension (2.9%) were rare but clinically treatable adverse effects. **Conclusions:** In hypertensive patients, intravenous dexmedetomidine (0.5 µg/kg) administered as a single pre-induction dosage is safe and efficient in reducing the hemodynamics of laryngoscopy and intubation while also enhancing cardiovascular stability throughout induction.

INTRODUCTION

Laryngoscopy and tracheal intubation are the tests that should also be conducted during general anesthesia, but which are also related to the extreme sympathetic reaction [1, 2]. The consequent outcome of such a reflex surge is an acute rise in heart rate (HR), systolic and diastolic blood pressure (SBP, DBP), as well as an increase in circulating catecholamine. Although these hemodynamic changes are tolerated by most healthy people, they expose patients with underlying cardiovascular or hypertension to the risk of myocardial ischemia, arrhythmias, left ventricular failure, or cerebrovascular accidents. The primary concern in the practice of anesthetics that must be attained to maintain cardiovascular stability in airway manipulation is the attenuation of these pressor reflexes [3]. There are various pharmacological interventions that have been tried over the years, and these are opioids, beta-blockers, calcium channel blockers, vasodilators, and local anesthetics [4-6]. Nevertheless, these drugs are not

DOI: https://doi.org/10.54393/pjhs.v7i2.3651

always effective, and the majority of them have dose effects, including bradycardia, hypotension, or slow recuperation. A new drug, dexmedetomidine, a robust selective agonist that acts on the 2 adrenergic receptors, is one of the most promising drugs due to its dose-dependent sedation, anxiolysis, sympatholytic effects, and minimal respiratory depression [7, 8]. Dexmedetomidine has a central locus coeruleus in the brainstem to counter sympathetic discharge and norepinephrine discharge, which results in a regulated drop in HR and blood pressure [9, 10]. Several randomized controlled trials and meta-analyses that have been performed over the recent decade have found that the pre-induction routine of dexmedetomidine is effective in counteracting the tachycardic and hypertensive effects of intubation [11, 12]. Nonetheless, their application can sometimes lead to bradycardia or hypotension, and there are still inconsistencies in the best dosage schedule, particularly in patients with regulated hypertension, a category that is especially susceptible to the exaggeration of pressor reactions during laryngoscopy [13, 14].

Although extensive data have been collected in normotensive or mixed patients, large-scale studies on the target population, namely controlled hypertensive people, are quite scarce. Since there is the possibility of overstimulation of sympathetic activity in such patients, the effectiveness of dexmedetomidine and its safety profile in this patient group need to be evaluated further. Controlled hypertension patients are a high-risk population in which peri-intubation hemodynamic surges may have severe clinical implications. The sympatholytic and cardioprotective properties of dexmedetomidine could provide a middle ground between these responses without affecting respiratory activity or hemodynamic stability. Nevertheless, the best dose and infusion rate for hypertensive patients is unclear. The current research was conducted to compare the effect of intravenous dexmedetomidine on the hemodynamic response to laryngoscopy and endotracheal intubation in patients with controlled hypertension.

METHODS

A prospective cohort study was conducted at the Department of Anesthesiology in the Sindh Institute of Urology and Transplantation (SIUT) from January 1st, 2025, to June 30th, 2025. The SIUT Ethical Review Committee (ERC) granted ethical approval, with approval number SIUT-ERC-2024/A-488. Before their involvement in the study, all individuals provided written informed consent. The sample size was calculated using Open Epi Version 3.01 for comparing two means, with an expected heart rate reduction of 7.04%, an estimated SD of 8 beats/min, alpha = 0.05, and power = 80%, assuming equal group sizes [15]. The formula used was $n=((Z1_{-\alpha/2}+Z_{1-\beta})^2\times2\times SD^2)/\Delta^2$, where Δ represents the expected group difference. To account for potential dropouts, 35 participants per group were recruited, totaling 70 participants. The method of non-probability consecutive sampling was utilized to select the eligible participants until the necessary sample size was obtained. The patients who were aged 20-70 years, who had controlled hypertension under the antihypertensive therapy, and who were ASA II were included [14]. Hypertension was recognized as a measurement of systolic blood pressure surpassing 140 mmHg or diastolic blood pressure over 90 mmHg, which was sufficiently controlled with medication. The exclusion criteria were severe cardiac arrhythmias, a history of myocardial infarction, severe valvular heart disease, uncontrolled diabetes, severe hepatic or renal dysfunction, use of beta-blockers, pregnancy, known allergy to study drugs, and an expected difficult airway. Baseline monitoring included non-invasive blood pressure, 5-lead ECG, pulse oximetry, end-tidal CO2, and capnography of all the participants. In 10 minutes, 0.5mg/kg dexmedetomidine in 20 mL 0.9per cent saline was given to the dexmedetomidine group, and 20 mL 0.9per cent saline was given to the control group. Infusions were made and administered by an anesthesiologist not involved in the care and data collection of the patients. Anesthesia induction was done with three minutes of mask ventilation of lignocaine. Laryngoscopy and tracheal intubation were done by experienced anesthesiologists directly, and the duration of the laryngoscopy was documented. Airoxygen mixture of isoflurane and mechanical ventilation was used to sustain anesthesia with an EtCO2 target of 35-40mmHg. Atropine 0.5 mg IV was given to control bradycardia (HR less than 50 bpm), and ephedrine 5mg IV was given to control hypotension (MAP less than 60 mmHg or more than 20% vs baseline). The parameters in the hemodynamic measurements were recorded at the baseline (T0), after the infusion (T1), before the intubation (T2), and 1, 3, and 5minutes following the intubation (T3, T4, and T5). The primary outcome was the change in HR one minute following intubation, and the secondary outcomes were the change in SBP and the adverse events or the necessity of vasoactivity interventions. The data were analyzed with SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to test the normality of the data. The report on the continuous variables indicated the mean with standard deviation (SD), and the group difference was determined with the independent-samples t-test when the data were normally distributed. ANOVA was applied repeatedly in the study of heart rate and systolic blood pressure with the passage of time. The assumption of sphericity was tested using the Mauchly test, and when the assumption of

DOI: https://doi.org/10.54393/pjhs.v7i2.3651

sphericity was violated, the test applied was the Greenhouse-Geisser correction. The intergroup difference and time x group interaction were assessed, and significant p-values of interaction demonstrated that attenuation of hemodynamic responses took place with time in the dexmedetomidine group. To adjust Type, I error caused by the multiple comparisons over six time points, Bonferroni post-hoc corrections were applied in all the pair-wise comparisons. The Chi-square and Fisher's exact test were used to analyse categorical data, which were later presented as frequencies and percentages. A p-value of less than 0.05 was used as a statistically significant value.

RESULTS

The dexmedetomidine group's mean age was 57.8 ± 7.9 years, while the non-dexmedetomidine groups was 56.9 ± 8.3 years (p=0.620). The baseline characteristics of both groups were comparable, indicating baseline comparability between groups. The p-values for age, sex distribution, body mass index (BMI), duration of laryngoscopy, baseline heart rate (HR), and baseline systolic blood pressure (SBP) were 0.620, 0.620, 0.660, 0.420, 0.680, and 0.630 respectively (Table 1).

Table 1: Demographic Characteristics of the Study Population (n=103)

Variables	Dexmedetomidine Group (n=35)	Control Group (n=35)	p-value
Age (Years)	57.8 ± 7.9	56.9 ± 8.3	0.620
Male	23 (65.7%)	21 (60.0%)	0.620
Female	12 (34.3%)	14 (40.0%)	
BMI (kg/m^2)	27.2 ± 3.8	27.6 ± 4.1	0.660
Duration of Laryngoscopy (s)	12.2 ± 1.8	12.5 ± 1.9	0.420
Baseline HR (beats/min)	78.6 ± 7.9	79.4 ± 8.1	0.680
Baseline SBP (mmHg)	138.0 ± 11.8	139.2 ± 12.1	0.630

At baseline, there was no difference in heart rate and systolic blood pressure between the groups. The dexmedetomidine group had a significantly lower heart rate and systolic blood pressure than the control group during infusion and the peri-intubation period (T1–T5) (p<0.001). Repeated-measures ANOVA demonstrated both variables to have a significant time × group interaction (p<0.001), indicating that there was a steady attenuation of hemodynamic responses over time in dexmedetomidine-treated patients (Table 2).

Table 2: Comparison of Hemodynamic Parameters Over Time among Study Participants

Time Point	HR Dexmed (beats/min)	HR Control (beats/min)	p-value (Between Groups)	Mean Difference (95% CI)	SBP Dexmed (mmHg)	SBP Control (mmHg)	p-value (Between Groups)	Time × Group Interaction p-value
T0 – Baseline	78.6 ± 7.9	79.4 ± 8.1	0.68	0.8 (–2.7 to 4.3)	138.0 ± 11.8	139.2 ± 12.1	0.630	–
T1 – Post-Infusion	72.4 ± 7.3	80.1 ± 8.2	<0.001	7.7 (4.1 to 11.3)	133.5 ± 11.2	140.0 ± 12.0	0.010	<0.001
T2 – Pre-Intubation	70.8 ± 7.0	81.5 ± 8.6	<0.001	10.7 (6.8 to 14.6)	131.8 ± 10.8	142.0 ± 12.5	<0.001	<0.001
T3 – 1 Min Post-Intubation	77.2 ± 9.0	95.2 ± 10.1	<0.001	17.9 (13.2 to 22.6)	138.6 ± 12.9	165.3 ± 15.8	<0.001	<0.001
T4 – 3 Min Post-Intubation	74.1 ± 8.2	88.6 ± 9.5	<0.001	14.5 (10.5 to 18.5)	135.0 ± 12.1	153.7 ± 14.2	<0.001	<0.001
T5 – 5 Min Post-Intubation	72.9 ± 7.8	83.5 ± 8.9	<0.001	10.6 (6.8 to 14.4)	133.2 ± 11.6	147.5 ± 13.7	<0.001	<0.001

The incidence of adverse events was low and comparable between the two groups, with no major complications reported. Bradycardia occurred in 5.7% of patients in the dexmedetomidine group and none in the control group (p=0.150), while hypotension was observed in 2.9% versus none (p=0.310). The requirement for atropine was slightly higher in the dexmedetomidine group (5.7%) compared to the control (0%) (p=0.150). Similarly, vasopressor use was noted in 2.9% of dexmedetomidine patients and 8.6% of controls (p=0.300) (Table 3).

Table 3: Incidence of Adverse Events among Study Participants (n=70)

Events	Dexmed Group (n=35)	95% CI	Control Group (n=35)	95% CI	p-value
Bradycardia (HR <50 bpm)	2 (5.7%)	0–13.4%	0 (0%)	0–0%	0.150
Hypotension (MAP <60 mmHg)	1 (2.9%)	0–8.4%	0 (0%)	0–0%	0.310
Atropine Use	2 (5.7%)	0–13.4%	0 (0%)	0–0%	0.150
Vasopressor Use	1 (2.9%)	0–8.4%	3 (8.6%)	0–17.8%	0.300
Major Adverse Events	0 (0%)	0–0%	0 (0%)	0–0%	–

DISCUSSION

The hemodynamic reaction to laryngoscopy and endotracheal intubation was significantly and clinically reduced by a single pre-induction infusion of dexmedetomidine at a dose of 0.5 µg/kg in this prospective cohort study of 70 ASA II patients with controlled hypertension. Heart rate and systolic blood pressure were considerably lower in the dexmedetomidine group from immediately following infusion to five minutes post-intubation, but initial findings were similar in both groups. These results demonstrate that a modest dose of dexmedetomidine reliably blunts peri-intubation sympathetic surges in patients with controlled hypertension, with a low incidence of major adverse events. [16, 17]. Current findings are consistent with several randomized trials and systematic reviews showing that dexmedetomidine reduces the tachycardic and hypertensive responses associated with airway manipulation. Misra et al. reported reduced HR and BP after nebulized dexmedetomidine compared with placebo

DOI: https://doi.org/10.54393/pjhs.v7i2.3651

during laryngoscopy and intubation, supporting the concept that dexmedetomidine, administered by different routes, attenuates the pressor response. Xiong and colleagues similarly found that dexmedetomidine premedication increased sedation and inhibited intubation-related stress in adults. A study by Jain et al. and other randomized trials have likewise reported significant reductions in peri-intubation HR and BP with doses in the 0.5–1.0 µg/kg range, corroborating our observation that 0.5 µg/kg is effective in the peri-intubation window [16, 18]. Several dose-comparison studies and meta-analyses have addressed the dose-response relationship of dexmedetomidine for attenuating intubation responses. While our study used 0.5 µg/kg, some trials found greater suppression with higher doses, suggesting a dose-dependent effect. Nevertheless, higher doses are also more likely to produce clinically relevant bradycardia or hypotension. The balance between efficacy and safety, therefore, supports use of moderate dosing (0.5 µg/kg) in many elective settings, especially when treating patients with controlled hypertension where excessive hypotension or bradycardia is undesirable. Our low rates of bradycardia (2/35) and hypotension (1/35), none of which led to major complications, echo the safety signals reported in other moderate-dose trials [19, 20]. Comparative and alternative strategies have also been evaluated in recent years. Trials comparing dexmedetomidine to other agents such as fentanyl, magnesium sulfate, esmolol, or labetalol have produced mixed results: some studies show comparable or superior attenuation with dexmedetomidine, whereas others found similar efficacy with shorter-acting agents but with different side-effect profiles. For example, head-to-head comparisons with beta-blockers or esmolol report that these drugs can blunt HR peaks rapidly but may be less effective on blood pressure or have different cardiovascular safety considerations. These different findings show that agent selection can also be tailored to each individual based on patient comorbidity, desired duration of effect, and clinician tolerance for bradycardia/hypotension. For example, in our cohort of hypertensive patients, dexmedetomidine afforded a sustained sympatholytic effect throughout the critical five-minute period post-intubation, which may be advantageous for patients at risk for acute hypertensive surges [21-23]. The route and timing of administration also affect outcomes. Studies examining pre-induction infusions of dexmedetomidine via IV (like the pre-induction of dexmedetomidine in the present trial) and alternative routes, such as nebulized or intranasal dexmedetomidine, have shown consistent benefit, but onset and peak effects differ. For example, nebulized or intranasal dexmedetomidine may be useful in situations where IV access or timing of administration is a concern. However, an infusion via an IV route provides precise titration, time to onset of action before laryngoscopy, and eliminates any concern for patient compliance or patient safety. The protocol we used, which involved an infusion of dexmedetomidine over ten minutes immediately before induction of anesthesia, was similar to other protocols, and the results were consistent with several randomized trials that demonstrated attainment of optimal attenuation of response without exaggerated sedation or respiratory depression [18, 24]. Safety is an essential consideration when using α2-agonists in hypertensive patients. Although dexmedetomidine reliably reduced HR and SBP, it can also precipitate bradycardia and hypotension. In our cohort, these events were infrequent and manageable with standard interventions (atropine for bradycardia, ephedrine for hypotension). This tolerability mirrors findings from other contemporary trials that report low but non-negligible rates of bradycardia/hypotension, typically dose dependent, and reinforces the need for appropriate patient selection, monitoring, and rescue protocols when employing dexmedetomidine perioperatively [16, 25]. The findings of our study are new since earlier literature has failed to adequately represent the higher-risk group of patients with controlled hypertension. The majority of previous investigations on the effects of dexmedetomidine on hemodynamic changes during laryngoscopy and intubation have incorporated mixed or normotensive cohorts. Through observation of a cohort with hypertension, we establish that even a moderate dose of dexmedetomidine (0.5 µg/kg) given before induction can help in attenuating the increase in heart rate and systolic blood pressure during airway manipulation without significantly increasing the number of adverse events. This clinical, empirical evidence justifies the implementation of this intervention in other patients, and this offers real-life advice on the peri-intubation hemodynamic support. The increased dosage may provide stronger attenuation, but it may also raise the chances of bradycardia or hypotension, and this is why efficacy and safety balance are of great importance. Recent clinical trials and registry data have demonstrated a growing interest in the use of dexmedetomidine among hypertensive patients, yet there is still a lack of high-quality data. Our future population contributes to this information, as it proves the hemodynamic advantage and safety of a moderate dose pre-induction regimen in a controlled population with hypertension. This prospective cohort study found that one pre-induction dexmedetomidine, 0.5 µg/kg, infusion was a strong suppressor of heart rate and systolic blood pressure responses to laryngoscopy and intubation in patients with controlled hypertension with an excellent

DOI: https://doi.org/10.54393/pjhs.v7i2.3651

short-term safety profile. These results advocate moderate dose of dexmedetomidine and its application as a practical and effective peri-intubation hemodynamic adjunct in high-risk patients with hypertension and provide significant evidence to an underrepresented population in past studies.

This was a single-center prospective cohort study with a relatively small sample size and absence of randomization, which may limit causal inference and external validity. Hemodynamic outcomes were assessed only in the immediate peri-intubation period, without evaluation of longer intraoperative or postoperative cardiovascular effects. Larger randomized controlled trials comparing dexmedetomidine with alternative agents in hypertensive patients are needed to define optimal dosing and long-term safety across different surgical settings.

CONCLUSIONS

In individuals who have controlled hypertension, pre-induction intravenous infusion of dexmedetomidine safely and efficiently reduces the hemodynamic response to intubation of the endotracheal tube and laryngoscopy. The medication had very minor, tolerable side effects and significantly reduced increases in heart rate and systolic blood pressure at all post-intubation time periods as compared to a placebo. The results validate the strong sympatholytic and cardioprotective effects of dexmedetomidine and show its clinical use as an addition to anesthesia for individuals susceptible to stress-induced increases in heart rate and blood pressure.

Authors' Contribution

Conceptualization: AS
Methodology: MQA
Formal analysis: AS, SMA, MQA, SM, SK
Writing and Drafting: AS, SMA, SM, VK
Review and Editing: AS, SMA, MQA, SM, VK, SK

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Wang L, Li H, Zhong Y, Ye S, Deng J, Pan T *et al.* Comparative Analysis of Hemodynamic Responses and Oropharyngeal Complications in Tracheal Intubation: Evaluating Conventional, Video, and Rigid Video Laryngoscopes Under General Anesthesia. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2024 Sep; 30: e944916-1. doi: 10.12659/MSM.944916.

[2] Pramanik M, Chattopadhyay U, Chaudhuri S, Hussain SS, Singh NK, Banerjee S *et al.* Comparison between Transtracheal and Intravenous 2% Lignocaine in Attenuating Hemodynamic Stress Response Following Direct Laryngoscopy and Endotracheal Intubation: A Randomized Controlled Trial. BioMed Central Anesthesiology. 2025 May; 25(1): 262. doi: 10.1186/s12871-025-03102-1.

[3] Saeed ZM, Jaafar H, Alburkiebh SH. Effect of Nebulized Lidocaine and Intravenous Lidocaine on Hemodynamic Responses to Laryngoscopy and Endotracheal Intubation. Iranian Journal of War and Public Health. 2024 Jan; 16(1): 67-74.

[4] Likhitha DN, Sriramula N, Reddy RR, Kumar KS. Comparison between Oral Clonidine and Oral Pregabalin as Premedication to Attenuate Pressor Response to Direct Laryngoscopy and Endotracheal Intubation. International Journal of Health and Clinical Research. 2022; 5(1): 680-683.

[5] Sapare V. Comparison of the Effects of Intravenous Esmolol and Intravenous Labetolol on the Hemodynamic Changes During Laryngoscopy and Intubation in Patients Undergoing Surgery under General Anesthesia. International Journal of Life Sciences, Biotechnology and Pharma Research. 2025 Apr; 14(4): 958-962.

[6] Khan MR, Ullah A, Deepa TC, Taskin R, Ibrahim K. Attenuation of Cardiovascular Responses to Laryngoscopy and Intubation by Intravenous Metoprolol. Bangladesh Medical College Journal. 2022; 27(2): 13-18.

[7] Liu X, Li Y, Kang L, Wang Q. Recent Advances in the Clinical Value and Potential of Dexmedetomidine. Journal of Inflammation Research. 2021 Dec: 7507-27. doi: 10.2147/JIR.S346089.

[8] Shehabi Y, Howe BD, Bellomo R, Arabi YM, Bailey M, Bass FE *et al.* Early Sedation with Dexmedetomidine in Critically Ill Patients. New England Journal of Medicine. 2019 Jun; 380(26): 2506-17. doi: 10.1056/NEJMoa1904710.

[9] Hansen N and Rediske AI. The Locus Coeruleus Noradrenaline System in Delirium. Frontiers in Aging Neuroscience. 2021 Dec; 13: 784356. doi: 10.3389/fnagi.2021.784356.

[10] Efe Mercanoglu E, Girgin Kelebek N, Turker G, Aksu H, Ozgur M, Karakuzu Z *et al.* Comparison of the Effect of Ketamine and Dexmedetomidine Combined with Total Intravenous Anesthesia in Laparoscopic Cholecystectomy Procedures: A Prospective Randomized Controlled Study. International Journal of Clinical Practice. 2022; 2022(1): 1878705. doi:

DOI: https://doi.org/10.54393/pjhs.v7i2.3651

10.1155/2022/1878705.

[11] Ismail EA, Mostafa AA, Abdelatif MM. Attenuation of Hemodynamic Response to Laryngoscopy and Endotracheal Intubation with Single Dose Dexmedetomidine in Controlled Hypertensive Patients: Prospective Randomized Double-Blind Study. Ain-Shams Journal of Anesthesiology. 2022 Jul; 14(1). doi: 10.1186/s42077-022-00255-w.

[12] Farooq S, Rizvi MF, Hashmi SU, Baig MA, Yousaf HS, Munir T. A Prospective Randomized Study to See the Effects of Dexmedetomidine Plus Propofol Versus Propofol Alone in Cardiac Surgery Patients. Professional Medical Journal. 2021 Apr; 28(4). doi: 10.29309/TPMJ/2021.28.04.5815.

[13] Wujtewicz M, Twardowski P, Jasiński T, Michalska-Małecka K, Owczuk R. Evaluation of the relationship between Baseline Autonomic Tone and Hemodynamic Effects of Dexmedetomidine. Pharmaceuticals. 2023 Feb; 16(3): 354. doi: 10.3390/ph16030354.

[14] Horvath B, Kloesel B, Todd MM, Cole DJ, Prielipp RC. The Evolution, Current Value, and Future of the American Society of Anesthesiologists Physical Status Classification System. Anesthesiology. 2021 Oct; 135(5): 904-19. doi: 10.1097/ALN.0000000000003947.

[15] Kamal M, Agarwal D, Singariya G, Kumari K, Paliwal B, Ujwal S. Effect of Dexmedetomidine on Attenuation of Hemodynamic Response to Intubation, Skin Incision, and Sternotomy in Coronary Artery Bypass Graft Patients: A Double-Blind Randomized Control Trial. Journal of Anesthesiology Clinical Pharmacology. 2020 Apr; 36(2): 255-60. doi: 10.4103/joacp.JOACP_353_18.

[16] Jain K, Sethi SK, KN H, Patodi V, Jain N, Meena D. Efficacy of Dexmedetomidine in Attenuating Pressor Response to Laryngoscopy and Endotracheal Intubation Under Bispectral Index Controlled Anesthesia: A Prospective Randomized Double-Blinded Study. Ain-Shams Journal of Anesthesiology. 2023 Mar; 15(1). doi: 10.1186/s42077-023-00314-w.

[17] Xiong J, Gao J, Pang Y, Zhou Y, Sun Y, Sun Y. Dexmedetomidine Premedication Increases Preoperative Sedation and Inhibits Stress Induced by Tracheal Intubation in Adult: A Prospective Randomized Double-Blind Clinical Study. BioMed Central Anesthesiology. 2022 Dec; 22(1): 398. doi: 10.1186/s12871-022-01930-z.

[18] Misra S, Behera BK, Mitra JK, Sahoo AK, Jena SS, Srinivasan A. Effect of Preoperative Dexmedetomidine Nebulization on the Hemodynamic Response to Laryngoscopy and Intubation: A Randomized Control Trial. Korean Journal of Anesthesiology. 2021 Apr; 74(2): 150-7. doi: 10.4097/kja.20153.

[19] Silpa AR, Koshy KA, Subramanian A, Pradeep KK. Comparison of the Efficacy of Two Doses of Dexmedetomidine in Attenuating the Hemodynamic Response to Intubation in Patients Undergoing Elective Cardiac Surgery: A Randomized Double-Blinded Study. Journal of Anesthesiology Clinical Pharmacology. 2020 Jan; 36(1): 83-7. doi: 10.4103/joacp.JOACP_235_18.

[20] Arora S, Govardhane BT, Srinivasan V, Karandikar G. Evaluation of Different Doses of Dexmedetomidine for Awake Fibreoptic Nasotracheal Intubation in Patients Undergoing Oromaxillofacial and Oral Malignancy Surgeries: A Randomized, Double-Blind Study. Indian Journal of Anesthesia. 2024 May; 68(5): 447-53. doi: 10.4103/ija.ija_1004_23.

[21] Shukla S, Kadni RR, Chakravarthy JJ, Zachariah KV. A Comparative Study of Intravenous Low Doses of Dexmedetomidine, Fentanyl, and Magnesium Sulfate for Attenuation of Hemodynamic Response to Endotracheal Intubation. Indian Journal of Pharmacology. 2022 Sep; 54(5): 314-20. doi: 10.4103/ijp.ijp_923_20.

[22] Saleh A, Kan S, Singhal S, Ouanounou A, Wong M. Effects of Dexmedetomidine vs Esmolol on Postintubation Hemodynamics: A Meta-Analysis. Anesthesia Progress. 2025 Mar; 72(1): 9-23. doi: 10.2344/23-0059.

[23] Neto MM, Paz MC, Crisóstomo AC, Rabelo IS, Luna BG, e Souza PF. Comparative Effects of Dexmedetomidine Versus Labetalol on Hemodynamic Stress Response to Laryngoscopy and Tracheal Intubation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Trends in Anesthesia and Critical Care. 2025 Aug: 101588. doi: 10.1016/j.tacc.2025.101588.

[24] Singh S, Gupta P, Dhar M, Pasha A. Effect of Preoperative Intravenous and Inhalational Dexmedetomidine on the Hemodynamic Response of Laryngoscopy: A Prospective Double-blinded Randomized Study. Journal of Research in Pharmacy Practice. 2023 Oct; 12(4): 123-9. doi: 10.4103/jrpp.jrpp_12_24.

[25] Wang W, Huo P, Wang E, Song W, Huang Y, Liu Z *et al.* Dexmedetomidine Infusion for Emergence Coughing Prevention in Patients Undergoing an Endovascular Interventional Procedure: A Randomized Dose-Finding Trial. European Journal of Pharmaceutical Sciences. 2022 Oct; 177: 106230. doi: 10.1016/j.ejps.2022.106230.

DOI: https://doi.org/10.54393/pjhs.v7i2.3524

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Effectiveness of Holter Monitoring in the Detection of Atrial Fibrillation after Ischemic Stroke

Hameed Ur Rehman[1*], Asif Hashmat[1], Mehwish Mustafa[1], Wali Rehma[1], Tariq Khan[1] and Farhan Tahir[1]

[1]Department of Neurology, Pak Emirates Military Hospital, Rawalpindi, Pakistan

ARTICLE INFO

Keywords:
Atrial Fibrillation, Ischemic Stroke, Holter Monitoring, Paroxysmal Atrial Fibrillation

How to Cite:
Rahman, H. U., Hashmat, A., Mustafa, M., Rehman, W., Khan, T., & Tahir, F. (2026). Effectiveness of Holter Monitoring in the Detection of Atrial Fibrillation after Ischemic Stroke: Holter Monitoring in the Detection of Atrial Fibrillation after Ischemic Stroke. Pakistan Journal of Health Sciences, 7(2), 26-31. https://doi.org/10.54393/pjhs.v7i2.3524

***Corresponding Author:**
Hameed Ur Rehman
Department of Neurology, Pak Emirates Military Hospital, Rawalpindi, Pakistan
drhameed0332@gmail.com

Received Date: 15th October, 2025
Revised Date: 2nd January, 2026
Acceptance Date: 9th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Atrial fibrillation (AF) is an important but often hidden cause of recurrent ischemic stroke, requiring early detection for timely anticoagulation. This study assessed the effectiveness of 72-hour Holter monitoring in identifying previously undiagnosed AF in acute ischemic stroke patients, particularly in resource-limited settings. **Objectives:** To determine the effectiveness of 72-hour Holter monitoring in identifying previously undiagnosed AF in acute ischemic stroke patients. **Methods:** This analytical cross-sectional study was conducted at the Department of Neurology, Pak Emirates Military Hospital, Rawalpindi, from May to September 2025, enrolling 256 patients with neuroimaging-confirmed ischemic stroke. Holter monitoring was initiated within 2 hours of admission and continued for 72-hours, accompanied by 8-hourly pulse checks and symptom logs to identify AF episodes lasting ≥30 seconds. Chi-square or Fisher's exact tests were used, keeping p≤0.05 statistically significant. **Results:** The mean age was 65.4±11.2 years; 59.4% were male. AF was detected in 17 patients (6.6%), with 72-hour Holter yielding significantly higher detection than baseline ECG (17(6.6%) vs.5(2.0%), p=0.002, with diagnostic accuracy of 95.3%. Cumulative detection increased over time: 29.4% within 24 hours, 70.6% by 48 hours, and 100% by 72 hours. AF was significantly associated with age ≥65 years (p=0.008), hypertension (p=0.047), and diabetes (p=0.029). **Conclusions:** 72-hour Holter monitoring is a useful non-invasive method of correctly detecting occult AF in patients after acute ischemic stroke, with superior diagnostic yield over baseline ECG. These results favor routine use of 72-hour Holter monitoring as part of post-stroke protocols.

INTRODUCTION

Ischemic stroke continues to be a major cause of morbidity and mortality globally, with atrial fibrillation (AF) recognized as an important modifiable risk factor in about 20-30% of cases [1]. AF, particularly paroxysmal forms, often goes undetected prior to stroke events, underscoring the need for effective post-stroke cardiac rhythm monitoring to guide anticoagulant therapy and prevent recurrence [2]. Holter monitoring, an ambulatory electrocardiography that is not invasive, has become a vital diagnostic tool for occult AF detection in this group, with longer durations having the potential to increase yield compared to standard 24-hour monitoring [3]. The AF detection background after ischemic stroke outlines how difficult subclinical or paroxysmal occurrence is to detect, sometimes not shown on routine electrocardiograms (ECGs) [4]. Current European Stroke Organization guidelines suggest monitoring of at least 48-72 hours in selected patients, but optimal duration and timing are controversial [5]. Detection rates have been shown to vary according to the length of monitoring and the characteristics of the patient in studies. For example, 7-day outpatient cardiac rhythm monitoring has identified new AF in 6.4 % of patients with ischemic stroke or transient ischemic attack (TIA) of undetermined etiology, with increased yield in diabetic or older patients [6]. In a similar way, 7-day wearable devices revealed an 8.7%

DOI: https://doi.org/10.54393/pjhs.v7i2.3524

detection rate in AF patients without a previous history of AF, beating traditional 7-day Holter in certain cohorts by facilitating earlier detection and treatment [7]. Long-term strategies, including insertable cardiac monitors, achieve better long-term detection versus short-term Holter (e.g., 24-48 hours), reducing stroke recurrence with timely anticoagulation, though at greater invasiveness [8]. Timing also matters; early inpatient 48-hour Holter recordings in patients with embolic stroke of undetermined source (ESUS) identify a 20% detection rate for previously undiagnosed AF, much higher than with delayed outpatient monitoring (5%), emphasizing the importance of early evaluation [9]. This study favors the use of extended Holter but underlines the necessity for context-dependent data, especially in resource-poor environments. This study addresses the critical gap in detecting AF, a major modifiable risk factor for ischemic stroke, which is often missed on routine ECG. Extended 72-hour Holter monitoring has shown superior diagnostic yield internationally, but local data are lacking, particularly in resource-limited hospital settings.

Despite guideline recommendations and growing evidence supporting extended cardiac rhythm monitoring, a substantial proportion of atrial fibrillation cases after ischemic stroke remain undetected when relying on routine ECG or short-duration Holter monitoring. There is a paucity of local, context-specific evidence evaluating the diagnostic yield of prolonged (72-hour) Holter monitoring for AF detection in post-stroke patients, particularly within resource-limited hospital settings. This study aimed to evaluate the diagnostic yield of prolonged Holter monitoring in detecting previously unrecognized AF after ischemic stroke, providing critical data to guide clinical decision-making and reduce recurrent stroke risk in the local population.

METHODS

This analytical cross-sectional study was carried out at the Department of Neurology, Pak Emirates Military Hospital, Rawalpindi, Pakistan, from May to September 2025. Ethical approval was obtained from the hospital under reference number A/28/ERC/03/2025. The Sample size was determined to be 256 patients, through OpenEpi sample size software as n = $DFFF.N.p(1\text{-}p) / d^2/Z^2_{1-\alpha/2}. (N\text{-}1) + p(1\text{-}p)$, keeping anticipated frequency of AF among ischemic stroke patients as 6.4% [6], confidence level of 95%, and 3% margin of error. The inclusion criteria were patients aged 18-85 years of either gender diagnosed with acute ischemic stroke through clinical evaluation and neuroimaging (computed tomography or magnetic resonance imaging) and no previously known history of AF. Patients with contraindications for Holter monitoring (e.g., skin conditions prohibiting electrode application), patients with severe comorbidities that would interfere with study participation (e.g., advanced cancers or terminal diseases), and patients with established pre-existing AF were excluded. All eligible patients after written consent underwent a standard 12-lead electrocardiogram (ECG) on admission, within 2 hours of hospital presentation, using a GE MAC 5500 ECG system (GE Healthcare, USA). ECGs were recorded at a paper speed of 25 mm/s and an amplitude of 10 mm/mV. A cardiologist interpreted all baseline ECGs for the presence of AF or other arrhythmias. Baseline ECG parameters, including rhythm classification (sinus rhythm or AF) and heart rate, were documented for each patient. Following baseline ECG, patients underwent continuous 72-hour Holter monitoring (initiated within 2 hours of admission) using the GE SEER 12 Holter system (GE Healthcare, USA). Recordings were obtained with three-channel ECG leads (V1, V3, V5) placed according to the modified Mason-Likar configuration, at a sampling rate of 200 Hz. AF episodes were defined as irregular R-R intervals without distinct P waves lasting ≥30 seconds, consistent with established guidelines [10]. All recordings were analyzed with GE MARS 8.1 Holter analysis software, with automatic detection confirmed by a cardiologist. Standard artifact rejection, filtering, and detection thresholds were applied according to manufacturer guidelines to ensure data reproducibility. During the monitoring interval, pulse rhythm was manually checked every 8 hours by neurology residents, and patients recorded any cardiac complaints (e.g., palpitations, presyncope) or hemodynamic instability (e.g., systolic BP variations >40 mmHg) in hourly symptom logs. All clinical observations were time-stamped and correlated with Holter recordings. The effectiveness of 72-hour Holter monitoring was defined as its ability to detect previously unrecognized AF compared to baseline ECG and clinical monitoring. Effectiveness was quantified by the number of newly detected AF cases or additional AF cases identified beyond baseline ECG, and diagnostic accuracy. Demographic and clinical data, including age, gender, and comorbidities (diabetes mellitus, hypertension, and ischemic heart disease), were collected through structured interviews and clinical records. Data were analyzed using IBM SPSS version 27.0. Continuous data like age and monitoring time were reported as mean ± standard deviation after normality was checked by the Shapiro-Wilk test. Categorical data like gender, comorbidities, Holter initiation delay, and AF detection rate were reported as frequencies and percentages. Potential modifiers of effect (gender, age, comorbidities, and delay in Holter monitoring) were adjusted by stratification. Post-stratification was compared by the Chi-square test or Fisher's exact test as deemed appropriate, with a p-value ≤0.05 being statistically significant.

DOI: https://doi.org/10.54393/pjhs.v7i2.3524

RESULTS

This study included 256 ischemic stroke patients with a mean age of 65.4 ± 11.2 years (range: 32–85), of whom 152 (59.4%) were male. Hypertension was the most common comorbidity (70.3%, n=180), followed by diabetes mellitus (39.8%, n=102) and ischemic heart disease (25.0%, n=64). The mean time from presentation to Holter initiation was 2.8 ± 0.9 hours (Table 1).

Table 1: Baseline Characteristics of Study Participants (n=256)

Variables		Mean ± SD, n (%)
Age	Years	65.4 ± 11.2
Gender	Male	152 (59.4%)
	Female	104 (40.6%)
Comorbidities	Hypertension	180 (70.3%)
	Diabetes	102 (39.8%)
	Ischemic Heart Disease	64 (25.0%)
Time to Holter Initiation	Hours	2.8 ± 0.9

The effectiveness of 72-hour Holter monitoring was evaluated by its ability to detect previously unrecognized AF in acute ischemic stroke patients. Baseline ECG identified AF in 5 (2.0%) patients, whereas 72-hour Holter monitoring detected AF in 17 (6.6%) patients, uncovering 12 (4.7%) additional cases that were missed initially. McNemar's test showed a statistically significant difference between the two diagnostic methods (p = 0.002), confirming that extended Holter monitoring has a superior diagnostic yield for detecting previously unrecognized AF. Most AF episodes (82.4%, n=14) lasted 30 seconds to 5 minutes, while 3 exceeded 5 minutes. The diagnostic accuracy of the 72-hour Holter was 95.3%, indicating that prolonged monitoring is a reliable tool for identifying new-onset AF in acute ischemic stroke patients (Table 2).

Table 2: Newly Diagnosed Atrial Fibrillation on Baseline ECG vs 72-Hour Holter Monitoring (n=256)

AF Detection Method	n (%)	p-value (McNemar Test) for ECG vs Holter
Baseline ECG	5 (2.0%)	0.002*
72-Hour Holter Monitoring	17 (6.6%)	
Additional AF Cases Identified by Holter	12 (4.7%)	–
Diagnostic Accuracy of 72-Hour Holter Monitoring	95.3%	–

*p-value= 0.002<0.05 is significant, calculated through the McNemar test

5 (29.4%) AF cases were detected within 24 hours, 7 (41.2%) between 24–48 hours, and 5 (29.4%) between 48–72 hours. Nearly 70% of AF cases would have been missed with only 24-hour monitoring, highlighting the value of prolonged assessment (Figure 1).

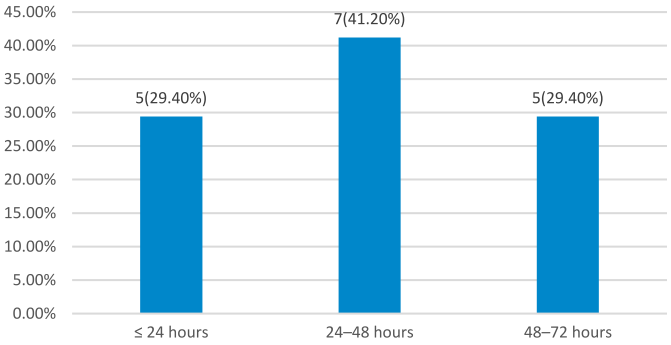

Figure 1: Percentage of Detection of Atrial Fibrillation Over 72-Hour Holter Monitoring

AF was significantly associated with patients aged ≥65 years, 14/120 (11.7%) (p=0.008). Hypertensive patients 15/180 (8.3%), and diabetic patients AF detection (6/64, 9.4% vs 11/192, 5.7%, p=0.029). No significant associations were observed with gender (p=0.661), ischemic heart disease (p=0.299), or delay in Holter initiation >2 hours (p=0.802) (Table 3).

Table 3: Association of Atrial Fibrillation Detection with Clinical and Demographic Characteristics (n=256)

Stratification Variables		AF Detected, n (%)	No AF, n (%)	p-value
Age	<65 Years (n=136)	3 (2.2%)	133 (97.8%)	0.008[a*]
	≥65 Years (n=120)	14 (11.7%)	106 (88.3%)	
Gender	Male (n=152)	11 (7.%2)	141 (92.8%)	0.661[a]
	Female (n=104)	6 (5.8%)	98 (94.2%)	
Hypertension	Yes (n=180)	15 (8.3%)	165 (91.7%)	0.047[b*]
	No (n=76)	2 (2.6%)	74 (97.4%)	
Diabetes Mellitus	Yes (n=64)	6 (9.4%)	58 (90.6%)	0.029[a*]
	No (n=192)	11 (5.7%)	181 (94.3%)	
Ischemic Heart Disease	Yes (n=64)	6 (9.4%)	58 (90.6%)	0.299[a]
	No (n=192)	11 (5.7%)	181 (94.3%)	
Delay in Holter (>2 Hours)	Yes (n=112)	8 (7.1%)	104 (92.9%)	0.802[a]
	No (n=144)	9 (6.3%)	135 (93.7%)	

[a]Chi-square test, [b]Fisher's exact test, as appropriate; * p-value ≤0.05 considered statistically significant

DISCUSSION

This study demonstrated that 72-hour Holter monitoring is an effective tool for detecting AF in patients with acute ischemic stroke (6.6% of cases). This detection rate is consistent with prior studies, such as a systematic review reporting a 6.27% prevalence of AF among stroke patients, with higher yields linked to prolonged monitoring [11]. Similarly, Bisson et al. observed new-onset AF in 5.9% of patients without prior AF after stroke, underscoring the importance of early cardiac rhythm evaluation [12]. Our higher detection rate compared to certain cohorts may relate to the early initiation of Holter monitoring within 4 hours of admission. The incremental diagnostic advantage of prolonged Holter monitoring over baseline ECG in our study (6.6% vs. 2.0%, p=0.002) highlights the value of

DOI: https://doi.org/10.54393/pjhs.v7i2.3524

extended surveillance for paroxysmal AF episodes. Comparable evidence shows that extending monitoring beyond 24 hours substantially improves detection rates. For instance, AF was identified in 4.5% of patients after 48 hours of Holter monitoring, while smartphone-based monitoring yielded even higher rates of 8.3% [13]. Dussault *et al.* similarly reported a three-fold increase in AF detection with extended monitoring compared to routine 24-hour assessment. Meta-analytic evidence also supports this, showing AF detection of 5.1% with ≤72 hours monitoring compared to 15% with ≥7 days [14]. Our findings align with this growing body of evidence that short-term ECG alone is insufficient and prolonged monitoring strategies are warranted. The temporal pattern of AF detection in our cohort further underscores the shortcomings of 24-hour monitoring. Only 29.4% of AF cases were detected in the first 24 hours, while 70.6% required the full 72 hours, consistent with prior work highlighting the incremental benefit of prolonged observation [15]. Enhanced monitoring approaches, such as 10-day Holter ECG or patch-type devices, have been shown to increase detection rates to 13.5% within six months [16]. Kwon *et al.* also reported that 72-hour adhesive patch monitoring increased AF detection by 1.6-fold compared with 24-hour Holter, particularly improving paroxysmal AF detection [17]. This study also identified significant associations between AF detection and clinical risk factors. Older age, hypertension, and diabetes mellitus were strongly linked to higher AF prevalence, in line with prior studies. For instance, Uhe *et al.* reported that AF detection rates rose from 6% in patients under 60 years to as high as 65% in those over 80 years using implantable monitors [18]. Similarly, Halimi *et al.* demonstrated that older age and hypertension were significantly associated with AF during 14-day continuous monitoring [19]. Diabetes and increasing comorbidity burden have also been identified as independent predictors of AF [6]. The clinical implications of these findings are significant. Continuous monitoring strategies, including wearable patches and implantable cardiac monitors, have demonstrated meaningful impacts on patient management, including the initiation of anticoagulation therapy and reductions in recurrent stroke risk [20]. These study findings support the incorporation of routine 72-hour Holter monitoring into post-stroke care, particularly in resource-constrained settings where longer-term or invasive monitoring is less feasible. Evidence also suggests that quality improvement initiatives using prolonged monitoring can increase AF detection and lead to more timely interventions [21].

Despite these strengths, our study has limitations. Being a single-center, and cross-sectional study limited its generalizability. The absence of long-term follow-up precludes assessment of recurrent stroke or the effectiveness of anticoagulation therapy. Furthermore, although 72-hour monitoring improves detection, very brief or late paroxysmal AF episodes may still be missed, as longer-term monitoring or implantable devices provide higher yields.

CONCLUSIONS

Seventy-two-hour Holter monitoring is a useful non-invasive method of correctly detecting occult AF in patients after acute ischemic stroke, with superior diagnostic yield over baseline ECG. These results favor routine use of 72-hour Holter monitoring as part of post-stroke protocols, especially in settings with limited resources, for early anticoagulant therapy initiation and prevention of recurrent stroke.

Authors' Contribution

Conceptualization: AH
Methodology: HUR, AH
Formal Analysis: AH, TK
Writing and Drafting: AH, MM, WR, FT
Review and Editing: HUR, AH, MM, WR, TK, FT

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Seiffge DJ, Cancelloni V, Räber L, Paciaroni M, Metzner A, Kirchhof P *et al.* Secondary Stroke Prevention in People with Atrial Fibrillation: Treatments And Trials. The Lancet Neurology. 2024 Apr; 23(4): 404-17. doi: 10.1016/S1474-4422(24)00037-1.

[2] Seet RC, Friedman PA, Rabinstein AA. Prolonged Rhythm Monitoring for the Detection of Occult Paroxysmal Atrial Fibrillation in Ischemic Stroke of Unknown Cause. Circulation. 2011 Jul; 124(4): 477-86. doi: 10.1161/CIRCULATIONAHA.111.029801.

[3] Sposato LA, Field TS, Schnabel RB, Wachter R, Andrade JG, Hill MD. Towards A New Classification of Atrial Fibrillation Detected After A Stroke or A Transient Ischaemic Attack. The Lancet Neurology. 2024 Jan; 23(1): 110-22. doi: 10.1016/S1474-4422(23)00326-5.

[4] Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J *et al.* Atrial Fibrillation in Patients with Cryptogenic Stroke. New England Journal of

DOI: https://doi.org/10.54393/pjhs.v7i2.3524

Medicine. 2014 Jun; 370(26): 2467-77. doi: 10.1056/NEJMoa1311376.

[5] Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C *et al.* 2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation Developed In Collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the Special Contribution of the European Heart Rhythm Association (EHRA) of the ESC. European Heart Journal. 2021 Feb; 42(5): 373-498.

[6] Van der Maten G, Meijs MF, van der Palen J, Brouwers PJ, Von Birgelen C, Van Opstal J *et al.* Atrial Fibrillation Detected with Outpatient Cardiac Rhythm Monitoring in Patients with Ischemic Stroke or TIA of Undetermined Cause. Journal of Stroke and Cerebrovascular Diseases. 2023 Dec; 32(12): 107400. doi: 10.1016/j.jstrokecerebrovasdis.2023.107400

[7] Saito T, Nishiyama Y, Otsuka T, Sakamoto Y, Okubo S, Iguchi Y *et al.* An Efficient Approach for Detecting Atrial Fibrillation in Ischemic Stroke Patients Using A Wearable Device: A Prospective Multicenter Substudy of the STABLED Trial. Frontiers in Neurology. 2025 Aug; 16: 1560495. doi: 10.3389/fneur.2025.1560495.

[8] Pantoni L, Mele F, Pescini F, Rafanelli M, Zivelonghi C, Tomasi L *et al.* Long-Term Detection of Subclinical Atrial Fibrillation in Cryptogenic Stroke Patients with Insertable Cardiac Monitors. European Journal of Neurology. 2025 Jun; 32(6): e70251. doi: 10.1111/ene.70251.

[9] Alwilly D, Srour S, Nordkin I, Honig A, Wiegler KB, Leker RR *et al.* The Importance of Timing in Performing a Holter ECG in Patients Diagnosed with an Embolic Stroke of Undetermined Source. Biomedicines. 2025 Mar; 13(4): 771. doi: 10.3390/biomedicines13040771.

[10] Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM *et al.* 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2024 Jan; 83(1): 109-279.

[11] Florentin M, Sagris D, Tasoudis P, Korompoki E, Veltkamp R, D'Anna L *et al.* Detection of Atrial Fibrillation After Stroke Due to Large or Small Vessel Disease: Systematic Review and Meta-Analysis. International Journal of Stroke. 2025 Apr; 20(4): 401-10. doi: 10.1177/17474930241292988.

[12] Bisson A, Clementy N, Bodin A, Angoulvant D, Babuty D, Lip GY *et al.* Relationship of Preexisting Cardiovascular Comorbidities to Newly Diagnosed Atrial Fibrillation After Ischemic Stroke. Stroke. 2017 Oct; 48(10): 2878-80. doi: 10.1161/STROKEAHA.117.018251.

[13] Linz D, Gawalko M, Betz K, Hendriks JM, Lip GY, Vinter N *et al.* Atrial Fibrillation: Epidemiology, Screening and Digital Health. The Lancet Regional Health–Europe. 2024 Feb; 37. doi: 10.1016/j.lanepe.2023.100786.

[14] Dussault C, Toeg H, Nathan M, Wang ZJ, Roux JF, Secemsky E. Electrocardiographic Monitoring for Detecting Atrial Fibrillation After Ischemic Stroke or Transient Ischemic Attack: Systematic Review and Meta-Analysis. Circulation: Arrhythmia and Electrophysiology. 2015 Apr; 8(2): 263-9. doi: 10.1161/CIRCEP.114.002521.

[15] Wachter R, Groeschel K, Gelbrich G, Hamann GF, Kermer P, Liman J *et al.* Holter-Electrocardiogram-Monitoring in Patients with Acute Ischaemic Stroke (Find-AFRANDOMISED): An Open-Label Randomised Controlled Trial. The Lancet Neurology. 2017 Apr; 16(4): 282-90. doi: 10.1016/S1474-4422(17)30002-9.

[16] Wachter R, Weber-Krüger M, Hamann GF, Kermer P, Liman J, Mende M *et al.* Long-Term Follow-Up of Enhanced Holter-Electrocardiography Monitoring in Acute Ischemic Stroke. Journal of Stroke. 2022 Jan; 24(1): 98-107. doi: 10.5853/jos.2021.01207

[17] Kwon S, Lee SR, Choi EK, Ahn HJ, Song HS, Lee YS *et al.* Comparison Between the 24-Hour Holter Test and 72-Hour Single-Lead Electrocardiogram Monitoring with an Adhesive Patch-Type Device for Atrial Fibrillation Detection: Prospective Cohort Study. Journal of Medical Internet Research. 2022 May; 24(5): e37970. doi: 10.2196/37970.

[18] Uhe T, Keilitz J, Berrouschot J, Wachter R. Age-Dependent Detection of Atrial Fibrillation with Implantable Cardiac Monitors in Patients with Cryptogenic Stroke. Thieme Open. 2024 Apr; 8(02): e202-8. doi: 10.1055/s-0044-1786015

[19] Halimi F, Sabouret P, Huberman JP, Cohen S, Ouazana L, Hoffman O *et al.* Atrial Fibrillation Diagnosis by A Systematic 14-Day Continuous ECG-Holter in Patients with High Cardiovascular Risk and Clinical Palpitation: The Prospective After Study. European Heart Journal. 2022 Oct; 43(Supplement_2): ehac544-404. doi: 10.1093/eurheartj/ehac544.404

[20] Verma A, Wachter R, Kowey PR, Halperin JL, Gersh BJ, Elkind MS *et al.* Changes in Management

DOI: https://doi.org/10.54393/pjhs.v7i2.3524

Following Detection of Previously Unknown Atrial Fibrillation by an Insertable Cardiac Monitor (from the REVEAL AF Study). The American Journal of Cardiology. 2019 Sep; 124(6): 864-70. doi: 10.1016/j.amjcard.2019.06.006.

[21] De Gregorio C, Di Franco A, Panno AV, Di Franco M, Scaccianoce G, Campanella F *et al.* Subclinical Atrial Fibrillation on Prolonged ECG Holter Monitoring: Results from the Multicenter Real-World SAFARI (Silent Atrial Fibrillation ANCE-Sicily Research Initiative) Study. Journal of Cardiovascular Development and Disease. 2023 Aug; 10(8): 336. doi: 10.3390/jcdd10080336.

DOI: https://doi.org/10.54393/pjhs.v7i2.3527

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Accuracy of Focused Assessment with Sonography in Trauma (FAST) In Detecting Visceral Injury Following Blunt Trauma with Computed Tomography (Ct) as A Gold Standard

Saad Saleem Qureshi[1*], Dawar Burhan[1], Nashmia Zubair[1], Saira Samnani[1] and Minaa Shahid[1]

[1]Department of Radiology, Aga Khan University Hospital, Karachi, Pakistan

ARTICLE INFO

Keywords:
Blunt Abdominal Trauma, Diagnostic Accuracy, Focused Assessment with Sonography in Trauma, Computed Tomography

How to Cite:
Qureshi, S. S., Burhan, D., Zubair, N., Samnani, S., & Shahid, M. (2026). Accuracy of Focused Assessment with Sonography in Trauma (FAST) In Detecting Visceral Injury Following Blunt Trauma with Computed Tomography (Ct) as A Gold Standard: FAST In Detecting Visceral Injury Following Blunt Trauma with Ct . Pakistan Journal of Health Sciences, 7(2), 32-37. https://doi.org/10.54393/pjhs.v7i2.3527

***Corresponding Author:**
Saad Saleem Qureshi
Department of Radiology, Aga Khan University Hospital, Karachi, Pakistan
qsaadsaleem@gmail.com

Received Date: 15th October, 2025
Revised Date: 3rd January, 2026
Acceptance Date: 12th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Blunt abdominal trauma is one of the major causes of morbidity and mortality around the world. The prompt identification of visceral damage is crucial for effective management, and FAST is a proven, widely adopted first-line imaging tool. **Objectives:** To investigate the diagnostic value of FAST for ascertaining the presence of visceral injuries after blunt abdominal injury, keeping the CT scan as the reference measure. **Methods:** A cross-sectional study was implemented at the Department of Radiology, Aga Khan University Hospital, Karachi, from June 2025 to September 2025. A population of 103 patients meeting eligibility criteria with blunt abdominal trauma was selected by non-probability consecutive sampling. FAST was performed on all patients, with the findings subsequently correlated with subsequent CT scans. A 2x2 contingency table in which the CT scan served as the gold standard was used to estimate sensitivity, specificity, positive and negative predictive values of FAST, and its diagnostic accuracy. SPSS version 26.0 was used to analyze data using the Shapiro-Wilk test. **Results:** FAST had a sensitivity of 88.24% and a specificity of 81.16%. Total diagnostic accuracy was 83.50%. The PPV was 69.77% and the NPV 93.33%. FAST was noted to be highly efficient for detecting intra-abdominal injuries; however, some false positives were also reported. **Conclusions:** FAST is a non-invasive, diagnostic measure as a preliminary assessment of blunt abdominal trauma with a good sensitivity and NPV, and hence turns out to be a useful screening test, particularly in resource-limited and emergency settings.

INTRODUCTION

Traumatic injury is one of the major causes of death among people under the age of 45 years and plays a substantial role in disease burden worldwide. Trauma is mostly blunt in nature, with about 80% mortality resulting from hypovolemic shock. Accurate and timely detection of internal bleeding is therefore critical; however, it remains a challenge, giving rise to one of the most important gaps in knowledge in resource-limited environments, where the optimized imaging strategies are not yet developed. Computed tomography (CT) is considered to be the gold standard for evaluating abdominal visceral injury in blunt trauma [1]. It is sensitive in the detection of solid organ parenchymal laceration, intraparenchymal hematoma, and hollow viscus injuries. In addition, CT can be used to obtain grades of injury, provide treatment guidance for associated thoracic or pelvic trauma, and aid in surgical or interventional planning [2]. Its multiplanar and contrast-enhanced functions offer important anatomical details, which are cardinal for trauma assessments [3]. Nevertheless, CT has shortcomings in acute trauma

DOI: https://doi.org/10.54393/pjhs.v7i2.3527

settings. For instance, the transportation of patients to the CT suite can delay resuscitation in unstable patients, leading to deterioration of outcomes. Other issues include exposure to ionizing radiation and the necessity of using iodinated contrast media, especially in children, pregnant patients, and those affected by renal issues [4]. In addition, CT is quite costly, involves heavy infrastructure, and requires human resources. Hence, the use of CT as a first-line imaging modality for all patients with blunt trauma, particularly those with hemodynamic instability, is clinically debatable [5]. On the other hand, ultrasound has logistical and safety benefits as it is easy to carry around, repeatable, non-ionizing, and can be performed without disrupting resuscitation efforts [6]. The current ultrasound technology allows real-time evaluation of the dynamic movement of intraperitoneal or pericardial fluid. These qualities have contributed to the high rates of the implementation of Focused Assessment with Sonography in Trauma (FAST) in pre-hospital and emergency department settings. FAST is primarily aimed at identifying free intraperitoneal or pericardial fluid that is a sign of internal hemorrhage. In the setting of blunt abdominal trauma, this indicates hemoperitoneum resulting from solid visceral injury, hollow viscus perforation, or both [7]. The presence of such fluids can be detected to institute timely triage, such as emergency laparotomy, interventional radiological procedures, or additional imaging. In view of these, FAST is often criticized over diagnostic performance, as it is operator-specific and is dependent on the education, experience, and knowledge of the sonographer about the trauma protocols [8]. FAST is sensitive in the detection of moderate to large fluid accumulation but is insensitive to small-volume hemoperitoneum or isolated parenchymal injury in the absence of free fluid [9].

In acute blunt abdominal trauma, reliance on computed tomography as the primary diagnostic modality is often impractical in hemodynamically unstable patients and resource-limited settings, while the true diagnostic reliability of FAST remains uncertain. There is limited local evidence directly correlating positive FAST findings with CT-confirmed visceral injuries, highlighting the need for context-specific validation of FAST accuracy in blunt abdominal trauma. This study aimed to establish the accuracy of positive FAST as a method of identifying visceral injury in blunt abdominal trauma, keeping CT as the gold standard.

METHODS

This was a cross-sectional diagnostic accuracy study designed to determine the sensitivity of FAST in visceral damage following blunt abdominal trauma, using CT as a reference tool [10]. The study was conducted in the Department of Radiology, Aga Khan University Hospital, Karachi, Pakistan, a tertiary care hospital that manages a high volume of emergency patients and is equipped with advanced diagnostic imaging facilities. Clearance was obtained from IRB (ID 2025-11517-35095) with an exemption of informed consent as per protocol following approval of synopsis by the CPSP (Ref no: CPSP/REU/RAD-2021-175-3541). The duration of this study was six months (June 2025 to September 2025). Ultrasound examinations were performed by sonographers and residents with at least 1 year of experience. CT scans were conducted using a Toshiba Aquilion 640 scanner. Sensitivity and specificity with sample size (103) were calculated with the help of the WHO sample size calculatoras shown in the population pyramid (Figure 1).

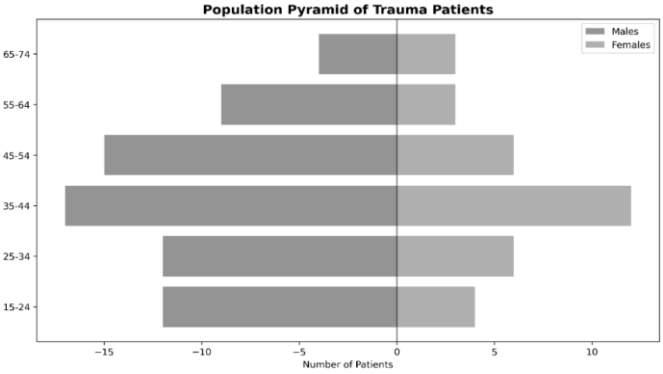

Figure 1: Population Pyramid of Trauma Patients

Prevalence of visceral injury in the study population was expected to be 20-40%, depending on the reported prevalence in general cohorts of blunt abdominal trauma. This is important because prevalence must be taken into account in estimating the numbers of diseased and non-diseased subjects. A few important terminologies and their definitions related to the study include diagnostic accuracy, which is the proportion of subjects correctly classified as having or not having the target condition. It is calculated as {TP + TN} / {TP + TN + FP + FN}. This measure is influenced by disease prevalence and is not independent of sensitivity and specificity. Blunt abdominal trauma is a non-penetrating injury of forceful impact, e.g., falls, vehicle accidents, or striking an object affecting the abdomen of a person. Positive CT refers to observations that confirm or validate positive FAST findings, i.e., presence of intra-abdominal injuries. Here, the outcomes can be segregated as: Sensitivity = TP / (TP + FN), Specificity = TN / (TN + FP), Positive Predictive Value (PPV) = TP / (TP + FP), Negative Predictive Value (NPV) = TN / (TN + FN). Patients who have had a history of blunt abdominal injuries and presented to the Emergency Room within one week of the insult, abdominal pain that persisted after blunt trauma, and all ages and genders of patients were included. Patients with a history of abdominal trauma, having known/pre-existing

DOI: https://doi.org/10.54393/pjhs.v7i2.3527

ascites (that could invert the results of FAST), and patients who were positive in FAST examination but failed to receive further evaluation in CT in AKUH were excluded. The major quantitative information was collected by means of observation (FAST examination, CT imaging) and analysis of the medical records. For secondary data, demographics were collected from hospital records following the Declaration of Helsinki research [11]. The safety of the patients was assured by the administration of masked identification codes rather than IDs to patients [12]. A consultant radiologist applied the standard FAST protocol, and records of data were recorded in a pre-designed proforma, which included Demographics: age, gender, mechanism of injury, location of impact point, use of other conditions that may alter the interpretation of ultrasound, FAST results, and CT results. The categorical variables (gender, mechanism of impact, site of impact, FAST results, CT findings) were illustrated in the form of frequencies and percentages. Continuous variables (age) were tested according to Shapiro Wilk whether they follow a normal distribution or not [13]. FAST sensitivity was estimated by the use of the 95% intervals of the study population. Similarly, specificity, PPV, NPV, and diagnostic accuracy were defined with 95% CI to estimate the parameters of the population [14]. SPSS version 26.0 was used to conduct the statistical analysis. Shapiro-Wilk was used for testing the normality of quantitative variables [15-17].

RESULTS

Out of the 155 patients who were first enrolled under blunt abdominal trauma, 52 patients were dropped, and this left 103 patients to be analyzed. The final sample consisted of 69 male (67%) and 34 female (33%) whose ages were between 18 and 80 years (mean age 42.6 ± 16.3 years). All participants had undergone FAST and abdominal/pelvic CT during a hospital admission. Spleen (n=12) and liver (n=8) were the most commonly injured organs among the 34 CT-positive cases, followed by combined liver/spleen (n=6), kidney (n=4), pancreas (n=2), duodenum (n=1), and colon (n=1). FAST detected splenic (91.7%) and liver injuries (90.9%) more often than kidney injuries (71.4%, p=0.038), because retroperitoneal bleeding occurs in the retroperitoneal space, which is harder to see on standard FAST scans compared to intraperitoneal hemorrhage (Figure 2).

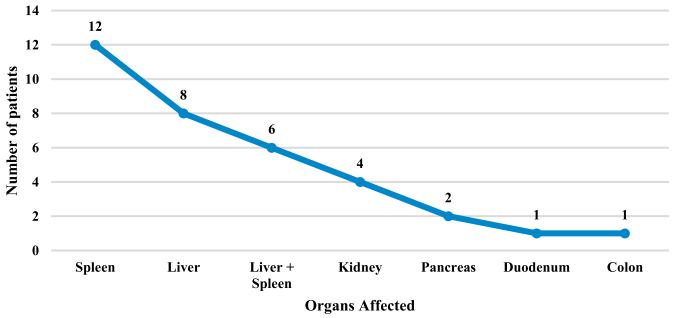

Figure 2: Distribution of Visceral Injuries in Blunt Abdominal Trauma

Diagnostic CT scan identified visceral injuries in 34 patients (33.0%) and no injuries in 69 patients (67.0%). FAST was positive in 43 patients (41.7%) and negative in 60 patients (58.3%). Using CT as the reference standard, FAST demonstrated 30 true positives, 56 true negatives, 13 false positives, and 4 false negatives. Figure 3 shows the breakdown of these diagnostic outcomes (Figure 3).

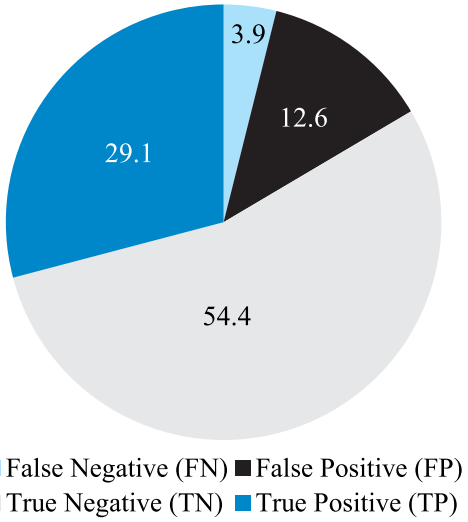

Figure 3: FAST Diagnostic Performance Breakdown

Diagnostic indices of FAST in the diagnosis of visceral injury were as follows: Sensitivity was 88.24% (95% CI: 74.2-95.8%), specificity was 81.16% (95% CI: ~70-89%), Positive Predictive Value (PPV) was 69.77%, Negative Predictive Value (NPV) was 93.33%, overall diagnostic accuracy was 83.50%, and F1 score was 77.78%. These findings suggest that FAST was sensitive in identifying most patients with CT-documented visceral injury and specific (excluding injury) (Table 1).

Table 1: Contingency Table for Diagnostic Performance of FAST in Detecting Visceral Injury Secondary to Blunt Abdominal Trauma, Using CT as Gold Standard (n=103)

Variables	CT Positive, Frequency (%)	CT Negative, Frequency (%)	Total Number
FAST Positive	30/43 (9.7%) TP	13/43 (30.3%) FP	43
FAST Negative	4/60 (6.7%) FN	56/60 (93.3%) T	60
Total Number	34	69	103

DOI: https://doi.org/10.54393/pjhs.v7i2.3527

The high NPV indicates that a negative FAST result was unlikely to miss important visceral injury in this population. FP (n=13) were found mainly in the presence of minimal peritoneal fluid of non-traumatic origin. In the 13 FPs, 84.6% had peritoneal fluid (less than 50 mL). This fluid was subsequently found to be non-traumatic, like normal pelvic fluid, fluid that was already present as ascites (incidental and not known to the patient), or fluid that developed as a result of inflammation. A Fisher's exact test validated the existence of a close association between small fluid volume and FP outcomes (p=0.001, odds ratio=12.4, 95% CI=3.2-48.1). FN (n=4) was common in isolated and solitary solid organ injuries in the absence of massive hemoperitoneum or bleeding volumes, too small to be detectable by FAST. All FNs (n=4, 100%) were caused by isolated solid-organ injuries in the presence of low-volume hemoperitoneum (<200 mL). Chi-square test was done to show that the factor of no moderate-large free fluid in isolated injury showed a significant FN (p=0.012). It also demonstrated that FAST failure was closely associated with low-volume hemoperitoneum (p=0.003). Sensitivity of 88.24% means that FAST missed approximately 12% of cases with visceral injury, while the specificity of 81.16% indicates a moderate rate of FP (Figure 4).

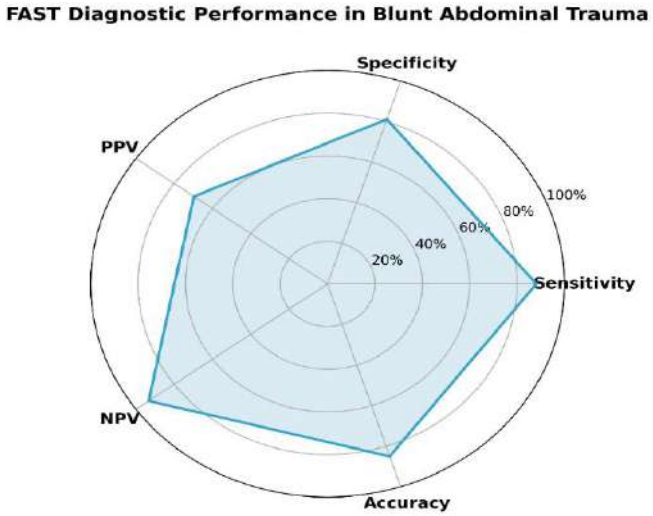

Figure 4: FAST Diagnostic Performance in Blunt Abdominal Trauma

Out of significance is the NPV 93.33% (95% CI: 84.2-97.4%), which meant that a negative FAST essentially eliminated any significant visceral injury in over 9 out of 10 cases. This large NPV favors the clinical utility of FAST as a high-speed screening tool in unstable trauma patients in the absence of urgent CT. However, the moderate PPV of 69.77% (95% CI: 55.2-81.3%), in turn, highlights the importance of confirmatory CT with positive FAST results to avoid unnecessary surgery or intervention. The sensitivity of 88.24% observed is higher than the benchmark of 80%. No statistically significant difference was detected in one-sample proportion testing (p=0.089), which may be because of the lack of sufficient data (n=34 true positives). However, the statistics validate that FAST has the lowest acceptable sensitivity limits, which means it can be used clinically.

DISCUSSION

This study presented a sensitivity of 88.24% (95%, CI: 73.4-95.4%), specificity of 81.16% (95%, CI: 70.4-88.7%), which demonstrates that FAST proves effective in the detection of visceral injuries and can be considered a valid triage assessment in resource-constrained environments where CT is not available. High sensitivity provides a high-level of detection of most patients with visceral injuries, which can be addressed by a timely surgical or interventional response. The study has a good range of sensitivity and specificity in relation to recent studies. Glia and Hamir and Rofananda *et al.* had greater sensitivity (98.3%) as they had highly trained operators and controlled conditions, though it appears that their specificity is low, indicating they over-interpret some results [18, 19]. Conversely, Jabbar *et al.* attained greater specificity (97.8%) due to optimized protocols in fixed cohorts [20]. Current findings are mirrored in studies by Glia and Hamir and Rashid *et al.* which indicate moderate-to-high performance that can be replicated in other similar clinical settings [18, 21]. The negative predictive value of 93.33% (95%, CI:84.1-97.4%) means that negative FAST predicts the absence of any significant visceral injury with a high degree of reliability in over 93% of patients. This large NPV is comparable to Rofananda *et al.* (91.2%) and higher than Salah *et al.* (88.5%), which confirms the validity of FAST in the emergency triage [19, 17]. Observation protocols are safe in hemodynamically stable patients with a negative FAST, without unnecessary radiation and costs, in case of the unavailability of urgent CT. The high NPV 93.33% (95% CI: 84.1-97.4%) indicates that clinicians can be sure that there is no serious visceral injury in hemodynamically unstable patients with a negative FAST, allowing clinicians to promptly focus on extra-abdominal sources of hemorrhage or to begin observation protocol even before a CT scan. Nevertheless, the FN rate was 6.7%, which requires serial tests and constant clinical follow-up. The positive predictive value of 69.77% implies that nearly 30% of positive FAST outcomes could be false. Our PPV is similar to Jabbar *et al.* [20] (72.4 %), but lower than Rashid *et al.* (85.3%) [21]. The FP (n=13) was primarily because of non-traumatic peritoneal fluid, like physiologic ascites or pelvic fluid, and this is why confirmatory CT of a stable patient with positive FAST is necessary to help avoid unnecessary surgery. FN (12% of real injuries) were primarily due to isolated solid organ injuries that did not have extensive hemoperitoneum. These instances illustrate that FAST is not able to detect

DOI: https://doi.org/10.54393/pjhs.v7i2.3527

smaller volumes of bleeding or lack of free fluid parenchymal injuries. This has clinical implications for serial FAST examination and close observation for trauma patients who are persistently abdominally tender even after the early negative FAST. The strengths of the study included prospective data collection, standardization of FAST protocols, and CT confirmation in each and every case, which gave high diagnostic accuracy. The clinical practice environment of the emergency department in the real-world setting increases the applicability of the results to other tertiary hospitals with resource constraints in the same area.

There are certain limitations, such as the variability of operators, since FAST exams were conducted by different radiologists and emergency physicians without standardized proficiency evaluation. Omission of penetrating injuries and cases without follow-up CT is a risk of biasing the sample to the hemodynamically stable cases. The sample size (n=103) is small for estimates with high accuracy, particularly in subgroups. Future studies should test longer FAST (E-FAST) protocols to diagnose pneumothorax and retroperitoneal trauma, adopt standardized operator training, and consider artificially intelligent assisted estimations as reported by computer scientists to lessen variability introduced by operators and enhance the accuracy of diagnosis in the Emergency Department.

CONCLUSIONS

FAST is a valid and quick screening method for identifying blunt intra-abdominal visceral injuries. The study supports its application in emergency and resource-constrained environments. Confirmatory CT is necessary for detailed assessment and characterization of injuries to guide subsequent management. FAST and CT are complementary methods that maximize the diagnostic accuracy, patient outcomes, and resource usage.

Authors' Contribution

Conceptualization: SSQ
Methodology: SSQ, DBK, NZ
Formal analysis: SSQ, DBK, NZ
Writing and Drafting: SSQ, DBK, NZ, SS, MS
Review and Editing: SSQ, DBK, NZ, SS, MS

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Ashley JR, Burczak KW, Cotton BA, Clements TW. Management of Blunt Abdominal Trauma. British Journal of Surgery. 2024 Jul; 111(7): znae168. doi: 10.1093/bjs/znae168.

[2] Ahmad R, Loke I, Saifullah F, Zafar H, Abbasi SH. Carcinoid Heart Disease Associated with Primary Ovarian Carcinoid Tumor: A Rare Presentation. Heart Views. 2024 Apr; 25(2): 106-9. doi: 10.4103/heartviews.heartviews_104_23.

[3] Park C, Loza-Avalos SE, Harvey J, Hirschkorn C, Dultz LA, Dumas RP *et al.* A Real-Time Automated Machine Learning Algorithm for Predicting Mortality in Trauma Patients: Survey Says It's Ready for Prime-Time. The American Surgeon™. 2024 Apr; 90(4): 655-61. doi: 10.1177/00031348231207299.

[4] Shao T, Gu Z, Liu Y, Wang X, Tang C, Chen N et al. Long-Term In Vivo Monitoring of Transplanted Mesenchymal Stromal Cells in Colitis Mice with Magnetic Particle Imaging. E-BioMedicine. 2025 Jun; 116. doi: 10.1016/j.ebiom.2025.105775.

[5] Marietta M and Burns B. Penetrating Abdominal Trauma. In StatPearls [internet]. 2025 Feb.

[6] Cormack CJ, Childs J, Kent F. Competencies Required by Sonographers Teaching Ultrasound Interprofessionally: A Delphi Consensus Study. BioMed Central Medical Education. 2024 Sep; 24(1): 970. doi: 10.1186/s12909-024-05933-x.

[7] Avila J, Smith BC, Guy M. Ultrasound for Trauma Evaluation. InAdvanced Point-of-Care Ultrasound: A Comprehensive Review. Cham: Springer Nature Switzerland. 2025 Aug: 25-37. doi: 10.1007/978-3-031-85308-1_3.

[8] Najjar R. Clinical Applications, Safety Profiles, and Future Developments of Contrast Agents in Modern Radiology: A Comprehensive Review. Iradiology. 2024 Oct; 2(5): 430-68. doi: 10.1002/ird3.95.

[9] Fagotti A, Costantini B, Fanfani F, Giannarelli D, De Iaco P, Chiantera V *et al*. Hyperthermic Intraperitoneal Chemotherapy in Platinum-Sensitive Recurrent Ovarian Cancer: A Randomized Trial on Survival Evaluation (HORSE; MITO-18). Journal of Clinical Oncology. 2025 Mar; 43(7): 852-60. doi: 10.1200/JCO.24.00686.

[10] World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Participants. Journal of the American Medical Association. 2025 Jan; 333(1): 71-4. doi: 10.1001/jama.2024.21972.

[11] Bašković M, Keretić D, Lacković M, Borić Krakar M, Pogorelić Z. The Diagnosis and Management of

DOI: https://doi.org/10.54393/pjhs.v7i2.3527

Pediatric Blunt Abdominal Trauma—A Comprehensive Review. Diagnostics. 2024 Oct; 14(20): 2257. doi: 10.3390/diagnostics14202257.

[12] Hussain K. Revolutionizing Healthcare: The Impact of Artificial Intelligence on Patient Care, Diagnosis, and Treatment. Jurnal Inovasi dan Humaniora. 2024 Feb; 1(5).

[13] Rahayu NI, Muktiarni M, Hidayat Y. An Application of Statistical Testing: A Guide to Basic Parametric Statistics in Educational Research Using SPSS. ASEAN Journal of Science and Engineering. 2024; 4(3): 569-82. doi: 10.17509/ajse.v4i3.76092.

[14] Xu L, Ding F, Zhang X, Zhu Q. Novel Parameter Estimation Method for Systems with Colored Noises Using a Filtering Identification Approach. Syst Control Lett. 2024 Apr; 186: 105774. doi: 10.1016/j.sysconle.2024.105774.

[15] George D and Mallery P. IBM SPSS Statistics 29 Step by Step: A Simple Guide and Reference. Routledge. 2024 Mar. doi: 10.4324/9781032622156.

[16] Monter-Pozos A and González-Estrada E. On Testing the Skew Normal Distribution by Using the Shapiro–Wilk Test. Journal of Computational and Applied Mathematics. 2024 Apr; 440: 115649. doi: 10.1016/j.cam.2023.115649.

[17] Salah EM, Ismaiel MT, Shabaan Hassan Khattab AS, Biomy SS. Accuracy of Focused Assessment with Sonography for Trauma in Blunt Abdominal Trauma in Comparison with Computed Tomography. Zagazig University Medical Journal. 2025 Apr; 31(4): 1656-65. doi: 10.21608/zumj.2025.362556.3854.

[18] Glia A and Hamir O. A Retrospective Analysis of FAST-Sonography Reliability for Blunt Abdominal Trauma Management at Abo-Slim Trauma Hospital: Surgical Outcomes and CT Comparisons. Libyan Medical Journal. 2025 Aug; 17(3): 355-61.

[19] Rofananda IF, Pratiwi AD, Jaya Putra ES, Budi Azhari SR, Setiawati R. Diagnostic Value of Focused Assessment with Sonography in Trauma (FAST) and Computed Tomography in Blunt Abdominal Trauma: A Systematic Review and Meta-analysis. Malaysian Journal of Medicine and Health Sciences. 2025 Mar; 21(2).

[20] Jabbar H, Ahmad M, Raza MA, Hanif N. Diagnostic Accuracy of Fast Scan in Blunt Abdominal Trauma Patients Taking Ct Abdominal as Gold Standard. Journal of Medical and Health Sciences Review. 2025 Feb; 2(1). doi: 10.62019/ss5j6941.

[21] Rashid CH, Shafi I, Khattak BH, Safran M, Alfarhood S, Ashraf I. ANN-Based Software Cost Estimation with Input from COCOMO: CANN Model. Alexandria Engineering Journal. 2025 Feb; 113: 681-94. doi: 10.1016/j.aej.2024.11.042.

DOI: https://doi.org/10.54393/pjhs.v7i2.3501

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Assessment of Maternal Risk Factors in Preterm Labor in A Tertiary Care Hospital of Pakistan

Arfa Rahman[1], Tahira Yasmin[1], Safoora Anjum[1], Sarah Hafeez[1], Sadaf Khurshid[1], Sanum Asif[1] and Hafiz Muhammad Zeeshan Raza[2*]

[1]Department of Obstetrics and Gynaecology, The University of Lahore Teaching Hospital, Lahore, Pakistan
[2]Department of Medicine, The University of Lahore Teaching Hospital, Lahore, Pakistan

ARTICLE INFO

Keywords:
Preterm Labor, Maternal Risk Factors, Urinary Tract Infection, Vaginal Discharge, Anemia, Gestational Hypertension

How to Cite:
Rahman, A., Yasmin, T., Anjum, S., Hafeez, S., Khurshid, S., Asif, S., & Raza, H. M. Z. (2026). Assessment of Maternal Risk Factors in Preterm Labor in A Tertiary Care Hospital of Pakistan: Assessment of Maternal Risk Factors in Preterm Labor. Pakistan Journal of Health Sciences, 7(2), 38-43. https://doi.org/10.54393/pjhs.v7i2.3501

***Corresponding Author:**
Hafiz Muhammad Zeeshan Raza
Department of Medicine, The University of Lahore Teaching Hospital, Lahore, Pakistan
hafizraza26@gmail.com

Received Date: 20th September, 2025
Revised Date: 30th December, 2025
Acceptance Date: 13th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Preterm labor remains a major contributor to perinatal morbidity and mortality, particularly in low- and middle-income countries. Identification of maternal risk factors is essential for prevention, timely intervention, and improved pregnancy outcomes. **Objectives:** To determine the frequency of maternal risk factors associated with preterm labor in a tertiary care setting. **Methods:** A descriptive cross-sectional study was conducted at the Department of Obstetrics and Gynaecology, University of Lahore Teaching Hospital, from May 3, 2025, to August 2, 2025. A total of 155 multigravida women aged 20–40 years with gestational age <37 weeks, diagnosed with preterm labor, were included through non-probability consecutive sampling. Data were collected using a structured proforma and analyzed in SPSS version 25.0. Descriptive statistics were calculated, and stratification was done with the chi-square test, considering $p \leq 0.05$ as significant. **Results:** The mean maternal age was 31.03 ± 5.89 years, and mean gestational age at delivery was 33.88 ± 1.43 weeks. The most frequent maternal risk factors were vaginal discharge (46.5%), urinary tract infection (45.2%), anemia in pregnancy (39.4%), previous cesarean section (23.9%), and gestational hypertension (18.1%). A history of previous preterm birth was present in 12.9% of women, leaking per vagina in 11.6%, and placental abruption in 2.6%. **Conclusions:** Infections, particularly vaginal discharge and urinary tract infection, were the leading maternal risk factors associated with preterm labor in this population. Routine screening and prompt management of maternal infections, alongside targeted antenatal interventions, may help reduce the burden of preterm births.

INTRODUCTION

Preterm labor, characterized as the commencement of labor before 37 weeks of gestation, represents a critical public health concern on a global scale and is a predominant contributor to neonatal morbidity and mortality [1]. Annually, there are approximately 15 million (11.1%) preterm births out of all births worldwide, with 13.3% of these occurrences taking place in South Asia exclusively [2]. A multitude of elements have been recognized as contributing factors to the occurrence of preterm birth. Socio-demographic variables, including maternal ethnicity, advanced maternal age, and tobacco use, have been documented as significant risk factors for preterm delivery [3]. Several studies have consistently demonstrated associations between maternal characteristics and the risk of preterm birth. Factors such as low educational attainment, poor nutritional status, and limited access to antenatal care services have been shown to elevate the likelihood of preterm delivery [4]. Similarly, obstetric determinants, including primigravity, prior preterm birth, and a history of cesarean section, have been

DOI: https://doi.org/10.54393/pjhs.v7i2.3501

linked with increased susceptibility [5]. However, the relative importance of these factors can vary according to regional disparities in healthcare access, socioeconomic conditions, and infection prevalence, which underscores the necessity of context-specific investigations. The scarcity of multicenter or hospital-based studies in Pakistan that quantify these associations using robust data limits the translation of findings into targeted clinical or preventive strategies [6]. In addition, infections such as urinary tract infection and bacterial vaginosis have been implicated as key contributors to preterm labor, with evidence suggesting that untreated genital or urinary infections may account for nearly 40% of spontaneous preterm deliveries in low- and middle-income countries [7]. In Pakistan, limited research has systematically evaluated the combined contribution of maternal infections and metabolic conditions to preterm labor outcomes. A cross-sectional study from Karachi reported that urinary tract infections and anemia were among the top predictors of spontaneous preterm birth, emphasizing the preventable nature of these factors in low-resource hospital settings [8]. Similarly, a study from Peshawar found that socioeconomic status and antenatal care access strongly influenced preterm birth rates, underscoring the multifactorial nature of the condition in Pakistani women [9].

Despite the known global and regional risk factors, preterm labor remains a leading cause of neonatal morbidity and mortality in Pakistan, with limited data to inform context-specific prevention and management strategies. There is a scarcity of systematic, hospital-based studies in Pakistan that comprehensively evaluate maternal sociodemographic, obstetric, and infectious risk factors, highlighting the need for localized evidence to guide clinical and public health interventions. To identify and quantify maternal risk factors associated with preterm labor in a tertiary care hospital setting in Pakistan.

METHODS

This descriptive cross-sectional study was conducted at the Department of Obstetrics and Gynaecology, University of Lahore Teaching Hospital, from May 3, 2025, to August 2, 2025. A total of 155 pregnant women were included in the study, with the sample size calculated using a 95% confidence level, 5% margin of error, and an estimated frequency of prior preterm birth at 11.14% [8]. The ethical approval of the research was obtained from the Institutional Review Board of University College of Medicine and Dentistry (UCMD), Lahore (ERC/91/23/08). Informed written consent was obtained from all participants after fully explaining the purpose, procedures, voluntary nature of participation, the right to withdraw, and measures taken to ensure confidentiality. Data were collected prospectively using a structured proforma designed to capture all relevant variables. Information was obtained through direct interviews and review of antenatal and delivery records. Participants were followed from their first antenatal visit until delivery. Follow-ups were scheduled regularly to track antenatal care utilization, maternal health conditions, and pregnancy outcomes. A non-probability consecutive sampling technique was employed. Women aged 20 to 40 years, who were multigravida with parity of one or more and a gestational age of less than 37 weeks, were included if diagnosed with preterm labor based on clinical signs such as regular uterine contractions, vaginal discharge of mucus plug or bloody show, cervical changes on examination, or transvaginal ultrasound (Mindray DC-30 (Shenzhen Mindray Bio-Medical Electronics Co., Ltd. China) measurement of cervical length. Women with multiple pregnancies, pre-existing maternal comorbidities, known fetal abnormalities, or those who declined to give consent were excluded. Maternal age, education level, socioeconomic status, area of residence, and smoking status were recorded. The body mass index (BMI) was calculated using pre-pregnancy or early pregnancy measurements of weight and height. Besides documenting current pregnancy risk factors, the obstetric history was also documented, including prior preterm birth (delivery before 37 weeks) and previous cesarean section, based on medical records and patient history. The number of antenatal care (ANC) visits was also recorded to assess care utilization. Maternal hemoglobin readings were taken as part of the routine laboratory tests, as documented in the patient files. The cases of gestational hypertension were determined by checking the antenatal and admission blood pressure values. The diagnosis was presumed when women had new-onset hypertension after 20 weeks of gestational age, which was systolic blood pressure of 140 mmHg and/or diastolic blood pressure of 90mmHg, measured on two or more occasions. Cases that had documented hypertension and had neither proteinuria nor systemic features indicating preeclampsia were characterized as gestational hypertension. The measurements of blood pressure were taken with standard sphygmomanometers during routine antenatal visits or hospitalization. Primary data on vaginal discharge were measured via patient-reported symptoms and clinical examination outcomes that were made available by the attending obstetrician. The diagnosis of UTI has been made according to the regular findings of antenatal or admission urinalysis, which can be found in the medical record of the patient. The procedure of collecting and testing midstream urine was conducted in an aseptic manner and through the conventional hospital laboratory tests, such as urine

DOI: https://doi.org/10.54393/pjhs.v7i2.3501

dipstick and urine microscopes. Descriptive statistical methods were employed using SPSS version 25.0. For continuous variables like maternal age, gestational age at delivery, and number of antenatal care (ANC) visits, the mean and standard deviation were computed. Categorical variables, including previous preterm birth history, presence of urinary tract infection (UTI), anemia, hypertensive disorders, and vaginal leakage, were presented as frequencies and proportions. Data stratification was performed based on maternal age, parity, body mass index (BMI), smoking behavior, educational attainment, socioeconomic standing, and residential location. Post-stratification analysis was carried out using the chi-square test. Statistical significance was determined at a threshold of $p \leq 0.05$.

RESULTS

A little over half were aged 31–40 years (83 women, 53.5%), while 72 women (46.5%) were 20–30 years, with a mean age of 31.03 ± 5.89 years. Regarding BMI, 84 women (54.2%) had a normal BMI, 51 (32.9%) were overweight, and 20 (12.9%) were obese, giving a mean BMI of 25.31 ± 3.38 kg/m^2. Slightly more participants were multiparous (82, 52.9%) than nulliparous/primiparous (73, 47.1%). Education levels varied: 51 (32.9%) had secondary, 50 (32.2%) primary, 39 (25.2%) tertiary, and 15 (9.7%) no formal schooling. Socioeconomic status was predominantly low (80, 51.6%), followed by middle (52, 33.5%) and high (23, 14.9%). Residence was evenly distributed between urban (80, 51.6%) and rural (75, 48.4%). Only 1 woman (0.6%) reported smoking, while 154 (99.4%) were non-smokers. The average number of antenatal care (ANC) visits was 4.55 ± 2.27, and the mean gestational age at delivery was 33.88 ± 1.43 weeks, confirming the preterm status. All participants delivered preterm, confirming that the study population exclusively comprised women with preterm labor (Table 1).

Table 1: Frequency Distribution of Different Variables (n=155)

Variables		Frequency (%), Mean ± SD
Age Groups	20-30 Years	72 (46.5%)
	31-40 Years	83 (53.5%)
	Mean Age (Years)	31.03 ± 5.89
BMI	Normal	84 (54.2%)
	Overweight	51 (32.9%)
	Obese	20 (12.9%)
	Mean Weight (kg)	16.30 ± 6.85
	Mean Height (cm)	161.02 ± 5.77
	Mean BMI (kg/m^2)	25.31 ± 3.38
Parity	Nulliparous/Primiparous	73 (47.1%)
	Multiparous	82 (52.9%)
Educational Level	No Formal Education	15 (9.7%)
	Primary	50 (32.2%)
	Secondary	51 (32.9%)
	Tertiary	39 (25.2%)
Socio-Economic Status	Low	80 (51.6%)
	Middle	52 (33.5%)
	High	23 (14.9%)
Residence	Rural	75 (48.4%)
	Urban	80 (51.6%)
Smoking	Yes	1 (0.6%)
	No	154 (99.4%)
Mean Number of ANC Visits		4.55 ± 2.27
Gestational Age on Delivery / Preterm Labor (<37 Completed Weeks)		33.88 ± 1.43

The most prevalent issues were vaginal discharge in 72 women (46.5%) and urinary tract infection (UTI) in 70 women (45.2%). Anemia was also common, affecting 61 women (39.4%). A history of cesarean section was reported in 37 women (23.9%), and gestational hypertension in 28 (18.1%). Fewer women had a history of preterm birth (20, 12.9%), leaking per vagina (18, 11.6%), or placental abruption (4, 2.6%). These values suggest that infectious and hematological conditions were more frequent contributors to preterm labor than obstetric complications (Table 2).

Table 2: Frequency Distribution of Maternal Risk Factors in Preterm Labor

Maternal Risk Factors in Preterm Labor	Frequency (%)
Previous Preterm Birth	20 (12.9%)
Previous C-Section	37 (23.9%)
Gestational Hypertension	28 (18.1%)
Urinary Tract Infection	70 (45.2%)
Vaginal Discharge	72 (46.5%)
Leaking Per Vagina	18 (11.6%)
Anemia In Pregnancy	61 (39.4%)
Placental Abruption	4 (2.6%)

The analysis demonstrated that maternal risk factors for preterm labor—such as previous preterm birth, gestational hypertension, urinary tract infection, vaginal discharge, and anemia were evenly distributed across demographic and socio-environmental groups, with no statistically significant associations (all $p>0.05$). Demographically, older, multiparous, and obese women showed slightly higher frequencies of anemia and previous preterm birth, though these differences were not meaningful. Socio-environmental comparisons revealed marginally higher infection-related risks (UTI and vaginal discharge) among women of low socioeconomic status and rural residence, while gestational hypertension and anemia appeared more common in rural areas (Table 3).

DOI: https://doi.org/10.54393/pjhs.v7i2.3501

Table 3: Stratification of Maternal Risk Factors in Preterm Labor by Demographic Characteristics

Variables	Age (20–30 Years)	Age (31–40 Years)	Normal BMI	Overweight	Obese	Nulli/Primiparous	Multiparous	p-value
Previous Preterm Birth	11.1%	14.5%	14.3%	5.9%	25.0%	9.6%	15.9%	0.083–0.535
Gestational Hypertension	20.8%	15.7%	16.7%	21.6%	15.0%	21.9%	14.6%	0.239–0.719
Urinary Tract Infection	45.8%	44.6%	50.0%	37.3%	45.0%	46.6%	43.9%	0.353–0.876
Vaginal Discharge	47.2%	45.8%	50.0%	43.1%	40.0%	46.6%	46.3%	0.611–0.977
Anaemia In Pregnancy	33.3%	44.6%	38.1%	37.3%	50.0%	31.5%	46.3%	0.089–0.577

The relationship between maternal risk factors for preterm labor and socio-environmental characteristics, including socioeconomic status, residential setting, and smoking habits, has also been presented. Although none of the associations reached statistical significance ($p>0.05$), distinct patterns were evident. Women from low socioeconomic backgrounds and rural areas demonstrated slightly higher rates of urinary tract infections, vaginal discharge, and anemia, suggesting possible links to limited healthcare access, hygiene disparities, and nutritional deficiencies. Gestational hypertension was also more prevalent among rural women, indicating potential environmental or lifestyle influences. Due to the very small number of smokers in the sample, results related to smoking could not be generalized (Table 4).

Table 4: Stratification of Maternal Risk Factors in Preterm Labor by Socio-Environmental Characteristics

Variables	Low SES	Middle SES	High SES	Rural	Urban	Smokers	Non-Smokers	p-value
Previous Preterm Birth	12.5%	11.5%	17.4%	14.7%	11.3%	100.0%	12.3%	0.129–0.775
Gestational Hypertension	17.5%	21.2%	13.0%	25.3%	11.3%	100.0%	17.5%	0.085–0.689
Urinary Tract Infection	51.2%	40.4%	34.8%	45.3%	45.0%	100.0%	44.8%	0.262–0.967
Vaginal Discharge	50.0%	44.2%	39.1%	48.0%	45.0%	0.0%	46.8%	0.350–0.708
Anaemia In Pregnancy	36.3%	40.4%	47.8%	49.3%	30.0%	0.0%	39.6%	0.084–0.595

DISCUSSION

Preterm labor is a multifactorial condition with complex interactions between maternal, fetal, and environmental factors, and remains a leading cause of neonatal morbidity and mortality worldwide. In the present study, the most frequent maternal risk factors were vaginal discharge (46.5%), urinary tract infection (45.2%), anemia in pregnancy (39.4%), previous cesarean section (23.9%), gestational hypertension (18.1%), and previous preterm birth (12.9%), with less common findings including leaking per vagina (11.6%) and placental abruption (2.6%). These findings align with the consensus that infectious etiologies and maternal comorbidities play a major role in the pathophysiology of preterm labor. Vaginal discharge, which in this study was reported in nearly half of the cases, has been previously documented as a strong indicator of genital tract infections leading to inflammatory cascades that precipitate uterine activity. A study conducted in Sub-Saharan Africa reported abnormal vaginal discharge in 38% of women presenting with preterm labor, which is slightly lower than the proportion in the present study, possibly due to regional variations in microbiological flora and access to early antenatal screening [10]. Similarly, Etil *et al.* documented a prevalence of 41%, which is also comparable, supporting the argument that untreated vaginal infections remain a persistent problem in low-resource settings despite antenatal care programs [11]. Urinary tract infection was present in 45.2% of the current cohort, reinforcing its status as a significant preventable risk factor for preterm birth. Several studies have reported similar associations, with prevalence rates ranging from 25% to 50%. For instance, a tertiary care hospital study in Nigeria found UTIs in 42% of preterm labor cases, while a South African study reported a prevalence of 36% [10, 12]. This consistency suggests that asymptomatic bacteriuria screening should be emphasized as part of routine antenatal visits, especially given that timely treatment can significantly reduce preterm birth risk. Anemia in pregnancy, observed in 39.4% of our participants, mirrors the burden reported in other South Asian populations, where nutritional deficiencies and limited access to supplementation remain challenges. In a study from rural Pakistan, anemia was found in 34% of preterm deliveries [13], while an Ethiopian study reported a higher prevalence of 46% [14]. The slightly higher rate in Ethiopia may be due to concurrent high rates of malaria and hookworm infections, which exacerbate iron deficiency. The association between anemia and preterm labor is biologically plausible through mechanisms of impaired oxygen delivery to the placenta and altered maternal immune response, further justifying aggressive nutritional interventions in antenatal care protocols. A history of previous cesarean section was noted in 23.9% of participants. This is comparable to the 21% reported in a Saudi Arabian cohort, though higher than the 15% observed in a Ugandan study in a systematic review [15]. Scar tissue from prior cesarean deliveries can alter uterine

DOI: https://doi.org/10.54393/pjhs.v7i2.3501

contractility and cervical competence, predisposing to preterm labor. Given rising cesarean rates globally, this factor warrants careful risk stratification in subsequent pregnancies. Gestational hypertension was reported in 18.1% of our cases, aligning with prevalence rates of 16% to 20% in studies from China and India [16, 17]. Hypertensive disorders in pregnancy can trigger early delivery through iatrogenic intervention or spontaneous onset due to placental dysfunction. The similarity in rates across diverse populations highlights the universality of this risk and the need for robust antenatal blood pressure monitoring programs. Previous preterm birth, present in 12.9% of participants, is a well-established predictor of recurrence. Studies in Rwanda and Ethiopia have reported similar proportions, ranging from 10% to 15% [18, 19]. This reinforces the need for heightened surveillance and targeted preventive measures, such as progesterone supplementation and cervical length monitoring, in women with such a history. Leaking per vagina, recorded in 11.6% of cases, is a marker of preterm pre-labor rupture of membranes (PPROM). This finding is consistent with a Tanzanian study reporting PPROM in 13% of preterm cases. Prompt diagnosis and antibiotic prophylaxis in such cases can reduce neonatal morbidity by mitigating the risk of ascending infection [20]. Placental abruption was rare in this cohort (2.6%), similar to the 2–4% prevalence reported in large multicenter studies. Although infrequent, its occurrence carries a high risk of adverse maternal and fetal outcomes, often necessitating urgent delivery [21]. Comparable rates have been documented in regional studies; for instance, a tertiary hospital study in Karachi found placental abruption in 2.8% of preterm deliveries, primarily associated with hypertensive disorders and maternal anemia [22]. Likewise, a study from Dubai reported a 3.1% prevalence, with similar associations between abruption, preeclampsia, and poor antenatal care utilization [23]. These findings highlight that even though placental abruption is uncommon, its impact on perinatal morbidity and mortality remains substantial.

This study was conducted at a single center with a limited sample size, which may affect the generalizability of the findings. Additionally, it relies on retrospective data and self-reported history, which may introduce reporting or selection bias. Prospective multicenter studies are needed to validate risk factors and develop targeted interventions for preventing preterm labor in high-risk populations.

CONCLUSIONS

This study identified vaginal discharge (46.5%), urinary tract infection (45.2%), and anemia (39.4%) as the leading maternal risk factors associated with preterm labor, followed by previous cesarean section, gestational hypertension, and prior preterm birth. A large share of preterm births in Pakistan could be prevented through routine antenatal screening and management of maternal infections, anemia, and hypertension.

Authors' Contribution

Conceptualization: TY
Methodology: SA[1], SH, SA[2], HMZR
Formal analysis: SA
Writing and Drafting: AR, SK
Review and Editing: AR, TY, SA[1], SH, SK, SA[2], HMZR

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Rubab F, Majid M, Zeb A, Shabbir S, Ali N, Ali S. Association of Urinary Tract Infection with Preterm Labor in Gravid Females in a Tertiary Care Hospital. Pakistan Armed Forces Medical Journal. 2023 Apr; 73(2): 357. doi: 10.51253/pafmj.v73i2.5515.

[2] Khanam R, Applegate J, Nisar I, Dutta A, Rahman S, Nizar A *et al.* Burden and Risk Factors for Antenatal Depression and Its Effect on Preterm Birth in South Asia: A Population-Based Cohort Study. PLOS One. 2022 Feb; 17(2): e0263091. doi: 10.1371/journal.pone.0263091.

[3] Etil T, Opio B, Odur B, Lwanga C, Atuhaire L. Risk Factors Associated with Preterm Birth Among Mothers Delivered at Lira Regional Referral Hospital. BioMed Central Pregnancy and Childbirth. 2023 Nov; 23(1): 814. doi: 10.1186/s12884-023-06120-4.

[4] Zafar T, Manzoor I, Farooq F. Assessment of Risk Factors Associated with Pre-Term Labour in Tertiary Care Hospitals, Lahore. Journal of Fatima Jinnah Medical University. 2021 Mar; 15(1): 13-7. doi: 10.37018/pobp2666.

[5] Hafeez S, Khan B, Khan M, Syed SZ, Waheed F, Mustafa R. Is Vaginal Progesterone More Effective to Treat Threatened Preterm Labour than Oral Nifedipine? Annals of PIMS-Shaheed Zulfiqar Ali Bhutto Medical University. 2023; 19(4): 441-5. doi: 10.48036/apims.v13i4.977.

[6] Akram S, Ahmad S, Maqsood K, Malik J, Iqbal MA, Ahmad H *et al.* Hormonal Biomarkers and Preterm Birth: Insights from A Study of Pregnant Women in Lahore, Pakistan. Endocrine Regulations. 2024; 58(1): 225-32. doi: 10.2478/enr-2024-0027.

DOI: https://doi.org/10.54393/pjhs.v7i2.3501

[7] Lalani S, Premji SS, Shaikh K, Sulaiman S, Yim IS, Forcheh N *et al.* Individual and Collective Contribution of Antenatal Psychosocial Distress Conditions and Preterm Birth in Pakistani Women. Plos one. 2023 Mar; 18(3): e0282582. doi: 10.1371/journal.pone.0282582.

[8] Qamar A, Aziz M, Riffat N, Tehseen S, Yaqoob S, Zaheer F. Association of Bacterial Vaginosis with Preterm Labour in Pregnant Women: Bacterial Vaginosis and Preterm Labor in Pregnant Women. Pakistan Journal of Health Sciences. 2024 Nov: 175-9. doi: 10.54393/pjhs.v5i11.2359.

[9] Khatoon A, Naz N, Ali S, Akhtar S, Zaman T, Khattak IU. Effectiveness of Educational Intervention on Risk Factors Leading to Preterm Labor Among Pregnant Women in Public Sector Hospital, Peshawar: Educational Intervention on Preterm Labor Risk Factors. Journal of Health and Rehabilitation Research. 2024 Sep; 4(3): 1-5. doi: 10.61919/jhrr.v4i3.1687.

[10] Makasa M, Kaonga P, Jacobs C, Silumesi K, Monde MW, Vwalika B. Magnitude of Perinatal Mortality in Sub-Saharan Africa: A Systematic Review and Meta-Analysis of Observational Studies. MedRxiv. 2025 Sep: 2025-09. doi: 10.1101/2025.09.16.25335956.

[11] Nkwabong E, Djientcheu Deugoue F, Fouedjio J. Pre-Eclampsia in a Sub-Saharan African Country and Maternal-Perinatal Outcome. Tropical Doctor. 2023 Jan; 53(1): 61-5. doi: 10.1177/00494755221113155.

[12] Sprong KE, Wright CA, Mabenge M, Govender S. Placental Histopathology, Maternal Characteristics and Neonatal Outcome in Cases of Preterm Birth in A High-Risk Population in South Africa. South African Medical Journal. 2023; 113(4): 1177-84. doi: 10.7196/SAMJ.2023.v113i4.16772.

[13] Dhaded SM, Saleem S, Goudar SS, Tikmani SS, Hwang K, Guruprasad G *et al.* The Causes of Preterm Neonatal Deaths in India and Pakistan (Purpose): A Prospective Cohort Study. The Lancet Global Health. 2022 Nov; 10(11): e1575-81.

[14] Tadese M, Getachew G, Kebede TN, Yesuf TE, Tessema SD, Damesa WA *et al.* Perinatal Outcomes and Predictors of Placental Abruption: A Retrospective Study in an Ethiopian Tertiary Care Center. Frontiers in Public Health. 2025 Jan; 12: 1453117. doi: 10.3389/fpubh.2024.1453117.

[15] Oltean I, Rajaram A, Tang K, MacPherson J, Hondonga T, Rishi A *et al.* The Association of Placental Abruption and Pediatric Neurological Outcome: A Systematic Review and Meta-Analysis. Journal of Clinical Medicine. 2022 Dec; 12(1): 205. doi: 10.3390/jcm12010205.

[16] Sureshbabu RP, Aramthottil P, Anil N, Sumathy S, Varughese SA, Sreedevi A *et al.* Risk Factors Associated with Preterm Delivery in Singleton Pregnancy in A Tertiary Care Hospital in South India: A Case-Control Study. International Journal of Women's Health. 2021 Apr: 369-77. doi: 10.2147/IJWH.S282251.

[17] Zhang L, Yang H, Sun Y, Liu S. Preterm Placental Abruption and Its Association with Adverse Maternal and Neonatal Outcomes: A Retrospective Study. BioMed Central Pregnancy and Childbirth. 2025 May; 25(1): 620. doi: 10.1186/s12884-025-07718-6.

[18] Ayele TB and Moyehodie YA. Prevalence of Preterm Birth and Associated Factors among Mothers Who Gave Birth in Public Hospitals of East Gojjam Zone, Ethiopia. BioMed Central Pregnancy and Childbirth. 2023 Mar; 23(1): 204. doi: 10.1186/s12884-023-05517-5.

[19] Rutayisire E, Mochama M, Ntihabose CK, Utumatwishima JN, Habtu M. Maternal, Obstetric and Gynecological Factors Associated with Preterm Birth in Rwanda: Findings from a National Longitudinal Study. BioMed Central Pregnancy and Childbirth. 2023 May; 23(1): 365. doi: 10.1186/s12884-023-05653-y.

[20] Rugumisa BT, Bongcam-Rudloff E, Lukumay MS, Lyantagaye SL. Factors Associated with Risk of Preterm Delivery in Tanzania: A Case-Control Study at Muhimbili National Hospital. International Journal of Gynecology and Obstetrics. 2021 Aug; 154(2): 318-23. doi: 10.1002/ijgo.13520.

[21] Deng K, Liang J, Mu Y, Liu Z, Wang Y, Li M et al. Preterm Births in China between 2012 and 2018: An Observational Study of More Than 9 million Women. The Lancet Global Health. 2021 Sep; 9(9): e1226-41. doi: 10.1016/S2214-109X(21)00298-9.

[22] Baloch F, Abro F, Chand P. Perinatal Stroke: Risk Factors and Outcome. A Study from Aga Khan University Hospital Karachi. Pakistan Armed Forces Medical Journal. 2022 Feb; 72(1): 215. doi: 10.51253/pafmj.v72i1.4863.

[23] Saquib S, Hamza LK, AlSayed A, Saeed F, Abbas M. Prevalence and Its Feto-Maternal Outcome in Placental Abruption: A Retrospective Study for 5 Years from Dubai Hospital. Dubai Medical Journal. 2020 Apr; 3(1): 26-31. doi: 10.1159/000506256.

DOI: https://doi.org/10.54393/pjhs.v7i2.3544

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Patterns and Outcomes of Adult Cardiac Surgery in a Tertiary Hospital in Pakistan: A Seven-Year Single-Surgeon Retrospective Study

Muhammad Sher i Murtaza[1], Muhammad Hamid Chaudhary[1*] and Khurram Hafeez[1]

[1]Department of Cardiac Surgery, Chaudhry Pervaiz Elahi Institute of Cardiology, Multan, Pakistan

ARTICLE INFO

Keywords:
Coronary Artery Bypass Grafting, Valvular Heart Disease, Rheumatic Heart Disease, Developing Country

How to Cite:
Murtaza, M. S. i, Chaudhary, M. H., & Hafeez, K. (2026). Patterns and Outcomes of Adult Cardiac Surgery in a Tertiary Hospital in Pakistan: A Seven-Year Single-Surgeon Retrospective Study: Patterns and Outcomes of Adult Cardiac Surgery . Pakistan Journal of Health Sciences, 7(2), 44-49. https://doi.org/10.54393/pjhs.v7i2.3544

***Corresponding Author:**
Muhammad Hamid Chaudhary
Department of Cardiac Surgery, Chaudhry Pervaiz Elahi Institute of Cardiology, Multan, Pakistan
dr.hamid632@gmail.com

Received Date: 11th October, 2025
Revised Date: 12th December, 2025
Acceptance Date: 16th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Cardiovascular disease is a major health burden in Pakistan, where access to cardiac surgery is limited. Understanding disease patterns and cardiac surgical procedures in high-burden societies can guide resource allocation to improve patient outcomes. **Objectives:** To evaluate retrospectively the pattern of adult cardiac surgical procedures and their outcomes performed by a single surgeon at a tertiary hospital in Pakistan. **Methods:** This retrospective observational study included 1,404 consecutive adult patients operated on by a single surgeon at CPEIC, Multan. Data were collected from all consecutive adult patients (≥15 years), of either sex, who underwent surgery by a single cardiac surgeon between May 2018 and July 2025. The data were obtained from a prospectively maintained surgeon's database. Fisher's exact test was used for small group comparisons. **Results:** A total of 1,404 patients underwent cardiac surgery. Coronary artery bypass grafting comprised 70.0% (on-pump 55.9%, off-pump 11.3%), valvular surgery 21.6%, congenital repairs 2.3%, aortic root 1.0%, and post-MI VSR repair 1.5%. In isolated CABG, the internal mammary artery was used in 92.4%, with a mean of 2.96 ± 0.93 grafts. Complications occurred in 20.4%. Early mortality was 3.1%, with the lowest rates in CABG (1.9%) and the highest in VSR repair (23.8%). Ventilation time and hospital stay were significantly longer in aortic root and redo procedures ($p<0.05$). **Conclusions:** Over seven years, CABG and valvular procedures predominated, with overall mortality and complication rates comparable to regional benchmarks. On-pump CABG provided more complete revascularization, while complex surgeries carried a higher risk.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide. More than half a billion people around the world are affected by cardiac diseases [1, 2]. In South Asia, there is an increasing trend of mortality among patients with ischemic heart disease, resulting in 0.16 years of loss of healthy life expectancy [3]. In South Asia, including Pakistan, rheumatic heart disease is more prevalent than in developed countries, resulting in a significantly increased need for mitral and aortic valve procedures. [4] However, contemporary institutional data describing the full range of cardiac procedures and associated early outcomes in Pakistan remain limited, with most published studies focusing on isolated procedures or small cohorts. Pakistan has a massive cardiovascular disease burden, with both incidence and mortality exceeding global averages. The Global Burden of Disease 2019 estimated the age-standardized incidence of CVD at 918 per 100,000 and the mortality rate at 358 per 100,000, which is significantly higher than the worldwide rates [3]. A multicenter cohort reported a 34.9% prevalence of coronary artery disease (CAD), with hypertension, diabetes, obesity, and smoking as major risk factors. [5] Local case–control data from Nawabshah further highlight obesity, hyperlipidemia, diabetes, and smoking as strongly associated with CAD [6].

DOI: https://doi.org/10.54393/pjhs.v7i2.3544

Cardiac surgery in Pakistan began in the late 1950s with closed-heart procedures, followed by the country's first open-heart surgery in 1967–68 at United Christian Hospital, Lahore [7, 8]. Postoperative morbidity after cardiac surgery is a key determinant of survival and resource utilization. Reporting outcomes is crucial for enhancing care and informing policy in resource-constrained settings. This study hypothesized that, despite a diverse and high-risk population, early morbidity and mortality at our center would be comparable to international standards.

Despite the high burden of cardiovascular disease and the growing need for diverse cardiac procedures in Pakistan, comprehensive institutional data on the full spectrum of adult cardiac surgeries and their early outcomes remain limited. Most available studies focus on isolated procedures or small cohorts, highlighting the need for single-center, longitudinal data to inform clinical practice, resource allocation, and policy in resource-constrained settings.

METHODS

The retrospective observational study was conducted at the Department of Cardiac Surgery, Chaudhry Pervaiz Elahi Institute of Cardiology, Multan, Pakistan. Data included all consecutive adult patients (>15 years) of either sex operated on by a single cardiac surgeon between May 2018 and July 2025, and the study was conducted from July to oct 2025. Before data collection commenced, institutional ethical approval was obtained (No. 238). Cardiovascular procedures like coronary artery bypass grafting, cardiac valve replacement or repair, aortic surgery, surgery on the pericardium, and adult congenital repairs were included. Patients operated on by other surgeons and minor vascular or cardiac procedures, e.g., arterial embolectomy, carotid endarterectomy, and pericardial effusion drainage, were excluded from the study. The study utilized a prospectively maintained surgeon's database, in which data were recorded in Microsoft Excel. Patients' preoperative, intraoperative, and postoperative characteristics were recorded. All procedures were carried out by a single experienced cardiac surgeon following standardized institutional protocols for anesthesia, myocardial protection, and postoperative management. For coronary artery bypass grafting (CABG), a median sternotomy was performed with cardiopulmonary bypass (CPB) established via aortic and right atrial cannulation; myocardial protection was provided with cold blood cardioplegia. In off-pump cases, mechanical stabilizers and intracoronary shunts were used. The left internal mammary artery (LIMA) was the preferred conduit for the left anterior descending artery, with additional venous or radial grafts used as needed. Valvular surgeries were conducted under CPB with aortic cross-clamping, utilizing mechanical or bioprosthetic valves as appropriate, and repairs were attempted when feasible. Procedures involving the aortic root and ascending aorta employed Composite tube grafts, while pericardiectomy was performed via median sternotomy. Adult congenital defects such as ASD and VSD were repaired under CPB with patch closure. Early mortality was defined as death during the initial hospitalization or within 30 days post-surgery, whereas late mortality referred to any death occurring after discharge but within six months of the operation. The collected variables comprise age, sex, and comorbidities like diabetes, hypertension, and smoking. Preoperative assessment included echocardiography (left ventricular ejection fraction, chamber dimensions, valvular morphology and severity, and pulmonary pressures) and coronary angiography (extent and severity of coronary artery disease). Additional variables recorded were HbA1c, serum creatinine, severity of carotid disease on carotid Doppler, abdominal ultrasonographic findings, priority status, operative details including type of procedure, use of cardiopulmonary bypass (CPB), use of left internal mammary artery (LIMA), coronary endarterectomy, cross-clamp and bypass durations, need of intraaortic balloon, and conversions from off-pump to on-pump techniques. Postoperative outcomes assessed were early mortality, defined as death during the index hospitalization or within 30 days of surgery; The primary morbidity outcome was defined as "any postoperative complication," referring to the occurrence of at least one adverse event following surgery. This composite measure included perioperative myocardial infarction (postoperative peak CK-MB ≥5× baseline), atrial or other arrhythmias, stroke, renal dysfunction (a ≥2-fold rise in serum creatinine from preoperative levels), re-exploration for bleeding or tamponade, pleural effusion requiring intervention, prolonged mechanical ventilation, and extended hospital stay. Patients who experienced more than one complication were counted only once in this composite outcome. Patients' contact information was documented, and postoperative follow-up was advised. Written informed consent was taken. The initial follow-up visit occurred two weeks after discharge in the Surgical Outpatient Department, followed by subsequent monthly visits for ongoing evaluation for 6 months after discharge. Data were analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between categorical variables were made using the Chi-square test or Fisher's Exact test, as appropriate, depending on expected cell frequencies.

DOI: https://doi.org/10.54393/pjhs.v7i2.3544

Where subgroup counts were small (<5), Fisher's Exact test Monte Carlo correction was applied.

RESULTS

Between May 2018 and July 2025, a total of 1,404 patients underwent cardiac surgery at Chaudhry Pervaiz Elahi Institute of Cardiology (CPEIC), Multan. The mean age was 49.2 ± 13.7 years (range 15–82), and 76.9% were male. Diabetes mellitus was present in 31.7%, hypertension in 37.2%, and smoking in 14.9% of the cohort. Carotid duplex revealed normal carotid arteries in 871 (62.0%) patients, mild disease in 495 (35.3%), moderate disease in 26 (1.9%), and Severe stenosis (≥50% internal carotid artery stenosis) in 12 (0.9%). Abdominal ultrasound was normal in 64% of cases, whereas 15.6% had fatty liver, 7.5% congested liver, 3.5% renal cysts, and 2.6% gallstones. The mean ejection fraction was 51.3 ± 9.6%, with corresponding mean left ventricular internal diameters of 48.1 ± 8.0 mm in diastole and 33.9 ± 7.0 mm in systole. Mean serum creatinine (n=1382) was 0.99 ± 0.29 mg/dL, and HbA1c (n=1278) was 6.58 ± 1.50%. Most operations were elective (91.6%), with 8.1% performed urgently and 0.3% emergently. Coronary artery bypass grafting (CABG) was the most commonly performed procedure (n=983, 70%). Isolated valvular heart disease constituted 21.0% of the operative workload, simple congenital surgery accounted for 2.9%, and ruptured sinus of Valsalva (RSOV) repair was performed in 7 cases (0.5%). Other operations included Aortic root surgery (n=15, 1.0%), post-MI VSR repair (n=21, 1.5%), minimally invasive cardiac surgery (n=8, 0.6%), left atrial myxoma excision (n=7, 0.5%), redo operations (n=6, 0.4%), and pericardiectomy (n=6, 0.4%) (Table1).

Table 1: Spectrum of Procedures Performed

Operations	Frequency (%)	Operations	Frequency (%)
OFF Pump CABG	158 (11.3%)	On Pump CABG	785 (55.9%)
On-Pump Beating	7 (0.5%)	AVR	63 (4.5%)
MVR	112 (8.0%)	DVR	50 (3.6%)
ASD Prim	1 (0.1%)	ASD Sec	23 1.6%)
ASD SV	7 (0.5%)	RSOV	6 (0.4%)
Redo Surgery	6 (0.4%)	VSR Repair	21 (1.5%)
Aortic Root Surgery	15 (1.1%)	MV Repair	3 (0.2%)
MICs	8 (0.6%)	LA Myxoma Excision	9 (0.6%)
Miscellaneous	6 (0.4%)	Pericardiectomy	6 (0.4%)
SAM	2 (0.1%)	RVOT	2 (0.1%)
CABG + MVR	7 (0.5%)	CABG + DVR	1 (0.1%)
CABG + ASD Repair	1 (0.1%)	TVR	1 (0.1%)
CABG + AVR	16 (1.1%)	MVR + TVR	52 (3.7%)
DVR + TVR	17 (1.2%)	ASD + MVR	4 (0.3%)
VSD	2 (0.1%)	AVR + VSD Repair	5 (0.4%)
CABG + Mv Repair	8 (0.6%)	–	–

Abbreviations: CABG, coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; AVR, aortic valve replacement; MVR, mitral valve replacement; DVR, double valve replacement; TVR, tricuspid valve replacement; MV repair, mitral valve repair; ASD, atrial septal defect (Prim = primum type; Sec = secundum type; SV = sinus venosus type); VSD, ventricular septal defect; RSOV, ruptured sinus of Valsalva; VSR, ventricular septal rupture (post-myocardial infarction); MICs, minimally invasive cardiac surgery; LA Myxoma, left atrial myxoma excision; SAM, subaortic membrane resection; RVOT, right ventricular outflow tract repair.

The left internal mammary artery (LIMA) was utilized in 92.4% of isolated CABG cases. In 1.7% of patients (n=16), the LIMA was harvested after establishing cardiopulmonary bypass (CPB) because of hemodynamic instability. In 7.3% of CABG cases, IMA was not used—either it was damaged during harvesting, had inadequate flow, or was not harvested due to technical difficulties, a poor-quality LAD target vessel, and a dilated left ventricle with poor function. Coronary endarterectomy was required in 4.6% of CABG cases. Intra-aortic balloon pump (IABP) support was used in 10 patients (0.7%). Among 158 patients undergoing OPCAB, 6 (3.8%) required conversion to on-pump surgery due to hemodynamic instability or technical difficulty. Comparative analysis revealed no statistically significant differences between on-pump and off-pump CABG in terms of early mortality (1.8% vs 1.9%), overall complications (20.4% vs 19.8%), ventilation time (5.4 ± 1.9 vs 5.2 ± 1.8, p=0.27), and hospital stay (6.3 ± 7.1vs 6.1 ± 6.8, p=0.589). However, on-pump CABG was associated with a significantly greater mean graft per patient (3.21 ± 0.76 vs 2.14 ± 0.86, p<0.001). A total of 1,117 patients (79.6%) had an uneventful postoperative course, while 287 (20.4%) developed one or more complications. The most frequent were atrial fibrillation (3.5%), re-exploration (2.7%), rhythm disturbances (2.4%), and renal dysfunction (1.4%). When stratified by procedure type, the highest complication rates occurred in post-MI VSR repair (33.3%) and redo surgeries (16.7%), reflecting the greater complexity and hemodynamic instability in these patients. The association between operation type and occurrence of postoperative complications was analyzed using the Fisher–Freeman–Halton Exact Test with Monte Carlo simulation (10,000 sampled tables, 99% confidence interval). Given that over 90% of expected cell frequencies were less than 5, this approach was preferred over the Pearson Chi-square test. The result showed a statistically significant relationship between procedure type and complications (Monte Carlo p = 0.003, 99% CI: 0.001–0.004) (Table 2).

DOI: https://doi.org/10.54393/pjhs.v7i2.3544

Table 2: Distribution of Major Postoperative Complications According to Surgery Groups (%)

Complications	CABG Only	CABG +Concomitant Surgery	Valvular	Congenital	Aortic Root Surgery	Post-MI VSR	MICS	Redo
No Complication	79.8%	75.8%	80.0%	80.6%		66.7%	100.0%	83.3%
Re-exploration (Reopening)	2.6%	0.0%	3.0%	4.5%	7.1%	0.0%	0.0%	0.0%
Atrial Fibrillation	3.6%	6.1%	4.3%	0.0%	0.0%	0.0%	0.0%	0.0%
Raised Creatinine	1.7%	6.1%	0.3%	0.0%	0.0%	0.0%	0.0%	0.0%
Rhythm Disturbances	2.2%	0.0%	2.3%	4.5%	7.1%	4.8%	0.0%	0.0%
Pleural Effusion	0.7%	0.0%	0.3%	3.0%	0.0%	0.0%	0.0%	0.0%
Stroke	0.4%	0.0%	0.3%	0.0%	0.0%	0.0%	0.0%	0.0%
Overall Complication	20.2%	24.2%	20.0%	19.4%	35.7%	33.3%	0.0%	16.7%

FisherExact Test (Monte Carlo simulation based on 10,000 samples, 99% CI 0.001–0.004): p=0.003.

Early mortality occurred in 43 patients (3.1%), while 12 patients (0.9%) died later within 6 months after surgery. Conventional CABG had the lowest early mortality (1.8%), whereas post-MI VSR repair (23.8%), aortic root surgery (8.3%), and combined CABG + AVR (12.5%) had the highest rates of early mortality. The association between operation type and postoperative mortality was analyzed using the Fisher Exact Test with Monte Carlo simulation (10 000 iterations, 99 % confidence interval 0.000–0.000). Given that over 75 % of expected cell counts were < 5, this approach was preferred over the Pearson Chi-square test. The relationship remained statistically significant (p<0.001). Includes all operations with ≥1 death. Percentages are within each operation type (denominator = N for that operation) (Table 3).

Table 3: Procedures with Mortality: Early, Late, and Total by Operation

Operations	n	Early Deaths, n (%)	Late Deaths, n (%)	Total Deaths, n (%)	Survival, n (%)
OPCAB	158	3 (1.9%)	0 (0.0%)	3 (1.9%)	155 (98.1%)
CABG	785	14 (1.8%)	3 (0.4%)	17 (2.2%)	768 (97.8%)
On-Pump Beating	7	1 (14.3%)	0 (0.0%)	1 (14.3%)	6 (85.7%)
AVR	63	1 (1.6%)	3 (4.8%)	4 (6.3%)	59 (93.7%)
MVR	112	3 (2.7%)	1 (0.9%)	4 (3.6%)	109 (96.4%)
ASD Prim	1	0 (0.0%)	1 (100.0%)	1 (100.0%)	0 (0.0%)
Redo Surgery	6	2 (33.3%)	1 (16.7%)	3 (50.0%)	3 (50.0%)
VSR Repair	21	5 (23.8%)	2 (9.5%)	7 (33.3%)	14 (66.7%)
Aortic Root Surgery	15	3 (20.0%)	0 (0.0%)	3 (20.0%)	12 (80.0%)
Miscellaneous	6	1 (16.7%)	0 (0.0%)	1 (16.7%)	5 (83.3%)
Pericardiectomy	6	1 (16.7%)	0 (0.0%)	1 (16.7%)	5 (83.3%)
SAM	2	1 (50.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)
CABG + MVR	7	1 (14.3%)	0 (0.0%)	1 (14.3%)	6 (85.7%)
CABG + AVR	16	2 (12.5%)	0 (0.0%)	2 (12.5%)	14 (87.5%)
MVR + TVR	52	2 (3.8%)	0 (0.0%)	2 (3.8%)	50 (96.2%)
DVR + TVR	17	2 (11.8%)	0 (0.0%)	2 (11.8%)	15 (88.2%)
CABG + Mvr	8	0 (0.0%)	1 (12.5%)	1 (12.5%)	7 (87.5%)
AVR + VSD Repair	5	1 (20.0%)	0 (0.0%)	1 (20.0%)	4 (80.0%)

Fisher–Freeman–Halton Exact Test (Monte Carlo simulation based on 10,000 samples, 99 % CI 0.000–0.000): p<0.001.

The mean ventilation time was 6.4 ± 7.5 hours, and the mean hospital stay was 5.4 ± 1.9 days. Aortic surgery and DVR cases had the most extended CPB durations (p<0.001), and both ventilation time and hospital stay were significantly prolonged in Aortic Root surgery and redo surgeries (p<0.001 and p=0.032, respectively).

DISCUSSION

Over the past seven years at CPEIC in Multan, our results for coronary artery bypass grafting (CABG) align closely with both regional and global data. The in-hospital mortality for isolated CABG (1.8%) was slightly lower than the 2.5–4% reported in other Pakistani series, reflecting consistent surgical performance [9]. These results also align with large international registries, where early mortality typically ranges between 1–2% [10]. Patients who needed coronary endarterectomy (CE) during CABG surgery experienced higher perioperative complications, consistent with global literature [11]. However, in patients with diffuse coronary artery disease (CAD), CE remains a valuable operative strategy, particularly in settings where hybrid or advanced percutaneous interventions (e.g., rotational/orbital atherectomy or intravascular lithotripsy) are not widely available [12]. Current findings reinforce that CE is a safe technique to achieve complete revascularization in diffuse CAD. A notable point in our study cohort is the relatively young age of patients (mean 49 years) compared with Western populations, where CABG is typically performed in the sixth or seventh decade of life [13]. This age disparity reflects the earlier onset and rapid progression of CAD among South Asians, emphasizing the urgent need for primary prevention and early screening programs to reduce cardiovascular disease in the region. High-risk subgroups, including patients undergoing repair of post-myocardial infarction ventricular septal rupture (VSR) or aortic root surgery, demonstrated predictably higher operative mortality. This is consistent with global experience [14]. Conversely, the reasonable outcomes of our limited aortic root cases suggest growing institutional expertise in complex aortic surgery, which is encouraging for capacity development in resource-limited centers. When comparing on-pump and off-pump CABG in our series, the data showed that although both operative armamentaria are safe, more complete revascularization is achieved during on-pump

DOI: https://doi.org/10.54393/pjhs.v7i2.3544

CABG. These findings are comparable with large international trials [15]. The overall postoperative complication rate was 20.4%, which matches regional data reporting 18–25% complications after heart surgery [16]. Atrial fibrillation was the most common complication at 3.5%, consistent with international studies showing rates between 2% and 5% [17]. The significant link between the type of surgery and complication rates ($\chi^2 = 322.5$, $p<0.001$) shows that more complex procedures, like redo surgeries and VSR repair, carry higher risks. Valvular procedures accounted for over one-fifth of our total cardiac procedures. The 6-month mortality ranged from 3.6% for mitral valve replacement (MVR) to 6.3% for aortic valve replacement (AVR), and corresponded closely with both national reports [18] and international benchmarks (2–7%) [19]. The intra-aortic balloon pump (IABP) support was used in only 0.7% of cases—lower than the international average of 2–4%—which points to a low-risk patient population, stable intraoperative conditions, and effective heart protection [20]. The short ventilation time (mean 6.4 hours) and hospital stay (mean 5.4 days) compare favorably with other regional centers [21], reflecting efficient postoperative recovery protocols. Predictably, longer ventilation and hospital stays were observed among aortic root and redo cases, consistent with their higher complexity. Preoperative imaging showed that over 97% of patients had normal or only mild carotid artery disease. This likely explains the low rate of stroke during surgery (0.4%). While coronary artery bypass grafting and valve replacements predominated, the overall spectrum also revealed relatively few cases of total arterial revascularization, mitral valve repair, and minimally invasive cardiac surgery (MICS). This reflects both patient selection and institutional practice patterns in a developingcountry setting, where resource constraints, late presentation, and limited expertise in advanced techniques may restrict their wider adoption. The low frequency of mitral valve repair highlights the ongoing challenge of rheumatic pathology, which often necessitates replacement rather than repair. Similarly, the limited use of total arterial grafting and MICS underscores the need for training and capacity building to expand these approaches to align with international standards.

The study's observational design may be prone to selection bias, as patient allocation to on-pump vs off-pump or complex procedures was not randomized. Additionally, variations in surgeon experience and perioperative management protocols could have influenced outcomes, limiting the ability to attribute results solely to the surgical approach. Future multicenter prospective studies with extended follow-up are needed to evaluate long-term outcomes and optimize surgical strategies in South Asian populations.

CONCLUSIONS

This seven-year retrospective study from a tertiary hospital in Pakistan demonstrates that CABG and valve surgeries predominated, with outcomes comparable to regional benchmarks. On-pump CABG achieved more complete revascularization, while complex procedures carried higher morbidity and mortality. Very few patients underwent mitral valve repair, total arterial bypass grafting, or minimally invasive surgery, underscoring the need for specialized training and adoption of advanced surgical strategies to improve outcomes in these subgroups.

Authors' Contribution

Conceptualization: MSIM
Methodology: MSIM, MHC
Formal analysis: MSIM, MHC
Writing and Drafting: MSIM, MHC, KH
Review and Editing: MSIM, MHC, KH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Lindstrom M, DeCleene N, Dorsey H, Fuster V, Johnson CO, LeGrand KE *et al.* Global Burden of Cardiovascular Diseases and Risks Collaboration, 1990-2021. Journal of the American College of Cardiology. 2022 Dec; 80(25): 2372-425. doi: 10.1016/j.jacc.2022.11.001.

[2] World Health Organization. Cardiovascular diseases (CVDs) [Internet]. Geneva: WHO. 2025 Jul. [Last accessed on 17 Nov 2025]. https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).

[3] World Health Organization. World Health Statistics 2025: Monitoring Health for the SDGS, Sustainable Development Goals. 2025 May. https://www.who.int/publications/i/item/9789240110496.

[4] Lamichhane P, Pokhrel KM, Pokharel P, Bhandari B, Lamichhane P, Regmi PR. Prevalence of Rheumatic Heart Disease in South Asia: A Systematic Review and Meta-Analysis. International Journal of Cardiology. 2022 Jul; 358: 110-9. doi: 10.1016/j.ijcard.2022.04.010.

[5] Hasnain M, Yasin S, Khan FR, Aslam K, Ihsan A, Farooq N. Prevalence and Risk Factors of Coronary Artery

DOI: https://doi.org/10.54393/pjhs.v7i2.3544

Disease in Pakistan: A Multicenter Cohort Study. Journal of Population Therapeutics and Clinical Pharmacology. 2024; 31(1): 2956-64. doi: 10.53555/hnwhqk98.

[6] Devkota S, Dhungana RR, Pandey AR, Poudel CM, Shrestha H, Bhattarai A. Risk Factors of Coronary Artery Disease: A Hospital-Based Study. Journal of Nepal Health Research Council. 2022; 20(02): 487-493.

[7] Jamali YA, Kazi S, Chandio MN, Nabeel SK, Kanhar AA, Riaz U *et al.* Prevalence and Risk Factors of Coronary Heart Disease in Nawabshah: A Case-Control Study: Prevalence and Risk Factors of Coronary Heart Disease. Pakistan Journal of Health Sciences. 2024 Oct: 194-8. doi: 10.54393/pjhs.v5i10.2102.

[8] Hosain N. The Early Days of Cardiac Surgery in South Asia: The History and Heritage. The Annals of Thoracic Surgery. 2017 Jul; 104(1): 361-6. doi: 10.1016/j.athoracsur.2017.01.039.

[9] National Institute of Cardiovascular Diseases (NICVD). History. 2025; 2(1).

[10] Vervoort D, Meuris B, Meyns B, Verbrugghe P. Global Cardiac Surgery: Access to Cardiac Surgical Care Around the World. The Journal of Thoracic and Cardiovascular Surgery. 2020 Mar; 159(3): 987-96. doi: 10.1016/j.jtcvs.2019.04.039.

[11] Jan A, Hayat MK, Khan MA, Ullah R. Trends in Perioperative Parameters and Postoperative Complications Associated with Coronary Artery Bypass Graft Surgery (CABG); A Four-Year Retrospective Study. Pakistan Journal of Medical Sciences. 2021 Nov; 37(7): 1734. doi: 10.12669/pjms.37.7.4315.

[12] Wang J, Gu C, Yu W, Gao M, Yu Y. Short-and Long-Term Patient Outcomes from Combined Coronary Endarterectomy and Coronary Artery Bypass Grafting: A Meta-Analysis of 63,730 Patients (PRISMA). Medicine. 2015 Oct; 94(41): e1781. doi: 10.1097/MD.0000000000001781.

[13] Hill JM, Kereiakes DJ, Shlofmitz RA, Klein AJ, Riley RF, Price MJ *et al.* Intravascular Lithotripsy for Treatment of Severely Calcified Coronary Artery Disease. Journal of the American College of Cardiology. 2020 Dec; 76(22): 2635-46. doi: 10.1016/j.jacc.2020.09.603.

[14] Wang C, Chen J, Gu C, Li J. Analysis of Survival After Coronary Endarterectomy Combined with Coronary Artery Bypass Grafting Compared with Isolated Coronary Artery Bypass Grafting: A Meta-Analysis. Interactive Cardiovascular and Thoracic Surgery. 2019 Sep; 29(3): 393-401. doi: 10.1093/icvts/ivz125.

[15] Inam H, Sohail AA, Aamir A, Ahmed KS, Asif N, Sharfuddin SS. Coronary Artery Bypass Grafting in Young Adults. History. 2024 Dec; 14: 10-45.

[16] Matteucci M, Ronco D, Corazzari C, Fina D, Jiritano F, Meani P *et al.* Surgical Repair of Postinfarction Ventricular Septal Rupture: Systematic Review and Meta-Analysis. The Annals of Thoracic Surgery. 2021 Jul; 112(1): 326-37. doi: 10.1016/j.athoracsur.2020.08.050.

[17] Hannan EL, Wu C, Smith CR, Higgins RS, Carlson RE, Culliford AT *et al.* Off-Pump Versus On-Pump Coronary Artery Bypass Graft Surgery: Differences in Short-Term Outcomes and Long-Term Mortality and Need for Subsequent Revascularization. Circulation. 2007 Sep; 116(10): 1145-52. doi: 10.1161/CIRCULATIONAHA.106.675595.

[18] Zia K, Mangi AR, Bughio H, Tariq K, Chaudry PA, Karim M. Initial Experience of Minimally Invasive Concomitant Aortic and Mitral Valve Replacement/Repair at a Tertiary Care Cardiac Centre of a Developing Country. Cureus. 2019 Sep; 11(9). doi: 10.7759/cureus.5707.

[19] Kytö V, Myllykangas ME, Sipilä J, Niiranen TJ, Rautava P, Gunn J. Long-Term Outcomes of Mechanical vs Biologic Aortic Valve Prosthesis in Patients Older Than 70 Years. The Annals of Thoracic Surgery. 2019 Nov; 108(5): 1354-60. doi: 10.1016/j.athoracsur.2019.04.012.

[20] Perazzo A, Steffen SP, Gaiotto FA, Santos RH, Jatene FB, Lorusso R. A Milestone in Cardiac Care: The Intra-Aortic Balloon Pump in Cardiac Surgery and Transplantation. Brazilian Journal of Cardiovascular Surgery. 2024 Jun; 39(2): e20240991. doi: 10.21470/1678-9741-2024-0991.

[21] Wang Q, Tao Y, Zhang X, Xu S, Peng Y, Lin L *et al.* The Incidence, Risk Factors, and Hospital Mortality of Prolonged Mechanical Ventilation among Cardiac Surgery Patients: A Systematic Review and Meta-Analysis. Reviews in Cardiovascular Medicine. 2024 Nov; 25(11): 409. doi: 10.31083/j.rcm2511409.

DOI: https://doi.org/10.54393/pjhs.v7i2.3540

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Natural Conception Rate in Sub-Fertile Couples Following Laparoscopy and Dye Test

Fatima Akram[1*], Aisha Taj[1], Rabia Rind[1], Nudrat Nazir[1] and Saima Rajab[1]

[1]Department of Gynecology and Obstetrics, Liaquat National Hospital, Karachi, Pakistan

ARTICLE INFO

Keywords:
Hypothyroidism, Laparoscopy, Nulligravida, Sub-Fertility, Tubal Blockage

How to Cite:
Akram, F., Taj, A., Rind, R., Nazir, N., & Rajab, S. (2026). Natural Conception Rate in Sub-Fertile Couples Following Laparoscopy and Dye Test: Natural Conception Rate in Sub-Fertile Couples Following Laparoscopy and Dye Test. Pakistan Journal of Health Sciences, 7(2), 50-56. https://doi.org/10.54393/pjhs.v7i2.3540

***Corresponding Author:**
Fatima Akram
Department of Gynecology and Obstetrics, Liaquat National Hospital, Karachi, Pakistan
akramfatima678@gmail.com

Received Date: 7th October, 2025
Revised Date: 4th December, 2025
Acceptance Date: 13th December, 2025
Published Date: 28th February, 2026

ABSTRACT

Infertility represents a major reproductive health issue, affecting between 8-12% couples worldwide. **Objectives:** To determine the natural conception rate in sub-fertile couples following laparoscopy and dye test (LDT). **Methods:** This single-center, prospective, observational, cohort study was performed at the Department of Obstetrics and Gynecology, Liaquat National Hospital, Karachi, Pakistan, during May 2024 to August 2025. A total of 131 couples with sub-fertility were consecutively enrolled if the female partner was scheduled for LDT. Baseline demographic and clinical data were recorded from both partners. All procedures were performed by experienced gynecologic surgeons. Participants were followed for six months to assess natural conception, confirmed clinically and by ultrasound. Statistical analyses included chi-square, t-test, or independent sample t-test, with $p<0.05$ considered significant. **Results:** Out of the 131 women, the mean age was 30.1 ± 6.0 years. The mean duration of subfertility was 25.6 ± 9.2 months. On laparoscopy, 69.5% had normal tubes, while unilateral and bilateral tubal abnormalities were seen in 16.0% and 8.4%. Natural conception within six months occurred in 76 (58.0%) women, with a mean interval to conception of 4.8 ± 1.1 months. Women who conceived were significantly younger (p=0.035), had lower BMI (p=0.003), and were more often nulligravid (p=0.001). Hypothyroidism was more prevalent among those who did not conceive (p=0.004). **Conclusions:** The study provides evidence supporting LDT as a valuable diagnostic and therapeutic modality in the management of sub-fertile couples. Younger age, lower BMI, and absence of hypothyroidism were associated with successful natural conception following LDT.

INTRODUCTION

Infertility represents a major reproductive health issue, affecting between 8-12% couples worldwide [1]. Infertility can lead to significant emotional, psychological, and social stress for those hoping to achieve parenthood [2, 3]. Structural abnormalities play a prominent role in subfertility [4]. Tubal factor infertility is estimated to account for almost one-third of female infertility cases across the globe [4]. Early and accurate diagnosis is vital for guiding appropriate management in infertility-affected couples [5]. In Pakistan, the prevalence of infertility is around 33%, with primary infertility at 5% and secondary infertility at 18% [6]. Laparoscopy with dye test (LDT) has become a leading diagnostic method in the evaluation of subfertility among women [7]. LDT is a minimally invasive procedure that allows direct visualization of the uterus, fallopian tubes, and ovaries, while also assessing whether the fallopian tubes are open or blocked through the injection of a colored dye. An additional advantage of laparoscopy is the ability to treat certain pelvic pathologies during the same procedure, which may restore natural fertility and reduce the need for advanced assisted reproductive techniques [8]. Despite its routine use in clinical practice, there is considerable variation in the reported rates of natural conception after LDT. Ikechebelu and colleagues reported a natural conception rate of 25% following the procedure [9]. Verhoeve et al. described a

DOI: https://doi.org/10.54393/pjhs.v7i2.3540

rate of 9.4%, whereas Mahtab *et al.* documented substantially higher conception rates of 62.9% in women with primary infertility [10, 11].

Data regarding the factors that may influence the chances of natural conception after LDT remain limited and diverse. Identifying these factors is essential for clinicians to provide accurate counseling, set realistic expectations, and design individualized treatment plans for sub-fertile couples. The findings of this study can help clarify the role of laparoscopy and dye test in the management of sub-fertility and may support clinicians in their decision-making process. Due to the wide variation in reported conception rates and limited data on influencing factors, this study aims to determine the natural conception rate in sub-fertile couples following LDT in our population.

METHODS

This single-centre, prospective, observational, cohort study was conducted at the Department of Obstetrics and Gynecology, Liaquat National Hospital, Karachi, Pakistan, during May 2024 to August 2025. Written informed consent was obtained from all participants, and institutional ethical approval was secured before study initiation (Ref: App # 1033-2024-LNH-ERC). Eligibility criteria included couples diagnosed with sub-fertility, where the female partner was scheduled to undergo a laparoscopy and dye test for diagnostic or therapeutic evaluation. Couples were excluded if the female partner had active genital infection, tuberculosis, overt tubal pathology such as hydrosalpinx, significant pelvic adhesions (American Fertility Society adhesion score > 10)[12], markedly distorted tubal anatomy (gross anatomical distortion) due to multiple uterine myomas, or distal tubal occlusion, as identified by preoperative assessment or intraoperative findings. Couples already pursuing fertility treatment or those with male partners having severely impaired semen parameters requiring IVF-ICSI were also excluded. All participants were recruited consecutively from couples presenting with subfertility. Sub-fertility was defined as failure to achieve conception after at least twelve months of regular, unprotected intercourse. Sample size calculation was performed using the Open-Epi online software, based on a 95% confidence level, with a 5% margin of error, and an estimated post-procedural natural conception rate of 9.4% [10], resulting in a required sample of 131 couples. Sample size was calculated using the formula: n = Z2 (1-α/2) * p * (1 - p) / e2. At enrollment, demographic and baseline clinical data were collected for both partners, including age, weight, and height. Female reproductive history, including parity and duration since attempting conception, was recorded. Both the pattern of menstrual cycles before and after laparoscopy (regular or irregular) and the presence of any comorbidities, specifically diabetes, hypertension, or hypothyroidism (as per history and medical record), were documented for both partners. Patterns of menstrual cycles, both before and after the laparoscopy, were classified as regular if menses occurred at predictable intervals of 21 to 35 days and as irregular if cycles fell outside this range or varied unpredictably. Information on previously diagnosed medical conditions, such as endometriosis or polycystic ovarian syndrome, was also collected. The reasons for laparoscopy with dye test were recorded. All enrolled women underwent laparoscopy with a dye test performed by experienced gynecologic surgeons (post-fellowship experience > 5 years) under standard protocols. Laparoscopy with dye test referred to a minimally invasive surgical procedure in which a laparoscope is used to visualize the pelvic organs, and a colored dye (methylene blue dye 0.1% solution) is injected through the cervix to assess the patency of the fallopian tubes and the overall anatomy of the uterine cavity. The successful passage of dye through one or both fallopian tubes, confirmed by its visual spill into the pelvic cavity, was considered evidence of tubal patency. Intraoperative findings, including tubal patency (normal, unilateral, or bilateral abnormalities), presence of pelvic adhesions, or other significant pelvic pathology, were meticulously documented. All procedures were performed using a Karl Storz 10-mm high-definition laparoscopic system (Germany) equipped with a xenon light source and HD camera unit. Dye testing was carried out using methylene blue 0.1% solution delivered transcervically through a Rubin's cannula under low-pressure infusion. Standard reusable laparoscopic instruments were employed, and all procedures were performed by consultants with over five years of post-fellowship experience. After the procedure, participants were followed for a period of six months to assess for natural conception, defined as a viable pregnancy achieved without assisted reproductive technologies. Pregnancy was confirmed through participant report, clinical evaluation, and ultrasound evidence of gestational sac development. For those who conceived, the interval from laparoscopy to conception in months was recorded. Follow-up assessments were conducted monthly, during which women were contacted through in-person visits or telephone interviews to document menstrual regularity, symptoms, and potential conception. Clinical evaluation and ultrasound were performed whenever pregnancy was suspected. Conception was defined as a clinically and ultrasonographically confirmed intrauterine pregnancy within six months of the procedure. Confirmation required visualization of a gestational sac on transvaginal ultrasound. The GE Voluson E8 ultrasound system was used with a 5–9 MHz transvaginal transducer, ensuring

DOI: https://doi.org/10.54393/pjhs.v7i2.3540

reproducibility and standardization of measurements. Women who did not achieve conception within six months of follow-up were recorded as having no conception. The conception rate was defined as the proportion of women who achieved clinically confirmed natural conception within six months following laparoscopy and dye test. The conception rate was calculated using the formula: Conception rate (%) = (Number of women with clinically confirmed natural conception / Total number of women undergoing LDT) X 100. All study data were maintained with strict confidentiality. Statistical analysis was conducted using IBM SPSS Statistics version 26.0. The primary outcome, natural conception within six months post-laparoscopy, was calculated as a proportion. Associations between baseline characteristics, intraoperative findings, and conception outcomes were evaluated using appropriate comparative statistical tests, including chi-square or Fisher's exact test for categorical variables, and t-test or Mann-Whitney U test for continuous variables (as per normal distribution of data checked by the Shapiro-Wilk test). Time to natural conception was analyzed using Kaplan–Meier survival curves, and the equality of distributions among subgroups was compared using the Log-Rank (Mantel–Cox) test. Statistical significance was set at $p<0.05$.

RESULTS

In a total of 131 women, the mean age and BMI were 30.1 ± 6.0 years and 28.0 ± 4.4 kg/m^2. There were 99 (75.6%) women who had regular menstrual cycles before laparoscopy. The mean duration since attempting to conceive naturally was 25.61 ± 9.19 months. Hypothyroidism, diabetes, and hypertension were the commonest comorbid conditions, documented among 37 (28.2%), 30 (22.9%), and 20 (15.3%) women, respectively. The primary indication for LDT was suspected tubal blockage, noted in 110 (84.0%) women, followed by pelvic pain investigation, reported in 5 (3.8%) women. On laparoscopy, the most common findings were normal tubes, noted in 91 (69.5%), unilateral tubal abnormalities in 21 (16.0%), bilateral tubal abnormalities in 11 (8.4%), and pelvic adhesions in 8 (6.1%). After LDT, 76 (58.0%) women conceived naturally within 6 months, while 55 (42.0%) did not. The mean duration required to conception was 4.79 ± 1.12 months among women who successfully achieved conception. Women who conceived were significantly younger (29.1 ± 7.1 vs. 31.4 ± 3.6 years, p=0.035), and had a significantly lower BMI (27.1 ± 3.9 vs. 29.4 ± 4.7 kg/m^2, p=0.003). Nulligravid status (9.5% vs. 3.6%, p=0.001) was more common among those who conceived. Hypothyroidism was significantly more prevalent among women who did not conceive (40.0% vs. 19.7%, p=0.004), whereas no significant differences were found for comorbid conditions like diabetes (p=0.415) or hypertension (p=0.214). There was no statistically significant difference in menstrual cycle regularity before or after laparoscopy, duration of attempting conception, or presence of polycystic ovarian syndrome between women who conceived or not. Among 76 women who conceived naturally, 42 (55.3%) had normal laparoscopic findings, while 19 (25.0%) had unilateral tubal abnormalities, 9 (11.8%) had bilateral abnormalities, and 6 (7.9%) had pelvic adhesions (p<0.001). Among 55 women who did not conceive, 49 (89.1%) had normal findings, and only 2 (3.6%) each showed unilateral, bilateral, or pelvic adhesions (p<0.001). Results showing the association of demographical and clinical characteristics of women undergoing laparoscopy and dye test with successful conception (Table 1).

Table 1: Association of Demographical and Clinical Characteristics of Women Undergoing Laparoscopy and Dye Test with Successful Conception Rate (n=131)

Characteristics		Conception, n (%)	No Conception, n (%)	p-value
Age	Years	29.13 ± 7.07	31.35 ± 3.62	0.035*
Body Mass Index	kg/m^2, Mean ± SD	27.08 ± 3.90	29.36 ± 4.70	0.003*
Gravidity	0	7 (9.5%)	2 (3.6%)	0.001*
	1	40 (54.1%)	13 (23.6%)	
	2	22 (29.7%)	29 (52.7%)	
	3	5 (6.8%)	11 (20.0%)	
Parity	0	72 (97.3%)	55 (100%)	0.219
	2	2 (2.7%)	–	
Menstrual Cycle Before Laparoscopy	Regular	60 (78.9%)	39 (70.9%)	0.291
	Irregular	16 (21.1%)	16 (29.1%)	
Comorbidities	Diabetes	14 (18.4%)	16 (29.1%)	0.415
	Hypertension	20 (26.3%)	–	0.214
	Hypothyrodism	15 (19.7%)	22 (40.0%)	0.004*
Time Since Trying to Conceive (Months)	Mean ± SD	25.03 ± 9.43	26.46 ± 8.84	0.388
Medical Conditions	Endometriosis	–	2 (3.6%)	0.098
	Polycystic Ovarian Syndrome	15 (19.7%)	14 (25.5%)	0.485
Reasons for Undergoing Laparoscopy and Dye Test	Suspected Blockage	65 (85.5%)	45 (81.8%)	0.419
	Endometriosis	–	2 (3.6%)	
	Pelvic Pain	3 (3.9%)	2 (3.6%)	
	Others	8 (10.5%)	6 (10.9%)	
Findings of Laparoscopy and Dye Test	Normal	42 (55.3%)	49 (89.1%)	<0.001*
	Unilateral Tubal Abnormalities	19 (25.0%)	2 (3.6%)	
	Bilateral Tubal Abnormalities	9 (11.8%)	2 (3.6%)	
	Pelvic Adhesions	6 (7.9%)	2 (3.6%)	
Menstrual Cycle after Laparoscopy	Regular	62 (81.6%)	37 (67.3%)	0.060
	Irregular	14 (18.4%)	18 (32.7%)	

Chi-square test/Fisher's exact test applied for the comparison of categorical data; Numeric data compared using an independent

DOI: https://doi.org/10.54393/pjhs.v7i2.3540

sample t-test. * Indicates statistically significant p-values (≤ 0.05).

Partners of women who conceived were significantly younger (30.6 ± 4.0 vs. 33.2 ± 3.8 years, p<0.001), and had significantly lower BMI (25.6±3.4 vs. 28.6 ± 3.4 kg/m^2, p<0.001). There were no significant differences in partner comorbidities, including diabetes (25.0% vs. 30.9%, p=0.512), hypertension (32.9% vs. 29.1%, p=0.571), or hypothyroidism(n=3, 3.9% vs. n=0; p=0.131)(Table 2).

Table 2: Association of Demographical and Clinical Characteristics of Partners with Natural Conception Rate (n=131)

Characteristics		Conception, n (%)	No Conception, n (%)	p-value
Age	Years, Mean ± SD	30.58 ± 4.02	33.18 ± 3.80	<0.001*
Body Mass Index	kg/m^2, Mean ± SD	25.59 ± 3.36	28.60 ± 3.36	<0.001*
Comorbidities	Diabetes	19 (25.0%)	17 (30.9%)	0.512
	Hypertension	25 (32.9%)	16 (29.1%)	0.571
	Hypothyroidism	3 (3.9%)	–	0.131

Chi-square test/Fisher's exact test applied for the comparison of categorical data; Numeric data compared using an independent sample t-test. *Indicates statistically significant p-values (≤0.05).

The mean time required for conception among cases with success was 4.79 months (standard error [SE]: 0.13; 95% confidence interval [CI]: 4.54–5.04). When stratified by the reason for undergoing LDT, women with suspected tubal blockage had a mean time of 4.82 months (SE: 0.13; 95% CI: 4.56–5.07). Those evaluated for pelvic pain investigation exhibited a mean time of 3.67 months (SE: 0.33; 95% CI: 3.01–4.32). A comparison of successful conception distributions among the three indication groups performed using the Log Rank (Mantel-Cox) test demonstrated a p-value of 0.028 across the different reasons for undergoing LDT, indicating that the reason for LDT was significantly associated with variations in time required to successful conception among the study population with the shortest mean time observed in the pelvic pain investigation group (Figure 1).

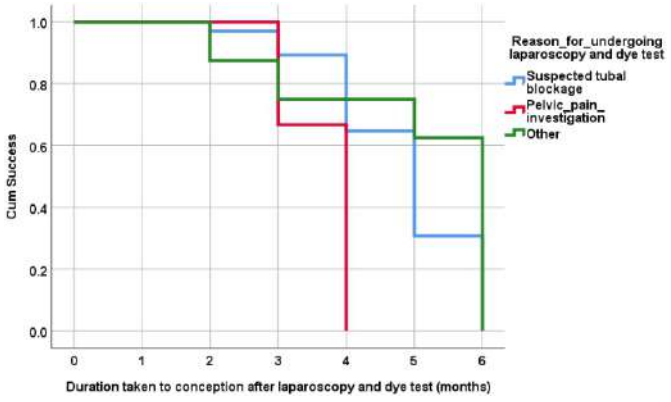

Figure 1: Kaplan-Meier Survival Curves by Time to Successful Conception Following Laparoscopy and Dye Test as Per Indications

Analysis of time to successful conception according to the findings of LDT revealed that the overall mean time to conception was 4.79 months (SE: 0.13; 95% confidence interval [CI]: 4.54–5.04). Among the subgroups, women with normal LDT findings had a mean time to conception of 4.67 months (SE: 0.17; 95% CI: 4.33–5.01), unilateral tubal abnormalities had a mean time to conception of 4.84 months (SE: 0.30; 95% CI: 4.26–5.43), bilateral tubal abnormalities had a mean time to conception of 5.33 months (SE: 0.17; 95% CI: 5.01–5.66), while those with pelvic adhesions, the mean time was 4.67 months (SE: 0.49; 95% CI: 3.70–5.64). Comparison of conception times among the LDT finding groups using the Log Rank (Mantel-Cox) test showed no statistically significant difference in time to conception (p=0.609)(Figure 2).

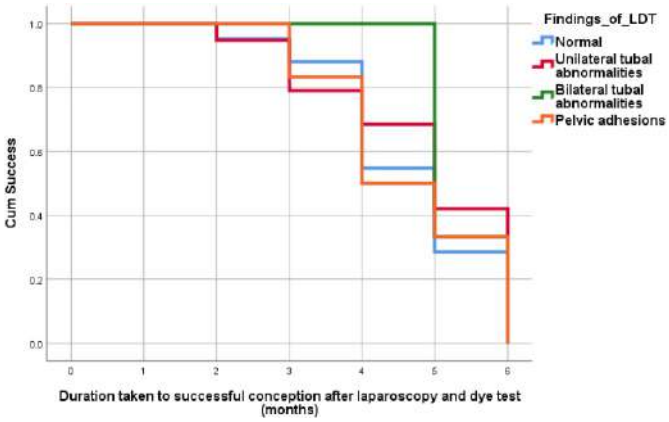

Figure 2: Kaplan-Meier Survival Curves by Time to Successful Conception Following Laparoscopy and Dye Test as Per Laparoscopy and Dye Test Findings

DISCUSSION

The present study explored the natural conception rate following LDT in sub-fertile couples and found a natural conception rate of 58% within six months. These findings position LDT as a potentially valuable tool in the fertility management algorithm for couples with unexplained or tubal-factor subfertility. Lee *et al.* documented a pregnancy rate of 41.9% over twelve months in infertile women with endometriosis, with nearly all conceptions occurring within six months postoperatively [13]. This timing reinforces the hypothesis that mechanical or physiological restoration effected by laparoscopy may facilitate early spontaneous conception in selected populations. In contrast, Younas *et al.* reported a slightly lower conception rate of 37.5% following LDT in women with minimal to mild endometriosis and pelvic adhesions, yet still found that 80% who conceived did so within eighteen months [14]. Differences in patient selection, the underlying cause of subfertility, and follow-up duration may explain variability in conception rates across these cohorts. The importance of patient selection and

DOI: https://doi.org/10.54393/pjhs.v7i2.3540

preoperative characteristics in predicting conception outcomes emerged in this study. Younger age among women and their partners was strongly associated with significantly higher conception rates following LDT. Zhang *et al.* identified patient age over 35 years as an independent risk factor for poor pregnancy outcomes after laparoscopic treatment in women with tubal infertility, a finding mirrored by a decline in conception rates with age in the current study population [15]. The effect of age is likely mediated by both oocyte quality and the cumulative impact of reproductive tract pathology, underscoring the urgency of timely intervention in younger women [16]. Another significant finding of this study was the association of BMI with successful natural conception following LDT, as both female, and their partners had significantly lower BMI who achieved natural conception post-LDT. Fataftah *et al.* also found a higher spontaneous pregnancy rate among non-obese women with unilateral proximal tubal obstruction following transcervical fallopian tube recanalization [17]. Elevated BMI is linked to multiple mechanisms detrimental to fertility, including ovulatory dysfunction, metabolic disturbances, and suboptimal endometrial receptivity, potentially diminishing the effectiveness of surgical intervention [18]. The duration of subfertility before LDT did not significantly differ between those who conceived and those who did not. This contrasts with findings from Zhang *et al.* where a longer duration of subfertility predicted poorer pregnancy outcomes [15]. Intraoperative findings remain critical for both prognosis and management. The highest conception rates were recorded among those with normal or unilateral tubal pathology, while those with bilateral tubal abnormalities or pelvic adhesions had lower, but not statistically different, rates. This trend resonates with the literature showing ongoing conception potential in women with proximal tubal blockage after selective salpingography and tubal catheterization [19, 20]. The diagnostic and therapeutic value of LDT is further supported by studies such as Mahtab *et al.* and Wankhede *et al.* which underscore the role of minimally invasive evaluation in identifying and correcting pelvic pathology [11, 20]. The finding that more than half (55.3%) of women who conceived had normal laparoscopy results, while 89.1% of those who failed to conceive also had normal findings, suggests that tubal patency alone does not guarantee successful conception. Unexplained subfertility often persists despite normal tubal morphology and spill, possibly due to subtle peritubal adhesions, impaired ciliary function, ovulatory or luteal phase defects, or unmeasured male factors. It may indicate that normal dye test results should be interpreted as a favourable but not definitive predictor of fertility potential. In the present study, nearly one-third of women were found to have comorbidities. The association between thyroid dysfunction and subfertility has been reported in the past, with thyroid hormone playing a crucial role in ovulation and endometrial receptivity [21]. Effective management of thyroid disorders may improve spontaneous conception rates following surgical intervention [22]. The presence of diabetes or hypertension did not show a significant association with conception outcomes in this study. This may reflect the multifactorial nature of sub-fertility, where metabolic and vascular comorbidities may influence fertility through indirect pathways or in conjunction with other risk factors [23]. In the current cohort, 1.5% women had a pre-existing diagnosis of endometriosis. Lee *et al.* reported that the severity of endometriosis and the type of laparoscopic intervention were not significantly associated with conception rate postoperatively [13]. Sharma *et al.* highlighted a high prevalence of endometriosis among women undergoing diagnostic laparoscopy, with no significant difference in demographic characteristics or BMI between those with and without the disease [24]. The study's strengths include prospective data collection, rigorous documentation of intraoperative findings, and systematic follow-up.

Several limitations merit consideration in interpreting these findings. The single-center nature of the study and relatively modest sample size may limit the generalizability of the results to other populations or settings. Selection bias may have been introduced by the exclusion of women with overt pelvic disease or those already pursuing assisted reproductive technologies. Outcome assessment relied on participant report, clinical evaluation, and ultrasound evidence, but potential for under-reporting of early pregnancy losses remains. Six-month of follow-up may have precluded identification of conceptions occurring later.

CONCLUSIONS

The study provides evidence supporting laparoscopy and dye test as a valuable diagnostic and therapeutic modality in the management of sub-fertile couples. Early conception post-procedure is facilitated by younger age, lower BMI, and absence of hypothyroidism, with favorable findings on laparoscopy further enhancing the likelihood of success.

Authors' Contribution

Conceptualization: AT
Methodology: FA, AT, RR, NN, SR
Formal analysis: RR
Writing and Drafting: FA
Review and Editing: AT, FA, RR, NN, SR

All authors approved the final manuscript and take responsibility for the integrity of the work.

DOI: https://doi.org/10.54393/pjhs.v7i2.3540

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Vander Borght M and Wyns C. Fertility and Infertility: Definition and Epidemiology. Clinical Biochemistry. 2018 Dec; 62: 2-10. doi: 10.1016/j.clinbiochem.2018.03.012.

[2] Hazlina NH, Norhayati MN, Bahari IS, Arif NA. Worldwide Prevalence, Risk Factors and Psychological Impact of Infertility Among Women: A Systematic Review and Meta-Analysis. British Medical Journal Open. 2022 Mar; 12(3): e057132. doi: 10.1136/bmjopen-2021-057132.

[3] Borumandnia N, Majd HA, Khadembashi N, Alaii H. Worldwide Trend Analysis of Primary and Secondary Infertility Rates Over Past Decades: A Cross-Sectional Study. International Journal of Reproductive Biomedicine. 2022 Feb; 20(1): 37. doi: 10.18502/ijrm.v20i1.10407.

[4] Ambildhuke K, Pajai S, Chimegave A, Mundhada R, Kabra P. A Review of Tubal Factors Affecting Fertility and Its Management. Cureus. 2022 Nov; 14(11). doi: 10.7759/cureus.30990.

[5] Garolla A, Pizzol D, Carosso AR, Borini A, Ubaldi FM, Calogero AE *et al.* Practical Clinical and Diagnostic Pathway for the Investigation of the Infertile Couple. Frontiers In Endocrinology. 2021 Jan; 11: 591837. doi: 10.3389/fendo.2020.591837.

[6] Sami N and Saeed Ali T. Perceptions and Experiences of Women in Karachi, Pakistan Regarding Secondary Infertility: Results from a Community-Based Qualitative Study. Obstetrics and Gynecology International. 2012; 2012(1): 108756. doi: 10.1155/2012/108756.

[7] Arab W. Diagnostic Laparoscopy for Unexplained Subfertility: A Comprehensive Review. Brazilian Journal of Assisted Reproduction. 2022 Jan; 26(1): 145. doi: 10.5935/1518-0557.20210084.

[8] Pantou A, Simopoulou M, Sfakianoudis K, Giannelou P, Rapani A, Maziotis E *et al.* The Role of Laparoscopic Investigation in Enabling Natural Conception and Avoiding in Vitro Fertilization Overuse for Infertile Patients of Unidentified Aetiology and Recurrent Implantation Failure Following In vitro Fertilization. Journal of Clinical Medicine. 2019 Apr; 8(4): 548. doi: 10.3390/jcm8040548.

[9] Ikechebelu JI, Eleje GU, Bhamare P, Joe-Ikechebelu NN, Okafor CD, Akintobi AO. Fertility Outcomes following Laparoscopy-Assisted Hysteroscopic Fallopian Tube Cannulation: A Preliminary Study. Obstetrics and Gynecology International. 2018; 2018(1): 7060459. doi: 10.1155/2018/7060459.

[10] Verhoeve HR, Coppus SF, van der Steeg JW, Steures P, Hompes PG, Bourdrez P *et al.* The Capacity of Hysterosalpingography and Laparoscopy to Predict Natural Conception. Human Reproduction. 2011 Jan; 26(1): 134-42.

[11] Mahtab NT, Mahmud N, Chowdhury TS, Chowdhury TA, Begum T. A Follow-Up Study on Fertility and Menstrual Pattern in Infertile Patients After Laparoscopy in a Tertiary Care Hospital in Bangladesh. BIRDEM Medical Journal. 2020 Jun; 10(2): 125-9. doi: 10.3329/birdem.v10i2.47744.

[12] Peers EM and Brown CB. American Fertility Society Score as a Measure of the Effectiveness of 4% Icodextrin in A Pivotal Adhesion Reduction Trial in the USA. Fertility and Sterility. 2005 Sep; 84: S160. doi: 10.1016/j.fertnstert.2005.07.392.

[13] Lee HJ, Lee JE, Ku SY, Kim SH, Kim JG, Moon SY *et al.* Natural Conception Rate Following Laparoscopic Surgery in Infertile Women with Endometriosis. Clinical and Experimental Reproductive Medicine. 2013 Mar; 40(1): 29. doi: 10.5653/cerm.2013.40.1.29.

[14] Younas K, Majoko F, Sheard K, Edwards C, Bunkheila A. Select and Treat at Laparoscopy and Dye Test Improves the Spontaneous Pregnancy. Human Fertility. 2014 Mar; 17(1): 56-9. doi: 10.3109/14647273.2014.880522.

[15] Zhang L, Jiang F, Qi R, Fu W, Wang Y, Gui D. Pregnancy Outcomes in Patients with Tubal Infertility Following Laparoscopic Treatment: A Multivariate Predictive Study. Annals of Palliative Medicine. 2021 Jan; 10(1): 46262-462. doi: 10.21037/apm-20-2347.

[16] Moghadam AR, Moghadam MT, Hemadi M, Saki G. Oocyte Quality and Aging. Brazilian Journal of Assisted Reproduction. 2022 Jan; 26(1): 105. doi: 10.5935/1518-0557.20210026.

[17] Fataftah J, Tayyem R, Al Rshoud F, Al-Omari M. Spontaneous Pregnancy Rate After Fallopian Tube Recanalization for Unilateral Obstruction with A Patent Contralateral Tube. Egyptian Journal of Radiology and Nuclear Medicine. 2022 Oct; 53(1): 227. doi: 10.1186/s43055-022-00916-8.

[18] Zheng L, Yang L, Guo Z, Yao N, Zhang S, Pu P. Obesity and Its Impact on Female Reproductive Health: Unraveling the Connections. Frontiers In Endocrinology. 2024 Jan; 14: 1326546. doi: 10.3389/fendo.2023.1326546.

[19] Papaioannou S, Afnan M, Girling AJ, Coomarasamy A, Ola B, Olufowobi O *et al.* Long-Term Fertility Prognosis

DOI: https://doi.org/10.54393/pjhs.v7i2.3540

Following Selective Salpingography and Tubal Catheterization in Women with Proximal Tubal Blockage. Human Reproduction. 2002 Sep; 17(9): 2325-30. doi: 10.1093/humrep/17.9.2325.

[20] Wankhede S, Thakare S, Goverdhan N, Shahane S. Evaluation of Cases of Infertility by Diagnostic Laparoscopy. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2017 Mar; 6(3): 924-30. doi: 10.18203/2320-1770.ijrcog20170557.

[21] Bartáková J, Potluková E, Rogalewicz V, Fait T, Schöndorfová D, Telička Z *et al.* Screening for Autoimmune Thyroid Disorders After Spontaneous Abortion Is Cost-Saving and It Improves the Subsequent Pregnancy Rate. BioMed Central Pregnancy and Childbirth. 2013 Nov; 13(1): 217. doi: 10.1186/1471-2393-13-217.

[22] Cima LN, Tarna M, Martin CS, Sirbu AE, Soare I, Panaitescu AM *et al.* Preconceptional Counseling in Women with Hyperthyroidism. Medicina. 2024 Jan; 60(2): 234. doi: 10.3390/medicina60020234.

[23] Westerman R and Kuhnt AK. Metabolic Risk Factors and Fertility Disorders: A Narrative Review of the Female Perspective. Reproductive Biomedicine and Society Online. 2022 Mar; 14: 66-74. doi: 10.1016/j.rbms.2021.09.002.

[24] Sharma S, Deb S, Ferdous T, Abusin F, Wijewardana I. Prevalence of Endometriosis in Sub-Fertile Women Confirmed at Laparoscopy: A Retrospective Analysis. Reproductive Medicine International. 2025 May; 7(1): 1-5. doi: 10.23937/2643-4555/1710026.

DOI: https://doi.org/10.54393/pjhs.v7i2.3550

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Gender Based Differences in Pain, Anxiety, and Disability in Response to Epidural Steroid Injection for Low Back Pain

Sadia Waheed Khan[1*], Ateeq Ur Rehman Ghafoor[1], Muhammad Ishaq[1], Asma Bhatti[1], Rabbiya Khalid[1], Ammar Khalid[1], Azeem Nasir[1] and Alishba Wamiq[2]

[1]Department of Anesthesia and Pain Medicine, Evercare Hospital, Lahore, Pakistan
[2]Department of Physical Therapy, Dundee University, Scotland, United Kingdom

ARTICLE INFO

Keywords:
Gender Difference, Epidural Steroid Injection, Low Back Pain

How to Cite:
Khan, S. W., Ghafoor, A. U. R., Ishaq, M., Bhatti, A., Khalid, R., Khalid, A., Nasir, A., & Wamiq, A. (2026). Gender Based Differences in Pain, Anxiety, and Disability in Response to Epidural Steroid Injection for Low Back Pain: Pain, Anxiety, and Disability in Epidural Steroid Injection for Low Back Pain. Pakistan Journal of Health Sciences, 7(2), 57-61. https://doi.org/10.54393/pjhs.v7i2.3550

***Corresponding Author:**
Sadia Waheed Khan
Department of Anesthesia and Pain Medicine, Evercare Hospital, Lahore, Pakistan
sadiawaheed7@gmail.com

Received Date: 10th October, 2025
Revised Date: 9th January, 2026
Acceptance Date: 22nd January, 2026
Published Date: 28th February, 2026

ABSTRACT

Emerging research suggests that pain perception, tolerance, and response to treatment may differ between males and females due to a complex interplay of biological, psychological and sociocultural factors. **Objective:** To determine gender differences in pain intensity, anxiety, depression, and disability outcomes following epidural steroid injection in patients with chronic low back pain. **Methods:** This comparative cross-sectional study was conducted from July 2024 to January 2025 after taking approval from the IRB of Evercare Hospital Lahore. Total 9 male and 9 female patients with low back pain were enrolled from the Anesthesia and Pain Medicine Department. Fluoroscopy-guided epidural injection was performed in all patients. Patients were followed at 3 and 6 weeks to assess pain, anxiety, depression, and disability. Data were analyzed using SPSS v26. **Results:** At both 3 and 6 weeks, females reported significantly lower mean Visual analogue scores (2.44 ± 0.53 and 2.11 ± 1.06, p=0.007) compared to males (5.11 ± 2.52 and 5.11 ± 2.26; p=0.002). Oswestry Disability scores were considerably lower in females at 3 weeks and 6 weeks; p=0.04. However, no significant gender differences were observed in HADS anxiety and depression scores at any follow-up point (p>0.05). **Conclusions:** The current study suggests that female patients demonstrated greater reductions in pain and disability scores than male patients following fluoroscopy-guided epidural steroid injection, whereas changes in anxiety and depression scores were comparable between genders. These findings indicate that gender may influence physical, but not psychological, recovery outcomes after the procedure.

INTRODUCTION

Chronic low back pain (LBP) is a prevalent medical condition and the leading cause of work-related limitations worldwide [1]. It is the second most frequently reported symptom prompting visits to primary healthcare [2]. Epidemiological data show that it affects up to 23% adults worldwide, with 24%-80% recurrence rates within one year. In Pakistan, through a telephonic survey conducted in 2021, its prevalence was found to be 15.75% [3]. LBP is characterized by discomfort lasting longer than 12 weeks, situated between the lower ribs and gluteal crease, and may or may not be accompanied by pain radiating to the legs [4]. The source of pain may include intervertebral discs, vertebral bones, spinal ligaments, or paraspinal muscles [5]. Multiple predisposing factors, genetic, environmental, social, neurological, and mechanical, contribute to its development. Notably, 85% of low back pain cases have no identifiable underlying etiology, while 97% are attributed to musculoskeletal causes [6, 7]. Diagnosis is primarily clinical, supplemented by imaging modalities when indicated [7]. Management of chronic LBP includes both non-pharmacological and pharmacological strategies. Pharmacological treatment may involve oral,

DOI: https://doi.org/10.54393/pjhs.v7i2.3550

topical, or injectable medications [8]. For patients not responding to conservative treatment, invasive procedures such as epidural steroid injections (ESIs) administered via transforaminal, interlaminar, or caudal routes serve as valuable non-surgical options for symptom relief and functional improvement [9]. Emerging research suggests that pain perception, tolerance, and response to treatment may differ between males and females due to the complex interplay of biological, psychological, and sociocultural factors [10].

However, literature specifically comparing gender-based responses to epidural steroid injections remains limited. Moreover, there is a paucity of local studies evaluating gender-based differences in response to epidural steroid injections in terms of pain relief, anxiety reduction, and disability improvement. This study aims to determine gender differences in pain intensity, anxiety, depression, and disability outcomes following epidural steroid injection in patients with chronic low back pain.

METHODS

This comparative cross-sectional study was conducted at the Department of Anesthesia and Pain Medicine, Evercare Hospital, Lahore, Pakistan. This study included 18 patients presenting to the pain clinic between July 2024 and January 2025 with complaints of low back pain (with or without radiculopathy). After institutional research and ethics committee approval, IRC/24/06/001, participants were recruited using a non-probability consecutive purposive sampling technique. Informed written consent was obtained from all patients before inclusion in the study. For sample size; WHO sample size calculator was used, and the formula applied was $n = 2\sigma 2(Z1\text{-}\alpha + Z1\text{-}\beta)2/(\mu 1\text{-}\mu 2)2$. The estimated sample size was 18 [9 in each group], using 20% level of significance, 80% power of the test, and an expected mean of pain among male taken as 7.3 ± 2.3 and in female as 6.1 ± 3.0 [11]. Patients of either gender aged between 30 and 80 years, classified as ASA I–III, with MRI-confirmed degenerative disc disease or herniated disc disease [with or without radiculopathy] and with a history of failed pharmacological and physical therapy, were eligible for inclusion. ASA I: normal healthy patient, ASA II: patient with mild systemic disease, and ASA III is defined as a patient with severe systemic disease that limits activity but is not incapacitating. This classification is based on the standard American Society of Anesthesiologists Physical Status Classification System [12]. Patients were excluded if they had contraindications to the procedure (local infection, bleeding disorders), allergy to any drugs used [contrast, steroids, local anesthetic], prior lumbar epidural injection within the past 6 months, history of psychiatric illness or opioid addiction, or diagnosis of fibromyalgia. Demographic details, including age, gender, ASA classification, and clinical history, were documented. Baseline assessment was conducted using the Visual Analog Scale (VAS) for pain [13], Hospital Anxiety and Depression Scale (HADS) [14], and the Oswestry Low Back Disability Questionnaire (ODI) [15]. The VAS for pain [13] consists of a 10-cm line ranging from 0 (no pain) to 10 (worst imaginable pain); higher scores indicate greater pain intensity. The Hospital Anxiety and Depression Scale (HADS) [14] include 14 items—7 for anxiety and 7 for depression—each scored from 0 to 3, giving subscale scores from 0 to 21. Scores of 0–7 are considered normal, 8–10 borderline, and 11–21 abnormal. The Oswestry Disability Index (ODI) [15] assesses functional disability related to low back pain through 10 items, each scored from 0 to 5, with a total score converted to a percentage (0–100%). Scores of 0–20% indicate minimal disability, 21–40% moderate, 41–60% severe, 61–80% crippled, and 81–100% bed-bound. Patients were divided into two equal groups based on gender (male and female). All patients underwent fluoroscopy-guided lumbar epidural steroid injection (interlaminar, transforaminal, or caudal) using triamcinolone 80 mg. The procedure was performed in the prone position after confirming needle placement by the spread of contrast. Post-procedure, patients were monitored in the post-anesthesia recovery unit for two hours using electrocardiography, pulse oximetry, and non-invasive blood pressure monitoring. Discharge was based on standard institutional criteria. Follow-up assessments were conducted at 3 weeks and 6 weeks post-procedure, using the same tools (VAS, HADS, ODI) to evaluate changes in pain, anxiety, depression, and disability levels. Data were analyzed using SPSS version 26. Quantitative variables were expressed as mean ± standard deviation for normally distributed data or as median (interquartile range) for non-normal data. Categorical variables were presented as frequencies and percentages. The independent sample t-test was used for normally distributed continuous variables, while the Mann-Whitney U test was used for non-normally distributed data. Chi-square was applied to compare qualitative variables. A $p\text{-value}<0.05$ was considered statistically significant.

RESULTS

A total of 18 patients were included; the mean age noted was higher in female (57.22 ± 12.60 years) compared to male (49.11 ± 14.24 years), though this variance was not statistically significant (p=0.219). ASA physical status was similar between groups, with the majority classified as ASA II. Radiculopathy was more common among female (88.9%) than male (55.6%), but this difference did not reach statistical significance (p=0.114). Both groups had an equal proportion of patients (88.9%) using NSAIDs pre-surgery (p=1.000). At baseline, there were no significant

DOI: https://doi.org/10.54393/pjhs.v7i2.3550

differences between male and female in terms of pain scores (VAS), disability (ODI), or psychological status (HADS-D and HADS-A). The mean baseline VAS was 8.00 ± 1.87 in female and 7.77 ± 1.98 in male (p=0.810). The mean baseline ODI was 21.33 ± 8.68 in female and 24.22 ± 9.48 in male (p=0.510). Mean HADS depression scores were 7.55 ± 4.61 in females and 10.22 ± 9.90 in males (p=0.475), while HADS anxiety scores were 9.25 ± 5.38 in female and 7.33 ± 5.40 in male (p=0.468) (Table 1).

Table 1: Comparison of Demographic Characteristics of Both Groups

Variables	Male (n=9), n (%), Mean ± SD	Female (n=9), n (%), Mean ± SD	p-value
Age (Years)	49.11 ± 14.24	57.22 ± 12.60	0.219
ASA Status (I)	1 (11.1%)	2 (22.2%)	0.513
ASA Status (II)	7 (77.8%)	7 (77.8%)	
ASA Status (III)	1 (11.1%)	0 (0%)	
Radiculopathy (Yes)	5 (55.6%)	8 (88.9%)	0.114
Radiculopathy (No)	4 (44.4%)	1 (11.1%)	
NSAIDS Pre Surgery (Yes)	8 (88.9%)	8 (88.9%)	1.000
NSAIDS Pre Surgery (No)	1 (11.1%)	1 (11.1%)	
Baseline VAS	7.77 ± 1.98	8.00 ± 1.87	0.810
Baseline HADS Depression score	10.22 ± 9.90	7.55 ± 4.61	0.475
Baseline HADS Anxiety score	7.33 ± 5.40	9.25 ± 5.38	0.468
Baseline ODI	24.22 ± 9.48	21.33 ± 8.68	0.510

Female exhibited significantly greater reduction in pain intensity as measured by VAS at both 3 weeks (2.44 ± 0.53) and 6 weeks (2.11 ± 1.06) compared to male (5.11 ± 2.52 at 3 weeks and 5.11 ± 2.26 at 6 weeks), with p-values 0.007 and 0.002, respectively. Disability scores, as assessed by ODI, were also significantly lower in females at both 3 weeks (5.88 ± 2.14 vs. 17.33 ± 15.23; p=0.04) and 6 weeks (3.55 ± 1.23 vs. 14.44 ± 14.95; p=0.04) compared to males. However, no statistically significant differences were observed between genders in HADS scores for either depression or anxiety at 3 or 6 weeks (p>0.05) (Table 2).

Table 2: Comparison of Outcome Variables among Male and Female Gender

Variables		Male (n=9)	Female (n=9)	p-value
VAS	3 Weeks	5.11 ± 2.52	2.44 ± 0.53	0.007*
	6 Weeks	5.11 ± 2.26	2.11 ± 1.06	0.002*
HADS Depression Score	3 Weeks	6.88 ± 6.62	3.55 ± 2.24	0.172
	6 Weeks	5.33 ± 3.97	5.66 ± 4.89	0.867
HADS Anxiety Score	3 Weeks	5.11 ± 4.31	4.55 ± 3.28	0.762
	6 Weeks	4.88 ± 4.72	4.55 ± 3.71	0.870
ODI	3 Weeks	17.33 ± 15.23	5.88 ± 2.14	0.040*
	6 Weeks	14.44 ± 14.95	3.55 ± 1.23	0.040*

*Statistically significant at p<0.05.

DISCUSSION

The gender-related differences observed in our study are partly consistent with previous research. Several studies suggest that females may respond more favorably to epidural steroid injections (ESI), potentially due to biological or pain-processing differences. Davison *et al.* reported that male patients were more likely to fail non-surgical management for low back pain compared to female [17], and Şencan *et al.* also noted higher ESI success rates among women, though the difference did not reach significance [18]. Pericot-Mozo *et al.* in contrast to our psychological findings, found lower median HADS scores in females than males at follow-up [16]. However, other studies, including Monzon *et al.* [19], Raak *et al.* [20], and Ross [21], found no meaningful gender-related differences in ESI outcomes, suggesting that the influence of gender may vary across populations and clinical settings. Chronic lumbar pain is closely linked with psychosocial factors such as anxiety, depression, maladaptive coping, and fear-avoidant behaviors that can intensify pain perception and hinder functional recovery [22, 23]. These variables may contribute to inconsistencies in the literature, as psychological status can affect treatment response regardless of gender. Supporting this, Inman *et al.* emphasized the roles of coping mechanisms, expectations, and anxiety when evaluating sex-related differences in ESI response [11]. Overall, while some evidence suggests that gender may influence physical recovery following ESI, psychological outcomes appear more strongly shaped by individual psychosocial profiles than by gender alone.

This study has several limitations. Firstly, the small sample size limits the statistical power and generalizability of our findings. Secondly, follow-up period of only 6 weeks may not fully capture long-term effects of ESI on pain relief, disability, or psychosocial outcomes. Thirdly, although baseline characteristics were comparable, residual confounding factors such as physical activity level, socioeconomic status, or comorbidities may have influenced the outcomes. Future research should use larger, multicenter cohorts with longer follow-up to clarify the interplay of gender and psychosocial factors in ESI outcomes.

CONCLUSIONS

The current study suggests that female patients demonstrated greater reductions in pain (VAS) and disability (ODI) scores than male patients following fluoroscopy-guided epidural steroid injection, whereas changes in anxiety and depression (HADS) scores were comparable between genders. These findings indicate that gender may influence physical, but not psychological, recovery outcomes after the procedure.

DOI: https://doi.org/10.54393/pjhs.v7i2.3550

Authors' Contribution

Conceptualization: SWK, AURG
Methodology: AURG, AB, AN
Formal analysis: MI, RK
Writing and Drafting: AB, RK, AK, AN, AW
Review and Editing: SWK, AURG, MI, AB, RK, AK, AN, AW

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Serranheira F, Sousa-Uva M, Heranz F, Kovacs F, Sousa-Uva A. Low Back Pain (LBP), Work and Absenteeism. Work. 2020 Feb; 65(2): 463-9. doi: 10.3233/WOR-203073.

[2] Nieminen LK, Pyysalo LM, Kankaanpää MJ. Prognostic Factors for Pain Chronicity in Low Back Pain: A Systematic Review. Pain reports. 2021 Apr; 6(1): e919. doi: 10.1097/PR9.0000000000000919.

[3] Amjad MA, Siddiqui AM, Bashir K, Ghafoor AU, Durrani RS. Prevalence of Chronic Pain in Pakistan—A National Survey. Journal of the Pakistan Medical Association. 2023 Jun; 73(6): 1217-20. doi: 10.47391/JPMA.6671.

[4] Li W, Gong Y, Liu J, Guo Y, Tang H, Qin S *et al.* Peripheral and Central Pathological Mechanisms of Chronic Low Back Pain: A Narrative Review. Journal of Pain Research. 2021 May: 1483-94. doi: 10.2147/JPR.S306280.

[5] Mohd Isa IL, Teoh SL, Mohd Nor NH, Mokhtar SA. Discogenic Low Back Pain: Anatomy, Pathophysiology and Treatments of Intervertebral Disc Degeneration. International Journal of Molecular Sciences. 2022 Dec; 24(1): 208. doi: 10.3390/ijms24010208.

[6] Ferreira ML, De Luca K, Haile LM, Steinmetz JD, Culbreth GT, Cross M *et al.* Global, Regional, and National Burden of Low Back Pain, 1990–2020, Its Attributable Risk Factors, and Projections to 2050: A Systematic Analysis of the Global Burden of Disease Study 2021. The Lancet Rheumatology. 2023 Jun; 5(6): e316-29. doi: 10.2139/ssrn.4318392.

[7] Chiarotto A and Koes BW. Nonspecific Low Back Pain. New England Journal of Medicine. 2022 May; 386(18): 1732-40. doi: 10.1056/NEJMcp2032396.

[8] Tagliaferri SD, Miller CT, Owen PJ, Mitchell UH, Brisby H, Fitzgibbon B *et al.* Domains of Chronic Low Back Pain and Assessing Treatment Effectiveness: A Clinical Perspective. Pain Practice. 2020 Feb; 20(2): 211-25. doi: 10.1111/papr.12846.

[9] Nicol V, Verdaguer C, Daste C, Bisseriex H, Lapeyre É, Lefèvre-Colau MM *et al.* Chronic Low Back Pain: A Narrative Review of Recent International Guidelines for Diagnosis and Conservative Treatment. Journal of Clinical Medicine. 2023 Feb; 12(4): 1685. doi: 10.3390/jcm12041685.

[10] Osborne NR and Davis KD. Sex and Gender Differences in Pain. In the International Review of Neurobiology. 2022 Jan; 164: 277-307. doi: 10.1016/bs.irn.2022.06.013.

[11] Inman SL, Faut-Callahan M, Swanson BA, Fillingim RB. Sex Differences in Responses to Epidural Steroid Injection for Low Back Pain. The Journal of Pain. 2004 Oct; 5(8): 450-7. doi: 10.1016/j.jpain.2004.07.004.

[12] Horvath B, Kloesel B, Todd MM, Cole DJ, Prielipp RC. The Evolution, Current Value, and Future of the American Society of Anesthesiologists Physical Status Classification System. Anesthesiology. 2021 Oct; 135(5): 904-19. doi: 10.1097/ALN.0000000000003947.

[13] Åström M, Thet Lwin ZM, Teni FS, Burström K, Berg J. Use of the Visual Analogue Scale for Health State Valuation: A Scoping Review. Quality of Life Research. 2023 Oct; 32(10): 2719-29. doi: 10.1007/s11136-023-03411-3.

[14] Wu Y, Levis B, Sun Y, He C, Krishnan A, Neupane D *et al.* Accuracy of the Hospital Anxiety and Depression Scale Depression Subscale (HADS-D) to Screen for Major Depression: Systematic Review and Individual Participant Data Meta-Analysis. British Medical Journal. 2021 May; 373. doi: 10.1136/bmj.n972.

[15] Jenks A, Hoekstra T, van Tulder M, Ostelo RW, Rubinstein SM, Chiarotto A. Roland-Morri's Disability Questionnaire, Oswestry Disability Index, and Quebec Back Pain Disability Scale: Which Has Superior Measurement Properties in Older Adults with Low Back Pain? Journal of Orthopedic and Sports Physical Therapy. 2022 Jul; 52(7): 457-69. doi: 10.2519/jospt.2022.10802.

[16] Pericot-Mozo X, Suñer-Soler R, Reig-Garcia G, Patiño-Masó J, Sitjar-Suñer M, Masià-Plana A *et al.* Quality of Life in Patients with Chronic Low Back Pain and Differences by Sex: A Longitudinal Study. Journal of Personalized Medicine. 2024 May; 14(5): 496. doi: 10.3390/jpm14050496.

[17] Davison MA, Lilly DT, Moreno J, Bagley C, Adogwa O. Gender Differences in the 3-Month Utilization of Nonoperative Therapies Before Primary Lumbar

DOI: https://doi.org/10.54393/pjhs.v7i2.3550

Microdiscectomy. Journal of Clinical Neuroscience. 2020 Jun; 76: 107-13. doi: 10.1016/j.jocn.2020.04.033.

[18] Şencan S, Çelenlioğlu AE, Asadov R, Gündüz OH. Predictive Factors for Treatment Success of Transforaminal Epidural Steroid Injection in Lumbar Disc Herniation-Induced Sciatica. Turkish Journal of Medical Sciences. 2020; 50(1): 126-31.

[19] Monzon M, De Schoenmacker I, Cina A, Enz R, Lanz C, Galbusera F *et al.* Chronic Low Back Pain Patient Satisfaction with Lumbar Steroid Injection: A Data-Driven Analysis. medRxiv. 2025 Apr: 2025-04. doi: 10.1101/2025.04.10.25325570.

[20] Raak CK, Ostermann T, Schönenberg-Tu AL, Fricke O, Martin DD, Robens S *et al.* No Gender Differences in Pain Perception and Medication After Lumbar Spine Sequestrectomy—A Reanalysis of a Randomized Controlled Clinical Trial. Journal of Clinical Medicine. 2022 Apr; 11(9): 2333. doi: 10.3390/jcm11092333.

[21] Ross JS. Do Epidural Injections with Local Anesthetic with Steroids Have Superiority Over Injections with Local Anesthetic Alone When Treating Chronic Back Pain Due to an Intervertebral Disc Herniation in Men and Women Over 18 Years Old? 2016.

[22] Neumann A and Hampel P. Long-Term Effects of Rehabilitation and Prevention of Further Chronification of Pain Among Patients with Non-Specific Low Back Pain. Journal of Back and Musculoskeletal Rehabilitation. 2022 Nov; 35(6): 1257-68. doi: 10.3233/BMR-210221.

[23] Varela AJ and Van Asselt KW. The Relationship Between Psychosocial Factors and Reported Disability: The Role of Pain Self-Efficacy. BioMed Central Musculoskeletal Disorders. 2022 Jan; 23(1): 21. doi: 10.1186/s12891-021-04955-6.

DOI: https://doi.org/10.54393/pjhs.v7i2.3566

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Comparison of Dexmedetomidine and Labetalol for Attenuating Stress Response in Hypertensive Patients

Rootaba Khalid[1*], Farrukh Afzal[2], Shaheer Nayyar[3], Sumayya Tariq[4], Shumaila Ashfaq[5], Sara Sabir[5] and Rehana Feroze[6]

[1]Department of Anesthesia, Lady Willingdon Hospital, Lahore, Pakistan
[2]Department of Anesthesia, King Edward Medical University, Mayo Hospital, Lahore, Pakistan
[3]Department of Anesthesia, Allama Iqbal Medical College, Jinnah Hospital, Lahore, Pakistan
[4]Department of Anesthesia, Sharif Medical City Hospital, Lahore, Pakistan
[5]Department of Anesthesia, Islam Medical and Dental College, Sialkot, Pakistan
[6]Department of Anesthesia, Kanad Hospital, Al Ain, United Arab Emirates

ARTICLE INFO

Keywords:
Dexmedetomidine, Labetalol, Laryngoscopy, Intubation, Intratracheal, Hemodynamics, Hypertension, General Anesthesia

How to Cite:
Khalid, R., Afzal, F., Nayyar, S., Tariq, S., Ashfaq, S., Sabir, S., & Feroze, R. (2026). Comparison of Dexmedetomidine and Labetalol for Attenuating Stress Response in Hypertensive Patients: Dexmedetomidine and Labetalol for Attenuating Stress Response in Hypertensive Patients. Pakistan Journal of Health Sciences, 7(2), 62-66. https://doi.org/10.54393/pjhs.v7i2.3566

***Corresponding Author:**
Rootaba Khalid
Department of Anesthesia, Lady Willingdon Hospital, Lahore, Pakistan
dr.rootaba@gmail.com

Received Date: 22nd October, 2025
Revised Date: 6th January, 2026
Acceptance Date: 22nd January, 2026
Published Date: 28th February, 2026

ABSTRACT

Laryngoscopy and tracheal intubation during general anesthesia provoke a sympathetic stress reaction that has significant hemodynamic changes. This can be risky, particularly in patients with controlled hypertension with compromised cardiovascular reserve. **Objective:** To compare the effect of dexmedetomidine and labetalol for attenuating stress response in hypertensive patients. **Methods:** A quasi-experimental study that involved 200 controlled hypertensive patients admitted to the elective surgery and placed under general anesthetic procedures. Patients received Intravenous dexmedetomidine (0.1 mcg/kg) or labetalol (0.1 mg/kg). It was observed that the mean heart rate and mean arterial blood pressure were measured at baseline and two minutes after endotracheal intubation. The statistics were performed using the independent sample t-test, which was used to compare the results observed between the two treatment groups. **Results:** The heart rate 2 minutes following intubation was much lower in Group D (78 ± 8.27 beats/minute) than in Group L (81 ± 5.30 beats/minute, p=0.0026). Further, the mean arterial blood pressure was declining remarkably in the dexmedetomidine group (98 ± 7.26 mmHg), compared to the labetalol group (101 ± 8.2 mmHg; p=0.0067). **Conclusions:** The present group of controlled hypertensive patients indicated that dexmedetomidine pre-induction, in comparison to labetalol, led to a significantly more significant reduction of hypertensive and tachycardic reaction to laryngoscopy and endotracheal intubation.

INTRODUCTION

Laryngoscopy and endotracheal intubation are obligatory parts of general anesthesia but are also known to be great triggering factors of substantial hemodynamic stress reactions. It is a sympathetic-mediated reflex that results in a short-lived but sharp increase in hemodynamic parameters [1, 2]. Though healthy individuals can withstand such changes, the reaction is risky in patients with cardiovascular comorbidities (especially hypertension). The acute rise in hemodynamic parameters in such individuals predisposes them to the onset of myocardial ischemia, cerebral vascular accidents, and perioperative arrhythmia [3]. This danger is also increased in hypertensive patients since chronic vascular remodeling, which reduces baroreceptor sensitivity in the process of buffering the sudden sympathetic stimulation [4]. There are many examples of pharmacologic agents:

DOI: https://doi.org/10.54393/pjhs.v7i2.3566

opioids, lidocaine, beta-blockers, and calcium channel blockers, which have been employed to reduce the intubation response [5]. Labetalol, an alpha-non-selective and beta-blocker, has proven to be the most popular in the perioperative units since it offers effective blood pressure regulation with no reflex tachycardia effect [6]. Research revealed that labetalol by the intravenous route has a greater effect in slowing the heart rate with a decrease in the elevation in blood pressure after laryngoscopy in hypertensive and cardiac-risk patients [7]. Dexmedetomidine is a very specific 2-adrenergic agonist that is very popular because it has strong sympatholytic, sedative, and analgesic but no respiratory depression properties [8]. Dexmedetomidine offers better hemodynamic stability during high-intensity noxious stimulation by decreasing the central sympathetic outflow. Different clinical trials indicated that dexmedetomidine pre-induction is very effective in blunting the hemodynamic effect of intubation and decreasing the amount of catecholamine release during peri-surgery [9, 10]. As much as the stress response around laryngoscopy has been proven to be reduced by both labetalol and dexmedetomidine separately, no head-to-head studies have been directly compared, especially in patients with well-managed hypertension. This group of individuals constitutes a special predicament, because continuous antihypertensive treatment might distort compensatory autonomic responses, and the choice of an agent is of paramount importance to prevent the occurrence of adverse cardiovascular events [11, 12]. It has been emphasized in recent literature that in hypertensive cohorts, special consideration should be directed towards the pharmacologic approach to assessment and evaluation since it has a disproportionately greater perioperative morbidity [13].

Enhancement of evidence in this field may make anesthetic practice safer in the perioperative management of a high-risk population. There is a lack of direct comparative evidence between intravenous dexmedetomidine and labetalol for attenuating the hemodynamic response to laryngoscopy and endotracheal intubation in patients with well-controlled hypertension. This study aimed to compare the effectiveness of intravenous dexmedetomidine and labetalol in the attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation in controlled hypertensive patients during elective surgery.

METHODS

A quasi-experimental study was conducted in the operating theaters of Mayo Hospital, Lahore, between March 20, 2019, and September 20, 2019, after getting permission from the ethics review committee (499/RC/KEMU). Two hundred potential patients were also identified and included in the ultimate analysis. The mean blood pressure in group D (70.50 ± 4.58) and group L (76.37 ± 5.52) was used to calculate the sample size by taking 80% power of the test, 5% margin of Error and 10% drop out rate is 136 (68 in each group) [14]. The inclusion criteria were: the presence of controlled hypertension (SBP less than 140 mmHg and DBP less than 90 mmHg on a single antihypertensive agent), both genders, and age between 18 and 70 years, and a scheduled elective surgery under general anesthesia. The patients predicted hard-to-manage airway (Mallampati class > 3), a laryngoscopy time longer than 30 seconds, or more than one attempt, pre-existing coagulation disorders (INR > 1.5), morbid obesity (BMI > 35kg/m2), uncontrolled hypertension, congestive heart failure, arrhythmias, acute bronchospasm, or initial hypotension were excluded from the study. After taking the informed and written consent, the patients were enrolled in the study. The treatment received was recorded by the researchers, and the patients were classified in the following way: Group D (Dexmedetomidine): Patients were treated with intravenous dexmedetomidine 0.1 mcg/kg before induction. Group L (Labetalol): Intravenous labetalol, 0.1mg/kg before induction. The study drugs were then ready prepared by the clinical team and were all diluted in normal saline to a billed volume of 10 mL and infused over 5 minutes before anesthesia induction. None of the observations were blinded; the study team was aware of the treatment administered. Upon arrival in the operating theatre, normal non-invasive monitoring was initiated: ECG, HR, NIBP, and peripheral oxygen saturation via a normal patient monitor. Once intravenous access had been achieved, nalbuphine 0.1 mg/kg was given to all the patients. Propofol 2mg/kg was administered intravenously to induce anesthesia. The Atracurium at 0.5mg per kilogram was administered after loss of consciousness to aid the endotracheal intubation. The anesthesia was maintained by isoflurane in 100% oxygen at 1.2MAC. An anesthetist who was senior carried out laryngoscopy and endotracheal intubation. With the help of hemodynamic parameters, the mean heart rate and the mean arterial pressure were measured at the induction (baseline) and at 2 minutes after intubation. Data analysis was conducted by SPSS version 25.0. The results of quantitative variables (age, BMI, heart rate, MAP) were in the form of mean standard deviation (SD). Frequencies and percentages were used to state qualitative variables (gender, ASA status). An independent sample t-test was utilized to compare the main outcome variables, mean heart rate and MAP, in the two non-randomized groups. A p-value of less than 0.05 was taken to be statistically significant.

DOI: https://doi.org/10.54393/pjhs.v7i2.3566

RESULTS

A total of 200 patients were enrolled and completed the study, with 100 patients receiving dexmedetomidine (Group D) and 100 receiving labetalol (Group L) based on the attending physician's standard clinical practice. The two groups were found to be comparable with respect to key baseline characteristics, including age, ASA physical status, and Body Mass Index. This finding suggests that major known confounders in these categories did not significantly differ between the observed groups (Table 1).

Table 1: Comparison of Demographic Characteristics of Both Groups

Characteristic	Group D, (n=100)	Group L, (n=100)	Total (n=200)
Age Group (Years)			
18-35	20 (20.0%)	21 (21.0%)	41 (20.5%)
36-50	50 (50.0%)	45 (45.0%)	95 (47.5%)
51-70	30 (30.0%)	34 (34.0%)	64 (32.0%)
ASA Physical Status			
ASA I	40 (40.0%)	45 (45.0%)	85 (42.5%)
ASA II	60 (60.0%)	55 (55.0%)	115 (57.5%)
Body Mass Index (kg/m^2)			
Normal (18-24.9)	41 (41.0%)	38 (38.0%)	79 (39.5%)
Overweight (25-29.9)	34 (34.0%)	39 (39.0%)	73 (36.5%)
Obese (30-35)	25 (25.0%)	23 (23.0%)	48 (24.0%)

Data are presented as n (%). ASA: American Society of Anesthesiologists

The primary findings of the study revealed a statistically significant difference in the observed hemodynamic response to intubation between the two treatment groups. At two minutes post-intubation, patients in Group D had a significantly lower mean heart rate and mean arterial pressure compared to patients in Group L (Table 2).

Table 2: Difference between the Hemodynamic Parameters 2 Minutes Post-Intubation

Parameters	Group D	Group L	p-value
Mean Heart Rate (beats/min)	78 ± 8.27	81 ± 5.30	0.006
Mean Arterial Pressure (mmHg)	98 ± 7.26	101 ± 8.20	0.007

Post-hoc stratification analysis was conducted to evaluate the outcomes across subgroups of age, ASA status, and BMI. The superior observed attenuating effect of dexmedetomidine was consistent across all subgroups. In every stratification for age, ASA status, and BMI, both mean heart rate and mean arterial pressure were significantly lower in the dexmedetomidine group compared to the labetalol group ($p<0.05$ for all comparisons). Table 3 presents a detailed stratification of the outcomes based on BMI (Table 3).

Table 3: Stratification of Hemodynamic Outcomes by Body Mass Index (BMI)

Parameters	BMI Category	Group D	Group L	p-value
Mean Heart Rate (beats/min)	Normal (18-24.9)	72.50 ± 3.40	76.35 ± 5.12	<0.001
Mean Heart Rate (beats/min)	Overweight (25-29.9)	75.00 ± 4.14	78.00 ± 3.77	0.001
Mean Heart Rate (beats/min)	Obese (30-35)	74.59 ±5.49	78.00 ± 2.40	0.008
Mean Arterial Pressure (mmHg)	Normal (18-24.9)	95.5 ± 2.5	97.0 ± 2.0	0.005
Mean Arterial Pressure (mmHg)	Overweight (25-29.9)	95.5 ± 3.6	97.8 ± 3.0	0.004
Mean Arterial Pressure (mmHg)	Obese (30-35)	97.6 ± 1.5	100.0 ± 2.71	0.002

DISCUSSION

The main observation of this observational study is that pre-induction dexmedetomidine was linked to a considerably superior decrease in the hemodynamic stress response. This implies that there is a possible efficacy benefit of dexmedetomidine compared to labetalol in clinical practice in the real world [15]. This noted excellent efficiency of dexmedetomidine is pharmacologically conceivable. Dexmedetomidine is a very selective 2-adrenergic CNS agonist; the stimulation of central nervous system presynaptic 2 receptors inhibit the release of norepinephrine, inhibiting sympathetic outflow and suppressing catecholamine response to noxious stimuli like intubation [16, 17]. Conversely, labetalol offers peripheral 2 and non-selective 3 adrenergic blockade, and this can be less efficient in managing the central sympathetic surge [16]. This process is in accordance with the earlier literature that indicated more hemodynamic stability in the presence of dexmedetomidine during airway control [18]. Further, the presence of uniform advantage in stratified subgroups (age, ASA status, BMI) confirms the clinical relevance of dexmedetomidine to represent a wide group of hypertensive patients [15, 19]. The effectiveness of the effect on such subgroups indicates that the hemodynamic benefits are not limited to a specific patient profile, but they might be extended to different demographic and physiologic backgrounds. A body of literature has substantiated these results. Recent controlled prospective, randomized, double-blind studies in hypertensive patients on intubation found that the single dose of dexmedetomidine showed significant lowering of HR and MAP at different time points after intubation, with no incidence of bradycardia or hypotension necessitating a response [17]. A meta-analysis of randomized trials also established the efficacy of dexmedetomidine in the attenuation of the hemodynamic reaction to tracheal intubation with decreased HR and MAP over placebo or none of dexmedetomidine [18]. Further, other controlled

DOI: https://doi.org/10.54393/pjhs.v7i2.3566

trials have continued to confirm dexmedetomidine's excellent profile during intubation stress response, such as decreased induction dosage and consistent hemodynamics [19, 20].

Our study should be limited by limitations. To begin with, causality cannot be well-established since it is observational research. Also, the two groups were well matched on measured variables (age, BMI, ASA), however, unmeasured confounders (e.g., clinician preference, baseline cardiovascular tone, frailty) could have contributed to the development of both drugs used and the final outcomes [15,22]. We did not test dose response relationships or other administration plans (e.g., continuous infusion), the effect of which may be different from our fixed single doses. With these constraints, future studies should incorporate multicenter randomized controlled trials between dexmedetomidine and labetalol, various dosing schedules (bolus vs infusion) as well as cardiovascular outcomes in the long run. These trials would aid in establishing causality and determining the most appropriate administration measures in hypertensive patients.

CONCLUSIONS

Pre-induction dexmedetomidine was associated with better attenuation of hemodynamic response to laryngoscopy and intubation in this group of patients with controlled hypertension than labetalol. These results clinically justify the use of dexmedetomidine to encourage improved perioperative hemodynamic stability in this predisposed group of patients. However, these observational relationships should be verified by randomized trials that have wider endpoints. This observation has direct clinical implications. It indicates that dexmedetomidine has the potential to be a better agent to use in the management of perioperative hemodynamic stability among vulnerable populations of patients, which may lessen the chances of cardiovascular complications associated with airway manipulation.

Authors Contribution

Conceptualization: RK
Methodology: RK, SN, ST
Formal analysis: FA, SS
Writing and Drafting: RK, SN, ST, SA, SS, RF
Review and Editing: RK, FA, SN, ST, SA, SS, RF

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Lakhe G, Pradhan S, Dhakal S. Hemodynamic Response to Laryngoscopy and Intubation Using Mccoy Laryngoscope: A Descriptive Cross-Sectional Study. Journal of the Nepal Medical Association. 2021 Jun; 59(238): 554. doi: 10.31729/jnma.6752.

[2] DeMasi SC, Casey JD, Semler MW. Evidence-Based Emergency Tracheal Intubation. American Journal of Respiratory and Critical Care Medicine. 2025 Jul; 211(7): 1156-64. doi: 10.1164/rccm.202411-2165CI.

[3] Stergiou GS, Palatini P, Parati G, O'Brien E, Januszewicz A, Lurbe E *et al.* 2021 European Society of Hypertension Practice Guidelines for Office and Out-of-Office Blood Pressure Measurement. Journal of Hypertension. 2021 Jul; 39(7): 1293-302. doi: 10.1097/HJH.0000000000002843.

[4] Suarez-Roca H, Mamoun N, Sigurdson MI, Maixner W. Baroreceptor Modulation of the Cardiovascular System, Pain, Consciousness, and Cognition. Comprehensive Physiology. 2011 Jan; 11(2): 1373-423. doi: 10.1002/j.2040-4603.2021.tb00152.x.

[5] Dangol S, Yadav RK, Bhatt P. Esmolol and Lidocaine in Blunting Hemodynamic Response to Extubation. Journal of College of Medical Sciences-Nepal. 2025 Jun; 21(2): 130-5. doi: 10.3126/jcmsn.v21i2.76102.

[6] Mathai C, Singh M, Abraham V. A Double Blind Comparative Study of the Efficacy of Labetalol and Esmolol in Low Doses in Attenuating the Hemodynamic Response to Laryngoscopy and Intubation. Journal of Applied Dental and Medical Sciences. 2022; 8: 1.

[7] Shetabi H, Nazemroaya B, Mahjobipoor H, Majidi S. Comparative Study of the Effect of Two Different Doses of Intravenous Labetalol on the Cardiovascular Response to Endotracheal Extubation. Journal of Cardiovascular and Thoracic Research. 2023 Jun; 15(2): 98. doi: 10.34172/jcvtr.2023.31623.

[8] Hu Y, Zhou H, Zhang H, Sui Y, Zhang Z, Zou Y *et al.* The Neuroprotective Effect of Dexmedetomidine and Its Mechanism. Frontiers in Pharmacology. 2022 Sep; 13: 965661. doi: 10.3389/fphar.2022.965661.

[9] Tariq S, Yaqoob KM, Shahid A, Abid K, Haq MM. Comparison of Intravenous Lignocaine and Intravenous Dexmedetomidine for Attenuation of Hemodynamic Stress Response to Laryngoscopy and Endotracheal Intubation. Pakistan Armed Forces

DOI: https://doi.org/10.54393/pjhs.v7i2.3566

Medical Journal. 2024 Aug; 74(4): 1138. doi: 10.51253/pafmj.v74i4.7000.

[10] Sadhukhan S, Sarkar M, Khanra M. Comparison Between Two Intravenous Doses of Dexmedetomidine in Attenuation of Hemodynamic Responses to Laryngoscopy and Endotracheal Intubation. International Journal. 2022 Mar; 5(2): 994.

[11] Neto MM, Paz MC, Crisóstomo AC, Rabelo IS, Luna BG, e Souza PF. Comparative Effects of Dexmedetomidine Versus Labetalol on Hemodynamic Stress Response to Laryngoscopy and Tracheal Intubation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Trends in Anesthesia and Critical Care. 2025 Aug: 101588. doi: 10.1016/j.tacc.2025.101588.

[12] Fazal S, Iqtdar R, Shah I, Zia K, Ahmed A, Iqbal A *et al.* Comparing Dexmedetomidine with Labetalol for Haemodynamic Response to General Anaesthesia during Elective Cardiac Surgery at a Tertiary Care Hospital. Pakistan Heart Journal. 2025 Sep; 58(s2): 103-8. doi: 10.47144/phj.v58is2.3201.

[13] Carey RM, Moran AE, Whelton PK. Treatment of Hypertension: A Review. Journal of the American Medical Association. 2022 Nov; 328(18): 1849-61. doi: 10.1001/jama.2022.19590.

[14] Swargiri K, Padun J, Basumatary B, Manivasagam R. A Comparative Study to Determine the Efficacy of Dexmedetomidine 1mcg/kg and Labetalol 0.25 Mg/Kg in Attenuating the Hemodynamic Stress Responses to Laryngoscopy and Endotracheal Intubation. African Journal of Biomedical Research. 2024 Nov; 27(3): 417-23. doi: 10.53555/AJBR.v27i3.2069.

[15] El-Shmaa NS and El-Baradey GF. The Efficacy of Labetalol vs Dexmedetomidine for Attenuation of Hemodynamic Stress Response to Laryngoscopy and Endotracheal Intubation. Journal of Clinical Anesthesia. 2016 Jun; 31: 267-73. doi: 10.1016/j.jclinane.2016.01.037.

[16] Sangeetha A and Saranya M. A Comparative Study of Dexmedetomidine and Labetalol for Attenuation of Hemodynamic Stress Response to Laryngoscopy and Intubation. Journal of Ayurveda and Integrative Medicine. 2021; 8(4): 86-93.

[17] Ismail EA, Mostafa AA, Abdelatif MM. Attenuation of Hemodynamic Response to Laryngoscopy and Endotracheal Intubation with Single Dose Dexmedetomidine in Controlled Hypertensive Patients: Prospective Randomized Double-Blind Study. Ain-Shams Journal of Anesthesiology. 2022 Jul; 14(1). doi: 10.1186/s42077-022-00255-w.

[18] De Cassai A, Boscolo A, Geraldini F, Zarantonello F, Pettenuzzo T, Pasin L *et al.* Effect of Dexmedetomidine on Hemodynamic Responses to Tracheal Intubation: A Meta-Analysis with Meta-Regression and Trial Sequential Analysis. Journal of Clinical Anesthesia. 2021 Sep; 72: 110287. doi: 10.1016/j.jclinane.2021.110287.

[19] Jarineshin H, Baghaei AA, Fekrat F, Kargar A, Abdi N, Navabipour S *et al.* Comparison of Two Different Doses of Dexmedetomidine in Attenuating Cardiovascular Responses During Laryngoscopy and Endotracheal Intubation: A Double Blind, Randomized, Clinical Trial Study. Journal of Medicine and Life. 2015; 8(Spec Iss 4): 45.

[20] Shah RM and Saba Ahad DS. Comparative Study of IV Dexmedetomidine and Lignocaine for Attenuation of Cardiovascular Stress Response to Laryngoscopy and Endotracheal Intubation. International Journal of Medical and Pharmaceutical Research. 2025 Nov; 6: 1104-10.

DOI: https://doi.org/10.54393/pjhs.v7i2.3033

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Positive Predictive Value of Dried Blood Sampling of TSH in Diagnosing Congenital Hypothyroidism in Neonates Born at a Tertiary Care Hospital

Wasif Ahmed Khan[1], Fizzah Naz[1], Muzna Arif[1], Shahiryar Khan[1], Hafsa Majid[2], Imran Nisar[1] and Khadija Nuzhat Humayun[1*]

[1]Department of Pediatrics and Child Health, Aga Khan University Hospital, Karachi, Pakistan
[2]Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan

ARTICLE INFO

Keywords:
Congenital Hypothyroidism, Dried Blood Samples of Thyroid-Stimulating Hormone, Newborn Screening, Positive Predictive Value, Neonates

How to Cite:
Khan, W. A., Naz, F., Arif, M., Khan, S., Majid, H., Nisar, I., & Humayun, K. N. (2026). Positive Predictive Value of Dried Blood Sampling of TSH in Diagnosing Congenital Hypothyroidism in Neonates Born at a Tertiary Care Hospital: PPV of Dried Blood Sampling of TSH in Diagnosing Congenital Hypothyroidism. Pakistan Journal of Health Sciences, 7(2), 67-72. https://doi.org/10.54393/pjhs.v7i2.3033

***Corresponding Author:**
Khadija Nuzhat Humayun
Department of Pediatrics and Child Health, Aga Khan University Hospital, Karachi, Pakistan
Khadija.humayun@aku.edu

Received Date: 10th April, 2025
Revised Date: 6th January, 2026
Acceptance Date: 8th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Congenital hypothyroidism (CH) is one of the most common preventable causes of intellectual disability in children. Early detection through newborn screening is essential for timely intervention. However, the predictive accuracy of DBS-TSH varies across populations, and limited local data are available from Pakistan. **Objectives:** To determine the positive predictive value (PPV) of dried blood samples of thyroid-stimulating hormone (DBS-TSH) in diagnosing congenital hypothyroidism (CH) in neonates. **Methods:** This retrospective cohort study using screening registry data was conducted at the newborn screening program, Aga Khan University Hospital, Karachi, from March 2023 to March 2024. Records of neonates screened from April 2019 to December 2022 were reviewed. Neonates with DBS-TSH >10 mIU/L were labeled screen-positive and underwent confirmatory testing with serum TSH and free T4 within two weeks. Neonates with Serum TSH (>20 mIU/L) were considered true positive for congenital hypothyroidism. **Results:** Of 30,402 neonates screened, 538 (1.76%) were screen positive. Mean DBS-TSH was 16.1 ± 12.6 mIU/L. Among them, 478 (88.8%) had 10–20 mIU/L (Group 1), and 60 (11.2%) had >20 mIU/L (Group 2). Confirmatory testing was available for 385 infants, of whom 33 were true cases of CH, yielding a PPV of 8.57% (95% CI: 5.9%–11.7%). Higher PPV was observed when sampling occurred at >48 hours. A DBS-TSH cutoff ≥35 mIU/L showed PPV of 95% (95% CI: 76.18 – 99.88), which may justify early treatment consideration. **Conclusions:** DBS-TSH screening at a cutoff of >10 mIU/L yields modest PPV for CH. Higher DBS-TSH values and appropriate sampling time significantly enhance predictive accuracy.

INTRODUCTION

Congenital hypothyroidism (CH) is one of the most common treatable endocrine disorders in neonates and a leading preventable cause of intellectual disability [1]. If untreated, thyroid hormone deficiency in early life leads to permanent cognitive impairment, motor dysfunction, and growth abnormalities [2, 3]. Recent global estimates suggest a rising prevalence, with reported rates ranging from 1 in 2,000 – 4,000 live births [4, 5]. The thyroid hormone plays a crucial role in brain maturation, particularly during the neonatal period [6]. Delays in detection and initiation of levothyroxine therapy are associated with irreversible neurological sequelae, whereas early treatment prevents long-term complications [2, 7]. This highlights the importance of effective and timely newborn screening programs. Dried blood spot thyroid-stimulating hormone (DBS-TSH) measurement has become the cornerstone of CH screening worldwide. It is inexpensive, minimally invasive, and well-suited for large-scale implementation, even in resource-limited settings [8, 9]. International studies demonstrate its predictive accuracy, though performance depends on the timing of sampling and cut-off thresholds. A large Chinese cohort study involving more

DOI: https://doi.org/10.54393/pjhs.v7i2.3033

than 50,000 newborns showed that optimal DBS-TSH cut-offs (9–11 mIU/L) improved both sensitivity and specificity [10]. Similarly, lowering TSH thresholds increased detection of mild CH cases but also raised false-positive rates [11]. Evidence also suggests that sampling after 48–72 hours reduce false positives compared to earlier collection [12]. Despite these global insights, data from Pakistan remains limited. Local studies have reported increasing trends of CH and highlighted gaps in newborn screening coverage [13, 14].

However, the positive predictive value (PPV) of DBS-TSH–based newborn screening has not been comprehensively evaluated in the Pakistani population, limiting evidence for optimizing national screening strategies. This study aimed to determine the PPV of DBS-TSH in diagnosing congenital hypothyroidism among neonates born at a tertiary care hospital, to inform refinement of national screening protocols.

METHODS

This retrospective cohort study using screening registry data was conducted at the Newborn Screening Program, Department of Pediatrics, Aga Khan University Hospital, Karachi, from March 2023 to March 2024. After obtaining approval from the Institutional Review Board (2023-8367-23754), data were retrieved for all neonates screened for congenital hypothyroidism (CH) between April 2019 and December 2022. As this study involved a retrospective review of existing medical records without direct patient contact, informed consent was not required. Patient confidentiality and anonymity were strictly maintained throughout the study. A DBS-TSH concentration greater than 10 mIU/L was considered screen-positive according to our hospital's newborn screening protocol. A non-probability consecutive sampling technique was used, whereby all screened positive neonates, with gestational age ≥33 weeks, during this period were included. Infants with incomplete records or missing follow-up data were excluded. Screen-positive infants were stratified into two groups: Group 1 (DBS-TSH 10–20 mIU/L) and Group 2 (DBS-TSH >20 mIU/L). Furthermore, screen-positive infants were also stratified based on age at the time of sampling. The sample size was calculated using the formula for estimating a single proportion, with the positive predictive value (PPV) of DBS-TSH in diagnosing congenital hypothyroidism as the primary outcome. Based on a previous regional study [6], which reported a PPV of 8.6%, and using a 95% confidence level (Z = 1.96) and a margin of error of 2.5%, the minimum required sample size was 478 screen-positive neonates. Accounting for an anticipated 20% loss to follow-up, the target sample size was increased to 600. The study included 538 screen-positive infants, meeting this calculated requirement. A non-probability consecutive sampling technique was used, whereby all screened positive neonates with gestational age ≥33 weeks during the study period were included. Data collection included demographic information like gestational age, birth weight, sex, and maternal thyroid and pregnancy history. Moreover, the age of neonates and TSH value through DBS and later confirmatory serum analysis were recorded along with FT4 from electronic medical records of Aga Khan University Hospital. DBS was collected at the hospital from neonates using standardized heel prick procedures onto filter paper cards for newborn screening. TSH levels were subsequently measured from these samples using liquid chromatography-tandem mass spectrometry (LC-MS/MS) at the AKUH Clinical Laboratories, Karachi. All samples were processed following institutional standard operating procedures to ensure quality and accuracy. Neonates with TSH levels >10mIU/L on DBS are advised to get confirmatory serum tests done, involving serum TSH for group 1 and serum TSH and free thyroxine (FT4) for Group 2, to confirm the presence of congenital hypothyroidism. Follow-up is done for all screen-positive cases within 48 hours of initial DBS-TSH results and continued for two weeks via telephonic messages, emails, and letters to the mailing address (whichever is available), and details of confirmatory testing, including date and results, were documented. Neonates are labelled as true positives for congenital hypothyroidism based on plasma TSH >20Miu/L and FT4 testing (<0.97 ng/dl). After extraction of data from medical records and NBS program registry statistical analysis was performed using Stata version 17 (Stata Corp, College Station, TX, USA). Continuous variables were expressed as mean ± standard deviation, while categorical data were summarized as frequencies and percentages. Positive predictive value was calculated as the proportion of screen-positive neonates who were confirmed to have congenital hypothyroidism on serum thyroid-stimulating hormone and free thyroxine testing, using the formula: Positive Predictive Value = (True Positives) / (True Positives + False Positives). Exact 95% confidence intervals were calculated using the Clopper–Pearson method for binomial proportions. Newborn screening was performed in 30402 neonates during the period of study, of which 538 (1.76%) were found to be screen positives (Figure 1).

DOI: https://doi.org/10.54393/pjhs.v7i2.3033

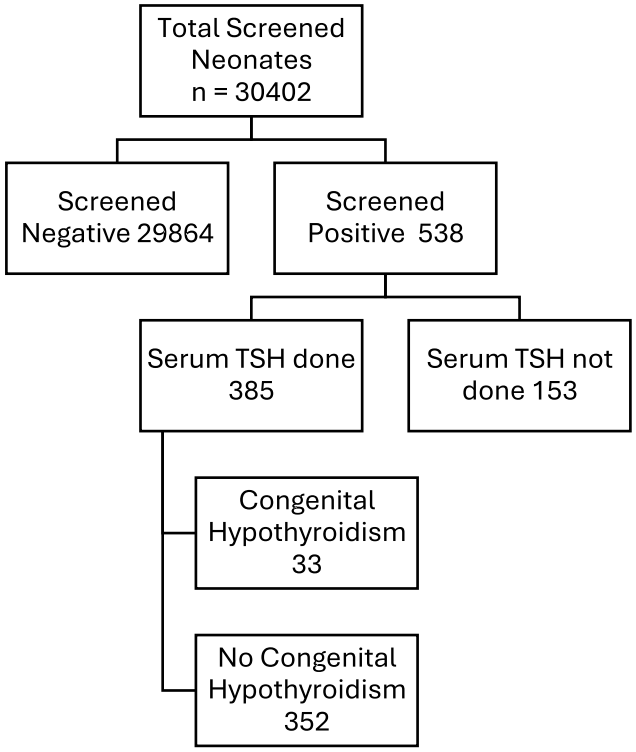

Figure 1: DBS-TSH screening and Serum TSH Confirmatory Testing in Neonates (n=30402)

RESULTS

The mean age of the neonates at the time of sampling was 38.3 ±18.8 hours. The majority of the DBS-TSH sampling was done within 24-48 hours of age, i.e., 315 (58.5%), while 37 (6.8%) was done before 24 hours of age, and 186 (34.5%) was sent after 48 hours of age. The cohort comprised 268 (49.8%) girls and 270 (50.2%) boys. The mean birth weight was 2853.8 ± 417.3 grams. Low birth weight (less than 2500 g) was observed in 86 (16%) of the neonates. The majority of the neonates were term infants, i.e., 466 (86.6%). The mean gestational age was 38.0 ±1.5 weeks. The mean DBS-TSH value was found to be 16.1 ±12.6 mIU/L. A total of 478 (88.8%) had DBS-TSH results between 10-20mIU/L (Group 1), whereas 60 (11.2%) had DBS-TSH results >20mIU/L (Group 2). Among the total cohort, 153 neonates (28.43%) were lost to follow-up, leaving 385 neonates (332 from group 1 and 53 from Group 2) (71.56%), who underwent confirmatory serum TSH testing. The mean serum TSH level among these neonates was 12.5 ± 28.7 mIU/L. Serum FT4 levels were measured in 90 neonates (16.7%), with a mean value of 1.5 ± 1.6 ng/dL. Of the 385 neonates who completed confirmatory TSH testing, congenital hypothyroidism was diagnosed in 33 cases, yielding a proportion of confirmed CH among screen-positive infants of 8.57% (Table 1).

Table 1: Descriptive Findings of Serum TSH, DBS-TSH, Final Diagnosis, and Serum FT4 (n=538)

Characteristics	Mean ± SD / Frequency (%)
DBS-TSH Results (mIU/L)	16.1 ± 12.6
Group 2 (DBS-TSH >20mIU/L)	60 (11.2%)
Group 1 (DBS-TSH 10-20mIU/L)	478 (88.8%)
Serum TSH done	385 (71.6%)
Serum TSH not done	153 (28.4%)
Contact established but not repeated by parents	117 (76.5%)
Contact not established	36 (23.5%)
Serum TSH Results (mIU/L), n=385	12.5 ± 28.7
Serum FT4 Levels, n=90	1.5 ± 1.6
Congenital Hypothyroidism	33 (8.57%)
No Congenital Hypothyroidism	352 (91.4%)

DBS: Dried blood sampling, PPV: Positive predicted value, SD: Standard deviation, TSH: Thyroid-stimulating hormone

The PPV of DBS-TSH in predicting congenital hypothyroidism was found to be 8.57% (95% CI: 5.9%–11.7%) in our cohort (Table 2).

Table 2: Positive Predictive Value of DBS-TSH in Diagnosing Congenital Hypothyroidism (n=385)

Final Diagnosis	DBS-TSH, Frequency (%)	PPV (%)	95% CI (%)
Congenital Hypothyroidism	33 (8.57%)	8.57%	5.97 – 11.38
No Congenital Hypothyroidism	352 (91.425)		
Total	385		

DBS: Dried blood sampling, PPV: Positive predicted value, TSH: Thyroid-stimulating hormone. The PPV confidence interval was calculated using the exact (Clopper–Pearson) binomial method to provide precise estimates of statistical uncertainty.

Stratification by predictor variables showed that the PPV of DBS-TSH increased with both sampling age and higher TSH concentrations. Neonates sampled after 48 hours of age had a PPV of 14.07% (95% CI: 8.69–21.10%) (Table 3).

Table 3: Stratification of Predictor Variables and Positive Predicted Value of DBS-TSH in Diagnosing Congenital Hypothyroidism (n=385)

Variables		Final Diagnosis, Frequency (%)		PPV (%)	95% CI (%)
		Congenital Hypothyroidism	No Congenital Hypothyroidism		
DBS-TSH Category					
Group 1 (10-20 mIU/L)	332	12 (3.6%)	320 (96.3%)	3.6	1.88 – 6.23
Group 2 (>20 mIU/L)	53	21 (39.6%)	32 (60.3%)	39.6	26.45 – 53.99
Age of Neonates at Time of Sampling					
<24 Hours	26	0 (0%)	26 (100%)	0	0 – 13.23
24-48 Hours	223	14 (6.27%)	209 (93.7%)	6.27	3.47 – 10.31
> 48 Hours	135	19 (14.07%)	116 (85.92%)	14.07	8.69 – 21.10

Further analysis of incremental DBS-TSH cutoff thresholds showed a progressive increase in PPV with rising TSH values. A DBS-TSH cutoff of ≥ 35 mIU/L yielded a PPV of

DOI: https://doi.org/10.54393/pjhs.v7i2.3033

95.2% (95% CI: 76.18–99.88%). Comparative PPV values for all evaluated cutoff points are summarized (Table 4).

Table 4: Comparison of Positive Predictive Values of Different DBS-TSH Cutoffs

DBS-TSH Cutoff Value (mIU/l)	No. of Screen Positives	No. of Screen Negatives	(Serum TSH >20 mIU/l) No. of True Positives	(Serum TSH >20 mIU/l)	(Serum TSH >20 mIU/l) No. of False Positives	(Serum TSH >20 mIU/l) No. of False Negatives	PPV (%)	95% CI (%)
≥ 10	385	0	33	0	352	0	8.57	5.97 – 11.83
≥ 11	326	59	33	59	293	0	10.1	7.07 – 13.93
≥ 12	252	133	31	131	221	2	12.3	8.51 – 17.00
≥ 13	197	188	28	183	169	5	14.2	9.66 – 19.88
≥ 14	142	243	26	236	116	7	18.3	12.32 – 25.67
≥ 15	110	275	24	266	86	9	21.8	14.51 – 30.70
≥ 16	96	289	23	279	73	10	23.9	15.83 – 33.75
≥ 17	77	308	22	297	55	11	28.5	18.88 – 40.00
≥ 18	64	321	21	309	43	12	32.8	21.59 – 45.69
≥ 19	59	326	21	314	38	12	35.5	23.55 – 49.13
≥ 20	54	331	21	319	33	12	38.8	25.92 – 53.12
≥ 25	38	347	21	335	17	12	55.2	38.30 – 71.38
≥ 30	28	357	21	345	7	12	75	55.13 – 89.31
≥ 35	21	364	20	351	1	13	95.2	76.18 – 99.88
≥ 40	18	367	17	351	1	16	94	72.71 – 99.86
≥ 50	16	369	16	351	0	17	100	79.41 – 100.0

DBS: Dried blood sampling, PPV: Positive predictive value, TSH: Thyroid-stimulating hormone, CI: Confidence Interval. PPV confidence intervals were calculated using the exact (Clopper–Pearson) binomial method to provide precise estimates of statistical uncertainty.

DISCUSSION

This study evaluated the positive predictive value (PPV) of DBS-TSH for neonatal screening of congenital hypothyroidism (CH) at a tertiary care center in Pakistan. The overall PPV was 8.57%, which is consistent with findings from other regions. Alameer *et al.* reported a PPV of 8.6% in Saudi Arabia [6]. while Liu *et al.* recently demonstrated wide variation in global prevalence and screening performance, reflecting differences in cutoffs and protocols across populations [3]. Current analysis showed that DBS-TSH ≥10 mIU/L identified 538 neonates, of whom 33 were confirmed to have CH, supporting this threshold as an effective screening cutoff. Importantly, a higher cutoff (≥35 mIU/L) yielded a PPV of 95%, suggesting that immediate treatment could be considered in such cases while awaiting confirmatory results. In addition, neonates sampled after 48 hours of life demonstrated higher PPVs, underscoring the importance of optimal timing for sample collection. These findings are consistent with recent European and international studies highlighting improved predictive value at higher TSH thresholds and later sampling [15-17]. These comparisons underscore the variability in PPV across different settings, influenced by factors such as screening protocols, cutoff values, and demographic characteristics of the neonates. Our study's findings contribute to the body of evidence supporting the effectiveness of DBS-TSH screening in identifying neonates at risk of congenital hypothyroidism, with implications for early detection and treatment to prevent adverse outcomes in our hospital and laboratory settings [18-20]. This study has several strengths. It is one of the few studies conducted in Pakistan that evaluates the PPV of DBS-TSH screening for congenital hypothyroidism in neonates. Current findings provide valuable insights into the performance of this screening method in a local context. Furthermore, the study included a relatively large sample size, enhancing the statistical power and reliability of our results. The identification of factors associated with higher PPV, such as age at the time of sampling and DBS-TSH levels, adds to the existing knowledge and can inform future screening strategies. Recent studies from Pakistan have reported that the true prevalence of congenital hypothyroidism in the Pakistani population is not available [10, 11]. Our study contributes to addressing the gap in knowledge regarding the true prevalence of congenital hypothyroidism in the Pakistani population by screening out cases with newborn screening, which would have been missed, but cannot provide prevalence estimates because nearly one-third of screen-positive infants did not undergo confirmatory testing. As a result, our findings are limited to the proportion of confirmed CH cases among those who completed follow-up rather than reflecting population-level prevalence. By evaluating the PPV of DBS-TSH for screening congenital hypothyroidism in neonates, our research provides valuable insights that can inform future epidemiological studies and screening strategies in Pakistan.

The study relied on DBS-TSH measurements without assessing full diagnostic parameters such as sensitivity, specificity, and negative predictive value. Additionally, incomplete follow-up limited the evaluation of long-term

DOI: https://doi.org/10.54393/pjhs.v7i2.3033

outcomes and may have led to underestimation of true disease burden. Future research should incorporate comprehensive screening performance measures, long-term neonatal follow-up, and evaluation of maternal and environmental factors affecting neonatal TSH levels.

CONCLUSIONS

Current study demonstrates that DBS-TSH screening in neonates has a PPV of 8.57% for diagnosing congenital hypothyroidism. Higher DBS-TSH levels and sampling after 48 hours were associated with increased predictive accuracy. These findings highlight the effectiveness of DBS-TSH as an initial screening tool for early detection of congenital hypothyroidism.

Authors' Contribution

Conceptualization: HM
Methodology: WAK, FN, KNH, IN
Formal analysis: SK
Writing and Drafting: WAK, FN, MA
Review and Editing: WAK, FN, MA, HM, IN, KHH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Cherella CE and Wassner AJ. Congenital Hypothyroidism: Insights Into Pathogenesis and Treatment. International Journal of Pediatric Endocrinology. 2017 Oct; 2017(1): 11. doi: 10.1186/s13633-017-0051-0.

[2] Klosinska M, Kaczynska A, Ben-Skowronek I. Congenital Hypothyroidism in Preterm Newborns-the Challenges of Diagnostics and Treatment: A Review. Frontiers in Endocrinology. 2022 Mar; 13: 860862. doi: 10.3389/fendo.2022.860862.

[3] Liu L, He W, Zhu J, Deng K, Tan H, Xiang L *et al.* Global Prevalence of Congenital Hypothyroidism among Neonates from 1969 To 2020: A Systematic Review and Meta-Analysis. European Journal of Pediatrics. 2023 Jul; 182(7): 2957-65. doi: 10.1007/s00431-023-04932-2.

[4] Yao YN, Yuan XL, Zhu J, Xiang LC, Li Q, Deng K *et al.* Geographic Variations in the Incidence of Congenital Hypothyroidism in China: A Retrospective Study Based on 92 million Newborns Screened in 2013-2018. Chinese Medical Journal. 2021 Sep; 134(18): 2223-30. doi: 10.1097/CM9.0000000000001613.

[5] Ahmad N, Irfan A, Al Saedi SA. Congenital Hypothyroidism: Screening, Diagnosis, Management, and Outcome. Journal of Clinical Neonatology. 2017 Apr; 6(2): 64-70. doi: 10.4103/jcn.JCN_5_17.

[6] Alameer S, Althobaiti E, Alshaikh S, Turjoman M, Badriq F, AlSofyani A *et al.* Diagnostic Comparison Between Cord Blood and Filter Paper for the Screening of Congenital Hypothyroidism. Journal of Clinical Laboratory Analysis. 2022 Jan; 36(1): e24149. doi: 10.1002/jcla.24149.

[7] Stroek K, Heijboer AC, Bouva MJ, Van der Ploeg CP, Heijnen ML, Weijman G *et al.* Critical Evaluation of the Newborn Screening for Congenital Hypothyroidism in the Netherlands. European Journal of Endocrinology. 2020 Sep; 183(3): 265-73. doi: 10.1530/EJE-19-1048.

[8] Di Dalmazi G, Carlucci MA, Semeraro D, Giuliani C, Napolitano G, Caturegli P *et al.* A Detailed Analysis of the Factors Influencing Neonatal TSH: Results from A 6-Year Congenital Hypothyroidism Screening Program. Frontiers in Endocrinology. 2020 Jul; 11: 456. doi: 10.3389/fendo.2020.00456.

[9] Caiulo S, Corbetta C, Di Frenna M, Medda E, De Angelis S, Rotondi D *et al.* Newborn Screening for Congenital Hypothyroidism: The Benefit of Using Differential TSH Cutoffs in A 2-Screen Program. The Journal of Clinical Endocrinology and Metabolism. 2021 Jan; 106(1): e338-49. doi: 10.1210/clinem/dgaa789.

[10] Mansoor S. Trends of Congenital Hypothyroidism and Inborn Errors of Metabolism in Pakistan. Orphanet Journal of Rare Diseases. 2020 Nov; 15(1): 321. doi: 10.1186/s13023-020-01602-6.

[11] Majid H, Jafri L, Ahmed S, Humayun K, Kirmani S, Ali NB *et al.* Perspective on Newborn Screening (NBS): Evidence Sharing on Conditions to be Included in NBS in Pakistan. Journal of the Pakistan Medical Association. 2022; 72(3): 526-531. doi: 10.47391/JPMA.01181.

[12] Zhang L, Lin K, Han X. Screening of 50,539 Newborns for Congenital Hypothyroidism: Optimization of TSH Cut-off Values and Seasonal Impact in Clinical Practice. Frontiers in Endocrinology. 2025 Jun; 16: 1616748. doi: 10.3389/fendo.2025.1616748.

[13] Teixeira Palla Braga N, Vilela Antunes JM, Colosimo EA, Alves Dias VM, Januário JN, Novato Silva I. Impact of Lowering TSH Cut-Off on Neonatal Screening for Congenital Hypothyroidism in Minas Gerais, Brazil. International Journal of Neonatal Screening. 2024 Jul; 10(3): 52. doi: 10.3390/ijns10030052.

[14] Wahoud F, Essadki S, Zirar K, Lamsyah R, Hajjaji W, Amrani R. Implementation of Neonatal Screening

DOI: https://doi.org/10.54393/pjhs.v7i2.3033

Program for Congenital Hypothyroidism in Eastern Morocco. International Journal of Neonatal Screening. 2025 Jul; 11(3): 55. doi: 10.3390/ijns11030055.

[15] Rahimpour A, Baxter J, Denning DA, Ray P, Rahman B, Denning D *et al.* Impact of Safety Device Features Upon Motor Vehicle Collision Facial Fracture Traumas: A Five-Year Retrospective Study in the Appalachian Tri-State Area. Cureus. 2024 Jun; 16(6). doi: 10.7759/cureus.61659.

[16] Yan X, Wang L, Chen X, Wang A. Analysis of Risk Factors and Screening Results of Neonatal Congenital Hypothyroidism in a Tertiary Care Center of Southern China. Journal of Multidisciplinary Healthcare. 2023 Dec: 741-9. doi: 10.2147/JMDH.S400804.

[17] Liu X, Liang J, Liu Y. Effects of Walking Speeds on Lower Extremity Kinematic Synergy in Toe Vertical Position Control: An Experimental Study. Medicine. 2024 May; 103(18): e38024. doi: 10.1097/MD.0000000000038024.

[18] Salerno M, Militerni R, Bravaccio C, Micillo M, Capalbo D, Di Maio S *et al.* Effect of Different Starting Doses of Levothyroxine on Growth and Intellectual Outcome at Four Years of Age in Congenital Hypothyroidism. Thyroid. 2002 Jan; 12(1): 45-52. doi: 10.1089/105072502753451968.

[19] Freire R, Monte O, Tomimori EK, Catarino RM, Sterza T, Rocha T *et al.* Sonographic Evaluation of the Thyroid Size in Neonates. Journal of Clinical Ultrasound. 2015 May; 43(4): 224-9. doi: 10.1002/jcu.22244.

[20] Aliyo A, Ashenafi G, Adem S. Evaluation of Transfusion Transmissible Infections Prevalence and Trend Among Blood Donors Attended at Bule Hora Blood Bank, West Guji, South Ethiopia. Health Services Research and Managerial Epidemiology. 2022 Nov; 9: 23333928221136717. doi: 10.1177/23333928221136717.

DOI: https://doi.org/10.54393/pjhs.v7i2.3478

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Association of Dry Socket (Alveolar osteitis) with Gender and Site of Extraction (Maxillary and Mandibular)

Zubair Ahmed[1*], Jehan Alam[1], Abubakar Saddique[2], Ruqaya Shah[1], Muhammad Saeed Azhar[3], Mehmood Ur Rehman[4], Mor Khan Shar[5] and Khursheed Ahmed[6]

[1]Department of Oral and Maxillofacial Surgery, Jinnah Post Graduate Medical Centre, Karachi, Pakistan
[2]Department of Maxillofacial Surgery, District Headquarters and Teaching Hospital, Timergara Dir Lower, Pakistan
[3]Department of Maxillofacial Surgery, Precision Dental Care, Karachi, Pakistan
[4]Department of General Dentistry, Al Khidmat Fareeda Yaqoob Hospital, Karachi, Pakistan
[5]Department of Oral and Maxillofacial Surgery, School of Dentistry, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan
[6]Tufts University School of Dental Medicine, Massachusetts, United States of America

ARTICLE INFO

Keywords:
Alveolar osteitis, Mandibular Extraction, Maxillary Extraction, Smoking, Oral Surgery Outcomes

How to Cite:
Ahmed, Z., Alam, J., Saddique, A., Shah, R., Azhar, M. S., Rehman, M. U., Shar, M. K., & Ahmed, K. (2026). Association of Dry Socket (Alveolar osteitis) with Gender and Site of Extraction (Maxillary and Mandibular): Dry Socket (Alveolar osteitis) and Its Association with Gender and Extraction Site. Pakistan Journal of Health Sciences, 7(2), 73-77. https://doi.org/10.54393/pjhs.v7i2.3478

***Corresponding Author:**
Zubair Ahmed
Department of Oral and Maxillofacial Surgery, Jinnah Post Graduate Medical Centre, Karachi, Pakistan
drzubaira94@gmail.com

Received Date: 10th September, 2025
Revised Date: 6th January, 2026
Acceptance Date: 13th January, 2026
Published Date: 28th February, 2026

ABSTRACT

American dentist James Young Crawford coined the phrase "dry socket" (Alveolar Osteitis) in 1896 to refer to an acute infection of alveolar bone surrounding the location of a tooth extraction. Severe pain, the lack of a blood clot inside the socket, and food particles inside the socket are clinical indicators of dry socket. Most frequently seen after the extraction of mandibular third molars, the incidence of dry socket ranges greatly, from 1% to over 25%. **Objectives:** To assess the frequency of dry socket and its association with gender and site of teeth extraction at a tertiary care hospital. **Methods:** The descriptive cross-sectional study was conducted at the Department of Oral and Maxillofacial Surgery of Jinnah Postgraduate Medical Center, Karachi. Demographic data, such as age and gender, and clinical data, such as the extraction site, smoking status, extraction type and extent, and the frequency of dry socket within five days after extraction. **Results:** Dry socket was found in 22.5% higher in male, 26.5% compared to female 17.3%. The incidence of dry socket was significantly greater in mandibular extractions 31.1% than in maxillary extractions 8.7% with a p-value of less than 0.01. Smokers exhibited a notably higher rate of dry socket 41.7% compared to non-smokers, 9.7%. Furthermore, 41% of surgical extractions resulted in dry socket, compared to 13.6% of non-surgical extractions. **Conclusions:** The reported frequency of dry socket was slightly higher in male as compared to female, and it was more commonly observed in patients who underwent mandibular tooth extractions.

INTRODUCTION

The American dentist James Young Crawford coined the phrase "dry socket" (Alveolar Osteitis) in 1896 to refer to an acute infection of the alveolar bone surrounding the location of a tooth extraction [1]. Severe pain, the lack of a blood clot inside the socket, and food particles inside the socket are clinical indicators of dry socket [2]. Most frequently seen after the extraction of mandibular third molars, the incidence of dry socket ranges greatly, from 1% to over 25% [3]. Several reasons have been related to an increased risk of developing alveolar osteitis, while some remain controversial [4]. These include the extraction location, smoking, being a woman, being younger, having had difficult or traumatic extractions, not practiced good dental hygiene, and had a history of dry socket episodes. Additionally, recent research points to the possible involvement of bacterial components in the

DOI: https://doi.org/10.54393/pjhs.v7i2.3478

pathophysiology of dry socket by indicating that individuals may have a unique microbiome. This underlines the importance of applying evidence-based strategies in routine dental practice to improve patient outcomes [5, 6]. Furthermore, a higher incidence of dry socket and other surgical problems has been associated with systemic health disorders such as diabetes and immunosuppression. Different incidence rates and gender distributions are reported by a number of studies in the literature [7]. For example, Chandran et al conducted a retrospective study in Chennai, India, and found that out of 1,341 extractions, 72 cases (5.37%) were complicated by dry socket. Among these, 44 (7.86%) were females, and 28 (6.18%) were males, with a higher prevalence in mandibular third molars (28.5%) compared to maxillary teeth (22.7%) [8]. According to a local cross-sectional survey, 9.0% of patients had dry socket, with female experiencing a slightly greater frequency (9.7%) than male (8.2%). In that study, the maxillary region accounted for 52.9% of dry socket instances, whereas the mandibular region accounted for 47.1% [9]. In contrast, Khan et al. reported that 75.7% of dry socket cases were in male and 24.2% in female, though they did not distinguish between maxillary and mandibular sites an important consideration, as mandibular extractions are known to be more commonly associated with dry socket [10]. Understanding the link between systemic health and oral health is crucial in developing individualized treatment plans for patients undergoing dental extractions. A comprehensive approach allows for tailored preventive and therapeutic interventions, ultimately improving patient care. The findings of this study will be used to inform future research and raise awareness in order to improve the quality of life for affected people.

Dry socket remains a frequent and painful complication following tooth extraction, with reported incidence and distribution varying widely across populations. Existing studies show inconsistent findings regarding its association with gender and extraction site, and local data remain limited and fragmented. This lack of uniform evidence makes it difficult to identify high-risk groups and plan targeted preventive strategies. This study aims to evaluate the association between dry socket and gender, as well as the extraction site (maxillary or mandibular), in the local population to support improved risk stratification and clinical decision-making.

METHODS

An analytical cross-sectional study was carried out at the Department of Oral and Maxillofacial Surgery at Jinnah Postgraduate Medical Centre in Karachi, with institutional ethical review committee clearance (No.F.2-81/2024-GENL/164/JPMC) from January 1, 2025, to July 15, 2025. The sample size was calculated using Open Epi Online software based on a reported dry socket prevalence of 8.2% in male 9, a 95% confidence level, and a 5% margin of error [9]. The study comprised 120 patients. Non-probability consecutive sampling was used to find the participants. All patients were recruited from the Outpatient Department after taking consent and a history with clinical examination. The study procedure, the reason for using their data for research, and the risks and advantages involved were all explained to the participants. Inclusion criteria consisted of patients aged between 18 and 60 years of either gender who presented to the outpatient department for permanent tooth extraction of mandibular or maxillary teeth. Patients with conditions that could affect the healing process, including osteopetrosis, ulcerative gingivitis, Paget's disease, malignancy, systemic diseases, osteomyelitis, coagulation disorders, or any other relevant medical conditions, were excluded. Pregnant women and those who did not provide consent were also excluded from the study. A structured Performa was used to collect data, which included clinical information such as the kind and extent of extraction, smoking status, the site of extraction, and the existence of dry socket within five days after extraction, in addition to demographic information such as age and gender. Dry socket, or alveolar osteitis, was defined as delayed healing without infection and was confirmed through a combination of the patient's complaint of pain beginning on the third postoperative day and clinical findings such as partial or complete loss of the blood clot and exposed bone, as assessed by a senior consultant. Smoking was defined as a history of smoking more than 10 cigarettes per day for a duration exceeding two years. SPSS version 27.0 version was used to analyze the data collected. The mean and standard deviation were used to display descriptive statistics like age, whereas frequency percentages were used to display categorical variables, including gender, smoking status, site, kind, and amount of extraction, and incidence of dry socket. The association was assessed by using chi square test, and a $p<0.05$ was considered significant.

RESULTS

A total of 120 patients were enrolled having mean age of the patients was 36.4 ± 11.2 years, ranging from 18 to 65 years. 68 (56.7%) were male, and 52 (43.3%) were female. Forty-eight patients (40%) were smokers, while 72 (60%) were non-smokers. The site of extraction was maxillary teeth in 46 patients (38.3%) and mandibular teeth in 74 patients (61.7%). In terms of extent, 85 patients (70.8%) underwent single-tooth extractions, whereas 35 (29.2%) had multiple teeth extracted. Regarding the type of procedure, 39 patients (32.5%) had surgical extractions and 81 (67.5%) had non-surgical extractions (Table 1).

DOI: https://doi.org/10.54393/pjhs.v7i2.3478

Table 1: Demographic and Clinical Characteristics of the Patients (n = 120)

Variables		Frequency (%), Mean ± SD
Age	Years	36.4 ± 11.2
Gender	Male	68 (56.7%)
	Female	52 (43.3%)
	Total	120 (100.0%)
Smoking Status	Smokers	48 (40.0%)
	Non-Smokers	52 (60.0%)
	Total	120 (100.0%)
Site of Extraction	Maxillary Teeth	46 (38.3%)
	Mandibular Teeth	74 (61.7%)
	Total	120 (100.0%)
Extent of Extraction	Single Tooth	85 (70.0%)
	Multiple Teeth	35 (29.2%)
	Total	120 (100.0%)
Type of Extraction	Surgical Extraction	39 (32.5%)
	Non- Surgical Extraction	81 (67.5%)
	Total	120 (100.0%)

The overall frequency of dry socket was 22.5% higher in male (26.5%) compared to female (17.3%) (p>0.05). The occurrence of dry socket was significantly greater in mandibular extractions (31.1%) than in maxillary extractions (8.7%), with a p-value of less than 0.01. Smokers exhibited a notably higher rate of dry socket (41.7%) compared to non-smokers (9.7%), and this association was highly significant (p<0.001). Additionally, dry socket occurred more frequently following surgical extractions (41%) than non-surgical extractions (13.6%) (p<0.01) (Table 2).

Table 2: Associations of Dry Socket with Demographic Characteristics

Group	Dry Socket (n)	Total (n)	Report Association (%)	p-value
Overall	27	120	22.5	–
Gender				
Male	18	68	26.5	>0.050
Female	9	52	17.3	
Site of Extraction				
Mandibular	23	74	31.1	<0.010*
Maxillary	4	46	8.7	
Smoking Status				
Smokers	20	48	41.7	<0.001*
Non-Smokers	7	72	9.7	
Type of Extraction				
Surgical	16	39	41.0	<0.010*
Non-Surgical	11	81	13.6	

*Indicates statistical significance at p≤0.05

DISCUSSION

In this study, the overall frequency of alveolar osteitis was reported as of 22.5%, which is higher than the typically reported range of 1% to 5% for routine extractions, but within the range of 20% to 30% for mandibular third molar extractions [11]. Several risk factors were evaluated, including gender, smoking status, site of extraction, type of extraction, and whether the procedure was surgical or non-surgical [12]. Most of the patients with dry socket were observed in the male gender (26.5%) compared to female (17.3%), although this difference was not statistically significant. This trend aligns with previous studies, such as the work by Nusair *et al.* and Asif *et al.* who also reported a higher frequency in male, attributing the difference to behavioral factors such as smoking [13, 14]. In a separate study conducted in Swat, Khan *et al.* reported that only 4% of patients developed dry socket following tooth extraction. The incidence was notably higher among male patients, particularly those within the 20 to 30-year age group. Additionally, the prevalence of dry socket was found to be significantly greater among smokers compared to non-smokers, indicating a strong association between smoking and the development of this postoperative complication [15]. The site of extraction showed a significant association with dry socket occurrence, with mandibular extractions (31.1%) being more prone compared to maxillary extractions (8.7%). This finding is consistent with the literature, indicating that mandibular teeth, especially molars, are at higher risk due to denser bone and lower vascularity, leading to compromised healing [16, 17]. Smoking was found to be a significant risk factor, with 41.7% of smokers developing dry socket compared to only 9.7% of non-smokers (p<0.001). This aligns with a study conducted by Saeed *et al.* in Bangladesh, which reported a non-significant association with smoking and the development of alveolar osteitis, suggesting that smoking did not appear to be a major contributing factor to the reported rate of dry socket in the study population [18]. Localized tissue ischemia may play a significant role in delayed wound healing and the development of thrombotic microvascular occlusion, potentially as a result of nicotine-induced vasoconstriction, which reduces blood flow to the surgical site. Additionally, nicotine can enhance platelet aggregation, further promoting the formation of microthrombi within small blood vessels, thereby exacerbating tissue hypoxia and impairing the normal healing process [19]. For instance, a study by Cardoso *et al.* revealed a 1% prevalence of dry socket [2], while Tandon *et al.* reported 20.6% at 48 h to 41.2% at two weeks post-extraction, with significant associations with smoking, poor oral hygiene, and surgical technique [20]. This is supported by findings from Sakka *et al.* who noted that surgical trauma increases fibrinolytic activity and delays healing, predisposing the socket to clot disintegration [21]. This study was limited by its observational design and lack

DOI: https://doi.org/10.54393/pjhs.v7i2.3478

of long-term follow-up, which may have underestimated delayed cases of alveolar osteitis. Additionally, factors such as oral hygiene, surgical technique variability, and patient compliance were not fully controlled, which could influence the results. Future research should include multicenter studies with standardized surgical protocols and comprehensive assessment of behavioral and clinical risk factors to better understand dry socket prevalence and prevention.

CONCLUSIONS

In this study, reported dry socket was notably higher in males and more commonly associated with extractions of lower teeth. These results indicate that gender and site of extraction had a role in the development of dry socket. For the understanding of this complication, it is important to introduce preventive measures in clinical practices and the conduct of large-scale studies.

Authors' Contribution

Conceptualization: ZA
Methodology: ZA, AS, MKS
Formal analysis: JA, MUR,
Writing and Drafting: RS, MSA
Review and Editing: ZA, JA, AS, RS, MSA, MUR, MKS, KA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Ekici Ö and Çalışkan İ. Retrospective Analysis of Alveolar Osteitis (Dry Socket) Cases Over Two Years. Clin Exp Health Sci. 2025; 15(1): 27-34. doi: 10.33808/clinexphealthsci.1359541.

[2] Cardoso RB, Soto VC, Gonçalves RCG, Pedroso AM, Jabur RO, Bortoluzzi MC. Prevalence and Factors Associated with Dry Socket Following Routine Dental Extractions. Med Oral Patol Oral Cir Bucal. 2024; 29 (3): 408-415. doi: 10.4317/medoral.26391.

[3] Bibi S, Basit A, Siddique U, Shabbir H, Ali M. Prevalence of Dry Socket Among the Patients Reporting for Extraction to Khyber College of Dentistry, Peshawar. Journal of Rehman College of Dentistry. 2023; 4(1): 17-20. doi: 10.52442/jrcd.v4i1.73.

[4] Zahid T and Ghafoor S. Molecular Events in the Clinicopathological Diagnosis of Alveolar Osteitis. Journal of the Pakistan Medical Association. 2021; 71: 508-13.

[5] Kuśnierek W, Brzezińska K, Nijakowski Surdacka K, A. Smoking as a Risk Factor for Dry Socket: A Systematic Review. Dentistry Journal (Basel). 2022; 10: 121. doi: 10.3390/dj10070121.

[6] Taberner-Vallverdú M, Camps-Font O, Gay-Escoda C, Sánchez-Garcés MA. Previous Dry Socket as a Risk Factor for Alveolar Osteitis: A Nested Case-Control Study in Primary Healthcare Services. Journal of Clinical and Experimental Dentistry. 2022; 14: 479-485. doi: 10.4317/jced.59586.

[7] Aguilar-Durán L, Figueiredo R, Seminago R, Roig FJ, Llorens C, Valmaseda-Castellón E. A Metagenomic Study of Patients with Alveolar Osteitis After Tooth Extraction. A Preliminary Case-Control Study. Clinical Oral Investigations. 2019; 23: 4163-4172. doi: 10.1007/s00784-019-02855-7.

[8] Chandran S, Alaguvelrajan M, Karthikeyan A, Ganesan K, Faiz MK, Vallabhaneni SS. Incidence of Dry Socket in South Chennai Population: A Retrospective Study. Journal of International Oral Health. 2016 Jan; 8(1): 119-122. doi: 10.4103/0976-7428.199496.

[9] Khan NB, Arsalan A, Yasir A, Azhar M, Ali M, Nawadat K. Frequency of Dry Socket Among Patients Undergoing Dental Extractions Presenting to a Teaching Hospital, Rawalpindi: Frequency of Dry Socket Among Patients Undergoing Dental Extractions. Pakistan Journal of Health Sciences. 2024; 30: 76-80. doi: 10.54393/pjhs.v5i09.1722.

[10] Khan ZA, Prabhu N, Maqsood A, Issrani R, Ahmed N, Abbasi MS *et al*. Frequency and Etiological Denominators of Alveolar Osteitis in Northern Province of the Kingdom of Saudi Arabia: An Observational Study. SAGE Open Medicine. 2023; 11: 1-8. doi: 10.1177/20503121231219420.

[11] Kolokythas A, Olech E, Miloro M. Alveolar Osteitis: A Comprehensive Review of Concepts and Controversies. International Journal of Dentistry. 2010; 2010(1): 1-10. doi: 10.1155/2010/249073.

[12] Noor S, Ahmed F, Batool S, Razzaq M, Shar MK. Does Aspirin Need to Be Discontinued Before an Elective Simple Tooth Extraction? BioMedica. 2024; 40(4): 181-185. doi: 10.24911/BioMedica/5-1176.

[13] Nusair YM and Younis MHA. Prevalence, Clinical Picture, and Risk Factors of Dry Socket in a Jordanian Dental Teaching Center. Journal of Contemporary Dental Practice. 2007; (8)3: 053-063. doi: 10.5005/jcdp-8-3-53.

[14] Asif M, Ullah A, Mujtaba H, Umer MF, Khurshid Z. Comparative Study of Frequency of Alveolar Osteitis, With and Without Using Platelet-Rich Fibrin in Mandibular Third Molar Surgery. International

DOI: https://doi.org/10.54393/pjhs.v7i2.3478

Journal of Dentistry. 2023 Mar; 2023(1): 1-5. doi: 10.1155/2023/2256113.

[15] Khan M, Ali S, Uroosa Zeb. Frequency of Dry Socket in Patients coming to the Dental Outpatient Department, Saidusharif Hospital, SWAT. Bulletin of Environment, Pharmacology and Life Sciences. 2020; 9: 94-99.

[16] Farhan A, Da'er S, Nasher A, Juain A, Alareqi N. Prevalence of Dry Socket in Yemeni Patients. Saudi Journal of Oral and Dental Research. 2023 May; 8(5): 146-151. doi: 10.36348/sjodr.2023.v08i05.001.

[17] Sulaiman NA, Al-Jewari SS, Salim HA. Dry Socket in Relation to Predisposing Factors in Mosul Dental Teaching Hospital Patients. Dental Cadmos. 2025; 93(3): 120-130. doi: 10.19256/d.cadmos.03.2025.07.

[18] Saeed MS, Khan A, Sohail S, Jamal M, Javed A, Murtaza M. Frequency of Dry Socket Among Patients Undergoing Dental Extraction Presenting to Ayub Teaching Hospital. Journal of University Medical & Dental College. 2022; 13(2): 387-390. doi: 10.37723 /jumdc.v13i2.618.

[19] Materni A, Pasquale C, Longo E, Frosecchi M, Benedicenti S, Bozzo M *et al.* Prevention of Dry Socket With Ozone Oil-Based Gel After Inferior Third Molar Extraction: a Double-Blind Split-Mouth Randomized Placebo-Controlled Clinical Trial. Gels. 2023 Apr; 9(4): 289. doi: 10.3390/gels9040289.

[20] Tandon P, Sahoo SK, Mohanty L, Jain N, Hittalamani V, Kamble SS *et al.* Dry Socket Prevalence and Risk Factors in Third Molar Extractions: A Prospective Observational Study. Cureus. 2024 Mar; 16(3): 1-6. doi: 10.7759/cureus.56721.

[21] Sakka S, Kharma MY, Al Rafedah A. Chlorhexidine Mouthwash and Augmentin to Prevent Alveolar Osteitis After Removal of Mandibular Third Molar: A Three-Arm Placebo-Controlled Randomized Clinical Trial. African Health Sciences. 2024 Jul; 24(2): 117-123. doi: 10.4314/ahs.v24i2.14.

DOI: https://doi.org/10.54393/pjhs.v7i2.3577

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Comparison of Efficacy of Ferric Carboxymaltose versus Iron Sucrose Complex for the Treatment of Iron Deficiency Anemia in Pregnancy

Florentina Prastish Javed[1], Sumaira Kanwal[1], Ayesha Azhar Khan[1], Asma Amin Baig[1], Muhammad Rabeet[1], Muhammad Owais Qurshi[2], Hafiz Muhammad Zeeshan Raza[3*] and Muhammad Imran Arif[4]

[1]Department of Gynaecology and Obstetrics, Rashid Latif Medical College, Arif Memorial Teaching Hospital, Lahore, Pakistan
[2]Department of Medicine, Lahore General Hospital, Lahore, Pakistan
[3]Department of Medicine, The University of Lahore Teaching Hospital, Lahore, Pakistan
[4]Xinjiang Medical University, Urumqi, China

ARTICLE INFO

Keywords:
Iron Deficiency Anemia, Pregnancy, Ferric Carboxymaltose, Iron Sucrose, Intravenous Iron, Hemoglobin, Parity, Adverse Effects, Maternal Health

How to Cite:
Javed, F. P., Kanwal, S., Khan, A. A., Baig, A. A., Rabeet, M., Qurshi, M. O., Raza, H. M. Z., & Arif, M. I. (2026). Comparison of Efficacy of Ferric Carboxymaltose versus Iron Sucrose Complex for the Treatment of Iron Deficiency Anemia in Pregnancy: Ferric Carboxymaltose versus Iron Sucrose Complex for Iron Deficiency Anemia in Pregnancy. Pakistan Journal of Health Sciences, 7(2), 78-83. https://doi.org/10.54393/pjhs.v7i2.3577

***Corresponding Author:**
Hafiz Muhammad Zeeshan Raza
Department of Medicine, The University of Lahore Teaching Hospital, Lahore, Pakistan
hafizraza26@gmail.com

Received Date: 9th December, 2025
Revised Date: 15th January, 2026
Acceptance Date: 24th January, 2026
Published Date: 28th February, 2026

ABSTRACT

During pregnancy, iron deficiency anemia (IDA) is a common complication that exposes both the mother and fetus to a lot of risks. **Objectives:** To compare intravenous ferric carboxymaltose (FCM) versus iron sucrose in the treatment of moderate to severe anemia in pregnant women. **Methods:** This quasi-experimental study was conducted in a tertiary care hospital in Lahore, which registered 62 pregnant women having 16-34 weeks of gestation and hemoglobin levels of 7-9 g/dl. The participants were randomly divided into two groups, with intravenous FCM in one of them and the other without. The level of base hemoglobin and post-treatment were taken three weeks after the completion. There was also the evaluation of effectiveness and adverse impacts. **Results:** The average basal hemoglobin was 7.88 ± 0.42 g/dl. The levels after treatment were significantly higher in the FCM group (10.93 ± 0.63 g/dl) compared to the IS group (9.98 ± 0.51 g/dl), with an increase in statistically significant HB ($p<0.001$). The efficacy was reported in 87.1% of patients treated with FCM versus 38.7% in the SI group. The adverse effects were remarkably lower in the FCM group (19.4%) compared to IS (61.3%) ($p=0.001$). Although multiparous women had significantly lower basal HB, both parity groups showed similar responses to treatment. **Conclusions:** Ferric carboxymaltose demonstrated superior efficacy and tolerability compared to iron sucrose in the first leg during pregnancy. Its ability to achieve rapid HB correction with fewer side effects supports its consideration as preferred intravenous iron therapy.

INTRODUCTION

Iron deficiency anemia (IDA) remains the most frequent hematological disorder that complicates pregnancy, affects millions worldwide, and raises important risks to maternal and fetal health [1]. During pregnancy, physiological changes, including the increase in plasma volume and the highest iron requirements for fetal growth and placental development, predispose women to iron exhaustion [2]. Worldwide, the highest load falls on low and middle-income countries, particularly in southern Asia and sub -Saharan Africa, where iron intake in the diet is inadequate, infections are common, and access to timely prenatal care is often limited [3]. A recent meta-analysis of 27 studies found a pooled prevalence of 70.4% for anemia in pregnant women, with even higher rates in Punjab at 77.4% [4]. Globally, IDA is regarded as one of the most common medical complications of pregnancy and is linked

DOI: https://doi.org/10.54393/pjhs.v7i2.3577

to poor maternal and neonatal outcomes (such as fatigue, predisposition to infection, preterm birth, and low birth weight) [5, 6]. Although oral iron supplementation is recommended as a first-line management, it is often insufficient because of gastrointestinal intolerance and lack of adherence as well as hematological response in women with moderate to severe anemia or advanced gestation [7]. In turn, intravenous iron therapy (IVI) has now been proven as a safe and reliable alternative to accelerate and guarantee successful iron replacement in pregnancy, especially when an embolism needs to be treated in time [8]. However, all preparations are not alike in terms of pharmacokinetics, dosing patterns, and infusion needs, which can affect the effectiveness of the treatment, compliance of the patient, and use of the health-care resources [9, 10].

Despite the existing data, the significant knowledge gaps persist with respect to the optimal choice of IVI in various populations, particularly in low -income environments, based on the community, where the logistics of treatment often dictate the clinical decisions and where both the load and the consequences of anemia are disproportionately high. Studies with adequate power and local contextualization are essential to inform the guidelines. This study aimed to compare the ferric carboxymaltose and the iron sucrose complex in the treatment of IDA, aiming to rigorously evaluate their relative effectiveness, safety, tolerability, and practical implications in the local context.

METHODS

This was a quasi-experimental study conducted from August to November 2025 in the Department of Obstetrics and Gynecology at Arif Memorial Hospital, affiliated with Rashid Latif Khan University (RLKU) Medical College, Lahore, Pakistan. The research was carried out following ethical approval given by the institutional review board of Hameed Latif Hospital, Lahore; the teaching institute of RLKU Medical College (HLH/ADM/IRB/2025-027). Informed consent was obtained from research participants before conducting this research, and confidentiality was maintained. A total of 62 pregnant women who were between 16 and 34 gestation weeks were recruited using non-probability consecutive sampling. The eligible study subjects were 18 to 40 years old; their hemoglobin was between 7.0 and 9.0 g/dl with serum ferritin below 30 ng/ml. The inclusion criteria were pregnant women found to have IDA through laboratory data. The exclusion criteria were a history of allergy to iron preparations, multiple pregnancy, chronic systemic disease (e.g., diabetes mellitus), renal or cardiac disease, hemoglobinopathies, non-iron deficiency anemia (i.e., antepartum bleeding), or intravenous iron or blood transfusion within the last three months. Group A was given FCM intravenously, and Group B was given intravenously as iron SEC. Basic demographic features such as age, parity, and gestational age were taken. Each subject was given albendazole 400 mg in a single oral dose before being administered iron therapy. In Group A, FCM would be diluted in 0.9% normal saline and infused intravenously within 15 to 30 minutes according to the dosage. The dosage of 100-500 mg was given in 100mL in a period of 15 minutes, whereas the 500-1000mg dosage was given in 200 mL in a period of 30 minutes. The highest single dose was 1000 mg with added doses on day 7 or 14 in case of need. Group B had iron sucrose, which was used in the form of 200 mg in 100 mL of 0.9% normal saline that was infused over 30 minutes on alternate days with a maximum dose of 600 mg per week. Total iron requirement was calculated using the formula: Total iron dose (mg) = 2.4 × body weight (kg) × (target Hb – actual Hb) + 500, with a target hemoglobin of 11 g/dL. The participants were carefully monitored throughout the infusion, when pulse, blood pressure, and fetal heart rate were monitored. All the negative experiences, like infusion reactions, were reported in detail. The main product was the hemoglobin concentration three weeks after therapy was completed, and this was measured with the help of an automated hematology analyzer. The secondary outcomes were treatment efficacy (successful increase of hemoglobin levels to 11g/dl or more or marked increase in comparison with baseline) and adverse effects. The Statistical Package for the Social Sciences (SPSS) version 29.0 was used to analyze the data. Quantitative variables were represented as mean standard deviation (SD). An independent samples t-test was employed in testing the difference in mean hemoglobin increase across groups. To evaluate the relationship between treatment groups and outcomes of efficacy and side effects, chi-square tests were used. Age, parity, and baseline hemoglobin stratification were done in order to control the potential confounders. The p-value below 0.05 was regarded as significant.

RESULTS

Sixty-two pregnant women with iron-deficient anemia were involved in the study. With a range of 6.65 to 8.61 g/dL, the mean baseline hemoglobin (Hb) level was 7.88 ± 0.42 g/dL. The mean post-treatment Hb level was 10.46 ± 0.75 g/dL, with a range of 8.99 to 12.31 g/dL. 39 (62.9%) were multiparous, and 23 (37.1%) were primiparous with respect to parity. 39 (62.9%) responded favorably (efficacy "Yes") to treatment efficacy, whereas 23 (37.1%) did not (efficacy "No"). Out of the subjects, adverse effects were evident in 25 (40.3%) and absent in 37 (59.7%). These results confirm that, in comparison to the control, the experimental intervention was linked to a statistically significant rise in hemoglobin and fewer negative side effects (Table 1).

DOI: https://doi.org/10.54393/pjhs.v7i2.3577

Table 1: Baseline and Post-Treatment Hemoglobin Levels, Parity Distribution, Treatment Efficacy, and Adverse Effects Among Pregnant Women with Iron Deficiency Anemia (n=62)

Variables	Category	Frequency (%)	Mean ± SD	Range
Baseline Hb (g/dL)	–	62 (100%)	7.88 ± 0.42	6.65 – 8.61
Post Hb (g/dL)	–	62 (100%)	10.46 ± 0.75	8.99 – 12.31
Parity	Multiparous	39 (62.9%)	–	–
	Primiparous	23 (37.1%)	–	–
Efficacy	Yes	39 (62.9%)	–	–
	No	23 (37.1%)	–	–
Adverse Effects	No	37 (59.7%)	–	–
	Yes	25 (40.3%)	–	–

The mean baseline hemoglobin (Hb) in the control group was 7.84 ± 0.37 g/dL, but in the experimental group it was marginally higher at 7.92 ± 0.46 g/dL. After therapy, the experimental group's mean post-treatment Hb improved significantly more than the control groups, rising to 9.98 ± 0.51 g/dL and 10.93 ± 0.63 g/dL. A better hemoglobin response to the experimental intervention was thus shown by the mean Hb rise, which was 3.01 ± 0.53 g/dL in the experimental group and 2.14 ± 0.37 g/dL in the control group. Regarding parity, multiparous women's baseline hemoglobin levels were lower at 7.70 ± 0.40 g/dL than those of primiparous women, who had 8.19 ± 0.21 g/dL. Following treatment, the mean hemoglobin levels in primiparous and multiparous women were 10.77 ± 0.63 g/dL and 10.27 ± 0.75 g/dL, respectively. Remarkably, the mean Hb rise was 2.57 ± 0.65 g/dL for multiparous women and 2.57 ± 0.61 g/dL for primiparous women (Table 2).

Table 2: Comparison of Baseline Hemoglobin, Post-Treatment Hemoglobin, and Mean Hemoglobin Rise Between Control (Iron Sucrose) and Experimental (Ferric Carboxymaltose) Groups

Variables	Group	n	Mean ± SD
Baseline Hb	Control	31	7.84 ± 0.37
	Experimental	31	7.92 ± 0.46
Post Hb	Control	31	9.98 ± 0.51
	Experimental	31	10.93 ± 0.63
Hb Rise	Control	31	2.14 ± 0.37
	Experimental	31	3.01 ± 0.53
Baseline Hb	Multiparous	39	7.70 ± 0.40
	Primiparous	23	8.19 ± 0.21
Post Hb	Multiparous	39	10.27 ± 0.75
	Primiparous	23	10.77 ± 0.63
Hb Rise	Multiparous	39	2.57 ± 0.65
	Primiparous	23	2.57 ± 0.61

With a mean difference of -0.493 g/dL (95% CI: -0.673 to -0.312), multiparous women's baseline hemoglobin (Hb) was substantially lower than that of primiparous women (t = -5.464, df = 60, p<0.001). Similarly, the post-treatment hemoglobin levels among multiparous women were significantly lower (t = -2.631, df=60, p=0.011), and the difference in hemoglobin levels between the two groups was -0.492 g/dL (95% CI: -0.867 to -0.118). However, no such significant differences were found in the Hb increase with parity groups (t=0.003, df=60, p=0.997), indicating that the reaction to treatment did not differ depending on parity. There was no significant difference in the baseline hemoglobin of the control group and experimental group when they were compared to the treatment groups (t = -0.744, df = 60, p=0.460). The post-treatment hemoglobin of the experimental group was significantly greater (t = -6.488, df = 60, p<0.001) with a mean of -0.950 g/dL (95% CI: -1.242 to -0.657). Also, since the mean difference between the experimental and control groups was -0.871 g/dL (95% CI: -1.104-0.637), the Hb increase was significantly greater in the experimental group (t = -7.470, df=60, p=0.001), which supported the better effect of the experimental treatment (Table 3).

Table 3: Comparison of Baseline Hemoglobin, Post-Treatment Hemoglobin, and Mean Hemoglobin Rise Between Multiparous and Primiparous Women

Variables	t	df	p-value	Mean Difference	95% CI (Lower–Upper)
Baseline Hb*Parity	-5.464	60	<0.001	-0.493	-0.673 to -0.312
Post Hb*Parity	-2.631	60	0.011	-0.492	-0.867 to -0.118
Hb Rise*Parity	0.003	60	0.997	0.0005	-0.335 to 0.336
Baseline Hb*Group	-0.744	60	0.460	-0.079	-0.291 to 0.133
Post Hb*Group	-6.488	60	<0.001	-0.950	-1.242 to -0.657
Hb Rise*Group	-7.470	60	<0.001	-0.871	-1.104 to -0.637

Efficacy and treatment group were shown to be significantly correlated (χ^2 = 15.552, df = 1, p<0.001). Total of 12 individuals in the control group and 19 in the experimental group demonstrated treatment efficacy. Likewise, there was a statistically significant correlation between the therapy group and negative outcomes (χ^2 = 11.328, df = 1, p=0.001). Six participants in the experimental group and 19 in the control group reported adverse effects, while 25 and 12 participants, respectively, were lost to follow-up. These results imply that the experimental medication was better tolerated with fewer side effects (Table 4).

Table 4: Association Between Treatment Group and Outcomes of Efficacy and Adverse Effects Using the Chi-Square Test

Variables	Group	Category	n	Pearson χ^2	df	p-value
Efficacy	Control	Yes	12	15.552	1	<0.001
		No	19			
	Experimental	Yes	27			
		No	4			
Adverse Effects	Control	Yes	19	11.328	1	0.001
		No	12			
	Experimental	Yes	6			
		No	25			

DOI: https://doi.org/10.54393/pjhs.v7i2.3577

DISCUSSION

Iron deficiency anemia (IDA) during pregnancy is a significant issue in health care worldwide, and the result of the study under consideration contributes to the existing number of studies that argue in favor of ferric carboxymaltose (FCM) over iron sucrose (IS) as intravenous iron replacement therapy. The mean increase in hemoglobin in FCM was 3.01 g/dL, which was statistically significant (p=0.001) when compared to the IS group, which had a mean increase in hemoglobin of 2.14 g/dL. This is in line with the results of Khan *et al.* who found a 2.9 g/dL hemoglobin increase with FCM and a 2.2 g/dL hemoglobin increase with IS at 12 weeks, and once again, a strong benefit of FCM [11]. The same findings were obtained by Alwan *et al.* who observed greater hemoglobin increase in the FCM group (3.96 ± 4.19 g/dL) compared to the iron sucrose group (2.11 ± 1.72 g/dL; p<0.05), but the standard deviations were greater, which is likely due to the higher heterogeneity of populations [12]. These studies suggest that the possibility of FCM to administer a bigger single dose is transferred into faster and more dependable hematological recovery in the course of pregnancy. In addition to the hemoglobin improvement, this study also established a much greater treatment efficacy with FCM since 87.1% of the patients met the therapeutic targets in contrast to 38.7% of those in the iron sucrose group. These results are also highly similar to those of Gupte *et al.* who found the efficacy rates of FCM and iron sucrose were 85.3% and 41.2% (p=0.001), respectively [13]. Equally, a phase IV trial by Saleem *et al.* had a larger percentage of pregnant women who were treated with FCM than the iron sucrose group, with more than 80% attaining target hemoglobin levels in under six weeks [14]. These variations are especially clinically relevant in late pregnancy, when the correction of anemia is required at a fast rate to prevent the threat of blood transfusion and adverse neonatal outcomes [13, 14]. The safety outcome is also vital in introducing the therapies during pregnancy. This research found that of women who got FCM, 19.4% of them had adverse effects, whereas 61.3% of the women who got iron sucrose had adverse effects (p=0.001). Bharadwaj *et al.* ratified such a difference, as they reported worse outcomes like infusion-site pain, nausea, and hypotension in 17% of patients who received FCM compared to 42% of those receiving iron sucrose [15]. Likewise, Lusingu and Maisonet established many fewer adverse effects of minor cases in the FCM group, as well as no severe cases of hypersensitivity in both groups [16]. These results show that the high tolerability of FCM is similar in various populations and study designs. Another secondary factor that was considered was parity. Baseline hemoglobin levels. Multiparous women had significantly lower (7.70 ± 0.40 g/ dL) hemoglobin levels compared to primiparous women (8.19 ± 0.21 g/dL; p<0.001). Nevertheless, the extent of hemoglobin elevation after the intervention was almost the same in the two groups (2.57 ± 0.65 g/dl vs. 2.57 ± 0.61 g/dl; p=0.997). Such a tendency is in line with the results of Singh *et al.* who proved that the higher parity, the lower the baseline iron stores, but has no impact on the responsiveness to intravenous iron therapy [17]. Similar findings to these were also made by Basha *et al.* Jin *et al.* and Xing *et al.* who stated that even though multiparous women start the treatment with a more severe iron deficiency, the hematologic response to intravenous iron in them is no worse than in primiparous women [18-20].

This research has also some limitations that must be acknowledged. As it was carried out in one tertiary care facility, and the sample consisted of non-probability consecutive, the findings cannot be closely applied to other clinical environments, such as primary or rural healthcare centers and other population groups. Also, the short-term follow-up of three weeks limited the assessment of long-term hematological sustainability, iron stores replenishment, and tardy adverse consequences. Future studies should include diverse healthcare settings with longer follow-up to evaluate sustained hematological outcomes and delayed complications.

CONCLUSIONS

The intravenous ferric carboxymaltose demonstrated greater improvement in hemoglobin levels, higher treatment efficacy, and better tolerability compared with iron sucrose among pregnant women with moderate to severe iron deficiency anemia. Although multiparous women presented with lower baseline hemoglobin levels, parity did not influence the hematological response to either intervention. Integrating FCM into the normal maternity anemia care practice can enhance the quality of care and minimize the anemia -related pregnancy complications.

Authors' Contribution

Conceptualization: SK
Methodology: AAK, AAB, HMZR
Formal analysis: AAK, MOQ
Writing and Drafting: FPJ, MR
Review and Editing: FPJ, SK, AAK, AAB, MR, MOQ, HMZR, MIA

All authors approved the final manuscript and take responsibility for the integrity of the work.

DOI: https://doi.org/10.54393/pjhs.v7i2.3577

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Obianeli C, Afifi K, Stanworth S, Churchill D. Iron Deficiency Anemia in Pregnancy: A Narrative Review from a Clinical Perspective. Diagnostics. 2024 Oct; 14(20): 2306. doi: 10.3390/diagnostics14202306.

[2] Jabeen M, Islam F, Azmaeen S. Injectable Ferric Carboxy Maltose Versus Oral Ferrous Fumerrate in Treatment of Iron Deficiency Anemia in Pregnancy-A Randomized Controlled Trial. Saudi J Med Pharm Sci. 2025; 11(8): 747-52. doi: 10.36348/sjmps.2025.v11i08.003.

[3] De Viñaspre-Hernández RR, Juárez-Vela R, Garcia-Erce JA, Nanwani-Nanwani K, González-Fernández S, Gea-Caballero V *et al.* Iron Deficiency Anemia During Pregnancy and Maternal and Neonatal Health Outcomes: A Prospective Study, Spain, 2021–2022. Heliyon. 2025 Jan; 11(1). doi: 10.1016/j.heliyon.2024.e41565.

[4] Mahar B, Shah T, Shaikh K, Shaikh SN, Uqaili AA, Memon KN *et al.* Uncovering the Hidden Health Burden: A Systematic Review and Meta-Analysis of Iron Deficiency Anemia among Adolescents, and Pregnant Women in Pakistan. Journal of Health, Population and Nutrition. 2024 Sep; 43(1): 149. doi: 10.1186/s41043-024-00643-y.

[5] Rahman H, Saikia T, Khalda E. Comparative Evaluation of Efficacy, Safety, Cost Effectiveness and Acceptability of Ferric Carboxymaltose Versus Iron Sucrose for Treatment of Iron Deficiency Anemia in Pregnancy: A Multicenter Open Label Randomized Controlled Trial. 2023.

[6] Sattar S, Sultana S, Shadab W, Afzal S, Salma UE, Mobeen A. Comparison of Safety and Efficacy of Ferric Carboxymaltose with Iron Sucrose for the Treatment of Iron Deficiency Anemia in Pregnancy. InMedical Forum Monthly. 2023: 34(2).

[7] Arzoo K, Jan S, Anwar R, Ali R, Masood A, Rehman MA. Efficacy of Intravenous Ferric Carboxymaltose Versus Iron Sucrose in the Treatment of Iron Deficiency Anemia of Pregnancy: Intravenous Ferric Carboxymaltose Versus Iron Sucrose for Iron Deficiency Anemia. Pakistan Journal of Health Sciences. 2025 Feb: 131-5. doi: 10.54393/pjhs.v6i2.2328.

[8] Papaniya TD, Parmar MT, Solanki HM. Comparison of Ferric Carboxymaltose and Iron Sucrose for Treatment of Iron Deficiency Anemia in Pregnancy at Tertiary Care Centre, Western India. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2023; 12(6): 1845. doi: 10.18203/2320-1770.ijrcog20231566.

[9] Jose A, Mahey R, Sharma JB, Bhatla N, Saxena R, Kalaivani M *et al.* Comparison of Ferric Carboxymaltose and Iron Sucrose Complex for Treatment of Iron Deficiency Anemia in Pregnancy-Randomized Controlled Trial. BioMed Central Pregnancy and Childbirth. 2019 Feb; 19(1): 54. doi: 10.1186/s12884-019-2200-3.

[10] Srimathi G, Revathy R, Bagepally BS, Joshi B. Clinical Effectiveness of Ferric Carboxymaltose (Iv) Versus Iron Sucrose (Iv) in Treatment of Iron Deficiency Anemia in Pregnancy: A Systematic Review and Meta-Analysis. Indian Journal of Medical Research. 2024 Jan; 159(1): 62-70. doi: 10.4103/ijmr.ijmr_246_23.

[11] Khan FH, Khalid AA, Alkwai HM, Alshammari RF, Alenazi F, Alshammari KF *et al.* The Effect of High Parity on the Occurrence of Anemia in Pregnant Women. Journal of the College of Physicians and Surgeons—Pakistan. 2023 Dec; 33(12): 1400-4.

[12] Alwan NA, Cade JE, McArdle HJ, Greenwood DC, Hayes HE, Simpson NA. Maternal Iron Status in Early Pregnancy and Birth Outcomes: Insights from the Baby's Vascular Health and Iron in Pregnancy study. British Journal of Nutrition. 2015 Jun; 113(12): 1985-92. doi: 10.1017/S0007114515001166.

[13] Gupte S, Mukhopadhyay A, Puri M, Gopinath PM, Wani R, Sharma JB *et al.* A Meta-Analysis of Ferric Carboxymaltose Versus Other Intravenous Iron Preparations for the Management of Iron Deficiency Anemia During Pregnancy. Revista Brasileira de Ginecologia e Obstetrícia. 2024 May; 46: e-rbgo21. doi: 10.61622/rbgo/2024AO21.

[14] Saleem K, Yaseen N, Saleem H, Noor L, Arif M, Nawaz MM. Comparison of Ferric Carboxymaltose Versus Iron Sucrose for Treatment of Iron Deficiency Anemia in Pregnant Women. Journal of The Society of Obstetricians and Gynaecologists of Pakistan. 2025 Jul; 15(3): 155-60. doi: 10.71104/jsogp.v15i3.896.

[15] Bharadwaj MK, Patrikar S, Singh Y. Comparative Analysis of Injection Ferric Carboxymaltose Vs Iron Sucrose for Treatment of Iron-Deficiency Anemia in Pregnancy: Systematic Review and Meta-Analysis. Journal of South Asian Federation of Obstetrics and Gynaecology. 2023 Oct; 15(5): 629-36. doi: 10.5005/jp-journals-10006-2311.

[16] Lusingu JP and Maisonet E. Ferric Carboxymaltose: A Potential Game Changer. The Lancet Global Health. 2024 Dec; 12(12): e1921-2. doi: 10.1016/S2214-109X(24)00455-8.

DOI: https://doi.org/10.54393/pjhs.v7i2.3577

[17] Singh S, Agarwal R, Sharma M, Singh N, Tyagi A. A Comparative Study between Efficacy of Ferric Carboxymaltose and Iron Sucrose Complex for Treatment of Iron Deficiency Anemia in Pregnancy. Journal of South Asian Federation of Obstetrics and Gynaecology. 2024 Jul; 16(4): 369-72. doi: 10.5005/jp-journals-10006-2448.

[18] Basha A, Ibrahim MI, Hamad A, Chandra P, Omar NE, Abdullah MA *et al.* Efficacy and Cost-Effectiveness of Intravenous Ferric Carboxymaltose Versus Iron Sucrose in Adult Patients with Iron Deficiency Anemia. PloS One. 2021 Aug; 16(8): e0255104. doi: 10.1371/journal.pone.0255104.

[19] Jin J, Ran Z, Noseda E, Roubert B, Marty M, Mezzacasa A *et al.* A Randomized, Controlled, Open Label Non-Inferiority Trial of Intravenous Ferric Carboxymaltose Versus Iron Sucrose in Patients with Iron Deficiency Anemia in China. Frontiers of Medicine. 2024 Feb; 18(1): 98-108. doi: 10.1007/s11684-023-1001-2.

[20] Xing Z, Mu S, Xue Q, Sun F, Hou G, Zhao Q. Economic Evaluation of Intravenous Iron Formulations for Patients with Iron Deficiency Anemia: A Systematic Review. Frontiers in Health Services. 2025 Nov; 5: 1690519. doi: 10.3389/frhs.2025.1690519.

DOI: https://doi.org/10.54393/pjhs.v7i2.3697

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Frequency and Factors of High-Degree Atrioventricular Block in Patients with Acute Anterior Wall Myocardial Infarction

Khadija Khan[1*], Mazhar Mahmood[1], Jebran Khan[2], Muhammad Farooq Azam Khan[1], Mashal Fatima[1] and Muhammad Waseem Hussain[2]

[1]Department of Cardiology, Rehman Medical Institute, Peshawar, Pakistan
[2]Department of Cardiology, Khyber Teaching Hospital, Peshawar, Pakistan

ARTICLE INFO

Keywords:
Myocardial Infarction, Atrioventricular Block, Anterior Wall Infarction, Heart Block, Electrocardiography, Cardiogenic Shock

How to Cite:
Khan, K., Mahmood, M., Khan, J., Khan, M. F. A., Fatima, M., & Hussain, M. W. (2026). Frequency and Factors of High-Degree Atrioventricular Block in Patients with Acute Anterior Wall Myocardial Infarction: High-Degree Atrioventricular Block with Acute Anterior Wall Myocardial Infarction. Pakistan Journal of Health Sciences, 7(2), 84-89. https://doi.org/10.54393/pjhs.v7i2.3697

***Corresponding Author:**
Khadija Khan
Department of Cardiology, Rehman Medical Institute, Peshawar, Pakistan
khajbangesh@gmail.com

Received Date: 15th December, 2025
Revised Date: 16th January, 2026
Acceptance Date: 3rd February, 2026
Published Date: 28th February, 2026

ABSTRACT

High-degree atrioventricular block (HAVB) is a serious complication of acute anterior wall myocardial infarction (AWMI), contributing significantly to early morbidity and mortality. Early identification of high-risk patients is essential for timely intervention. **Objectives:** To determine the frequency, clinical predictors, and in-hospital outcomes of HAVB among patients presenting with acute AWMI. **Methods:** This cross-sectional study included 78 acute AWMI patients presenting at Rahman Medical Institute from June 2024 to July 2025. Demographic data, clinical characteristics, and ECG findings were recorded. Patients were monitored continuously for the development of HAVB. Outcomes included cardiogenic shock, ICU admission, pacing requirements, and in-hospital mortality. Associations were analyzed using chi-square and logistic regression, with $p<0.05$ considered significant. **Results:** The mean age of patients was 56.8 ± 8.2 years, predominantly male 51(65.4%). The majority of patients were in the age group 51–60 years, 31(39.7%). HAVB occurred in 7(9%)patients. Older age (>60 years)and diabetes mellitus were significantly associated with HAVB ($p=0.03$) and ($p=0.04$), respectively. HAVB was strongly associated with cardiogenic shock ($p=0.01$), ICU admission ($p=0.002$), and need for temporary pacing ($p<0.001$). In-hospital mortality was significantly higher in the HAVB group ($p=0.04$). On multivariate analysis, HAVB independently predicted mortality (aOR 4.9, $p=0.03$). **Conclusions:** HAVB is an important predictor of adverse outcomes in AWMI, particularly among older and diabetic patients. Early monitoring and timely pacing interventions are crucial to improving survival.

INTRODUCTION

Acute myocardial infarction (AMI) is a major global health burden characterized by obstruction of coronary blood flow leading to myocardial damage [1], with anterior wall myocardial infarction (AWMI) being particularly severe due to involvement of the left anterior descending (LAD) artery and a larger myocardial territory [2]. Despite advancements in treatment that have reduced in-hospital AMI mortality from 26.7% in the 1960s to 7.2% in recent years, AMI still accounted for approximately 8.9 million deaths worldwide in 2019 [3]. A critical complication during AMI is atrioventricular (AV) block, a conduction abnormality ranging from first-degree delay to complete third-degree block, with high-degree AV block, such as Mobitz II and complete heart block, representing the most clinically significant forms [4]. Patients who develop high-grade AV block during AMI experience substantially higher mortality rates (15% vs. 4.9%) [5], underscoring the importance of early recognition. This complication is particularly concerning in AWMI, where extensive septal involvement increases vulnerability to conduction disturbances and

DOI: https://doi.org/10.54393/pjhs.v7i2.3697

contributes to adverse outcomes. The relationship between AWMI and AV block is clinically significant, primarily due to the involvement of the LAD artery, which supplies the septal branches responsible for maintaining normal cardiac conduction [6]. This complication is often accompanied by hemodynamic instability, heart failure, and arrhythmias, frequently requiring pacing interventions [7]. Early recognition is therefore essential, as timely management not only improves clinical outcomes but may also reverse conduction abnormalities in some cases following successful revascularization [8, 9].

Despite the recognized association between AWMI and HAVB, there remains a paucity of contemporary, region-specific data from Pakistan regarding its frequency, factors, and in-hospital outcomes. Most available evidence is derived from Western populations, which may not be fully generalizable due to differences in patient demographics, comorbidities, and healthcare infrastructure. Therefore, this study aims to determine the frequency and factors of HAVB among patients presenting with acute AWMI and to identify its clinical predictors and associated in-hospital outcomes.

METHODS

This cross-sectional study was conducted at the Department of Cardiology, Rehman Medical Institute from June 2024 to July 2025 on 78 patients, calculated using an Open epi software, keeping confidence level of 95%, anticipated prevalence of HAVB in AWMI as 5.34% [10] and 5% margin of error, using formula the following formula $n = DEFF \times N \times p(1-p) / d2/Z^2_{1-\alpha/2} \times (N-1) + p(1-p)$. The population was recruited through consecutive sampling. Data collection began after getting approval from the institutional review board under ref: RMI-REC/Ethical Approvals/CPSP Synopsis/57. Either gender patients, aged 40–70 years, presenting within 48 hours of symptom onset with acute anterior wall ST-segment elevation myocardial infarction (AW-STEMI) were included. AW-STEMI was defined as ST-segment elevation ≥0.1 mV in at least two contiguous anterior leads (V1–V6) on admission electrocardiography. High-degree atrioventricular (AV) block comprised second-degree block (2:1 conduction or Wenckebach phenomenon with narrow QRS) and third-degree block (complete AV dissociation with atrial rate exceeding ventricular rate). Patients with electrolyte abnormalities involving potassium, calcium, or magnesium were excluded. Eligible patients presenting to the cardiac emergency department were enrolled after written informed consent. Demographic characteristics, clinical variables, cardiovascular risk factors, and comorbidities were recorded using a structured proforma. Patients received primary percutaneous coronary intervention or thrombolytic therapy when indicated, followed by standard guideline-based management. All participants were monitored throughout hospitalization until discharge, with outcomes prospectively documented.

SPSS version 27.0 was used for analysis. Quantitative variables such as age, height, weight, BMI, time with symptoms, left ventricular ejection fraction, and hospital stay were checked for normality using Shapiro-Wilk tests and were expressed as mean ± SD. Qualitative variables like gender, residence, DM, Hypertension, Smoking status, Family history of cardiovascular diseases, and other comorbidities were expressed in frequency and percentage format. Post-stratification Fisher's Exact tests were used, with a significance level set at 0.05. Logistic regression analysis was conducted to predict risk factors for HAVB.

RESULTS

This study included 78 patients with acute AWMI, with a mean age of 56.8 ± 8.2 years. The majority of patients were aged 51–60 years, 31 (39.7%), followed by 61–70 years, 25 (32.1%), and 40–50 years, 22 (28.2%), predominantly male, 51 (65.4%). The mean body mass index (BMI) was 26.4 ± 4.1 kg/m^2, with 32 (41.0%) as overweight, and 18 (23.1%) as obese. Regarding symptom duration before presentation, 34 (43.6%) patients presented within 6 hours, 22 (28.2%) within 6–12 hours, 15 (19.2%) within 13–24 hours, and 7 (9.0%) within 25–48 hours. Two-thirds of the study patients resided in urban areas 52 (66.7%), while 26 (33.3%) were from rural areas. Additionally, 28 (35.9%) patients were active smokers, and 19 (24.4%) reported a family history of cardiovascular disease (Table 1).

Table 1: Demographic, Anthropometric, and Clinical Characteristics of Patients Presenting with AWMI (n=78)

Variables	n (%), Mean ± SD
Age	
Years	56.8 ± 8.2
Age Groups	
40-50 Years	22 (28.2%)
51-60 Years	31 (39.7%)
61-70 Years	25 (32.1%)
Gender	
Male	51 (65.4%)
Female	27 (34.6%)
BMI	
(kg/m^2)	26.4 ± 4.1
Normal (18.5-24.9)	28 (35.9%)
Overweight (25.0-29.9)	32 (41.0%)
Obese (≥30.0)	18 (23.1%)
Duration of Symptoms	
<6 Hours	34 (43.6%)
6-12 Hours	22 (28.2%)
13-24 Hours	15 (19.2%)
25-48 Hours	7 (9.0%)

DOI: https://doi.org/10.54393/pjhs.v7i2.3697

Residence	
Urban	52 (66.7%)
Rural	26 (33.3%)
Others	
Smoking Status	28 (35.9%)
Family History of CVD	19 (24.4%)

Regarding the comorbid status of these acute AWMI patients, the majority 53.9% was presented with dyslipidemia, followed by hypertension (48.7%) and DM (39.7%). Previous myocardial infarction was seen in 10.3% of cases (Figure 1).

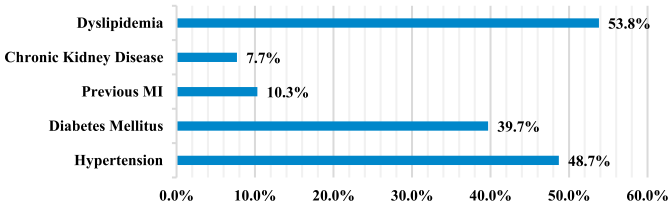

Figure 1: Comorbidity Status

Most of the patients 35.9% was presented with one comorbidity, closely followed by two-comorbidities 30.8%, and almost 17.9% of the patients had three or more related comorbidities. A small proportion of patients 15.4% has comorbid free status (Figure 2).

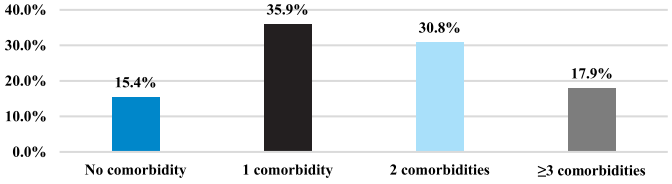

Figure 2: Patients Presented with Several Comorbidities

The frequency of HAVB was 7 (9.0%), among which 4 (5.1%) of patients had Second-degree AV block, including Type I (Wenckebach) in 2 (2.6%) and Type II (Mobitz II) in 2 (2.6%) patients. Third-degree AV block occurred in 3 (3.9%) patients. The onset of HAVB was most frequent within 6 hours of presentation in 4 (5.1%) patients, followed by 6–24 hours in 2 (2.6%) and after 24 hours in 1 (1.3%) patient. The mean time to HAVB resolution was 3.2 ± 1.8 days. Resolution occurred before discharge in 5 (6.4%) patients, while 2 (2.6%) patients had persistent HAVB at discharge (Table 2).

Table 2: Frequency, Types, Timing of Onset, and Resolution of HAVB among AWMI Patients (n=78)

Variables	n (%)	95% CI
HAVB		
Overall	7 (9.0%)	2.7-15.3
Type of HAVB		
Second-degree AV block	4 (5.1%)	0.2-10.0
Type I (Wenckebach)	2 (2.6%)	0.0-6.1
Type II (Mobitz II)	2 (2.6%)	0.0-6.1
Third-degree AV block	3 (3.9%)	0.0-8.2
Timing of HAVB Onset		
Within 6 hours	4 (5.1%)	0.2-10.0
6-24 hours	2 (2.6%)	0.0-6.1
>24 hours	1 (1.3%)	0.0-3.8
HAVB Resolution		
Time To Resolution (Days)	3.2 ± 1.8	–
Resolved Before Discharge	5 (6.4%)	0.8-12.0
Persistent At Discharge	2 (2.6%)	0.0-6.1

Patients with HAVB were older and had a higher prevalence of diabetes mellitus than those without HAVB, while sex, BMI, hypertension, family history, and symptom duration were comparable. Left ventricular ejection fraction showed a nonsignificant trend toward lower values in the HAVB group. Reperfusion strategy, procedural features, treatment timelines, and post-procedural TIMI flow did not differ significantly between groups. In contrast, HAVB was associated with significantly worse clinical outcomes, including prolonged hospitalization, higher in-hospital mortality, increased cardiogenic shock, greater need for mechanical ventilation and ICU care, longer ICU stays, and a higher requirement for temporary and permanent pacing (all $p<0.05$) (Table 3).

Table 3: Clinical Features, Management, and in-Hospital Outcomes Stratified by HAVB

Variables	HAVB Present (n= 7), Mean ± SD, n (%)	HAVB Absent (n= 71), Mean ± SD, n (%)	p-value
Age (Years)	62.1 ± 6.8	56.2 ± 8.1	0.042*
Male	4 (57.1%)	47 (66.2%)	0.619
Female	3 (42.9%)	24 (33.8%)	–
BMI (kg/m^2)	27.8 ± 3.9	26.2 ± 4.1	0.298
Hypertension	5 (71.4%)	33 (46.5%)	0.168
Diabetes Mellitus	5 (71.4%)	26 (36.6%)	0.046*
Family History of CVD	3 (42.9%)	16 (22.5%)	0.194
Symptom Duration (hours)	8.0 ± 5.7	7.0 ± 4.6	0.421
Left Ventricle Ejection Fraction (%)	38.2 ± 8.5	43.1 ± 9.2	0.165
Reperfusion Strategy (Primary PCI)	6 (85.7%)	54 (76.1%)	0.548
Reperfusion Strategy (Thrombolysis)	1 (14.3%)	17 (23.9%)	–
Door-to-Balloon Time (minutes)	82.1 ± 18.7	78.1 ± 22.7	0.632
Door-to-Needle Time (minutes)	35.0	32.2 ± 9.1	0.745
TIMI Flow Post-Procedure (TIMI 0-1)	2 (28.6%)	6 (8.5%)	0.068
TIMI Flow Post-Procedure (TIMI 2)	2 (28.6%)	13 (18.3%)	–
TIMI Flow Post-Procedure (TIMI 3)	3 (42.8%)	52 (73.2%)	–
Multivessel Disease	4 (57.1%)	30 (42.3%)	0.409
Culprit Vessel - LAD	7 (100.0%)	71 (100.0%)	–
Stent Deployment	6 (100.0%)	52 (96.3%)	0.652
Length of Hospital Stay (days)	6.7 ± 2.4	4.2 ± 1.8	0.001*
In-Hospital Mortality	2 (28.6%)	3 (4.2%)	0.014*
Cardiogenic Shock	3 (42.9%)	9 (12.7%)	0.025*
Re-Infarction	1 (14.3%)	2 (2.8%)	0.158
Mechanical Ventilation	3 (42.9%)	5 (7.0%)	0.004*
ICU Admission	6 (85.7%)	18 (25.4%)	0.001*

DOI: https://doi.org/10.54393/pjhs.v7i2.3697

ICU Stay (days)	4.5 ± 2.1	2.4 ± 1.7	0.018*
Temporary Pacing	4 (57.1%)	0 (0.0%)	<0.001*
Permanent Pacemaker	2 (28.6%)	0 (0.0%)	<0.001*

Fisher's Exact Test was used to calculate the p-value. * p<0.05 is significant

On logistic regression analysis, age >60 years and DM were independent predictors of high-degree AV block (HAVB). Other variables, including female gender, BMI >30 kg/m^2, hypertension, smoking, family history of cardiovascular disease, symptom duration >12 hours, reduced ejection fraction, multivessel disease, and thrombolysis versus PCI, were not significantly associated with HAVB after adjustment (Table 4).

Table 4: Logistic Regression Analysis for Predictors of High-Degree AV Block (HAVB)

Variables	Univariate Analysis OR (95% CI)	p-value	Multivariate Analysis OR (95% CI)	p-value
Age >60 Years	5.2 (1.4–19.8)	0.015*	4.8 (1.2–19.4)	0.027*
Female Gender	1.4 (0.3–6.2)	0.619	1.2 (0.2–6.8)	0.812
BMI >30 kg/m^2	1.2 (0.2–6.4)	0.826	–	–
Diabetes Mellitus	4.3 (1.0–18.6)	0.046*	3.9 (1.1–14.2)	0.038*
Hypertension	2.9 (0.6–14.2)	0.183	2.1 (0.4–11.8)	0.364
Smoking	0.7 (0.1–3.6)	0.654	–	–
Family History of CVD	2.6 (0.6–11.2)	0.208	1.8 (0.3–9.4)	0.521
Symptom Duration >12 h	1.8 (0.4–8.1)	0.432	–	–
Ef <40%	2.3 (0.5–10.4)	0.276	1.9 (0.4–9.2)	0.421
Multivessel Disease	1.8 (0.4–8.1)	0.432	–	–
Thrombolysis vs PCI	0.5 (0.1–4.2)	0.548	–	–

Note: Variables showing p < 0.20 in univariate analysis and those with established clinical relevance were entered into multivariate regression. The final model was derived using backward elimination. *p < 0.05 statistically significant

Multivariate logistic regression identified age, presence of high-degree AV block, cardiogenic shock, and peak troponin levels as independent predictors of in-hospital mortality. Other variables, including DM, EF <35%, female gender, multivessel disease, and TIMI flow <3, were not significantly associated with mortality after adjustment (Table 5).

Table 5: Logistic Regression Analysis for Predicting in-Hospital Mortality

Variables	Univariate Analysis OR (95% CI)	p-value	Multivariate Analysis OR (95% CI)	p-value
Age (Years)	1.15 (1.04–1.28)	0.008*	1.12 (1.02–1.23)	0.019*
HAVB Present	9.07 (1.37–60.1)	0.022*	9.3 (1.4–62.1)	0.021*
Cardiogenic Shock	10.7 (1.78–64.2)	0.010*	12.5 (2.1–74.8)	0.006*
Diabetes Mellitus	2.41 (0.40–14.5)	0.340	–	–
EF <35%	4.58 (0.76–27.6)	0.097	3.2 (0.5–20.4)	0.221
Female Gender	3.06 (0.51–18.4)	0.227	–	–
Multivessel Disease	2.03 (0.34–12.2)	0.441	–	–
TIMI Flow <3	3.98 (0.66–24.0)	0.133	–	–
Peak Troponin	1.03 (1.01–1.06)	0.012*	1.02 (1.00–1.05)	0.048*

*Statistically significant at p<0.05

DISCUSSION

HAVB was identified as a clinically important complication associated with AWMI, adverse hemodynamic status, increased healthcare resource utilization, and significantly higher in-hospital mortality. In the present study, the incidence of HAVB was 9%, placing it in the upper range compared with reports from larger registries, where incidence rates among patients with acute myocardial infarction range from 1.5% to 8.6% [7, 11]. This higher incidence may be attributed to the study's greater focus on anterior infarctions, delayed presentation, and a higher prevalence of comorbid conditions, particularly DM. Consistent with prior studies, complete heart block accounted for a substantial proportion of HAVB cases and has been reported in up to 15.8% of anterior STEMI, where it is associated with worse outcomes compared with non-anterior infarctions [12]. In our study, high-degree AV block, including Mobitz II and complete heart block, was associated with early presentation, hemodynamic instability, and increased need for supportive interventions. Most events occurred within the first six hours, supporting the concept that AV block in anterior myocardial infarction reflects extensive septal ischemia involving the cardiac conduction system [13]. In our study, age >60 years and DM emerged as independent predictors of HAVB, consistent with prior evidence identifying advanced age as a major risk factor [7]. Unlike previous studies that have linked male sex and right coronary artery involvement with HAVB, all patients in our study had left anterior descending artery occlusion due to the anterior infarct distribution, likely explaining the lack of association with RCA involvement. The association with diabetes remains variable across studies; however, our findings suggest increased susceptibility of the diabetic myocardium to ischemia-related conduction disturbances [14]. Patients with HAVB experienced significantly worse clinical outcomes, including prolonged hospitalization, higher rates of cardiogenic shock, increased need for mechanical ventilation, and greater dependence on temporary and permanent pacing, in line with earlier reports [5, 15]. In-hospital mortality was markedly higher in the HAVB group and comparable to rates reported in other populations (15–28.6%) [7, 16]. Although literature indicates that HAVB loses independent prognostic significance after adjustment for confounders [7, 16], multivariate analysis identified HAVB as an independent predictor of in-hospital mortality, alongside age, cardiogenic shock, and peak troponin levels. This finding likely reflects the predominance of extensive LAD-territory infarction in our

DOI: https://doi.org/10.54393/pjhs.v7i2.3697

cohort, underscoring the prognostic importance of HAVB in anterior myocardial infarction. Even though the vast majority of HAVB patients in our research received timely PCI, post-operative TIMI-3 flow was less often observed in this group of patients, indicating a higher level of myocardial damage or microvascular blockage. This is also in line with other studies, which have shown that HAVB is linked with poor post-procedural perfusion and worse TIMI flow grades [17]. The increased incidence of pacemaker implantation in our cohort is also in agreement with the global statistics, where HAVB occurring in hospitalization would be an indicator of decreased chances of spontaneous recovery and the necessity of permanent pacing [18]. Despite the pathophysiological differences between TAVI-related HAVB and ischemic HAVB, there are some similarities between them in terms of hemodynamic compromise, the necessity of pacing, and a long hospital stay. The relevance of conduction disturbances as indicators of cardiac instability in various patient settings is highlighted by these similarities [19, 20].

The limitation of the study is that it is a single-center, retrospective study and not a large-scale one; therefore, its findings might be limited in their generalizability. Emphasis on a particular group of patients (AWMI with LAD involvement) precludes the presence of other types of infarcts and can potentially cause selection bias. Long-term outcomes and the finer timing of the conduction recovery data were also not available. These predictors and outcomes should be confirmed by prospective, multicenter, larger, and more diverse cohort studies. The study ought to examine the prognosis of survivors of HAVB in the long run and the best time to install permanent pacemakers. Additional investigation of the pathophysiological connection of diabetes, micro-vascular dysfunction, and conduction impairments is also justified.

CONCLUSIONS

This study illustrates that HAVB is an important complication of AWMI and is associated with cardiogenic shock, increased intensive care requirement, long hospitalization, and increased in-hospital mortality. HAVB was significantly predicted by older age and DM. Most of the cases occurred early during the first six hours, which underscores the importance of early diagnosis and constant supervision.

Authors' Contribution

Conceptualization: MM
Methodology: MM, MFAK
Formal analysis: MM, MF
Writing and Drafting: KK, MM, JK, MWH
Review and Editing: KK, MM, JK, MFAK, MF, MWH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Anderson JL and Morrow DA. Acute Myocardial Infarction. New England Journal of Medicine. 2017 May; 376(21): 2053-64. doi: 10.1056/NEJMra1606915.

[2] Bansal K, Gore M, Afzal M, Shams P, Nalabothu P. Anterior Myocardial Infarction. In Stat Pearls [Internet]. 2024 Feb.

[3] Ferrero L. In-Hospital Mortality of Acute Myocardial Infarction. In Epidemic Preparedness and Control. 2023 Nov. doi: 10.5772/intechopen.1001453.

[4] Khan MA, Sammar K, Naz R, Tauqeer S, Shafiq M, Naz S. Frequency of Complete Heart Block in Patients Presenting with Acute Anterior Wall Myocardial Infarction. Journal of Ayub Medical College Abbottabad. 2024 Jun; 36(2): 310-5. doi: 10.55519/JAMC-02-13024.

[5] Olivito N, Foster Witassek F, Rickli H, Roffi M, Radovanovic D, Pedrazzini G. Impact of High-Grade Atrioventricular Block on Outcomes in Patients with Acute Myocardial Infarction. European Heart Journal: Acute Cardiovascular Care. 2025 Sep: zuaf123. doi: 10.1093/ehjacc/zuaf123.

[6] Yadav S, Yadav H, Dwivedi SK, Parashar NK, Chandra S, Chaudhary G *et al.* The Time to Reversal of Complete Atrioventricular Block and Its Predictors in Acute ST-Segment Elevation Myocardial Infarction. Journal of Electrocardiology. 2020 Nov; 63: 129-33. doi: 10.1016/j.jelectrocard.2020.10.008.

[7] Velásquez-Rodríguez J, Vicent L, Díez-Delhoyo F, Valero Masa MJ, Bruña V, Sousa-Casasnovas I *et al.* Prognostic Implications of High-Degree Atrio-Ventricular Block in Patients with Acute Myocardial Infarction in the Contemporary Era. Journal of Clinical Medicine. 2023 Jul; 12(14): 4834. doi: 10.3390/jcm12144834.

[8] Malekrah A, Fattahian A, Majidifard I, Resident C, Asgary N, Kazemisaeed A *et al.* Hibernation of the

DOI: https://doi.org/10.54393/pjhs.v7i2.3697

Conduction System and Atrioventricular Block Reversibility Following Revascularization in Patients without Acute Coronary Syndrome. The Journal of Innovations in Cardiac Rhythm Management. 2023 Dec; 14(12): 5697. doi: 10.19102/icrm.2023.14125.

[9] Shah MA, Asim M, Mehmood S, Iqbal J, Tayyeb M. Prevalence of Left Ventricular Clot and Its Associated Factors in Anterior Wall Myocardial Infarction Patient Presenting to Mardan Medical Complex, Mardan. Insights-Journal of Health and Rehabilitation. 2025 Jul; 3(4 (Health and Rehabilitation)): 302-309. doi: 10.71000/htjxn683.

[10] Ullah F, Din IU, Adil I, Ali U, Khan MA, Abbas F. High Degree Av Block in Patients Presenting with Acute Myocardial Infarction. Pakistan Heart Journal. 2019; 52(3).

[11] Babar MZ, Majid A, Chaudhary AW, Baig MA. Atrio-Ventricular Block: Incidence of High Degree Atrio-Ventricular Block Complicating Acute Myocardial Infarction and Its Effects on in-Hospital Mortality. The Professional Medical Journal. 2016; 23(08): 1017-21. doi: 10.17957/TPMJ/16.3518.

[12] Margolis G, Levi Y, Abu Fanne R, Saada M, Kobo O, Kazatsker M *et al.* In-Hospital Outcomes of Anterior Versus Non-Anterior St Elevation Myocardial Infarction Complicated with Complete Atrioventricular Block. Europace. 2024 May; 26(Supplement_1): euae102-295. doi: 10.1093/europace/euae102.295.

[13] Kalsi J, Suffredini J, Pickett JK, Alam M, Kayani W, Jia X. Ischemic Evaluation and Revascularization in Patients Presenting with Advanced Atrioventricular Block Without Concomitant Acute Myocardial Infarction. Texas Heart Institute Journal. 2024 Apr; 51(1). doi: 10.14503/THIJ-23-8257.

[14] Kosmidou I, Redfors B, Dordi R, Dizon JM, McAndrew T, Mehran R *et al*. Incidence, Predictors, and Outcomes of High-Grade Atrioventricular Block in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention (from the HORIZONS-AMI Trial). The American Journal of Cardiology. 2017 May; 119(9): 1295-301. doi: 10.1016/j.amjcard.2017.01.019.

[15] Weferling M, Lan Cheong Wah S, Fischer-Rasokat U, Hain A, Renker M, Charitos EI *et al.* Incidence and Predictors of Hemodynamic Compromise Due to High-Grade AV Block After TAVI. Frontiers in Cardiovascular Medicine. 2023 Jun; 10: 1161871. doi: 10.3389/fcvm.2023.1161871.

[16] Kawamura Y, Yokoyama H, Kitayama K, Miura N, Hamadate M, Nagawa D *et al*. Clinical Impact of Complete Atrioventricular Block in Patients with ST-Segment Elevation Myocardial Infarction. Clinical Cardiology. 2021 Jan; 44(1): 91-9. doi: 10.1002/clc.23510.

[17] Ramesh RS, Velappan P, Thampi L. Influence of PCI Timing on Pre-and Post-Procedural TIMI Flow and No-Reflow Rates in Pharmacoinvasive PCI for Anterior STEMI Patients. European Journal of Cardiovascular Medicine. 2025 Nov; 15: 8-13.

[18] Lu R, Glaser N, Sartipy U, Dismorr M. Long-Term Outcomes Associated with Permanent Pacemaker Implantation in Low-Risk Surgical Aortic Valve Replacement. Journal of the American College of Cardiology: Advances. 2024 Aug; 3(8): 101110. doi: 10.1016/j.jacadv.2024.101110.

[19] Elhadi M, Alabdaljabar MS, Lane C, Deshmukh AJ, Gulati R, Cha YM *et al.* Incidence and Predictors of High-Grade AV Block in Patients with Initially Unchanged Electrocardiogram After TAVR. Journal of the Society for Cardiovascular Angiography and Interventions. 2025 May: 103666. doi: 10.1016/j.jscai.2025.103666.

[20] Özilhan MO, Açıkgöz SK, Karaaslan ÖÇ, Eriş E, Gökalp G, Selçuk H *et al*. Predictors of Complete Atrioventricular Block Following Transcatheter Aortic Valve Replacement. Journal of Updates in Cardiovascular Medicine. 2023 Sep; 11(3). doi: 10.32596/ejcm.galenos.2023.2023-3-10.

DOI: https://doi.org/10.54393/pjhs.v7i2.3626

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Genotype-Phenotype Correlation in Idiopathic Cerebral Palsy

Madiha Sarwat[1*], Aisha Farid[1], Shazia Maqbool[1], Fatima Rahman[1], Stephanie Efthimyou[2] and Henry Houlden[2]

[1]Department of Developmental and Behavioral Pediatrics, University of Child Health Sciences, Children's Hospital, Lahore, Pakistan
[2]Department of Neuromuscular Disorders, University College London, Queen Square Institute of Neurology, London, United Kingdom

ARTICLE INFO

Keywords:
Cerebral Palsy, Exome Sequencing, Consanguinity, Phenotype, Genetics

How to Cite:
Sarwat, M., Farid, A., Maqbool, S., Rahman, F., Efthimyou, S., & Houlden, H. (2026). Genotype-Phenotype Correlation in Idiopathic Cerebral Palsy: Genotype–Phenotype: Idiopathic Cerebral Palsy. Pakistan Journal of Health Sciences, 7(2), 90-95. https://doi.org/10.54393/pjhs.v7i2.3626

***Corresponding Author:**
Madiha Sarwat
Department of Developmental Behavioral Pediatrics, University of Child Health Sciences, Children's Hospital, Lahore, Pakistan
msarwat2013@gmail.com

Received Date: 20th November, 2025
Revised Date: 12th January, 2026
Acceptance Date: 27th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Genetic etiology is an important cause of idiopathic cerebral palsy, especially in consanguineous populations. **Objectives:** To determine the genotype-phenotype correlation in idiopathic cerebral palsy at a tertiary care hospital in Lahore, Pakistan. **Methods:** This retrospective descriptive cross-sectional study was conducted in the Department of Developmental and Behavioral Pediatrics, University of Child Health Sciences, Lahore. The data on cerebral palsy children with Whole Exome Sequencing was collected from January 2022 to January 2025. The study duration for all patients with reports available from March to August 2025 was included using nonprobability consecutive sampling. **Results:** Eighty-two patients were included after receiving their whole exome sequencing reports, and 35 genes were identified in 58 patients, showing a diagnostic yield of WES as 70.2%. There were 52 (63.4%) males. The average age was 8.3 ± 4.1 years (SD). The phenotype of positive patients showed spastic cerebral palsy to be the most common (79%), with a predominant quadriplegic subtype (55%). Seventeen genes (SYNE 1, PYCR2, PTS, SEPSECS, MOCS1, SERAC1, DEGS1, ECHS1, HPDL, ALS2, BLM, ITPA, PARD3, RIF1, CHD2, RAB3GAP1, ADAD2, WDR62) were associated with quadriplegic type, five (TBC1D14, CENPJ, ADAMDEC1, AMPD2 and TKTL1) with spastic diplegic, five (BICRA, ADGRG, CENPF, MAGEL2, TXNDC11) with hemiplegic, five (MIX23, EXOSC8, METTL5, GNG7, EZH1) with dyskinetic and two (SLC25A12, LPIN1) with mixed type. **Conclusions:** Epilepsy was present in 69%, feeding issues in 84%, drooling in 74%, recurrent chest infections in 60%, sleep issues in 60%, and constipation in 79%. GMFCS level V and MACS level V were the most common. Genotype–phenotype correlations in idiopathic cerebral palsy will help in comorbidity management and prognosis.

INTRODUCTION

Cerebral palsy (CP) is characterized by permanent, non-progressive problems with movement, posture, and motor function of variable extent due to an insult in growing brain. It may be associated with intellectual disability, feeding difficulties, constipation, drooling, epilepsy, sleep issues, and visual and hearing impairment [1]. Cerebral palsy has been divided into multiple types, such as spastic, dyskinetic, and mixed [2]. It is a leading cause of childhood disability worldwide. The prevalence of cerebral palsy is 3.4 per 1000 live births in low- and middle-income countries, while it is 1.6 per 1000 live births in high-income countries [3]. The prevalence has decreased from 2.2-2.5 to 1.6 per thousand in developed countries (high-income countries). A small study in Swabi showed the prevalence of cerebral palsy in Pakistan to be around 2.2/1000. However, the exact prevalence is unknown due to the lack of a national registry [4]. Risk factors of cerebral palsy include prematurity, hypoxic ischemic encephalopathy, maternal infections, kernicterus, neonatal brain infections, and others [5]. However, no risk factors can be defined in many children with cerebral palsy, and they fall under the umbrella of CP mimics. It is proposed that such children need to be investigated for inborn errors of metabolism and genetic disorders so that they can benefit from specific disease-modifying therapeutic options [6]. The existing literature on genetic studies showed that as many as one third cases

DOI: https://doi.org/10.54393/pjhs.v7i2.3626

of cerebral palsy are thought to have an underlying genetic cause [7]. A study carried out by May HJ at New York Presbyterian Hospital included 20 patients with idiopathic cerebral palsy, who showed that 11 (55%) had genetic mutations on whole exome sequencing. The incidence of epilepsy and severity of motor impairment were found to be higher in children with cerebral palsy with underlying genetic mutations [8]. In another multicenter study conducted in China by Wang et.al., including 1578 children with cerebral palsy, researchers utilized whole exome sequencing to successfully identify genetic causes in 24.5% (n=387) of the participants. A total of 219 genes were isolated [9]. Another US study by Chopra et.al. with 50 patients shows that a high number of patients diagnosed with CP possess single-gene mutations on whole exome sequencing, with 13 children (26%) having a positive result [10]. Consanguinity is one of the major factors in gene-related disorders, including disabilities like developmental delay, cerebral palsy, spasticity, and epilepsy [11].

Pakistan is a highly consanguineous population, and there is limited data on genetics with respect to cerebral palsy mimics and genetic etiology. As per the researcher's knowledge, very few studies have been done in Pakistan to identify the genetic makeup and severity of symptoms in cerebral palsy. This study aims to fill the gap in knowledge of genetic heterogeneity in cerebral palsy. To determine the genotype-phenotype correlation in idiopathic cerebral palsy at a tertiary care hospital in Lahore, Pakistan.

METHODS

The Retrospective descriptive cross-sectional study was carried out on children with cerebral palsy in the Department of Developmental and Behavioral Pediatrics, University of Child Health Sciences and Children's Hospital, Lahore, whose samples for genetic analysis by whole exome sequencing were sent to UCL, London. The data were collected from January 2022 to January 2025. Eighty-two children had reports available during the study period from March 2025 to August 2025. Certificate of ethical approval (No.1076/CH-UCHS) for this research was taken from the IRB Committee of the University of Child Health Sciences, Children's Hospital, Lahore. Children were enrolled by non-probability consecutive sampling. Informed written consent was taken from parents, and confidentiality was ensured. Children with cerebral palsy having positive genetic reports of both genders born to consanguineous parents with a family history of developmental delay or miscarriage/ intrauterine death of a sibling were included. Children with identifiable known syndromes were excluded. Data was entered using a well-designed questionnaire. Demographic information was collected, including age and gender. A developmental behavioral pediatrician examined and classified each patient with cerebral palsy according to the Rosenbaum criteria. The phenotype of children with positive reports was studied in detail. ICD-11 classification of cerebral palsy was used to classify children into spastic (its subtypes), dyskinetic, and mixed forms of cerebral palsy based on clinical examination. Comorbidities like the presence of epilepsy, feeding difficulty, drooling, sleep issues, constipation, and behaviour issues were also documented. Severity of participants' disability was assessed by GMFCS (Gross Motor Function Classification System), MACS (Manual Ability Classification System), and BMFM (Bimanual Fine Motor Function) scale from level 1 to level V. Data was entered & analyzed by using SPSS version 25.0. Quantitative variable (age) was calculated as Mean ± SD. The diagnostic yield of whole-exome sequencing was calculated as a percentage of children with positive genetic reports. Qualitative variables like gender, type of cerebral palsy, presence of comorbidities, and levels of GMFCS, MACS, and BMFM were calculated as frequency and percentage. The association of comorbidities was compared between different types of cerebral palsy by using the chi-square test, and a p-value≤0.05 was taken as significant. Genomic DNA was extracted from peripheral blood samples according to standard procedures of phenol-chloroform extraction and enriched according to the Agilent Sure Select Target Enrichment Kit V7. Libraries were sequenced with the HiSeq or MiSeq sequencer (Illumina) with 50x coverage. Quality assessment of the sequence reads was performed by generating QC statistics with Fast QC. Priority was given to rare variants (<0.01% in public databases, including 1000 Genomes project, NHLBI Exome Variant Server, Complete Genomics 69, and Exome Aggregation Consortium) that were fitting dominant or a de novo model or variants in genes previously linked to neurological disorders. Variants of interest were confirmed with Sanger sequencing. For Sanger sequencing validation, genomic DNA was amplified by PCR using gene-specific primers designed with Primer3 software. Primer sequences, annealing temperatures, and expected amplicon sizes were carefully selected. PCR amplification was performed using FastStart PCR Master mix (Roche), and PCR products were purified using Exo-SAP (Exonuclease I and Shrimp Alkaline Phosphatase). Sequencing PCR was performed bi-directionally using an ABI 3730xl DNA Analyzer, and chromatograms were analysed using Geneious. The significance of the identified variant was classified according to American College of Medical Genetics and Genomics (ACMG) criteria using the Varsome tool [10].

DOI: https://doi.org/10.54393/pjhs.v7i2.3626

RESULTS

Positive gene mutation was seen in 58 out of 82 children with cerebral palsy, showing 70% diagnostic yield of the whole exome sequencing. Among 58 children with positive gene reports, 35 unique genes were identified. Mean age of presentation for children with positive reports was 6.9 years ± 4.2 SD. The most common age group of presentation was 10 years and above (34.5%), and 69%(n=40) of children were male (Table 1).

Table 1: Age Groups of Children With Positive Genetic Reports

Age Groups	Spastic Quadriplegic	Spastic Diplegic	Spastic Hemiplegic	Dyskinetic	Mixed	Total
0-1 Year 11 Months	4	1	0	0	1	6 (10.3%)
2 -4 Years 11 Months	9	0	2	2	1	13 (22.4%)
5 Years-9 Years 11 Months	11	3	0	0	2	19 (31.8%)
10 Years and Above	8	4	6	6	0	20 (34.5%)

The most common type of CP (phenotype) among the children with positive genetic etiology is spastic CP (79%, n=46), with quadriplegic cerebral palsy (55%, n=32) being the predominant subtype. Seventeen genes (SYNE 1, PYCR2, PTS, SEPSECS, MOCS1, SERAC1, DEGS1, ECHS1, HPDL, ALS2, BLM, ITPA, PARD3, RIF1, CHD2, RAB3GAP1, ADAD2, WDR62) were associated with this phenotype. Five genes (TBC1D14, CENPJ, ADAMDEC1, AMPD2, and TKTL1) were associated with spastic diplegic cerebral palsy, five (BICRA, ADGRG, CENPF, MAGEL2, TXNDC11) with spastic hemiplegic type, five (MIX23, EXOSC8, METTL5, GNG7, EZH1) with dyskinetic, and two (SLC25A12, LPIN1) with mixed form of cerebral palsy (Table 2).

Table 2: Genes and Their Type of CP (Phenotype)

Spastic Quadriplegic	Spastic Diplegic	Spastic Hemiplegic	Dyskinetic	Mixed
SYNE 1, PYCR2, PTS, SEPSECS, MOCS1, SERAC1, DEGS1, ECHS1, HPDL, ALS2, BLM, ITPA, PARD3, RIF1, CHD2, RAB3GAP1, ADAD2, WDR62)	TBC1D14, CENPJ, ADAMDEC1, AMPD2 and TKTL1	BICRA, ADGRG, CENPF, MAGEL2, TXNDC11	MIX23, EXOSC8, METTL5, GNG7, EZH1	SLC25A12, LPIN1

Novel genes (ADGRG, PTS, METTL5, and SLC25A12) had been reconfirmed by Sanger sequencing. All genes had an autosomal recessive pattern of inheritance except MAGEL2 and CHD2, which were autosomal dominant. The EZH1 gene had both dominant and recessive inheritance (Figure 1).

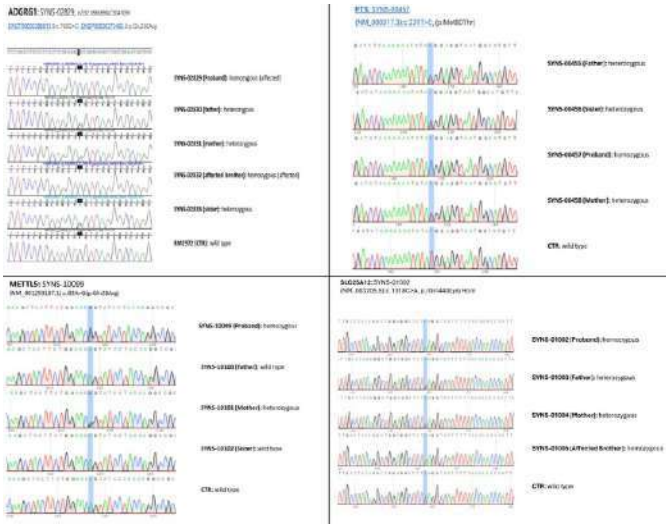

Figure 1: Sanger Sequence Images of Genes PTS, ADGRG, METTL5, and SLC25A12

Overall, epilepsy was present in 69%(n=40) feeding issues in 84%(n=49), sleep issues in 60%(n=35), recurrent chest infections in 60%(n=35), drooling in 74%(n=43), constipation in 79%(n=46) and behavior issues in 39%(n=23) of children. The highest percentage of comorbidities was seen in children with spastic quadriplegic cerebral palsy. Co-morbidities like feeding issues, drooling, sleep disturbance, recurrent chest infections, and constipation had a statistically significant association ($p<0.05$) with subtypes of CP (phenotype) except epilepsy and behavioural issues (Table 3).

Table 3: Association of Co-Morbidities with Subtypes of CP

Type of Cerebral Palsy	No. of Patients	Epilepsy	Feeding Issues	Drooling	Sleep Disturbance	Chest Infections	Constipation	Behavior Issues
p-values	–	0.510	<0.001	<0.001	<0.001	<0.001	<0.001	0.247
Spastic Quadriplegic	32	22 (69%)	32 (100%)	30 (94%)	27 (84%)	25 (78%)	31 (96%)	14 (44%)
Spastic Hemiplegic	6	4 (66%)	3 (50%)	1 (17%)	2 (33.3%)	0 (0%)	4 (67%)	4 (67%)
Spastic Diplegic	8	4 (50%)	7 (87%)	4 (50%)	0 (0%)	4 (50%)	4 (50%)	1 (12%)
Dyskinetic	8	6 (75%)	3 (38%)	4 (50%)	2 (25%)	2 (25%)	3 (38%)	2 (25%)
Mixed	4	4 (100%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)	2 (50%)
Total Patients In Each Column	58 (100%)	40 (69%)	49 (84%)	43 (73%)	35 (60%)	35 (60%)	46 (79%)	23 (39%)

Among 58 children with positive reports, most had a high level of motor impairment, showing GMFCS level V in 42 patients

DOI: https://doi.org/10.54393/pjhs.v7i2.3626

(72.4%), MACS level V in 38 patients (65.5%), and BMFM level V in 40 patients (69%) (Table 4).

Table 4: Level of Severity of Motor Impairment

Scales	Level I	Level II	Level III	Level IV	Level V
GMFCS	0 (0%)	10 (17.2%)	5 (8.6%)	1 (1.7%)	42 (72.4%)
MACS	0 (0%)	9 (15.5%)	4 (6.9%)	7 (12.1%)	38 (65.5%)
BMFM	0 (0%)	4 (6.9%)	7 (12.1%)	7 (12.1%)	40 (69%)

DISCUSSION

Cerebral palsy is a clinical diagnosis for a nonprogressive disorder of motor impairment. According to Van-Eyk *et al.* around one-third of the cases have an underlying genetic etiology [12]. A meta-analysis study done by Romeo *et al.* showed male predominance in all 57 articles included in the study [13]. Al-Sowi *et al.* found spastic cerebral palsy to be the most common type [14]. Studies have shown that there are multiple underlying etiologies in children presented with clinical signs of cerebral palsy. Numerous inborn errors of metabolism, CNS malformations, leukodystrophies, developmental epileptic encephalopathies, and rare syndromes with developmental delay can be diagnosed as cerebral palsy on clinical grounds [6]. Some children having genes for inborn errors of metabolism like Hyperphenylalaninemia (PTS), Molybdenum cofactor synthetase deficiency (MOCS1), and 3-methylglutaconic aciduria (SERAC1) presented with a clinical picture suggestive of quadriplegic cerebral palsy [15]. It has been observed that early detection and identification of genetic mutations in children with inborn errors of metabolism can change their prognosis. Infantile-onset leukodystrophies can also overlap in clinical picture with cryptogenic cerebral palsy. Discovery of leukodystrophy-related genes in our study (PYCR2 and DEGS1 gene) in the quadriplegic cerebral palsy group is consistent with previous literature reporting onset in infancy, developmental delay, and spasticity [16]. A neurodegenerative disorder of Developmental and epileptic encephalopathy (DEE), which presents with seizures in early infancy and developmental delay, mimics spastic cerebral palsy on clinical examination. DEE may be a result of both genetic and other causes. The ITPA gene has been associated with DEE and mimics spastic cerebral palsy when assessed clinically [17]. Similarly, CHD2 and SLC25A12 genes have been listed as pathogenic genes for DEE [18]. CNS malformation-related genes were another significant group we came across in our study. Pontocerebellar hypoplasia-related genes were more common (AMPD2, SEPSECS, and EXOSC8) as compared to genes related to cortical malformation (ADGRG, WDR62). Early detection of pathogenic/likely pathogenic genes. help in the genetic counselling of families [19, 20]. Epilepsy was present in 69% of our patients, with the highest prevalence in mixed type, followed by spastic quadriplegic CP. Bertoncelli *et al.* postulated that spastic quadriparesis is associated with the highest incidence of epilepsy and functional impairment [21]. A systematic review of literature on feeding difficulties in cerebral palsy by Calderone *et al.* highlighted that oropharyngeal dysphagia was more prevalent (81.5%) in children with cerebral palsy. Other significant feeding difficulties in cerebral palsy are problems with mastication and spasticity of muscles around the mouth [22]. Hassanein *et al.* state that three-fourths of all cerebral palsy children have constipation and may benefit from oral magnesium therapy, stretching exercises, and use of lactulose [23]. According to Spoto *et al.* recurrent chest infections in CP children leading to multiple admissions and hospital visits pose a significant burden on healthcare systems as well as the family of the patient [24]. Functional ability and severity of motor impairment of children with cerebral palsy are assessed by standardized scales like GMFCS, MACS, and BMFM. In our study, most of the children with CP had Level V in all scales, which signifies complete dependence. In a study conducted in South India by Brien *et al.* GMFCS level V is the most encountered class in lower-middle-income countries [25].

Limitations of the study includes retrospective cross-sectional study design, which can lead to data loss. More robust prospective study designs can shed more light on patients' prognosis. Selection bias among children with cerebral palsy due to inclusion criteria with affected sibling or intrauterine demise is also a limitation and might not represent the true proportion of genetic causality in cerebral palsy mimics. More resources need to be employed to ensure genetic testing for a wider group of patients and ideally for all patients with cerebral palsy, with or without a predisposing risk factor [26]. Significant work still needs to be done on understanding the genetic etiology of developmental delay, and not just cerebral palsy. Further studies can be carried out on comorbidities and functional impairment associated with each gene. Data is still insufficient even in high-resource setups, regarding exploring genetic causes in cerebral palsy, and it is being proposed that genetic testing should be done in every child with cerebral palsy.

CONCLUSIONS

Genetic etiology should be considered in idiopathic cerebral palsy to identify CP mimics, especially in consanguineous populations. Correlating genotype with phenotype will help in management options of comorbidities and prognosis in these children. Significant work still needs to be done to understand the genetic etiology of idiopathic cerebral palsy in resource-limited settings like Pakistan.

DOI: https://doi.org/10.54393/pjhs.v7i2.3626

Authors' Contribution

Conceptualization: MS, AF, SM, FR, SE, HH
Methodology: MS, AF, FR, SE, HH
Formal analysis: MS, SE, HH
Writing and Drafting: MS, AF, SM, FR, SE, HH
Review and Editing: MS, AF, SM, FR, SE, HH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Baxter P, Morris C, Rosenbaum P, Paneth N, Leviton A, Goldstein M *et al.* The Definition and Classification of Cerebral Palsy. Developmental medicine and child neurology. 2007 Feb; 49: 1-44.

[2] Cans C, Dolk H, Platt MJ, Colver A. Recommendations from the SCPE Collaborative Group for Defining and Classifying Cerebral Palsy. Developmental Medicine and Child Neurology. 2007 Feb; 49: 35. doi: 10.1111/j.1469-8749.2007.tb12626.x.

[3] McIntyre S, Goldsmith S, Webb A, Ehlinger V, Hollung SJ, McConnell K, Arnaud C et al. Global Prevalence of Cerebral Palsy: A Systematic Analysis. Developmental Medicine and Child Neurology. 2022 Dec; 64(12): 1494-1506. doi: 10.1111/dmcn.15346.

[4] Ahmad A, Akhtar N, Ali H. Prevalence Of Cerebral Palsy In Children Of District Swabi, Khyber Pakhtunkhwa, Pakistan. Khyber Medical University Journal. 2017 Apr; 9(2): 1-4.

[5] Sadowska M, Sarecka-Hujar B, Kopyta I. Cerebral Palsy: Current Opinions on Definition, Epidemiology, Risk Factors, Classification and Treatment Options. Neuropsychiatric Disease and Treatment. 2020 Jun: 1505-1518. doi: 10.2147/NDT.S235165.

[6] Pearson TS, Pons R, Ghaoui R, Sue CM. Genetic Mimics of Cerebral Palsy. Movement Disorders. 2019 May; 34(5): 625-636. doi: 10.1002/mds.27655.

[7] Van Eyk C, MacLennan SC, MacLennan AH. All Patients with a Cerebral Palsy Diagnosis Merit Genomic Sequencing. Journal of the American Medical Association Pediatrics. 2023 May; 177(5): 455-456. doi: 10.1001/jamapediatrics.2023.0015.

[8] May HJ, Fasheun JA, Bain JM, Baugh EH, Bier LE, Revah-Politi A. New York Presbyterian Hospital/Columbia University Irving Medical Center Genomics Team. Genetic Testing in Individuals with Cerebral Palsy. Developmental Medicine and Child Neurology. 2021; 63(12): 1448-1455. doi: 10.1111/dmcn.14948.

[9] Wang Y, Xu Y, Zhou C, Cheng Y, Qiao N, Shang Q et al. Exome Sequencing Reveals Genetic Heterogeneity and Clinically Actionable Findings in Children With Cerebral Palsy. Nature Medicine. 2024 May; 30(5): 1395-1405. doi: 10.1038/s41591-024-02912-z.

[10] Chopra M, Gable DL, Love-Nichols J, Tsao A, Rockowitz S, Sliz P *et al.* Mendelian Etiologies Identified with Whole Exome Sequencing in Cerebral Palsy. Annals of Clinical and Translational Neurology. 2022 Feb; 9(2): 193-205.

[11] Mehdi MA, Ali NT, Saleh R. Genetic Disorders Caused by Consanguineous Marriage in Radfan Districts-Yemen. BioMed Central Genomics. 2025 Dec; 18(1): 199. doi: 10.1186/s12920-025-02267-5.

[12] Van Eyk CL, Fahey MC, Gecz J. Redefining Cerebral Palsies as a Diverse Group of Neurodevelopmental Disorders with Genetic Aetiology. Nature Reviews Neurology. 2023 Sep; 19(9): 542-555. doi: 10.1038/s41582-023-00847-6.

[13] Romeo DM, Venezia I, Pede E, Brogna C. Cerebral Palsy and Sex Differences in Children: A Narrative Review of the Literature. Journal of Neuroscience Research. 2023 May; 101(5): 783-795. doi: 10.1002/jnr.25020.

[14] Al-Sowi AM, AlMasri N, Hammo B, Al-Qwaqzeh FA. Cerebral Palsy Classification Based on Multi-Feature Analysis Using Machine Learning. Informatics in Medicine Unlocked. 2023 Jan; 37: 101197. doi: 10.1016/j.imu.2023.101197.

[15] Jones DE, Klacking E, Ryan RO. Inborn Errors of Metabolism Associated with 3-Methylglutaconic Aciduria. Clinica Chimica Acta. 2021 Nov; 522: 96-104. doi: 10.1016/j.cca.2021.08.016.

[16] Torii T, Shirai R, Kiminami R, Nishino S, Sato T, Sawaguchi S *et al.* Hypomyelinating leukodystrophy 10 (HLD10)-Associated Mutations of PYCR2 form Large Mitochondria, Inhibiting Oligodendroglial Cell Morphological Differentiation. Neurology International. 2022; 14(4): 1062–1080. doi: 10.3390/neurolint14040085.

[17] Garg M, Goraya J, Kochar G, Jain V. ITPA-Associated Developmental and Epileptic Encephalopathy: Characteristic Neuroradiological Features with Novel Clinical and Biochemical Findings. Epileptic Disord. 2022; 24(3): 583–588. doi: 10.1684/epd.2022.1424.

[18] Pardo B, Herrada-Soler E, Satrústegui J, Contreras L, Del Arco A. AGC1 Deficiency: Pathology and Molecular and Cellular Mechanisms of the Disease. International Journal of Molecular Sciences. 2022 Jan; 23(1): 528. doi: 10.3390/ijms23010528.

[19] Zhao R, Zhang L, Lu H. Analysis of the Clinical Features and Imaging Findings of Pontocerebellar

DOI: https://doi.org/10.54393/pjhs.v7i2.3626

Hypoplasia Type 2D Caused by Mutations in the SEPSECS Gene. The Cerebellum. 2023 Oct; 22(5): 938-946. doi; 10.1007/s12311-022-01470-9.

[20] Zaki MS, Abdel-Ghafar SF, Abdel-Hamid MS. A Missense Variant in EXOSC8 Causes Exon Skipping and Expands the Phenotypic Spectrum of Pontocerebellar Hypoplasia Type 1C. Journal of Human Genetics. 2024 Feb; 69(2): 79-84. doi: 10.1038/s10038-023-01207-4.

[21] Bertoncelli CM, Dehan N, Bertoncelli D, Bagui S, Bagui SC, Costantini S *et al.* Prediction Model for Identifying Factors Associated with Epilepsy in Children With Cerebral Palsy. Children. 2022 Dec; 9(12): 1918. doi: 10.3390/children9121918.

[22] Calderone A, Militi D, Cardile D, Corallo F, Calabrò RS, Militi A. Swallowing Disorders in Cerebral Palsy: A Systematic Review of Oropharyngeal Dysphagia, Nutritional Impact, and Health Risks. Italian Journal of Pediatrics. 2025 Dec; 51(1): 1-47. doi: 10.1186/s13052-025-01903-1.

[23] Hassanein SM, Deifallah SM, Bastawy HA. Efficacy of Oral Magnesium Therapy in the Treatment of Chronic Constipation in Spastic Cerebral Palsy Children: A Randomized Controlled Trial. World Journal of Pediatrics. 2021 Feb; 17(1): 92-98. doi: 10.1007/s12519-020-00401-0.

[24] Spoto G, Accetta AS, Grella M, Di Modica I, Nicotera AG, Di Rosa G. Respiratory Comorbidities and Complications of Cerebral Palsy. Developmental Neurorehabilitation. 2024 Aug; 27(6): 194-203. doi: 10.1080/17518423.2024.2374959.

[25] Brien M, Krishna D, Ponnusamy R, Cameron C, Moineddin R, Coutinho F. Motor Development Trajectories of Children With Cerebral Palsy in a Community-Based Early Intervention Program in Rural South India. Research in Developmental Disabilities. 2024 Nov; 154: 104829. doi: 10.1016/j.ridd.2024.104829.

[26] Wang Y, Zhu C, Xing Q. Insights into the Genetic Landscape of Cerebral Palsy. Clinical and Translational Medicine. 2025 Jul; 15(7): 70412. doi: 10.1002/ctm2.70412.

DOI: https://doi.org/10.54393/pjhs.v7i2.3647

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Morphological Variations of the Cusp of Carabelli in Permanent Maxillary First Molars and Their Correlation with Caries Risk in the Peshawar Population

Farhan Dil[1], Syed Umer Farooq[2*], Asma Sattar[1], Naheed Imran[1], Ammar Khattak[1] and Muhammad Adnan Khan[3]

[1]Department of Oral Biology, Khyber College of Dentistry, Peshawar, Pakistan
[2]Department of Oral Pathology, Khyber College of Dentistry, Peshawar, Pakistan
[3]Eastman Dental Institute, University College London, United Kingdom

ARTICLE INFO

Keywords:
Cusp of Carabelli, Dental Morphology, Maxillary First Molar, Decayed, Missing, Filled Teeth, Caries Risk, Arizona State University Dental Anthropology System

How to Cite:
Dil, F., Syed Umer Farooq , Sattar, A., Imran, N., Khattak, A., & Khan, M. A. (2026). Morphological Variations of the Cusp of Carabelli in Permanent Maxillary First Molars and Their Correlation with Caries Risk in the Peshawar Population: Cusp of Carabelli in Permanent Maxillary First Molars and Their Correlation with Caries Risk. Pakistan Journal of Health Sciences, 7(2), 96-101. https://doi.org/10.54393/pjhs.v7i2.3647

***Corresponding Author:**
Syed Umer Farooq
Department of Oral Pathology, Khyber College of Dentistry, Peshawar, Pakistan
umer.farooq@kcd.edu.pk

Received Date: 1st December, 2025
Revised Date: 5th January, 2026
Acceptance Date: 14th January, 2026
Published Date: 28th February, 2026

ABSTRACT

The Cusp of Carabelli is a common non-metric morphological trait of permanent maxillary first molars. Although its anthropological significance is well recognized, its clinical relevance in relation to dental caries remains controversial, with limited regional data from Khyber Pakhtunkhwa. **Objectives:** To determine the prevalence and morphological patterns of the Cusp of Carabelli and evaluate their association with caries risk in a young population of Peshawar. **Methods:** A descriptive cross-sectional study was conducted at the Dental Outpatient Department of Khyber College of Dentistry, Peshawar. A total of 103 participants aged ≥12 years were examined using non-probability consecutive sampling. The Cusp of Carabelli was assessed on teeth 16 and 26 using the ASUDAS/Dahlberg classification (Types 0–6). Caries experience was recorded using the DMFT index. Oral hygiene behaviors were obtained through a structured questionnaire. Data were analyzed using descriptive statistics, chi-square, independent t-test, and Pearson correlation. **Results:** The Cusp of Carabelli was present in 62.1% of participants, with a mean severity score of 1.47 ± 1.41. The mean DMFT score was 4.48 ± 2.42, and 53.4% were classified as high caries risk. No significant associations were observed between Carabelli morphology, side expression, or severity score and caries experience ($p>0.05$). Oral hygiene behaviors also showed no significant association with caries risk. **Conclusions:** The Cusp of Carabelli is common in the studied population; however, its presence and morphology do not significantly influence caries risk and should be regarded primarily as a normal anatomical variation.

INTRODUCTION

The Cusp of Carabelli is a well-recognized non-metric morphological trait located on the palatal surface of permanent maxillary first molars and is understood to represent genetic and developmental dental variation rather than a functional anatomical feature. This trait exhibits a wide spectrum of expression, from minor pits and grooves to distinct, well-developed cusps, reflecting its complex ontogeny and multifactorial genetic influences [1, 2]. Morphological dental traits such as the Cusp of Carabelli have long served as important markers in dental anthropology, forensic science, and human population studies, demonstrating variations in expression among different ethnic and regional groups worldwide [3, 4]. Systematic meta-analyses indicate that the prevalence of the Cusp of Carabelli in permanent maxillary first molars globally hovers around 59%, although individual studies report broad variation depending on population characteristics and grading systems used [5]. European

DOI: https://doi.org/10.54393/pjhs.v7i2.3647

populations generally show higher expression frequencies, whereas Asian and African populations display intermediate to lower rates, highlighting marked inter-ethnic variability [6, 7]. Within the South Asian context, including Pakistan, published prevalence estimates for this trait vary considerably. A recent study using ASUDAS criteria found the Cusp of Carabelli in 46.5% of maxillary first molars in a Lahore population, with morphological types ranging from shallow grooves to pronounced cusps [3]. Hospital-based research from Peshawar Dental Hospital reported a 39.3% prevalence in a Peshawar population and noted associated caries in the Carabelli groove in 17.7% of cases, although no significant gender differences were observed [8]. Another local investigation in Multan identified the trait in 53.75% of patients, reinforcing the notion of regional variation within Pakistan itself [9]. These findings suggest that underlying genetic heterogeneity and environmental factors may influence trait distribution across Pakistani subpopulations. Despite its long-standing use in anthropological research, the clinical implications of the Cusp of Carabelli, particularly in caries etiology, remain unclear. Some recent studies indicate that deeper or more pronounced expressions of the trait may create retentive niches conducive to plaque accumulation and subsequent caries development, especially in the grooves at the mesiolingual surface of first molars [10]. However, other regional studies have contradicted this association, reporting no significant relationship between Carabelli morphology and overall caries experience when controlling for behavioral and hygiene factors [11, 12]. This inconsistency suggests that the trait's impact on caries risk might be conditional on a complex interplay with oral hygiene behaviors, dietary patterns, fluoride exposure, and socioeconomic determinants, rather than a direct causal factor in isolation. Furthermore, interstudy differences in methodology, particularly grading systems for Carabelli expression (e.g., ASUDAS) and criteria for caries assessment, have contributed to the lack of consensus. These methodological disparities complicate cross-population comparisons, as some studies restrict analyses to the presence/absence of the trait, while others incorporate detailed morphological scoring [5, 13].

Given the high burden of dental caries in many low- and middle-income contexts and the scarcity of robust dental morphologic data from Khyber Pakhtunkhwa, region-specific research is essential. Understanding whether morphological variants like the Cusp of Carabelli contribute to increased caries susceptibility beyond established risk factors can inform targeted preventive strategies in local public dental health initiatives. This study aimed to determine the prevalence and morphological patterns of the Cusp of Carabelli and evaluate their association with caries risk in a young population of Peshawar.

METHODS

This descriptive cross-sectional study was conducted from 26 September to 26 November 2025 at the Dental Outpatient Department (OPD) of Khyber College of Dentistry, Peshawar. Ethical approval was obtained from the Institutional Ethics Committee of Khyber College of Dentistry (Reference No. 110/ADR/KCD), and written informed consent was obtained from all participants before enrollment. The sample size comprised 103 participants and was calculated using the standard cross-sectional formula $n = (Z^2 \times P \times (1–P)) / d^2$, where $Z = 1.96$ (95% confidence), P was based on previously reported regional prevalence [14], and d was set between 0.08 and 0.10. To compensate for possible non-responses and improve precision, a final sample size of 103 was included. A non-probability consecutive sampling technique was employed. Demographic information, including age, gender, residence, and socioeconomic status, was collected through a structured interviewer-administered questionnaire at the time of clinical examination. Oral hygiene practices such as brushing frequency, fluoride toothpaste use, and snack frequency were recorded using the same questionnaire. Participants aged 12 years and above with fully erupted permanent maxillary first molars and intact crown morphology were included. Participants were excluded if maxillary first molars were grossly carious, fractured, hypoplastic, restored with full-coverage crowns, orthodontically altered, or if any systemic or developmental condition known to affect tooth formation was present. Intra-oral examination was performed under ambient clinical lighting using a disposable mouth mirror and periodontal probe. Both maxillary first molars (teeth 16 and 26) were examined. The Cusp of Carabelli was assessed using the Arizona State University Dental Anthropology System (ASUDAS) / Dahlberg classification [15], which categorizes the trait on a scale from Type 0 (absence of the cusp) to Type 6 (well-developed prominent cusp). Types 1–2 represent pits and shallow depressions, Types 3–4 represent grooves and small cusps, and Types 5–6 represent moderately to well-developed cusps. Side expression (unilateral/bilateral) was also recorded. Caries experience was assessed using the DMFT index (Decayed, Missing, Filled Teeth) according to the World Health Organization (WHO) Oral Health Surveys criteria Basic Methods (5th edition), which provides standardized criteria for epidemiological recording of dental caries [16]. To ensure reliability, all examinations were performed by a single calibrated examiner. Intra-examiner reliability was assessed on a subset of participants before data collection, and consistent scoring

DOI: https://doi.org/10.54393/pjhs.v7i2.3647

was achieved. Data were analyzed using IBM SPSS version 26.0. Descriptive statistics were used to summarize demographic, oral hygiene, and morphological variables. Chi-square tests were applied to assess associations between categorical variables. An independent samples t-test was used to compare mean DMFT scores between groups with and without the Cusp of Carabelli. Pearson's correlation coefficient was used to evaluate the relationship between Carabelli severity scores and DMFT values. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

The mean age of the participants was 18.49 ± 3.05 years, with the majority (60.2%) belonging to the 17–21-year age group. Females comprised 56.3% of the sample, and 57.3% were urban residents. With respect to oral hygiene practices, 38.8% brushed once daily, 33.0% brushed twice daily, and 28.2% brushed irregularly, while 78.6% reported using fluoride toothpaste. The demographic and behavioral characteristics of the study participants are summarized in table 1.

Table 1: Frequency of Demographic, Oral Hygiene, and Dietary Characteristics (n=103)

Variables	Category	n (%)
Age (Years)	Mean ± SD	18.49 ± 3.05
Age Groups	12–16	22 (21.4%)
	17–21	62 (60.2%)
	>21	19 (18.4%)
Gender	Male	45 (43.7%)
	Female	58 (56.3%)
Residence	Urban	59 (57.3%)
	Rural	44 (42.7%)
Socioeconomic Status	Low	31 (30.1%)
	Middle	54 (52.4%)
	High	18 (17.5%)
Brushing Frequency	Once daily	40 (38.8%)
	Twice daily	34 (33.0%)
	Irregular	29 (28.2%)
Fluoride Toothpaste	Yes	81 (78.6%)
	No	22 (21.4%)
Snack Frequency	<1/day	24 (23.3%)
	1–2/day	51 (49.5%)
	≥3/day	28 (27.2%)

The study demonstrates the prevalence and morphological expression of the Cusp of Carabelli. The cusp was present in 62.1% of participants, with 58.3% showing bilateral expression. The mean severity score was 1.47 ± 1.41, indicating predominantly mild expression. The most frequent morphology was Type 0 (37.9%), followed by Type 1 (12.6%) and Type 5 (12.6%), as shown in table 2.

Table 2: Tooth-Related Findings and Morphology of the Cusp of Carabelli

Variables	Category	n (%)
Tooth Examined	16	50 (48.5%)
	26	53 (51.5%)
Side Expression	Bilateral	60 (58.3%)
	Unilateral	43 (41.7%)
Presence of CC	Present	64 (62.1%)
	Absent	39 (37.9%)
Severity Score	Mean ± SD	1.47 ± 1.41
Morphology	Type 0	39 (37.9%)
	Type 1	13 (12.6%)
	Type 2	9 (8.7%)
	Type 3	8 (7.8%)
	Type 4	8 (7.8%)
	Type 5	13 (12.6%)
	Type 6	13 (12.6%)

Results summarize the overall caries experience of the study participants using the DMFT index and its association with the Cusp of Carabelli. The mean DMFT score was 4.48 ± 2.42, with the decayed component contributing the largest share (2.87 ± 2.09), indicating an overall moderate caries burden. More than half of the participants (53.4%) were classified as having high caries risk, while 24.3% and 22.3% were categorized as low and moderate risk, respectively. Comparison of mean DMFT scores between individuals with and without the Cusp of Carabelli showed no statistically significant difference (p=0.529), and severity score did not correlate with DMFT (r=0.001, p=0.996), indicating that Carabelli morphology did not influence caries experience, as shown in table 3.

Table 3: Caries Status, Risk Distribution, and Association with Cusp of Carabelli (n=103)

Variables	Category / Statistic	Mean ± SD / n (%)	p-value
DMFT Components	Decayed (D)	2.87 ± 2.09	–
	Missing (M)	0.12 ± 0.40	
	Filled (F)	1.49 ± 1.15	
	Total DMFT	4.48 ± 2.42	
Caries Risk Categories	Low	25 (24.3%)	–
	Moderate	23 (22.3%)	
	High	55 (53.4%)	
Mean DMFT by CC Presence	CC Present	4.59 ± 2.40	0.529
	CC Absent	4.28 ± 2.47	
Correlation Analysis	Severity Score vs DMFT	r = 0.001	0.996

The study demonstrates the association between Carabelli morphology, side expression, and caries risk. A higher proportion of individuals with the Cusp of Carabelli had high caries risk (56.3%) than those without it (48.7%); however, this difference was not statistically significant (p=0.714). Similarly, bilateral (53.3%) and unilateral (53.5%) expressions showed comparable high-risk proportions,

DOI: https://doi.org/10.54393/pjhs.v7i2.3647

with no significant association between side expression and caries risk (p=0.318). Furthermore, different Carabelli morphological types did not demonstrate statistically significant variation in caries risk categories (p=0.693), indicating that Carabelli morphology did not influence caries susceptibility in this population, as shown in table 4.

Table 4: Association of Carabelli Features with Caries Risk (n=103)

Features	Category	High, n (%)	Low, n (%)	Moderate, n (%)	Total	χ^2 (Cramer's V)	p-value
CC Presence	Present	36 (56.3%)	14 (21.9%)	14 (21.9%)	64	0.673	0.714
	Absent	19 (48.7%)	11 (28.2%)	9 (23.1%)	39		
Side Expression	Bilateral	32 (53.3%)	12 (20.0%)	16 (26.7%)	60	0.149	0.318
	Unilateral	23 (53.5%)	13 (30.2%)	7 (16.3%)	43		
CC Morphological Type	Type 0	19 (48.7%)	11 (28.2%)	9 (23.1%)	39	9.121	0.693
	Type 1	7 (53.8%)	4 (30.8%)	2 (15.4%)	13		
	Type 2	3 (33.3%)	2 (22.2%)	4 (44.4%)	9		
	Type 3	4 (50.0%)	2 (25.0%)	2 (25.0%)	8		
	Type 4	5 (62.5%)	2 (25.0%)	1 (12.5%)	8		
	Type 5	10 (76.9%)	0 (0.0%)	3 (23.1%)	13		
	Type 6	7 (53.8%)	4 (30.8%)	2 (15.4%)	13		

The results present the relationship between oral hygiene behaviors and caries risk categories. Although higher proportions of high caries risk were observed among participants who brushed twice daily (64.7%) and those consuming ≥3 snacks per day (64.3%), brushing frequency (p=0.566), fluoride toothpaste use (p=0.920), and snack frequency (p=0.184) did not show statistically significant associations with caries risk. These findings indicate that oral hygiene behaviors were not independent predictors of caries susceptibility in this study population, as shown in table 5.

Table 5: Association of Oral Hygiene Behaviors with Caries Risk (n=103)

Behaviors	Category	High, n (%)	Low, n (%)	Moderate, n (%)	p-value
Brushing Frequency	Twice Daily	22 (64.7%)	7 (20.6%)	5 (14.7%)	0.566
	Once Daily	19 (47.5%)	10 (25.0%)	11 (27.5%)	
	Occasionally	14 (48.3%)	8 (27.6%)	7 (24.1%)	
Fluoride Toothpaste Use	Yes	44 (54.3%)	19 (23.5%)	18 (22.2%)	0.920
	No	11 (50.0%)	6 (27.3%)	5 (22.7%)	
Snack Frequency	<1/Day	9 (37.5%)	10 (41.7%)	5 (20.8%)	0.184
	1–2/Day	28 (54.9%)	10 (19.6%)	13 (25.5%)	
	≥3/Day	18 (64.3%)	5 (17.9%)	5 (17.9%)	

Scatter plot showing no correlation between CC severity and DMFT (r=0.001, p=0.996). Evidence suggests no significant relationship, as the point distribution lacks a clear linear pattern, and the trendline is almost flat. This aligns with the results from the cusp severity and caries experience correlation test (r=0.001; p=0.996), which showed no statistically significant correlation between cusp severity and caries experience (Figure 1).

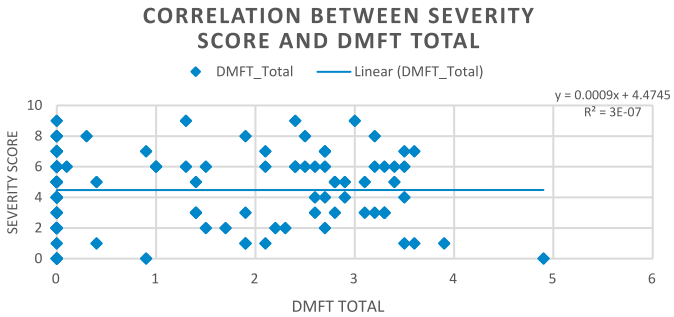

Figure 1: Correlation Between Severity Score and DMFT Total

DISCUSSION

The present study demonstrated a high prevalence of the Cusp of Carabelli (62.1%) among permanent maxillary first molars in the Peshawar population, with predominantly mild morphological expressions, and found no statistically significant association between Carabelli morphology and caries experience. These findings are consistent with recent international and regional literature. A global systematic review and meta-analysis by Kotsanos *et al.* reported an overall prevalence of approximately 59%, confirming that Carabelli expression is common worldwide but highly variable across populations [4]. Comparable results were observed in Pakistan, where Shahbaz *et al.* reported a prevalence of 46.5% using ASUDAS classification in Lahore [3], while Khan *et al.* from Peshawar and Qamar *et al.* from Multan documented similarly moderate to high frequencies of the trait [17, 18]. Studies from neighboring regions further support these findings. Zichao *et al.* in China documented moderate prevalence rates and substantial inter-individual variation [19]. German orthodontic research also emphasized the genetic basis and bilateral nature of Carabelli expression [20], reinforcing that this trait primarily reflects inherited crown morphology rather than pathological change.

DOI: https://doi.org/10.54393/pjhs.v7i2.3647

Importantly, the absence of a significant association between Carabelli morphology and caries experience in the present study aligns with multiple regional and international investigations. Zichao *et al.* in Peshawar [19] and Matti *et al.* in Iraq [6] similarly reported that Carabelli expression did not independently predict dental caries when oral hygiene behaviors and other confounders were considered. These observations suggest that Carabelli morphology alone does not constitute a clinically meaningful caries risk factor. Conversely, a few studies have reported slightly increased caries susceptibility in deeper Carabelli groove types, particularly in the Bangladeshi population [21] and in a cohort study by Bhavyaa *et al.* [22]. However, these studies also noted that the observed associations were modest and strongly influenced by oral hygiene practices, dietary habits, and fluoride exposure. The predominance of shallow, easily cleanable Carabelli expressions and relatively high fluoride toothpaste use in the present cohort may explain the lack of association observed. Overall, the current findings support the growing body of evidence that regards the Cusp of Carabelli as a genetically determined non-metric dental trait with limited independent clinical relevance in caries etiology. While its documentation remains valuable for anthropological, forensic, and population studies, its role as a predictive indicator for dental caries appears minimal.

This study was conducted in a single city with a limited sample, which may not represent the wider population. Additionally, the cross-sectional design and focus on mild Carabelli expressions limited assessment of potential effects of extreme morphologies on caries risk. Future longitudinal investigations with larger sample sizes are warranted to elucidate whether pronounced morphological expressions may contribute to caries development under varying behavioral and environmental conditions.

CONCLUSIONS

The present study demonstrates that the Cusp of Carabelli is a prevalent morphological feature of permanent maxillary first molars among young individuals in Peshawar, predominantly expressed in mild forms. Despite a moderate overall caries burden in the study population, no statistically significant associations were identified between Carabelli presence, side expression, morphological type, or severity score and caries risk or DMFT values. These findings indicate that Carabelli morphology does not independently influence dental caries susceptibility and should be regarded primarily as a normal anatomical variation rather than a clinical risk indicator.

Authors' Contribution

Conceptualization: FD
Methodology: FD, MAK
Formal analysis: SUF, AS, NI, AK, MAK
Writing and Drafting: FD, SUF, AS, NI, AK
Review and Editing: FD, SUF, AS, NI, AK, MAK

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Madalena IR, Resende HG, Blancato AB, de Menezes-Oliveira MA, Baratto-Filho F, Santos PF *et al.* Exploring the Association Between Third Molar Agenesis and Carabelli Traits: A Cross-Sectional Study. Dentistry Journal. 2025 Jan; 13(1): 23. doi: 10.3390/dj13010023.

[2] Pillai JP, Parmar G, Vyas JM, Babu R. The Nonmetric Cusp Traits of Maxillary Molars in Tamil Population: A Cross-Sectional, Descriptive and Sex Identification Study using the Turner Scott dental Anthropology Standards. Indian Journal of Dental Research. 2024 Jul; 35(3): 320-5. doi: 10.4103/ijdr.ijdr_229_23.

[3] Shahbaz M, Zaheer N, Zaheer U, Bilal MH, Sajid A, Ali J *et al.* Morphological Traits and Caries Susceptibility of the Cusp of Carabelli in Permanent Maxillary Molars: A Study in Lahore, Pakistan. Archives of Oral Biology. 2025 Sep: 106406. doi: 10.1016/j.archoralbio.2025.106406.

[4] Kotsanos N, Papagerakis P, Sarnat H, Bloch-Zupan A. Developmental Defects of the Teeth and Their Hard Tissues. In Pediatric Dentistry. Cham: Springer International Publishing. 2022 Jan: 415-463. doi: 10.1007/978-3-030-78003-6_17.

[5] Bhavyaa R, Sujitha P, Muthu MS, Nirmal L, Patil SS. Prevalence of the Cusp of Carabelli: a systematic review and meta-analysis. Annals of Human Biology. 2021 Nov; 48(7-8): 572-84. doi: 10.1080/03014460.2022.2032339.

[6] Matti MQ, Hadi RJ, Rashid SY. Clinical Evaluation of the Occurrence of Cusp of Carabelli and its Caries Susceptibility in Specific Population in Baghdad. Thi-qar Medical Journal. 2024 Nov; 28(2): 299-308. doi: 10.32792/jmed.v28i2.594.

[7] Yılancı HÖ, Özkan G, Akkaya N, Boyacıoğlu H. The Frequency and Degree of Expression of Carabelli's Trait on the Permanent Maxillary Molars in a Sample

DOI: https://doi.org/10.54393/pjhs.v7i2.3647

of Turkish Individuals. International Dental Research. 2022 Dec; 12(3): 112-9. doi: 10.5577/intdentres.2022.vol12.no3.2.

[8] Arbab S, Khattak MA, Shah SA. Frequency of Cusp of Carabelli in Maxillary Permanent First Molars and Its Association with Dental Caries in Patients Visiting Peshawar Dental Hospital, Peshawar. The Professional Medical Journal. 2021 Aug; 28(08): 1101-6. doi: 10.29309/TPMJ/2021.28.08.4959.

[9] Zafar R, Shakoor A, Haider MU, Muhammad U, Baloch N. The Presence/Absence of Cusps of the Carabelli in Patients Presenting to the Dental Outdoor Department in a Teaching Hospital in Multan, Pakistan. The Professional Medical Journal. 2023 Jan; 30(02): 281-4. doi: 10.29309/TPMJ/2023.30.02.7153.

[10] Riaz S, Khamis MF, Ahmad WM, Abdullah JY, Alam MK. Potential Use of the Cusp and Crown Areas of the Maxillary Posterior Teeth Measured with A Two-Dimensional Stereomicroscope for Sex Determination. Forensic Science, Medicine, and Pathology. 2024 Jun; 20(2): 452-61. doi: 10.1007/s12024-023-00651-0.

[11] Al-Azzawi AS, Aswad FG, Rasheed AK, Abdulrazak MA, Ibrahim FA. Prevalence of Cusp of Carabelli in Upper First Molars in Salahdin Governate and Its Caries Susceptibility. Tikrit Journal for Dental Sciences. 2024 Jun; 12(1): 172-8. doi: 10.25130/tjds.12.1.19.

[12] Sureshbabu S, Ramadoss R, Arthanari A, Ramalingam K. Dental Anomalies: An Identification Marker in Forensics. Cureus. 2024 May; 16(5). doi: 10.7759/cureus.59922.

[13] Nair HR, Mishra S, Panda S, Srivastava G. Frequency and Degree of Inter-Trait Association of Maxillary Non-Metric Dental Crown Traits in the Permanent Dentitions of Two States of India. The Journal of Forensic Odonto-Stomatology. 2020 May; 38(1): 18.

[14] Khan DB, Khan MA, Khattak M. Prevalence of Cusp of Carabelli in Permanent Teeth in a Group from Khyber Pakhtunkhwa, Pakistan. Pakistan Oral and Dental Journal. 2011 Dec; 31(2).

[15] Ortiz A. 2012 Dahlberg Award Winner Dental Morphological Variation among Six Pre-Hispanic South American Populations with Implications for the Peopling of the New World. Dental Anthropology Journal. 2013; 26(1-2): 20-32. doi: 10.26575/daj.v26i1-2.45.

[16] World Health Organization. Oral Health Surveys: Basic Methods. World Health Organization. 2013.

[17] Khan SH, Akram S, Masood M, Nawadat K, Moazzam M, Saqib S. Frequency of Carabelli's Cusp and its Association with Dental Caries in Maxillary Permanent First Molars in Relation to Gender. Annals of Punjab Medical College. 2022 Dec; 16(4): 356-9.

[18] Qamar W, Qayum M, Ali A, Idrees S. Frequency and trends of cusp of Carabelli in Maxillary First Molars of Patients Visiting Dental Teaching Hospital in Mardan, Pakistan. Pakistan Orthodontic Journal. 2018 Aug; 10(1): 27-9.

[19] Zichao Z, Daorui W, Qianxia Z, Yidan, Aiyun C, Jianing L *et al.* The Carabelli's Traits on Permanent Maxillary Molars in 803 Han Chinese College Students. Stomatology. 2024; 44(8): 586-589.

[20] Blancato AB, Paddenberg-Schubert E, Proff P, Hueb de Menezes-Oliveira MA, Beisel-Memmert S *et al.* Frequency and Variability of Nonmetric Dental Crown Traits of Primary and Permanent Molars in A Group of Orthodontic Patients. Journal of Orofacial Orthopedics/Fortschritte der Kieferorthopädie. 2025 Sep; 86(5): 298-313. doi: 10.1007/s00056-024-00532-3.

[21] Emon KE, Sarmin S, Rafique T, Hossin MI, Al Mamun A, Rahman M *et al.* Morphological Prevalence and Clinical Implications of the Cusp of Carabelli in Maxillary First Molars: A Cross-Sectional Study among the Bangladeshi Population. Scholars Journal of Dental Sciences. 2025 Jul; 6: 90-3. doi: 10.36347/sjds.2025.v12i06.002.

[22] Bhavyaa R, Sujitha P, Muthu MS, Kirthiga M. Prevalence of Cusp of Carabelli and Its Caries Susceptibility–An Ambidirectional Cohort Study. Australian Dental Journal. 2020 Dec; 65(4): 294-301. doi: 10.1111/adj.12795.

DOI: https://doi.org/10.54393/pjhs.v7i2.3700

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Evaluating The Role of Point-of-Care Lactate Measurement in Predicting Severity and Outcomes of Diabetic Ketoacidosis in Emergency Settings

Imtiaz Manzoor[1], Rajesh Jamna Dass[2], Faryal Aman[3], Sana Ilyas[4], Faiza Zaib[5] and Sidra Anwar[6*]

[1]Department of Medicine, Chiniot General Hospital, Karachi, Pakistan
[2]Department of Medicine, United Medical and Dental College, Karachi, Pakistan
[3]Karachi Medical and Dental College, Karachi, Pakistan
[4]Department of Emergency Medicine, Ziauddin University Hospital, Karachi, Pakistan
[5]Department of Medicine, Jinnah Medical and Dental College, Karachi, Pakistan
[6]Civil Hospital, Karachi, Pakistan

ARTICLE INFO

Keywords:
Diabetic Ketoacidosis, Severity, Point of Care Lactate, In-Hospital Mortality, Hyperglycemia

How to Cite:
Manzoor, I., Dass, R. J., Aman, F., Ilyas, S., Zaib, F., & Anwar, S. (2026). Evaluating The Role of Point-of-Care Lactate Measurement in Predicting Severity and Outcomes of Diabetic Ketoacidosis in Emergency Settings: Point-of-Care Lactate for Predicting Severity and Outcomes in Diabetic Ketoacidosis. Pakistan Journal of Health Sciences, 7(2), 102-107. https://doi.org/10.54393/pjhs.v7i2.3700

***Corresponding Author:**
Sidra Anwar
Civil Hospital, Karachi, Pakistan
sidra_sms23@outlook.com

Received Date: 22nd November, 2025
Revised Date: 13th January, 2026
Acceptance Date: 17th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Diabetic ketoacidosis is one of the severe diabetic emergencies with hyperglycaemia, acidosis, and ketonemia, and an increased level of lactate is an indicative feature of metabolic stress and unfavourable prognosis, necessitating urgent assessment and immediate care. **Objectives:** To assess the frequency of elevated point-of-care lactate in patients presenting with diabetic ketoacidosis (DKA) and to evaluate its association with DKA severity and in-hospital mortality. **Methods:** Data were prospectively collected from patients after obtaining verbal consent. Both quantitative and qualitative data were collected and analysed using SPSS version 23.0. Chi-square tests were applied, with a p-value of ≤0.05 considered significant. The study employed a descriptive cross-sectional design, conducted over six months (January 7, 2023, to June 7, 2023) at the Department of Medicine, Civil Hospital, Karachi. **Results:** A total of 131 patients were included, with a mean age and duration of T2DM of 47.14 ± 16.49 years and 1.72 ± 1.24 years, respectively. Among the participants, 71 (54.2%) were male, and 60 (45.8%) were female. Out of 131 patients, 64 (48.9%) had elevated point-of-care lactate, while 67 (51.1%) did not. In-hospital mortality occurred in 14 (60.9%) patients with elevated point-of-care lactate. The majority of patients presented with moderate DKA. **Conclusions:** The findings conclude that initial lactate levels in DKA patients are significantly associated with the need for critical care, suggesting that lactate can be used as a reliable marker for monitoring and managing DKA patients.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a severe diabetic complication characterized by insulin deficiency, which causes hyperglycemia, acidosis, and ketonemia and has prevailed in approximately 8 per 1000 diabetics each year with a mortality rate of less than 5% [1]. Even though high levels of lactate can be used to anticipate sepsis, burns, myocardial infarction, and trauma, the data on the relationship between lactate and DKA severity are scarce and contradictory [2]. Measurement of lactate on-site may be an effective prognostic indicator for a patient in DKA because a higher level of lactate indicates an increased severity of the disease and increased chances of fatality in the hospital. Lactate may develop in numerous body tissues (kidney, erythrocyte, skeletal muscle, brain). The liver metabolizes the majority of the lactate, with the help of the kidney and skeletal muscle coming next [3]. At the moment of patient presentation, point-of-care lactates were assessed by means of a portable lactate reading

DOI: https://doi.org/10.54393/pjhs.v7i2.3700

instrument. The criteria used to classify the levels as being elevated were above 2 mmol/L, which is the standard clinical reference range of hyperlactatemia. [4]. In DKA, high levels of lactate are due to hypoperfusion, tissue hypoxia, and high levels of anaerobic glycolysis caused by insulin deficiency. With no insulin, more lipolysis, free fatty oxidation, and ketone bodies will be formed, leading to metabolic acidosis [5]. The presence of lactic acidosis also complicates acid-base imbalances, thereby complicating the management of the patient. Multiple studies suggest that the rise in lactate during DKA is not tissue hypoxia in all cases but is associated with the modified glucose metabolism and increased catecholamine levels, with the potential to cause hyperlactatemia [6]. Thus, hyperlactatemia in DKA must be well-defined to guide the diagnosis, the proposed management, and the prognostic assessment, and receive appropriate clinical attention [7]. Diabetic ketoacidosis (DKA) is a life-threatening condition mostly faced by patients with unregulated diabetes mellitus. Therefore, its early recognition and prompt treatment are paramount. Point-of-care lactate levels are increasingly noted as a marker of tissue hypoperfusion and worse outcomes in critically ill patients. However, the importance of elevated point-of-care lactate levels in DKA is still insufficiently understood, especially regarding the levels of DKA-related acidosis and the overall in-hospital outcome [8]. Recently, Kumar et al. researched the impact of late lactate clearance on DKA outcomes and noted that patients with late lactate clearance had longer stays at both the ICU and the hospital [9]. Furthermore, Elfiky et al. studied that in pediatric DKA and found that higher lactate levels correlated inversely with pH and positively with inflammatory markers, though did not consistently predict recovery time [10]. Also, Munsakul et al. formulated a predictive score for in-hospital mortality for DKA and included lactate in the score as one of the biochemical predictors [11].

Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes marked by hyperglycemia, acidosis, and ketonemia, yet the role of lactate as a prognostic marker in DKA remains unclear. Existing studies suggest associations between elevated lactate, disease severity, and in-hospital outcomes, but findings are inconsistent and mostly derived from non-local populations. Limited local evidence hampers the ability to use point-of-care lactate effectively for risk stratification and management decisions in DKA patients. This study aims to assess point-of-care lactate levels in DKA patients presenting to a tertiary care hospital, evaluating their relationship with disease severity and clinical outcomes to inform timely and evidence-based management.

METHODS

This descriptive cross-sectional study design was done in the Department of Medicine, Civil Hospital, Karachi, for six months, from January 7, 2023, to June 7, 2023, after approval of the research synopsis from the review board (IRB No. CIVL/AL/2023-064). Data were prospectively collected from patients after obtaining verbal consent; 131 patients were included in the study. The sample size was calculated through WHO software based on 68% prevalence of elevated point-of-care lactate with 8% margin of error and 95% confidence level [12]. Participants for the study were recruited using a non-probability consecutive sampling technique. The study included all male and female patients aged between 20 and 70 years who presented with diabetic ketoacidosis using a consecutive (non-probability) sampling technique. Patients were excluded if they had a history of hepatocellular carcinoma, blood or solid tumor malignancies, sepsis, or hospitalization within the previous month. Additionally, individuals with known endocrine or chronic systemic conditions, including hypothyroidism, hyperthyroidism, chronic obstructive pulmonary disease (COPD), asthma, myocardial infarction, congestive heart failure, or chronic renal failure, were also excluded to minimize confounding factors and ensure accurate assessment of metabolic parameters related to diabetic ketoacidosis. Patients meeting the study criteria were recruited from the Department of Emergency, Civil Hospital Karachi. Demographics, comorbidities, and clinical data were recorded, and blood samples were collected for point-of-care lactate measurement. Patients were classified based on lactate levels, and outcomes, including DKA severity and in-hospital mortality, were documented in a predesigned proforma. The researcher performed data entry and analyses using SPSS version 23.0. Frequency distribution and post-stratification Chi-square test were applied for statistical analysis with a significance level of $p \leq 0.05$. For normally distributed variables, means ± standard deviations were reported, while medians and interquartile ranges were reported for non-normally distribute. For the categorical variables, reported values were frequencies and percentages of gender, residence status, hypertension, dyslipidemia, smoking status, family monthly income, educational status, severity of DKA, elevated point-of-care lactate, and in-hospital mortality (Yes/No).

RESULTS

The findings indicated that the patients who were diagnosed with diabetic ketoacidosis and met the criteria were predominantly middle-aged adults of middle age with different durations of having diabetes mellitus type 2. The majority of them resided in the cities, and both genders

DOI: https://doi.org/10.54393/pjhs.v7i2.3700

were equally represented. Almost half of the patients had increased point-of-care levels of lactate, with a substantial proportion of such patients dying in-hospital. The less prevalent comorbidities were hypertension and dyslipidemia. The moderate level of DKA was the most prevalent. Statistical analysis found that there is a significant correlation between a high level of lactate and some demographic and socioeconomic variables, but not other clinical variables. One hundred and thirty-one patients (mean age 47.14 ± 16.49 years; mean T2DM duration 1.72 ± 1.24 years) took part in the research, consisting of 71 (54.2%) male and 60 (45.8%) female. High point-of-care lactate was detected in 64 (48.9%) patients, and in-hospital mortality was experienced by 23 (17.6%) of them. The median age, urban dwelling, and protracted T2DM (>2 years) were fairly high, where 64.1% of the patients were aged 64 years and above, 83.2% dwelling in urban areas, and 64.1% with diabetes exceeding two years (Table 1).

Table 1: Demographic and Clinical Characteristics of the Study Participants (n=131)

Variables	Categories	Frequency (%)
Age (Years)	Mean ± SD	47.14 ± 16.49
	Range	29 – 75
Age Groups	20 – 45 years	47 (35.9%)
	46 – 70 years	84 (64.1%)
Gender	Male	71 (54.2%)
	Female	60 (45.8%)
Residence	Urban	109 (83.2%)
	Rural	22 (16.8%)
Duration of T2DM (years)	Mean ± SD	1.72 ± 1.24
	≤ 2 years	47 (35.9%)
	> 2 years	84 (64.1%)
Point-of-Care Lactate Levels	Elevated	64 (48.9%)
	Not Elevated	67 (51.1%)
In-Hospital Mortality	Yes	23 (17.6%)
	No	108 (82.4%)

Of 131 patients, 33 (25.2%), 77 (58.8%), and 21 (16%) had mild, moderate, and severe DKA, respectively. There were 42 (32.1%), 19 (15.3%), and 20 (15.3%) hypertension cases, dyslipidemia cases, and smokers, respectively. The majority of patients were earning more than 75,000 PKR monthly (66.4%) and were highly educated (51.1%). It was found that lactate levels were elevated in 42.6 percent of patients between the ages of 20-45 years and 52.4 percent of those between the ages of 46-70 years, without a significant age difference in levels (p=0.28) (Table 2).

Table 2: Clinical and Demographic Characteristics Related to Severity of DKA (n=131)

Variables	Categories	Frequency (%)
Severity of DKA	Mild	33 (25.2%)
	Moderate	77 (58.8%)
	Severe	21 (16.0%)
Hypertension	Present	42 (32.1%)
	Absent	89 (67.9%)
Dyslipidemia	Present	19 (15.3%)
	Absent	111 (84.7%)
Smoking Status	Smoker	20 (15.3%)
	Non-Smoker	111 (84.7%)
Family Monthly Income (PKR)	≤ 75,000	44 (33.6%)
	> 75,000	87 (66.4%)
Educational Status	Illiterate	7 (5.3%)
	Primary	12 (9.2%)
	Secondary	45 (34.4%)
	Higher Education	67 (51.1%)
Age Group (years)	20 – 45 years (Elevated Lactate)	20 (42.6%)
	46 – 70 years (Elevated Lactate)	44 (52.4%)
	20 – 45 years (Normal Lactate)	27 (57.4%)
	46 – 70 years (Normal Lactate)	40 (47.6%)
p-value	–	0.28

The gender difference was found to be significant in the cases of elevated levels of lactate via stratified analysis, as 35.2% of males and 65% of females had been affected. There was no significant relationship with residence (urban 50.5% vs rural 40.9%, p=0.41), T2DM duration (length of less than 2 years 42.6% vs length of greater than 2 years 52.4%, p=0.28), hypertension (50% vs 48.3%), and dyslipidemia (47.4% vs 49.1%) (Table 3).

Table 3: Stratification of Elevated Point-of-Care Lactate Levels with Respect to Different Variables

Variables	Category	Elevated Lactate (n, %)	Normal Lactate (n, %)	p-value
Gender	Male (n=71)	25 (35.2%)	46 (64.8%)	0.01
	Female (n=60)	39 (65.0%)	21 (35.0%)	
Residence	Urban (n=109)	55 (50.5%)	54 (49.5%)	0.41
	Rural (n=22)	9 (40.9%)	13 (59.1%)	
Duration of T2DM	≤ 2 years (n=47)	20 (42.6%)	27 (57.4%)	0.28
	> 2 years (n=84)	44 (52.4%)	40 (47.6%)	
Hypertension	Present (n=42)	21 (50.0%)	21 (50.0%)	0.85
	Absent (n=89)	43 (48.3%)	46 (51.7%)	
Dyslipidemia	Present (n=19)	9 (47.4%)	10 (52.6%)	0.88
	Absent (n=112)	55 (49.1%)	57 (50.9%)	

Elevated lactate did not significantly correlate with smoking (45% vs. 49.5%; p=0.70) or the severity of DKA (54.5% mild, 42.9% moderate, 61.9% severe; p=0.22), according to stratified analysis. Patients with higher education (56.7%; p=0.03) and household income >75,000 PKR (57.5%; p=0.01) had substantially higher levels of elevated lactate. In-hospital deaths had increased lactate

DOI: https://doi.org/10.54393/pjhs.v7i2.3700

as 60.9% as compared to 46.3% of survivors (p=0.20) (Table 4).

Table 4: Stratification of Elevated Point-of-Care Lactate with Respect to Various Variables (n=131)

Variables	Category	Elevated Lactate (n, %)	Normal Lactate (n, %)	p-value
Smoking Status	Smoker	9 (45.0%)	11 (55.0%)	0.70
	Non-Smoker	55 (49.5%)	56 (50.5%)	
Monthly Income (PKR)	≤ 75,000	14 (31.8%)	30 (68.2%)	0.01
	> 75,000	50 (57.5%)	37 (42.5%)	
Educational Status	Illiterate	0 (0.0%)	7 (100%)	0.03
	Primary	6 (50.0%)	6 (50.0%)	
	Secondary	20 (44.4%)	25 (55.6%)	
	Higher	38 (56.7%)	29 (43.3%)	
Severity of DKA	Mild	18 (54.5%)	15 (45.5%)	0.22
	Moderate	33 (42.9%)	44 (57.1%)	
	Severe	13 (61.9%)	8 (38.1%)	
In-Hospital Mortality	Yes	14 (60.9%)	9 (39.1%)	0.20
	No	50 (46.3%)	58 (53.7%)	

DISCUSSION

Increased metabolic stress and tissue hypoperfusion are reflected in elevated lactate levels in diabetic ketoacidosis (DKA), which suggests a more severe illness, a larger need for rapid treatment, and a higher chance of unfavorable outcomes, such as in-hospital mortality. Lactate metabolism is key to understanding DKA, as insulin deficiency and altered glucose utilization increase lactate production and impair clearance, reflecting metabolic stress during acute diabetic emergencies [13]. Tissue hypoperfusion, hypoxia, insulin deficiency-driven increased anaerobic glycolysis, and stress hormone-mediated accelerated glycolysis are the causes of hyperlactatemia in DKA. Effective metabolic treatment requires careful fluid resuscitation, insulin therapy, and lactate level monitoring since these mechanisms worsen metabolic acidosis [14]. The hyperlactatemia develops with the loss of the pyruvate oxidation and the gain of the pyruvate to lactate process because of the condition of insulin deficiency. Besides that, the fact that the pyruvate and acetyl-CoA are converted into ketones and not gluconeogenic can be interpreted as less lactate being involved and more excreted [15]. It is due to the metabolic imbalance that enables the high levels of lactate: it shows the amount of lactate-related metabolic stress and hypoperfusion when compared to lactate and hypoxia that cause tissue and oxygen transportation damage [16]. The metabolism of DKA through lactate is the key to fluid and insulin therapy judicious use, hyperlactatemia assessment, and, above all, metabolic recoveries to diseased states assessment during the treatment process [17]. Several mechanisms can account for high levels of lactate in DKA that encompass anaerobic glycolysis, soaring levels of catecholamine, and stifled tissue oxygenation [18]. This, nonetheless, focuses on the perception of the lactate levels considering other metabolic and hemodynamic conditions [19]. More importantly, the alterations in the lactate sample are indications of the direct intervention effects and, therefore, the effects of an intervention as a whole because enhancing the levels of lactate indicates enhancing the clinical condition. In addition to that, demographic and socioeconomic characteristics such as age, location, and income level also affect the prevalence rates of high lactate levels in DKA [20]. In our research, it is demonstrated that point-of-care lactate has a prognostic value in DKA, which is increased in metabolic stress, is correlated with the severity of DKA, and has a correlation with increased in-hospital mortality. Out of 131 patients (mean age 47.14 ± 16.49 years; mean T2DM duration 1.72 ± 1.24 years), 48.9% had high levels of lactate, and 60.9% of deaths were found within the group, and most patients reported with moderate levels of DKA.

The study's observational design and relatively small sample size may limit the strength of causal inferences, and unmeasured confounders such as comorbidities, infection severity, and concurrent medications could have influenced lactate levels. Lactate was measured only at admission, preventing assessment of trends during treatment. Future research should include larger, longitudinal studies with serial lactate measurements to better understand its prognostic role in DKA management.

CONCLUSIONS

To sum up, point-of-care testing with lactate is useful in the management of diabetic ketoacidosis since it provides quick, practical data regarding the metabolic condition of the patient. It enables timely evaluation of the risk, contributes to early introduction of individualized measures, and can even influence improved results. The prognostic significance of the socioeconomic status elements is represented in the high level of lactate in patients with regard to their demographic and socioeconomic factors in a significant portion of patients. However, these consequences should be diluted with clinical studies, established guidelines, and a fair amount of anticipation of the pitfalls in the diagnostic. As the burden of diabetes continues to increase in the world today, particularly in the lower- and middle-income nations, point-of-care lactate detection will play a central role in timely detection of patients at high-risk with acute metabolic crisis and improved management of the situation.

DOI: https://doi.org/10.54393/pjhs.v7i2.3700

Authors' Contribution

Conceptualization: IM
Methodology: IM, RJD, SI, FZ
Formal analysis: RJD, FA, FZ
Writing and Drafting: SI, SA
Review and Editing: IM, RJD, FA, SI, FZ, SA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Taşkın G, Yılmaz M, Yılmaz S, Şirin H, Sapmaz H, Taşlıgil S *et al.* Lactate Kinetics in Intensive Care Unit Admissions Due to Diabetic Ketoacidosis. Gulhane Medical Journal. 2021 Sep; 63: 212-217. doi: 10.4274/gulhane.galenos.2021.29290.

[2] Stewart C, Chan PS, Kennedy K, Swanson MB, Girotra S. American Heart Association. Hospital Variation in Epinephrine Administration Before Defibrillation for Cardiac Arrest Due to Shockable Rhythm. Critical care medicine. 2024 Jun; 52(6): 878-886. doi: 10.1097/CCM.0000000000006203.

[3] Sheryazdanova D and Laryushina Y. 1, 5-Anhydroglucitol in Type 2 Diabetes Mellitus Patients with ST Elevation Myocardial Infarction. Journal of Clinical Medicine of Kazakhstan. 2021; 18(4): 52-57. doi: 10.23950/jcmk/11042.

[4] Bjerg LN, Thomsen HH, Sandfeld-Paulsen B. Evaluating Agreement Between Separate Capillary Sampling Sites and Venous Concentrations Of B-Hydroxybutyrate Measured by a Point-Of-Care Device and Liquid Chromatography Tandem Mass Spectrometry. Scandinavian Journal of Clinical and Laboratory Investigation. 2025 Jan; 85(1): 58-63. doi: 10.1080/00365513.2025.2460198.

[5] Adeva-Andany M, López-Ojén M, Funcasta-Calderón R, Ameneiros-Rodríguez EA, Donapetry-García C, Vila-Altesor M *et al.* Comprehensive Review of Lactate Metabolism in Human Health. Mitochondrion. 2014 Jul; 17: 76-100. doi: 10.1016/j.mito.2014.05.007.

[6] Söbü E, Yükselmiş U, Köle MT, Akın Y, Esen FH. Lactate Levels in Diabetic Ketoacidosis: Is There an Association Between the Severity of Acidosis and Length of Hospital Stay with Elevated Lactate Levels? Istanbul Medical Journal. 2025 Feb; 26(1): 11-15. doi: 10.4274/imj.galenos.2024.39024.

[7] Yang Y, Zhou T, Zhao X, Cai Y, Xu Y, Gang X *et al.* Main Mechanisms and Clinical Implications of Alterations in Energy Expenditure State Among Patients with Pheochromocytoma and Paraganglioma: A Review. Medicine. 2024 Apr; 103(17): 37916. doi: 10.1097/MD.0000000000037916.

[8] Eledrisi MS and Elzouki AN. Management of Diabetic Ketoacidosis in Adults: A Narrative Review. Saudi Journal of Medicine and Medical Sciences. 2020 Sep; 8(3): 165-173. doi: 10.4103/sjmms.sjmms_478_19.

[9] Kumar A, Anstey C, Doola RE, McIlroy P, Whebell S, Shekar K *et al.* Associations Between Late Lactate Clearance and Clinical Outcomes in Adults with Hyperlactataemia in the Setting of Diabetic Ketoacidosis. Journal of Clinical Medicine. 2024 Aug; 13(16): 4933. doi: 10.3390/jcm13164933.

[10] Elfiky OA, Assar E, Rachwan MT, Mohamed S. Frequency and prognostic significance of serum lactate in children with diabetic ketoacidosis. Benha Medical Journal. 2023; 40: 137–145. doi: 10.21608/bmfj.2023.186933.1745.

[11] Munsakul N, Manosroi W, Buranapin S. Predictors and Predictive Score of In-Hospital Mortality in Diabetic Ketoacidosis: A Retrospective Cohort Study. Medicina. 2024 Nov; 60(11): 1833. doi: 10.3390/medicina60111833.

[12] Moraes RB, Friedman G, Lisboa T, Viana MV, Hirakata V, Czepielewski MA. Comparison of Cumulative Incidence Analysis and Kaplan-Meier for Analysis of Shock Reversal in Patients with Septic Shock. Journal of Critical Care. 2012 Jun; 27(3): 317. doi: 10.1016/j.jcrc.2011.06.006.

[13] Lee S, Song J, Lee S, Kim SJ, Han KS, Lee S. Impact of Point-of-Care Lactate Testing for Sepsis on Bundle Adherence and Clinical Outcomes in the Emergency Department: A Pre–Post Observational Study. Journal of Clinical Medicine. 2024 Sep; 13(18): 5389. doi: 10.3390/jcm13185389.

[14] Wang J and Ji M. The 6-Hour Lactate Clearance Rate in Predicting 30-Day Mortality in Cardiogenic Shock. Journal of Intensive Medicine. 2024 Jul; 4(3): 393-399. doi: 10.1016/j.jointm.2024.01.003.

[15] Liu Y, Mo W, Wang H, Shao Z, Zeng Y, Bi J. Feature Selection and Risk Prediction for Diabetic Patients with Ketoacidosis Based on MIMIC-IV. Frontiers in Endocrinology. 2024 Mar; 15: 1344277. doi: 10.3389/fendo.2024.1344277.

[16] Suarez DF, Ancona R, Schneider RM, Haas N, Griffey RT. Triage Point-of-Care Ketone Measurements: Association with Diabetic Ketoacidosis and Severity. Journal of Diabetes Science and Technology. 2025

DOI: https://doi.org/10.54393/pjhs.v7i2.3700

Aug: 1-2. doi: 10.1177/19322968251345500.

[17] Mutuku PM, Joshi MD, Genga EK, Kagima JW. Point-of-Care Lactate as a Predictor of 7-Day Morbidity and Mortality in Critically Ill Patients Presenting to the Emergency Department in Kenyatta National Hospital. Journal of the Pan-African Thoracic Society. 2023; 4(3): 115-23. doi: 10.25259/JPATS_8_2023.

[18] Aydin Ö and Yurttaş TA. Acil Serviste Diyabetik Ketoasidozda Mortalite Prediktörü Olarak Laktat Düzeyleri. Turkish Journal of Clinics and Laboratory. 2025; 16(1): 1-7.

[19] Song C, Dhaliwal S, Bapat P, Scarr D, Bakhsh A, Budhram D *et al*. Point-of-Care Capillary Blood Ketone Measurements and The Prediction of Future Ketoacidosis Risk in Type 1 Diabetes. Diabetes Care. 2023 Nov; 46(11): 1973-1977. doi: 10.2337/dc23-0840.

[20] Eltom EH, Alali AO, Alanazi RK, Alanazi AA, Albalawi MA, Alanazi SA *et al*. Exploring Awareness Levels of Diabetic Ketoacidosis Risk Among Patients with Diabetes: A Cross-Sectional Study. Clinics and Practice. 2024 Dec; 14(6): 2681-2692. doi: 10.3390/clinpract14060211.

DOI: https://doi.org/10.54393/pjhs.v7i2.3887

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Frequency of Post-Thyroidectomy Hypoparathyroidism in Surgical Patients

Hassan Shoukat[1*], Hafiz Ashfaq Ahmad[2], Abbas Hassnain Kazmi[1], Kiran Abdul Rasheed[3], Nasir Mukhtar[1], Madeeha Shahid[1] and Tuba Binte Qasim[4]

[1]Department of Surgery, Niazi Medical and Dental College, Sargodha, Pakistan
[2]Department of Surgery, Dr. Faisal Masood Teaching Hospital, Sargodha, Pakistan
[3]Department of Surgery, Ghurki Trust Teaching Hospital, Lahore, Pakistan
[4]Barking Havering and Redbridge University Hospitals, National Health Service Trust, United Kingdom

ARTICLE INFO

Keywords:
Hypoparathyroidism, Post-Thyroidectomy Hypoparathyroidism, Total Thyroidectomy, Post-operative

How to Cite:
Shoukat, H., Ahmad, H. A., Kazmi, A. H., Rasheed, K. A., Mukhtar, N., Shahid, M., & Qasim, T. B. (2026). Frequency of Post-Thyroidectomy Hypoparathyroidism in Surgical Patients: Post-Thyroidectomy Hypoparathyroidism in Surgical Patients. Pakistan Journal of Health Sciences, 7(2), 108-111. https://doi.org/10.54393/pjhs.v7i2.3887

***Corresponding Author:**
Hassan Shoukat
Department of Surgery, Niazi Medical and Dental College, Sargodha, Pakistan
hassanshoukat1984@gmail.com

Received Date: 10th December, 2025
Revised Date: 23rd January, 2026
Acceptance Date: 29th January, 2026
Published Date: 28th February, 2026

ABSTRACT

The risk of post-operative hypoparathyroidism is increased after thyroidectomy. It can be transient or permanent, potentially leading to severe neuromuscular and respiratory complications. **Objectives:** To identify postoperative hypoparathyroidism based on serum post-thyroidectomy hypoparathyroidism (PTH) levels after total thyroidectomy. **Methods:** This was a cross-sectional study, conducted after total thyroidectomy on 88 participants at the Department of Surgery, Niazi Welfare Foundation Teaching Hospital, Sargodha, from 1st October, 2024 to 30th November, 2025. Patients with an age range of 22 to 62 years undergoing total thyroidectomy were included in this study, while others with hyperparathyroidism, a history of neck radiotherapy, preoperative hypocalcemia, or preoperative suspicion of malignancy were excluded. A predesigned form was used to collect data regarding demographics, personal habits, comorbidities, reasons for performing total thyroidectomy, and postoperative hypoparathyroidism. Serum PTH level of <10 pg/ml was marked as diagnostic criteria for postoperative hypoparathyroidism. SPSS version 26.0 was used to analyze data. **Results:** In this Study, out of 88 participants, there were 25 male patients and 63 females. The patients' ages ranged from 22 to 62 years, with a mean age of 40.56 ± 8.23 years. 30 participants belong to the age group of 22-42 years, whereas 58 participants were in the age range of 43 to 62 years. Post-operative hypoparathyroidism was revealed in 19 (21.59%) participants. **Conclusions:** Postoperative hypoparathyroidism was observed in the majority of patients after total thyroidectomy.

INTRODUCTION

Thyroid surgery is a commonly performed and generally safe procedure used to treat various benign as well as malignant disorders. However, it carries risks of hemorrhage, laryngeal nerve injury, and, potentially leading to voice changes or airway obstruction—infection, hypothyroidism, and hypoparathyroidism (HPT) [1]. The most frequent surgical procedure leading to hypoparathyroidism is total thyroidectomy [2]. HPT results from parathyroid gland dysfunction caused by damage, inadvertent removal, or devascularization of parathyroid glands in the surgical process [3]. Hypoparathyroidism is also considered a major complication of neck surgeries, especially those involving the anterior triangle. Approximately 75% cases of anterior neck surgery progress to acquired hypoparathyroidism [4]. Postoperative hypoparathyroidism may be transient or permanent [5, 6]. Many patients who experience immediate postoperative hypoparathyroidism are classified as transient cases [7]. However, if normal function is not restored within six months, the condition is classified as permanent hypoparathyroidism [8]. Transient hypoparathyroidism risk after thyroid surgery ranges from

DOI: https://doi.org/10.54393/pjhs.v7i2.3887

6.9% to 46% and, 0.4% to 33% of cases progress to permanent hypoparathyroidism [9]. Certain thyroid conditions, like thyrotoxicosis, Graves' disease, thyroid carcinoma, and recurrent goiter, are related with an increased risk of both transient and permanent postoperative hypoparathyroidism [10]. Additional risk factors include low preoperative calcium levels, failure to identify all parathyroid glands during surgery, and parathyroid auto-transplantation [11]. 1.7% to 68% thyroidectomy cases present with postoperative hypocalcemia due to hypoparathyroidism and manifest as elevated or high-normal serum phosphorus levels, potentially leading to severe neuromuscular and respiratory complications [12]. The clinical manifestations of hypoparathyroidism vary in severity, ranging from tingling sensations to paresthesia, and muscle cramps leading to tetany, abnormal cardiac rhythms, seizures, cardiac failure, and laryngospasm [13]. The incidence of hypoparathyroidism has significantly declined due to improved anatomical knowledge and the presence of specialized endocrine units with high case volumes and experienced professionals. The occurrence of permanent hypoparathyroidism following thyroid surgery ranges from 0.9% to 1.6% [14].

Limited data are available on this research. So, this study doesn't work with a large sample size. As a result, a desire to establish whether the early postoperative serum parathyroid hormone (PTH) can be used as a reliable indicator of hypoparathyroidism in the immediate postoperative period in the situation of total thyroidectomy, particularly in cases where the sample sizes are small and surgical outcomes can be surgeon-dependent. Iatrogenic injury to the parathyroid glands or their blood supply is largely preventable when handled by skilled surgeons. This study aimed to identify postoperative hypoparathyroidism based on serum PTH levels after total thyroidectomy.

METHODS

A cross-sectional study was done during the period of 1st October, 2024 to 30th November, 2025 at the Department of Surgery, Niazi Welfare Foundation Teaching Hospital (NWFTH), Sargodha, after taking ethical approval letter (NM&DC-IRB-96) from the Institutional Review Board (IRB) committee having Ref No: IRB/NM&DC/598. Data collection was done after informed consent from patients and attendants. Sample size was calculated on open Epi software with the data of post-operative hypoparathyroidism from a previous research study [15] using 95% confidence interval and 7% margin of error, and the calculated sample size of the study was 88. A non-probability convenience sampling was utilized to collect data from study participants. Patients with an age range of 22 to 62 years undergoing total thyroidectomy were included in this study. An exclusion criterion was patients with hyperparathyroidism, a history of neck radiotherapy, preoperative hypocalcemia, or preoperative suspicion of malignancy. A predesign form was used to document preoperative history pertaining to patients' demographics, physical examination findings, thyroid function test, lab investigation including PTH and serum calcium levels, and ultrasound result of thyroid gland. Total thyroidectomy was done through the capsular dissection technique by experienced surgeons specialized in thyroid surgery. Consultants performed the procedure with careful identification and preservation of the parathyroid glands along with their vascular supply. After 2 days of total thyroidectomy, patients' PTH levels were again investigated to compare pre- and post-data, and serum PTH level of <10 pg/ml was marked as diagnostic criteria for postoperative hypoparathyroidism [16].

The data were gathered and processed in SPSS 26.0. Frequencies and percentages were determined in qualitative variables, whereas means and standard deviation (SD) were used to determine the quantity of the qualitative variables in the quantitative variables. Fisher's exact test was applied to see the gender and age-wise distribution of hypoparathyroidism post-operatively at a significance level of <0.05.

RESULTS

Eighty-eight patients were referred for a total thyroidectomy. A total of 88 patients (25 men and 63 women) were subjects in this study. The age of the patients was varied between 22 and 62 years, with a mean age of 40.56 and a standard deviation of 8.23 years. 30 patients were in the age group of 22-42 years, and 58 patients were in the age group of 43-62 years. In study participants, mean BMI was 26.77 ± 3.48 Kg/m^2, height was 155.4 ± 8.46 cm, and weight was 72.2 ± 10.23 Kg (Table 1).

Table 1: Demographics of Study Participants

Variables	n	Mean ± SD
Gender		
Male	25	–
Female	63	
Age in Years		
22-42	30	40.56 ± 8.23
43-62	58	
Others		
BMI (kg/m^2)	–	26.77 ± 3.48
Height (cm)	–	155.4 ± 8.46
Weight (kg)	–	72.2 ± 10.23

Post-operative hypo-parathyroidism was revealed in 19(21.59%) participants. Gender distribution depicted that out of 25 male participants, hypo-parathyroidism was

DOI: https://doi.org/10.54393/pjhs.v7i2.3887

evident in 9 patients, while 10 females were identified as having PTH <10pg/ml. According to age category,12 patients in the age group 22-42 years had PTH levels less than 10pg/ml, and similarly 7 patients of hypoparathyroidism were in the age group of 43-62 years. Mean pre- and post-operatively PTH levels were 25.76 ± 9.78 and 16.78 ± 2.34, respectively (Table 2).

Table 2: Age- and Gender-Based Categorization of Hypoparathyroidism in the Participants

Characteristics	Hypoparathyroidism (PTH<10pg/ml)		p-value
	Yes	No	
Gender			
Male	9	16	0.040
Female	10	53	
Age (Years)			
22-42	12	18	0.005
43-62	7	51	

DISCUSSION

The surgery of benign multinodular diseases was still an issue of debate over the years particularly to determine whether the option of total thyroidectomy or near-total thyroidectomy should be regarded as a gold standard. Thyroid surgery carries the risk of hypoparathyroidism (parathyroid insufficiency) and recurrent laryngeal nerve damage [7]. Both can significantly impact the quality of life and strain healthcare resources. Hypoparathyroidism after thyroid surgery is less common in hospitals with specialized thyroid units, but it does tend to occur more frequently in older women [17, 18]. This study found a 21.59% rate of hypoparathyroidism, which can be attributed to surgical trauma to the gland, resulting in postoperative hypoparathyroidism. A Pakistani study showed a much higher rate (47.5%) of hypoparathyroidism after total thyroidectomy [19]. Additionally, one study found no significant difference in PTH levels during and immediately after thyroidectomy [20]. These findings align with the results of the current study. Similarly, a prospective study reported 17.2% hypoparathyroidism cases after total thyroidectomy [21]. Another study found that the incidence of transient hypoparathyroidism was also found to be highly increased in the total thyroidectomy (TT) group, which is in line with the results of the study [8]. On the same note, a different study has noted a reduced incidence of hypoparathyroidism among patients undergoing near-total thyroidectomy than those undergoing total thyroidectomy [17]. Akgun et al. also reported hypoparathyroidism cases following total thyroidectomy, particularly when combined with radical neck dissection. These findings are consistent with the results of the study [22].

This study was conducted at a single center with a limited sample size and short follow-up, which restricts the generalizability of the findings. Additionally, it focused solely on immediate postoperative outcomes. Future research should include multicenter follow-up studies with larger sample sizes to enhance the applicability of the results. Although the study offers valuable insights for improving postoperative management in patients undergoing total thyroidectomy.

CONCLUSIONS

The study reveals that postoperative hypoparathyroidism is a serious and potentially life-threatening outcome after total thyroidectomy. The early recognition using PTH levels is crucial for minimizing the risk of hypoparathyroidism in clinical practice.

Authors' Contribution

Conceptualization: HS
Methodology: HS, HAA, NM, MS
Formal analysis: AHK, TBQ
Writing and Drafting: HAA, KAR
Review and Editing: HS, HAA, AHK, KAR, NM, MS, TBQ

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Hussein M, Toraih E, Issa PP, Omar M, Aboueisha M, Buti Y *et al.* From Ablation to Operation: Unraveling the Surgical Outcomes and Complications of Thyroidectomy After Radiofrequency Ablation. Surgery. 2024 Jan; 175(1): 146-52. doi: 10.1016/j.surg.2023.09.025.

[2] Aghdam AM and Rousta F. Investigating the Risk Factors of Hypoparathyroidism after Total Thyroidectomy. Eurasian Journal of Chemical, Medicinal and Petroleum Research. 2023 May; 2(2): 147-58.

[3] Clarke BL. Hypoparathyroidism: Update Of Guidelines from the 2022 International Task Force. Archives of Endocrinology and Metabolism. 2022 Dec; 66(5): 604-10. doi: 10.20945/2359-3997000000549.

[4] Rao SS, Rao H, Moinuddin Z, Rozario AP, Augustine T. Preservation of Parathyroid Glands During Thyroid and Neck Surgery. Frontiers in Endocrinology. 2023 May; 14: 1173950. doi: 10.3389/fendo.2023.1173950.

[5] Hadedeya D, Kay J, Attia A, Omar M, Shalaby M, Youssef MR *et al.* Effect of Postsurgical Chronic

DOI: https://doi.org/10.54393/pjhs.v7i2.3887

Hypoparathyroidism on Morbidity and Mortality: A Systematic Review and Meta-Analysis. Gland Surgery. 2021 Oct; 10(10): 3007. doi: 10.21037/gs-21-181.

[6] Sitges-Serra A. Etiology and Diagnosis of Permanent Hypoparathyroidism After Total Thyroidectomy. Journal of Clinical Medicine. 2021 Feb; 10(3): 543. doi: 10.3390/jcm10030543.

[7] Hamny I, Chanson P, Borson-Chazot F. New directions in the Treatment of Hypoparathyroidism. In Annales d'Endocrinologie. 2023 Aug; 84(4): 460-465. doi: 10.1016/j.ando.2023.04.001.

[8] Graceffa G, Lopes A, Orlando G, Mazzola S, Vassallo F, Curione F *et al*. Risk Factors for Transient Hypoparathyroidism After Total Thyroidectomy: Insights from A Cohort Analysis. Journal of Clinical Medicine. 2024 Jun; 13(11): 3326. doi: 10.3390/jcm 13113326.

[9] Maheshwari M and Khan IA. Risk Factors for Transient and Permanent Hypoparathyroidism Following Thyroidectomy: A Comprehensive Review. Cureus. 2024 Aug; 16(8). doi: 10.7759/cureus.66551.

[10] Ning K, Yu Y, Zheng X, Luo Z, Jiao Z, Liu X *et al.* Risk Factors of Transient and Permanent Hypoparathyroidism After Thyroidectomy: A Systematic Review and Meta-Analysis. International Journal of Surgery. 2024 Aug; 110(8): 5047-62. doi: 10.1097/JS9.0000000000001475.

[11] Privitera F, Centonze D, La Vignera S, Condorelli RA, Distefano C, Gioco R *et al*. Risk Factors for Hypoparathyroidism After Thyroid Surgery: A Single-Center Study. Journal of Clinical Medicine. 2023 Mar; 12(5): 1956. doi: 10.3390/jcm12051956.

[12] Jan BS, Alamri AH, Alkaff HH, Almuqati WQ, Sayed SI, Abdelmonim SK *et al.* Risk Factors for Postoperative Hypocalcemia Following Total Thyroidectomy: A Retrospective Study. Annals of Saudi Medicine. 2024 Jan; 44(1): 39-47. doi: 10.5144/0256-4947.2024.39.

[13] Cipriani C and Bilezikian JP. Clinical Presentation of Hypoparathyroidism. Journal of the Endocrine Society. 2021 Mar; 5(3): bvab003. doi: 10.1210/jendso/bvab003.

[14] Annebäck M, Hedberg J, Almquist M, Stålberg P, Norlén O. Risk of Permanent Hypoparathyroidism After Total Thyroidectomy for Benign Disease: A Nationwide Population-Based Cohort Study from Sweden. Annals of Surgery. 2021 Dec; 274(6): e1202-8. doi: 10.1097/SLA.0000000000003800.

[15] Naushad A, Sattar S, Salik M, Wajid M, Khalid F, Hussain A *et al.* Frequency and Risk Factors of Permanent Hypoparathyroidism After Total Thyroidectomy: An Experience at A Tertiary Care Hospital in Pakistan. Ear, Nose and Throat Journal. 2025 Dec; 104(12): NP846-51. doi: 10.1177/0145561323 1173455.

[16] Aimon S, Altaf HN, Latif S, Farooqui F, Khan S, Amir M. Role of Postoperative Intact Parathyroid Hormone Levels in Predicting Hypocalcaemia After Thyroidectomy. Journal of College of Physicians and Surgeons Pakistan. 2024 Jul; 34(7): 828-31. doi: 10.29271/jcpsp.2024.07.828.

[17] Wang X, Wang SL, Cao Y, Li CQ, He W, Guo ZM. Postoperative Hypoparathyroidism After Thyroid Operation and Exploration of Permanent Hypoparathyroidism Evaluation. Frontiers in Endocrinology. 2023 May; 14: 1182062. doi: 10.3389/fendo.2023.1182062.

[18] Nagel K, Hendricks A, Lenschow C, Meir M, Hahner S, Fassnacht M *et al*. Definition and Diagnosis of Postsurgical Hypoparathyroidism After Thyroid Surgery: Meta-Analysis. British Journal of Surgery. 2022 Oct; 6(5): zrac102. doi: 10.1093/bjsopen/zrac 102.

[19] Randhawa SR, Iqbal MS, Fatima T, Khalid I, Sajid M. Comparison of Frequency of Hypoparathyroidism in Total Thyroidectomy (TT) versus Near-Total Thyroidectomy (NTT) Patients. Journal of University Medical and Dental College. 2023 Jan; 14(1): 560-3. doi: 10.37723/jumdc.v14i1.753.

[20] Metere A, Biancucci A, Natili A, Intini G, Graves CE. PTH After Thyroidectomy as a Predictor of Post-Operative Hypocalcemia. Diagnostics. 2021 Sep; 11(9): 1733. doi: 10.3390/diagnostics11091733.

[21] Rani S. Risk Factors of Hypoparathyroidism After Total Thyroidectomy. Journal of Surgery Pakistan. 2023 Dec; 28(4): 118-21.

[22] Akgun IE, Unlu MT, Aygun N, Kostek M, Tufan AE, Yanar C *et al.* The Reality of Hypoparathyroidism After Thyroidectomy: Which Risk Factors Are Effective? Single-Center Study. Sisli Etfal Hastanesi Tip Bulteni. 2022 Jun; 56: 262-9. doi: 10.14744/SEMB.2022.24356.

DOI: https://doi.org/10.54393/pjhs.v7i2.3709

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Frequency of ACS among Patients Presenting with Atypical Presentation in the National Institute of Cardiovascular Diseases Emergency Room

Masroor Tariq[1*], Kamran Ahmed Khan[1], Rabel Shafi[1], Kanwal Fatima Aamir[1] and Iram Jehan Balouch[1]

[1]Department of Adult Cardiology, National Institute of Cardiovascular Diseases, Karachi, Pakistan

ARTICLE INFO

Keywords:
Acute Coronary Syndrome, Atypical Presentation, Dyspnea, Emergency Department, Troponin

How to Cite:
Tariq, M., Khan, K. A., Shafi, R., Aamir, K. F., & Balouch, I. J. (2026). Frequency of ACS among Patients Presenting with Atypical Presentation in the National Institute of Cardiovascular Diseases Emergency Room: Frequency of ACS among Patients Presenting with Atypical Presentation . Pakistan Journal of Health Sciences, 7(2), 112-116. https://doi.org/10.54393/pjhs.v7i2.3709

***Corresponding Author:**
Masroor Tariq
Department of Adult Cardiology, National Institute of Cardiovascular Diseases, Karachi, Pakistan
masroortariq@gmail.com

Received Date: 29th November, 2025
Revised Date: 31st January, 2026
Acceptance Date: 3rd February, 2026
Published Date: 28th February, 2026

ABSTRACT

Acute coronary syndrome (ACS) classically presents with chest pain; however, many patients present atypically, which can delay diagnosis and treatment. **Objectives:** To determine the frequency of ACS among patients presenting with atypical symptoms to the emergency room of the National Institute of Cardiovascular Diseases (NICVD), Karachi. **Methods:** This prospective cross-sectional study was conducted in the NICVD emergency room from 28 May to 27 September 2025. Adults aged 18-80 years presenting with atypical symptoms (dyspnea, fatigue, epigastric pain, dizziness, or syncope ± chest pain) were consecutively enrolled (n=165). ACS was defined by ischemic ECG changes and/or elevated troponin I/T and confirmed by a consultant cardiologist. Associations were assessed using Chi-square or Fisher's exact tests; $p<0.05$ was considered statistically significant. **Results:** Mean age was 61.8 ± 12.6 years; 54.5% were male. ACS was diagnosed in 49 patients (29.7%). Dyspnea was the most common symptom (40.0%) and was significantly associated with ACS (51.0% vs 35.3%; p = 0.031). ACS was more frequent in patients aged ≥60 years (36.5% vs 18.9%; p=0.012). Hypertension (p=0.021), diabetes (p=0.038), and obesity (p=0.047) were significantly associated with ACS. **Conclusions:** Approximately one in three patients presenting atypically in the NICVD emergency room had ACS. Older age, dyspnea, hypertension, diabetes, and obesity were significantly associated with ACS, supporting early ECG and troponin testing in atypical presentations.

INTRODUCTION

Acute coronary syndrome (ACS) includes a spectrum of conditions caused by an acute reduction in myocardial blood flow and remains a major cause of emergency presentations worldwide [1, 2]. Typical ACS symptoms include central chest pain or pressure with radiation to the arm or jaw, often accompanied by autonomic symptoms or dyspnea [3]. However, a clinically important proportion of patients present without classical chest pain and instead report non-classical symptoms such as dyspnea, fatigue, epigastric discomfort, dizziness, or syncope [3-6]. These atypical presentations increase diagnostic uncertainty in the emergency department (ED) and can contribute to delayed recognition, delayed reperfusion/medical therapy, and worse outcomes [6, 7]. Multiple studies have shown that ACS without chest pain is not rare and may account for roughly one-quarter to one-third of ACS cases in some cohorts [8, 9]. Older adults and patients with cardiometabolic comorbidities may be more likely to present atypically and may experience greater diagnostic delays [10, 8]. Because ED triage and early decision-making frequently rely on symptoms, atypical presentations pose a consistent challenge and may lead to missed ischemia if objective testing is not performed promptly [11].

In Pakistan, local evidence regarding the frequency of ACS

DOI: https://doi.org/10.54393/pjhs.v7i2.3709

among patients presenting with atypical symptoms in high-volume emergency cardiac settings remains limited. This study defines this gap. This study aimed to determine the frequency of ACS among adults presenting with atypical symptoms to the NICVD emergency room in Karachi and to identify clinical factors significantly associated with ACS, to support earlier recognition and reduce delays in care.

METHODS

This prospective cross-sectional study was conducted at the Emergency Room of the National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan, from 28 May to 27 September 2025. Ethical approval was obtained from the Institutional Review Board of NICVD, Karachi (IRB Ref No: IRB-08/2025). Written informed consent was taken from all participants before enrollment. A total of 165 patients were enrolled using consecutive non-probability sampling. The sample size was calculated using the World Health Organization (WHO) formula for a single proportion, assuming a 30% prevalence of ACS among atypical presentations, a 7% margin of error, and a 95% confidence level. Adults aged 18–80 years presenting with atypical symptoms such as dyspnea, fatigue, epigastric pain, dizziness, or syncope, with or without chest pain, and who provided informed consent were included. Patients were excluded if they had: prior diagnosed ACS, known structural heart disease, previous revascularization (PCI or CABG), non-cardiac causes of hemodynamic instability, or use of anti-arrhythmic or anticoagulant therapy at presentation. Atypical symptoms were defined as presentations not classically associated with ischemic chest pain, including dyspnea, fatigue, epigastric pain, dizziness, or syncope without typical ischemic chest pain. [ACS was defined by ischemic ECG changes (ST-segment deviation and/or T-wave abnormalities suggestive of myocardial ischemia) and/or elevated cardiac troponin I or T, in accordance with established guidance, and the final diagnosis was confirmed by a consultant cardiologist [19]. Demographic and clinical information, including age, sex, residence, body mass index (BMI), smoking history, and comorbidities (hypertension, diabetes mellitus, dyslipidemia, and family history of coronary artery disease), were recorded on a structured proforma. All participants underwent physical examination, routine investigations, and a 12-lead ECG within six hours of presentation. Troponin I or T was measured at arrival according to the emergency room protocol. Data were collected daily by trained emergency medicine residents under the supervision of a senior cardiologist; all identifiers were removed before analysis.

Data were analyzed using IBM SPSS Statistics version 25. Continuous variables were summarized as Mean ± SD, and categorical variables as Frequency (%). Normality of continuous variables was assessed using the Shapiro–Wilk test. Associations between ACS and clinical variables were evaluated using Chi-square or Fisher's exact test as appropriate; $p<0.05$ was considered statistically significant. Unadjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated for key clinical risk factors and diagnostic tests to quantify associations.

RESULTS

A total of 165 patients presenting with atypical symptoms suggestive of ACS were included. The mean age was 61.8 ± 12.6 years (range: 24–80 years). Most participants were male (54.5%), and 21.2% were obese (BMI ≥30 kg/m^2). Demographic characteristics are presented. Findings summarize baseline demographic characteristics of adults presenting with atypical symptoms (n=165). Continuous variables are shown as Mean ± SD and categorical variables as Frequency (%). BMI categories are defined using standard cutoffs (Table 1).

Table 1: Demographic Characteristics of Patients with Atypical Symptoms (n=165)

Variables	Frequency (%) / Mean ± SD
Age	
Years	61.8 ± 12.6
Age Range	
Years	24–80
Gender	
Male	90 (54.5%)
Female	75 (45.5%)
Body Mass Index (kg/m^2)	
Normal (18.5–24.9)	58 (35.2%)
Overweight (25.0–29.9)	72 (43.6%)
Obese (≥30.0)	35 (21.2%)
Residence	
Urban	98 (59.4%)
Rural	67 (40.6%)

Dyspnea was the most common atypical symptom (40.0%), followed by fatigue (21.8%), epigastric pain (18.2%), dizziness (12.1%), and syncope (7.9%). Dyspnea showed a statistically significant association with ACS (51.0% vs 35.3%; p=0.031), whereas the other atypical symptoms were not significantly associated with ACS (p>0.05). Results present the frequency of atypical symptoms among participants and compare the ACS vs non-ACS groups. Values are shown as Frequency (%). The p-values were calculated using Chi-square or Fisher's exact test where appropriate (Table 2).

Table 2: Frequency of Atypical Symptoms among Study Participants (n=165)

Symptoms	Total, Frequency (%)	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	p-value
Dyspnea	66 (40.0%)	25 (51.0%)	41 (35.3%)	0.031

DOI: https://doi.org/10.54393/pjhs.v7i2.3709

Fatigue	36 (21.8%)	13 (26.5%)	23 (19.8%)	0.247
Epigastric Pain	30 (18.2%)	10 (20.4%)	20 (17.2%)	0.592
Dizziness	20 (12.1%)	6 (12.2%)	14 (12.0%)	0.971
Syncope	13 (7.9%)	4 (8.2%)	9 (7.8%)	0.934

Cardiovascular risk factors were also compared between the ACS and non-ACS groups. Hypertension was the most prevalent risk factor (61.8%), followed by diabetes mellitus (47.9%) and dyslipidemia (32.7%). Hypertension was significantly associated with ACS (p=0.021), and diabetes mellitus was also significantly associated with ACS (p=0.038). Obesity (BMI ≥30 kg/m^2) was significantly more common among ACS patients (28.6% vs 18.1%; p=0.047). Dyslipidemia, smoking history, and family history of CAD were not significantly associated with ACS (p>0.05). The study compares cardiovascular risk factors between ACS and non-ACS groups. Values are shown as Frequency (%). CAD indicates coronary artery disease. P-values were calculated using Chi-square or Fisher's exact test where appropriate. Additionally, diagnostic findings were evaluated explicitly. Ischemic ECG changes were observed in 41.2% of all participants, and elevated troponin I/T levels in 35.2%. Among patients diagnosed with ACS, ischemic ECG changes were present in 87.8% and elevated troponin in 79.6%, compared with 21.6% and 16.4%, respectively, in non-ACS patients (both p<0.001). The combined positivity of both ECG and troponin was also strongly associated with ACS (p<0.001). The study presents key diagnostic test findings (ECG and troponin) and compares ACS vs non-ACS groups. Values are shown as Frequency (%). ECG indicates electrocardiogram; troponin refers to troponin I or T (Table 3).

Table 3: Distribution of Cardiovascular Risk Factors among Patients and Diagnostic Test Findings among Patients with Atypical Symptoms (n=165)

Symptoms	Total, Frequency (%)	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	p-value
Hypertension	102 (61.8)	38 (77.6)	64 (55.2)	0.021
Diabetes Mellitus	79 (47.9)	29 (59.2)	50 (43.1)	0.038
Dyslipidemia	54 (32.7)	18 (36.7)	36 (31.0)	0.482
Smoking History	51 (30.9)	18 (36.7)	33 (28.4)	0.311
Family History of CAD	31 (18.8)	11 (22.4)	20 (17.2)	0.418
Obesity (BMI ≥30 kg/m^2)	35 (21.2)	14 (28.6)	21 (18.1)	0.047
ECG Changes Suggestive of Ischemia	68 (41.2%)	43 (87.8%)	25 (21.6%)	<0.001
Elevated Troponin I/T	58 (35.2%)	39 (79.6%)	19 (16.4%)	<0.001
Both ECG and Troponin Positive	46 (27.9%)	36 (73.5%)	10 (8.6%)	<0.001

Age ≥60 years was significantly associated with a higher incidence of ACS. Specifically, ACS was more frequent among participants aged ≥60 years compared with those <60 years (36.5% vs 18.9%; p=0.012). There was no significant association between gender and ACS (p=0.871). These results stratify ACS by age group and gender to address the reviewer's statistical questions. Values are shown as Frequency (%). P-values were calculated using the Chi-square test (Table 4).

Table 4: Stratification of ACS by Age and Gender (n=165)

Variables	Category	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	p-value
Age Group (Years)	<60	17 (18.9%)	73 (81.1%)	0.012
	≥60	32 (36.5%)	43 (63.5%)	
Gender	Male	27 (30.0%)	63 (70.0%)	0.871
	Female	22 (29.3%)	53 (70.7%)	

To quantify the strength of association, unadjusted odds ratios (ORs) with 95% CI were calculated for key clinical risk factors and diagnostic tests. Age ≥60 years (OR 3.20), dyspnea (OR 1.91), hypertension (OR=2.81), diabetes mellitus (OR 1.91), and obesity (OR 1.81) showed increased odds for ACS. ECG ischemic changes and elevated troponin had the highest ORs, reflecting a strong diagnostic association with ACS. These results provide unadjusted odds ratios to support reviewer requests regarding "key risk factors" and diagnostic tests. ORs are unadjusted and calculated from the 2×2 group frequencies. CI indicates confidence interval; ECG indicates electrocardiogram (Table 5).

Table 5: Odds Ratios for ACS Based on Key Risk Factors and Diagnostic Findings

Variables	ACS (n=49), Frequency (%)	Non-ACS (n=116), Frequency (%)	OR (95% CI)
Age ≥60 Years	32 (65.3%)	43 (37.1%)	3.20 (1.59–6.43)
Dyspnea	25 (51.0%)	41 (35.3%)	1.91 (0.97–3.75)
Hypertension	38 (77.6%)	64 (55.2%)	2.81 (1.31–6.03)
Diabetes Mellitus	29 (59.2%)	50 (43.1%)	1.91 (0.97–3.77)
Dyslipidemia	18 (36.7%)	36 (31.0%)	1.29 (0.64–2.60)
Obesity (BMI ≥30 kg/m^2)	14 (28.6%)	21 (18.1%)	1.81 (0.83–3.95)
ECG Ischemic Changes	43 (87.8%)	25 (21.6%)	26.09 (9.97–68.27)
Elevated Troponin I/T	39 (79.6%)	19 (16.4%)	19.91 (8.50–46.64)

DISCUSSION

This study provides evidence on the burden of ACS among adults presenting with atypical symptoms in a tertiary cardiac emergency setting in Karachi. Nearly one-third of patients presenting atypically were diagnosed with ACS (29.7%), highlighting that non-classical symptoms in the ED should not be considered low risk by default. Current guideline-based pathways emphasize rapid ECG and cardiac biomarker testing to reduce missed ACS, and our findings support applying these principles even in atypical presentations [12, 13]. Dyspnea was the most common atypical symptom in our cohort (40.0%). Importantly, dyspnea showed a significant association with ACS

DOI: https://doi.org/10.54393/pjhs.v7i2.3709

(p=0.031). This supports prior international observations that ACS can present without chest pain and that dyspnea may be a key "warning symptom," particularly in older adults and comorbid patients [8, 9]. Since dyspnea is common in multiple non-cardiac conditions, the clinical implication is not to over-diagnose ACS, but rather to ensure objective testing (ECG and troponin) is performed early in dyspneic patients with potential ischemic risk features [14, 15]. Age ≥60 years was significantly associated with ACS in this atypical cohort (p=0.012). This finding aligns with literature showing that older adults may have more atypical ischemic symptoms and may face greater diagnostic delays [10, 8]. Hypertension (p=0.021), diabetes mellitus (p=0.038), and obesity (p=0.047) were also significantly associated with ACS in our study. Diabetes is well known to be linked to altered symptom perception and atypical or silent ischemia, and outcomes may be worse when recognition is delayed [16]. Hypertension and obesity reflect increased baseline cardiovascular risk and may contribute to a higher probability of ACS even when presentations are non-classical [17]. ECG ischemic changes and elevated troponin were strongly associated with ACS (both p<0.001), with very high odds ratios. This reinforces the central diagnostic role of ECG and cardiac troponins in suspected ACS and aligns with contemporary recommendations supporting structured ED strategies for rapid rule-out and rule-in [18-20]. Our results emphasize that early ECG and troponin should be prioritized during triage, particularly for older patients or those with hypertension, diabetes, obesity, or dyspnea. From an emergency medicine perspective, these findings support maintaining a low threshold for early ECG and troponin testing among patients presenting atypically, especially those with age ≥60 years or cardiometabolic risk factors. Implementing protocol-based triage pathways may reduce missed ischemia and improve timely management decisions in resource-limited, high-volume settings [7, 14].

This study has limitations. First, it was a single-center study conducted at a tertiary cardiac institute, which may limit generalizability to primary or rural hospitals. Second, the study design was observational and not blinded, raising the possibility of residual confounding. Third, symptom reporting may be affected by recall bias, especially among older or more unwell patients. Finally, the odds ratios presented are unadjusted; larger multicenter studies using multivariable models are recommended to determine independent predictors more robustly.

CONCLUSIONS

Approximately one in three adults presenting with atypical symptoms in the NICVD emergency room had ACS. Dyspnea, age ≥60 years, hypertension, diabetes mellitus, and obesity were significantly associated with ACS. These findings support early ECG and troponin testing for atypical emergency presentations, particularly in older adults and patients with cardiometabolic comorbidities, to reduce diagnostic delay and improve outcomes.

Authors' Contribution

Conceptualization: MT, IJB
Methodology: MT, KAK, KFA, IJB
Formal analysis: KAK, RS, KFA, IJB
Writing and Drafting: MT, KAK, RS, KFA, IJB
Review and Editing: MT, KAK, RS, KFA, IJB

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Rao SV, O'Donoghue ML, Ruel M, Rab T, Tamis-Holland JE, Alexander JH *et al.* 2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients with Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2025 Jun; 85(22): 2135-237.

[2] Byrne R, Rossello X, Coughlan J, Barbato E, Berry C, Chieffo A *et al.* 2023 ESC Guidelines for the Management of Acute Coronary Syndromes. European Heart Journal. 2023 Oct; 44(38): 3720-826.

[3] Van Damme A, Vanderheeren P, De Backer T, Desimpel F. Atypical Presentation of Acute Coronary Syndrome (ACS): A Case Report. Acta Clinica Belgica. 2018 Nov; 73(6): 453-9. doi: 10.1080/17843286.2018.1460019.

[4] Kraler S, Mueller C, Libby P, Bhatt DL. Acute Coronary Syndromes: Mechanisms, Challenges, and New Opportunities. European Heart Journal. 2025 May: ehaf289. doi: 10.1093/eurheartj/ehaf289.

[5] Shehata MA, AlDawsari AA, Saeedi AH, Ibrahim AlAyshan M, Saleh MA *et al.* Acute Coronary Syndrome Diagnosis & Management Approach in Emergency Department: Literature Review. World Journal of Environmental Biosciences. 2022; 11(2-2022): 61-4. doi: 10.51847/Gihy97OwCC.

[6] Hwang SY, Park EH, Shin ES, Jeong MH. Comparison of Factors Associated with Atypical Symptoms in Younger and Older Patients with Acute Coronary Syndromes. Journal of Korean Medical Science.

DOI: https://doi.org/10.54393/pjhs.v7i2.3709

2009 Sep; 24(5): 789. doi: 10.3346/jkms.2009.24.5.789.

[7] Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR *et al.* Missed Diagnoses of Acute Cardiac Ischemia in the Emergency Department. New England Journal of Medicine. 2000 Apr; 342(16): 1163-70. doi: 10.1056/NEJM200004203421603.

[8] Brieger D, Eagle KA, Goodman SG, Steg PG, Budaj A, White K *et al.* Acute Coronary Syndromes without Chest Pain, an Underdiagnosed and Undertreated High-Risk Group: Insights from the Global Registry of Acute Coronary Events. Chest. 2004 Aug; 126(2): 461-9. doi: 10.1378/chest.126.2.461.

[9] Perona M, Cooklin A, Thorpe C, O'Meara P, Rahman MA. Symptomology, Outcomes and Risk Factors of Acute Coronary Syndrome Presentations without Cardiac Chest Pain: A Scoping Review. European Cardiology Review. 2024 Jul; 19: e12. doi: 10.15420/ecr.2023.45.

[10] Canto JG, Rogers WJ, Goldberg RJ, Peterson ED, Wenger NK, Vaccarino V *et al.* Association of Age and Sex with Myocardial Infarction Symptom Presentation and In-Hospital Mortality. Jama. 2012 Feb; 307(8): 813-22. doi: 10.1001/jama.2012.199.

[11] Thompson A, Fleischmann KE, Smilowitz NR, de Las Fuentes L, Mukherjee D, Aggarwal NR *et al.* 2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2024 Nov; 84(19): 1869-969.

[12] Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA *et al.* Fourth Universal Definition of Myocardial Infarction (2018). Journal of the American College of Cardiology. 2018 Oct; 72(18): 2231-64. doi: 10.1016/j.jacc.2018.08.1038.

[13] Ataman MG, Sariyer G, Saglam C, Karagoz A, Unluer EE. Factors Relating to Decision Delay in the Emergency Department: Effects of Diagnostic Tests and Consultations. Open Access Emergency Medicine. 2023 Dec: 119-31. doi: 10.2147/OAEM.S384774.

[14] Torralba F, Navarro A, la Hoz JC, Ortiz C, Botero A, Alarcón F *et al.* HEART, TIMI, and GRACE Scores for Prediction Of 30-Day Major Adverse Cardiovascular Events in the Era of High-Sensitivity Troponin. Arquivos Brasileiros de Cardiologia. 2020 Mar; 114: 795-802.

[15] Jaffe AS, Body R, Mills NL, Aakre KM, Collinson PO, Saenger A *et al.* Single Troponin Measurement to Rule Out Myocardial Infarction: JACC Review Topic of the Week. Journal of the American College of Cardiology. 2023 Jul; 82(1): 60-9. doi: 10.1016/j.jacc.2023.04.040.

[16] Stampouloglou PK, Anastasiou A, Bletsa E, Lygkoni S, Chouzouri F, Xenou M *et al.* Diabetes Mellitus in Acute Coronary Syndrome. Life. 2023 Nov; 13(11): 2226. doi: 10.3390/life13112226.

[17] D'Agostino RB, Grundy S, Sullivan LM, Wilson P, CHD Risk Prediction Group. Validation of the Framingham Coronary Heart Disease Prediction Scores: Results of a Multiple Ethnic Groups Investigation. Journal of the American Medical Association. 2001 Jul; 286(2): 180-7. doi: 10.1001/jama.286.2.180.

[18] Li Z, Tao J, Wang H, Zhang Q, Liu Q, Wang Q *et al.* High-sensitivity Cardiac Troponin I in the Diagnosis of Acute Myocardial Infarction: A Study in Patients with Renal Insufficiency. American Heart Journal Plus: Cardiology Research and Practice. 2025 Oct: 100631. doi: 10.1016/j.ahjo.2025.100631.

[19] Heart Foundation Working Group. Comprehensive Australian Clinical Guideline for Diagnosing and Managing Acute Coronary Syndromes. 2025.

[20] D'Agostino Sr RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM *et al.* General Cardiovascular Risk Profile for Use in Primary Care: The Framingham Heart Study. Circulation. 2008 Feb; 117(6): 743-53. doi: 10.1161/CIRCULATIONAHA.107.699579.

DOI: https://doi.org/10.54393/pjhs.v7i2.3813

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Emotional Intelligence and Academic Performance among MBBS students in Blended Learning Environment: A Correlational Study

Sadia Yaseen[1*], Mamoona Shabbir[2], Nosheen Khurram[3] and Muhammad Ali Raza[1]

[1]Department of Medical Education, Rashid Latif Medical College, Lahore, Pakistan
[2]Department of Medical Education, University of Health Sciences, Lahore, Pakistan
[3]Department of Pathology, Rashid Latif Medical College, Lahore, Pakistan

ARTICLE INFO

Keywords:
Distance Education, Emotional Intelligence, Academic Performance, Blended Learning, Educational Measurement, Examination

How to Cite:
Yaseen, S., Shabbir, M., Khurram, N., & Raza, M. A. (2026). Emotional Intelligence and Academic Performance among MBBS students in Blended Learning Environment: A Correlational Study: EI and Academic performance among MBBS students in Blended Learning Environment. Pakistan Journal of Health Sciences, 7(2), 117-122. https://doi.org/10.54393/pjhs.v7i2.3813

***Corresponding Author:**
Sadia Yaseen
Department of Medical Education, Rashid Latif Medical College, Lahore, Pakistan
sadiayaseendme@gmail.com

Received Date: 10th December, 2025
Revised Date: 31st January, 2026
Acceptance Date: 10th February, 2026
Published Date: 28th February, 2026

ABSTRACT

Emotional intelligence (EI) is a critical factor influencing academic performance (AP) and professional competence in medical education. **Objectives:** To assess the correlation between EI and AP among MBBS students across different professional years, age groups, gender, and achievement levels within a blended learning environment. **Methods:** A correlational study was conducted at Rashid Latif Medical College, Lahore, from January to June 2023 after ethical approval. Stratified random sampling selected 300 MBBS students eligible for their annual professional examination, with full exposure of students to a blended learning curriculum. EI was measured using the validated National Health Service emotional intelligence questionnaire, and AP was assessed using annual professional marks. Data analysis was performed in SPSS version 25.0. Non-normal variables were reported as median IQR, and normally distributed variables as mean ± SD. Spearman's rank correlation evaluated the relationship between EI and AP, and Kruskal-Wallis tests compared groups. Statistical significance was set as $p<0.05$ and 95% confidence interval. **Results:** Overall, EI showed a moderate positive correlation with AP ($r=0.557$, $p<0.001$). The strongest correlation was observed in final year students ($r=0.747$, $p<0.001$). Third Year students had the highest mean emotional intelligence (202 ± 12.8, $p<0.001$). Positive correlation was consistent across genders and age groups. High achievers demonstrated significantly higher emotional intelligence than low achievers. **Conclusions:** Blended learning can enhance emotional intelligence and academic performance, particularly in early clinical years. Integrating structured emotional intelligence development into blended curricula may improve engagement and professional preparedness, including unforeseen challenges such as future pandemics.

INTRODUCTION

Emotional intelligence (EI) has been recognized as a critical non-cognitive skill for success in medical education and practice [1, 2]. High EI is associated with better communication, empathy, stress management, and adaptability. These competencies are essential for MBBS students coping with demanding academic and clinical workloads. Academic performance (AP) is typically measured through continuous assessment and professional examinations, and remains a central benchmark of medical students' success; however, it is influenced by multiple factors like cognitive, emotional, and environmental factors [3, 4]. The COVID-19 pandemic triggered a paradigm shift in medical education with institutions rapidly adopting a hybrid or blended learning model, a structured combination of face-to-face and online teaching modalities [5-7]. In this environment, students explore both physical and virtual platforms requiring greater self-directed learning and digital literacy. These conditions can alter the dynamics between emotional competencies and learning outcomes. The

DOI: https://doi.org/10.54393/pjhs.v7i2.3813

reduced in-person contact may challenge emotional regulation in online interaction, while asynchronous learning demands sustained self-motivation, both areas where EI can play a decisive role [8]. While literature documents a modest but significant relationship between EI and academic performance in traditional medical education settings, most evidence predates the widespread implementation of hybrid learning [2]. Effective e-learning requires appropriate use of modern educational tools as well as attention to emotional attitude towards online learning [9, 10].

Current studies often overlook detailed influences of demographic variables such as age, gender, and year of study, and almost none examined this relationship exclusively within a hybrid learning context, which leaves a critical knowledge gap. No recent studies in South Asian medical schools and very few globally have systematically explored the correlation between EI and academic outcomes across diverse demographic strata within a hybrid/ blended learning framework. Given the rapid post-pandemic institutionalization of blended model, understanding this relationship is essential to inform student support, curriculum design, and targeted intervention. By examining EI and academic performance among MBBS students engaged in blended learning, this study provides timely and context-specific evidence to guide interventions that fosters both emotional skills and academic achievement. This study aims to determine the correlation between emotional intelligence and academic performance among MBBS students of different age groups, all professional years exposed to a hybrid learning environment, as well as to find the level of emotional intelligence among high achievers and low achievers.

METHODS

This correlational study was conducted at Rashid Latif Medical College, Lahore (RLMC), in six months (January-June 2023) to find relationships between EI and AP. Stratified random sampling was used via the lottery method. MBBS students eligible for their annual professional examination (more than 75% attendance) and who had full exposure to blended learning during the academic year were included. Students who were excluded from the examination were excluded from the study. The blended learning model at RLMC combined 60% online and 40% face-to-face instruction using platforms like Zoom, Google Meet, Socrative, and Kahoot for content delivery and assessment purposes. The targeted population was MBBS students from all professional years enrolled at RLMC. The sample size was calculated using a 5% significance level, 90% study power, and an anticipated correlation coefficient of 0.51, resulting in 60 students per year (Total n=300) [11]. Ethical approval was sought from the ethical review board of the University of Health Sciences and the Institutional Review Board of Rashid Latif Medical College (Approval no RLMC-IRB-2021/018). Written informed consent was obtained from all participants, with confidentiality and anonymity ensured. Data collection involved two components. First, EI was measured using the open-access validated National Health Services Emotional Intelligence Questionnaire [12]. Each item was rated on a five-point Likert scale (1=strongly disagree to 5= strongly agree). Details of the questionnaire are shown in Figure 1. Second, AP data in the form of percentage marks from the annual professional examination were taken from official institutional records. Data were collected in the classroom on a hard copy of a proforma comprising three sections: demographic information, emotional intelligence, and academic performance (Figure 1).

Figure 1: NHS Emotional Intelligence Questionnaire Detail

The hybrid/ blended learning context during the study period reflected post-pandemic adaptation. Blended instructional delivery combined asynchronous and synchronous online lectures, small group face-to-face clinical teaching, and technology-enhanced and technology-mediated assessments. Faculty used interactive tools to sustain engagement and align learning activities with curricular objectives [13].

Data analysis was conducted in SPSS version 25,0. Normality was assessed with the Shapiro-Wilk test. Non-normal continuous variables (emotional intelligence scores, raw marks) were reported as median with interquartile range, while normally distributed variables, i.e., percentage marks, were summarized as mean and standard deviation. Categorical variables were presented as frequencies and percentages. The relationship between emotional intelligence and academic performance was tested using Spearman's rank correlation coefficient.

DOI: https://doi.org/10.54393/pjhs.v7i2.3813

Group comparisons were conducted with a Kruskal-Walli's test. The statistical significance was set as a p-value less than 0.05 and a confidence interval of 95%.

RESULTS

A total of 300 MBBS students participated in the study with the mean age of 21.22 ± 2.5 years (median 21.0: IQR 20.0-24.0). Most of the students (56.3%) belonged to the 17-21 years age group, while 43.7% were between 22-24 years of age. The age variable exhibited a non-normal distribution. Demographic details are shown in table 1.

Table 1: Demographic Characteristics of Study Participants (n=300)

Variables	Category / Statistics	n % or Value
Age (years)	Mean ± SD	21.22 ± 2.5
	Median (IQR)	21.0 (20.0-24.0)
	Distribution	Non normal
Age Groups (years)	17-21	169 (43.7%)
	22-24	131 (56.3%)
Gender	Males	101 (33.7%)
	Females	199 (66.3%)

Comparison across professional years revealed significant differences in both Academic Performance and Emotional Intelligence EI. The highest mean emotional intelligence score was observed in 3rd year students (Mean=202, SD=12.8, n=60, 95% CI= 198.8-205.2) Which is significantly higher than other years (p<0.001). Correlation analysis demonstrated a moderate positive correlation between emotional intelligence and academic performance in the first year (r=0.502) 2nd year (r=0.590). 4th year students (r=0.659). A weaker correlation was noted among 3rd-year students. Whereas final year students showed a strong positive correlation (r=0.747). All correlations were statistically significant (p<0.001) as shown in table 2.

Table 2: Correlation of Emotional Intelligence with Academic Performance Among MBBS Students of Years

Study of the Year	Mark's Percentage Obtained (Mean ± SD)	Emotional Intelligence (Mean ± SD)	Correlation Coefficient	p-value[a]
First-Year	73.3 ± 5.9	194.9 ± 14.0	0.502	<0.001*
Second Year	72.1 ± 5.4	194.3 ± 14.2	0.590	<0.001*
Third Year	73.0 ± 4.1	202.5 ± 12.8	0.288	<0.001*
Fourth Year	70.6 ± 4.2	195.4 ± 14.0	0.659	<0.001*
Fifth Year	67.2 ± 3.6	195.0 ± 12.5	0.747	<0.001*
Overall	71.2 ± 5.2	196.4 ± 13.8	0.557	<0.001*
p-value[b]	<0.001*	0.004*	–	

[a]Spearman's rho correlation, [b]Kruskal-Walli's test. *Significant

The correlation between emotional intelligence and academic performance remained moderately positive for both genders (r = 0.587) for males and r=0.531 for females, indicating that higher emotional intelligence was consistently associated with better academic outcomes, irrespective of gender. Students aged 17-21 years obtained significantly higher academic scores compared to those aged 22-25 years (69.1 ± 4.3) (p<0.001). However, the difference in mean emotional intelligence score between the younger (197.2 ± 14.0) and older groups (195.5 ± 13.4) was not statistically significant (p=0.268). Correlation analysis revealed a moderate positive correlation between emotional intelligence and academic performance in both groups, with r=0.480 for the younger group and r=0.687 for the older group, both statistically significant (p<0.001). Students were categorized as high achievers (>70% marks) and low achievers (<70% marks). High achievers scored significantly higher in total EI score, i.e., total emotional intelligence score was 203.4 ± 11.2 among high achievers versus 186.8 ± 10.9 among low achievers. Correlational findings revealed a moderate positive correlation between academic performance and EI (r=0.557), and it was statistically significant (p<0.001). Overall, the findings consistently indicated that higher EI correlated with better academic performance across genders, age groups, achievement levels, and most professional years, particularly in the context of blended learning.

DISCUSSION

The study explored the relationship between emotional intelligence and different variables (academic performance, low and high achievers, different age groups, and both genders) among students of all professional years exposed to a blended learning environment. Mostly, the findings revealed a positive correlation with variation in strength among various subgroups. Our study reported the highest mean EI Score in third year MBBS students (202 ± 12.8, n=60, 95% CI = 198.8-205.2). A previous study conducted in Sweden among first year and fifth year students demonstrated a significant increase in emotional intelligence during medical training, where fifth year students demonstrated higher trait EI (F (5,423=2.39, p=0.037)). Although this supports enhanced EI during progression in medical training, EI can be at peak during early clinical years, as in the case of our study, rather than at the terminal stage of training [14]. In contrast to our findings, a previous study using the Universal Emotional Intelligence Questionnaire-Inventory reported the lowest score for third-year MBBS students (2.27%) and the highest for first and final-year MBBS students (2.90%). The study was conducted with a traditional curriculum with classroom pedagogy. Our findings on students exposed to a blended learning system suggest that contextual factors like implemented curriculum (blended vs onsite) and student support system may have an impact on EI difference, with the highest in the third year, underscoring the importance of EI development over the years in teaching learning environment [15]. Our study found a

DOI: https://doi.org/10.54393/pjhs.v7i2.3813

moderate positive correlation between academic performance and emotional intelligence among all cohorts of MBBS students, with a strong correlation in final year MBBS students (r=0.747). A study conducted in Spain among students reported a positive association of EI with academic performance, as well as resilience, positive emotions, and self-determined motivation, and this association was statistically significant and was confirmed through structural equation modelling. (χ^2/df = 3.24, IFI = 0.95, CFI = 0.95, RMSEA = 0.062, SRMR = 0.057). These results augment the significance of the results of our study [16]. Ranasinghe et al. performed binary logistic regression to find the predictors of academic performance, including gender, choice of study medicine, and emotional intelligence. Among these factors, female gender (OR=1.98) and satisfaction with the choice to study medicine (OR=3.69) were significantly associated with passing the exam, while EI was not a strong and significant predictor [17]. Taken together, generally EI is better correlated with academic performance, but different confounding factors, mode of teaching and learning (online vs, on site vs blended), and educational stages, particularly in medical training, may cause variation in the association of EI and academic performance. Our study demonstrated a moderately positive correlation between EI and AP among both genders exposed to blended teaching and learning (r=0.587) for males and (r = 0.531) for females. But there was no significant difference between the two groups regarding the impact of EI on academic performance. Consistent results were reported in previous literature in a study that male medical students have a statistically significant but slight association with self-esteem, while emotional intelligence exerted a stronger and more consistent effect across both genders. Considerably, no evidence suggested that the positive association between emotional intelligence and GPA was limited to one gender, indicating that emotional intelligence works as a universal facilitator for academic performance without gender discrimination among university students [18]. Contrarily, A study conducted in Lebanon on online teaching and learning found a significant gender difference, with women showing higher self-perceived performance, academic engagement, and emotionality factor in trait EI, while men scored higher in self-control [19]. In another study conducted in a traditional class learning environment reported significant gender differences were reported between different domains of Emotional intelligence among both genders (p<0.05), with females scoring higher in emotional attention and academic self-concept. Additionally, most of the students fell in the remarkable category of academic performance; females showed higher academic performance overall, with greater representation in the remarkable category (66.9%) as compared to males (27.1%) [20]. In another study on blended learning environments, although cognitive engagement mediated the positive relationship between emotional intelligence and study habits, gender also exerted a modest but significant influence (B=0.117, p<0.05), suggesting that while EI enhances academic performance across students in blended learning, female and male students may differ slightly in the way they engage with study practices [21]. These observed discrepancies may be attributed to differences in sample characteristics and use of domain specific vs global measures of emotional intelligence, as well as learning environment. Data analysis of our study demonstrated that students aged 17-21 years obtained significantly higher academic scores compared to those aged 22–25 years, while there was an insignificant difference between the mean emotional intelligence of both age groups. Correlational analysis revealed there was a moderate positive correlation between emotional intelligence and academic performance of MBBS students exposed to a blended teaching and learning system in both groups, with r=0.480 for the younger group and r=0.687 for the older group, both statistically significant. In a study on online learning during COVID-19, Age and gender showed minimal association with both emotional competence and academic outcomes, while emotional competence was moderately related to online learning readiness, but academic performance remains the strongest predictor of academic achievement during COVID-19 [22]. Contrasting results were reported in a study conducted in private universities of Bangladesh that age was a potential factor influencing the development of emotional intelligence. Regression analysis confirmed that age didn't significantly predict academic performance (B=0.012, p=0.438), whereas emotional intelligence showed a strong and positive effect [23]. In another study, emotional intelligence exhibited age-related changes during adolescence, with overall EI increasing modestly with age, particularly in girls (B=0.82, β=0.13, p<0.001). Gender-specific analysis revealed that girls show improvement in emotional management over time, while boys experienced a slight decline in emotional perception [24]. A blended learning environment can effectively enhance emotional intelligence and academic performance, particularly during early clinical years. Integrating structured EI development within blended curricula can prepare students for adaptive and resilient learning and professional functioning in the face of unforeseen challenges, including future pandemics. Tailoring interventions to different students' subgroups may optimize students' engagement and academic outcomes.

DOI: https://doi.org/10.54393/pjhs.v7i2.3813

This single-institution, cross-sectional study limits generalizability and causal inference. Self-reported EI may be influenced by bias, and contextual factors like prior training exposure to EI and the mental support system for students were not studied. The study didn't analyze emotional intelligence separately for synchronous and asynchronous components of blended learning. Examining EI in different contexts could provide different insights and represent a potential direction for research.

CONCLUSIONS

Emotional intelligence was positively correlated with academic performance across all MBBS years, gender, age group, and achievement level in a blended learning environment, peaking in early clinical years. High-achieving students consistently demonstrated high emotional intelligence, highlighting its role in academic success. These findings suggest that integrating structured EI development in medical curricula as a longitudinal module can enhance resilient and adaptive learning, thus preparing the students for unforeseen challenges, especially a pandemic. Tailored intervention may further optimize student engagement and academic outcomes.

Authors' Contribution

Conceptualization: SY
Methodology: SY, NK
Formal analysis: MS, MAR
Writing and Drafting: SY, MS, NK, MAR
Review and Editing: SY, MS, NK, MAR

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Shengyao Y, Xuefen L, Jenatabadi HS, Samsudin N, Chunchun K, Ishak Z. Emotional Intelligence Impact on Academic Achievement and Psychological Well-Being among University Students: The Mediating Role of Positive Psychological Characteristics. BioMed Central Psychology. 2024 Jul; 12(1): 389. doi: 10.1186/s40359-024-01886-4.

[2] Maity S, De Filippis SM, Aldanese A, McCulloch MA, Sandor AP, Perez Cajigas JE *et al.* Enhancing Emotional Intelligence in Medical Education: A Systematic Review of Interventions. Frontiers in Medicine. 2025 Jul; 12: 1587090. doi: 10.3389/fmed.2025.1587090.

[3] Alabbasi AM, Alabbasi FA, AlSaleh A, Alansari AM, Sequeira RP. Emotional Intelligence Weakly Predicts Academic Success in Medical Programs: A Multilevel Meta-Analysis and Systematic Review. BioMed Central Medical Education. 2023 Jun; 23(1): 425. doi: 10.1186/s12909-023-04417-8.

[4] Chung EK, Yun H, Yang JH, Shin MH, Han ER. Factors Associated with Academic Performance among Medical Students at a Medical School in South Korea: A Retrospective Cohort Study. Plos One. 2024 Feb; 19(2): e0296682. doi: 10.1371/journal.pone.0296682.

[5] Wang X, Liu J, Jia S, Hou C, Jiao R, Yan Y *et al.* Hybrid Teaching After COVID-19: Advantages, Challenges, and Optimization Strategies. BioMed Central Medical Education. 2024 Jul; 24(1): 753. doi: 10.1186/s12909-024-05745-z.

[6] Kabi A, Nayak BC, Ray SS, Gupta S, Epari V, Sahoo J. Impact of COVID-19 Pandemic on Online Medical Education–an Online Survey of Students' Perspective. Journal of Family Medicine and Primary Care. 2024 May; 13(5): 1755-9. doi: 10.4103/jfmpc.jfmpc_1047_23.

[7] Zhao Y, Sun T, Zhang X, Wang X, Hu W. The Evolution of Medical Education in the Era of Covid-19 and Beyond: A Longitudinal Study. BioMed Central Medical Education. 2024 Nov; 24(1): 1289. doi: 10.1186/s12909-024-06271-8.

[8] Jaleel A, Iqbal SP, Cheema KM, Iftikhar S, Bashir MZ. Navigating Undergraduate Medical Education: A Comparative Evaluation of a Fully Online Versus a Hybrid Model. BioMed Central Medical Education. 2024 Aug; 24(1): 895. doi: 10.1186/s12909-024-05865-6.

[9] Alenezi AM. The Relationship of Students'emotional Intelligence and the Level of Their Readiness for Online Education: A Contextual Study on the Example of University Training in Saudi Arabia. Образование и наука. 2020; 22(4): 89-109. doi: 10.17853/1994-5639-2020-4-89-109.

[10] Vezne R, Yildiz Durak H, Atman Uslu N. Online Learning in Higher Education: Examining the Predictors of Students' Online Engagement. Education And Information Technologies. 2023 Feb; 28(2): 1865-89. doi: 10.1007/s10639-022-11171-9.

[11] Ashwini AP, Kumar N, Gunasegeran P, Sivagamy SM, Rong LZ, Sujatha PP. A Survey-Based Study of Emotional Intelligence as It Relates to Gender and Academic Performance of Medical Students. Education for Health. 2016 Sep; 29(3): 255-8.

[12] HRB National Drugs Library. Emotional Intelligence Questionnaire. Outcomes Measurement Tool:

DOI: https://doi.org/10.54393/pjhs.v7i2.3813

Attitudes and Feelings - Emotional Intelligence. 2016. https://www.drugsandalcohol.ie/26776/.

[13] El Seifi OS, Albishi N, Albalawi GA, Alzahrani L, AlOmari LI, Albalawi DM *et al.* Relationship between Emotional Intelligence and Academic Performance among Medical Students at University of Tabuk (2021). Cureus. 2023 Nov; 15(11). doi: 10.7759/cureus.49301.

[14] Bitar A, Amnelius L, Kristoffersson E, Boman J. Emotional Intelligence among Medical Students in Sweden–A Questionnaire Study. BioMed Central Medical Education. 2023 Aug; 23(1): 603. doi: 10.1186/s12909-023-04570-0.

[15] Daud N, Rahim AF, Pa MN, Ahmad A, Yusof NA, Hassan NM *et al.* Emotional Intelligence Among Medical Students and Its Relationship with Burnout. Education in Medicine Journal. 2022 Sep; 14(3). doi: 10.21315/eimj2022.14.3.4.

[16] Trigueros R, Aguilar-Parra JM, Cangas AJ, Bermejo R, Ferrandiz C, López-Liria R. Influence of Emotional Intelligence, Motivation and Resilience on Academic Performance and the Adoption of Healthy Lifestyle Habits Among Adolescents. International Journal of Environmental Research and Public Health. 2019 Aug; 16(16): 2810. doi: 10.3390/ijerph16162810.

[17] Ranasinghe P, Wathurapatha WS, Mathangasinghe Y, Ponnamperuma G. Emotional Intelligence, Perceived Stress and Academic Performance of Sri Lankan Medical Undergraduates. BioMed Central Medical Education. 2017 Feb; 17(1): 41. doi: 10.1186/s12909-017-0884-5.

[18] Salih SA, Omar AM, Atrous MH, Ali TS, Hamad MM, Bashir WA *et al.* The Relationship of University Students' Academic Achievement with Emotional Intelligence and Self-esteem: A Descriptive Correlation Study Design at Jouf University, Saudi Arabia, 2023. Sudan Journal of Medical Sciences. 2024 Oct; 19(3). doi: 10.18502/sjms.v19i3.13167.

[19] Sanchez-Ruiz MJ, Khalaf T, Tadros N, Nauffal D, Nader J, Diab R *et al.* Positive Affect and Self-Care Mediate the Relationship Between Trait Emotional Intelligence and Academic Engagement in Lebanese Undergraduates: Lessons Learned from an Online Setting. International Journal of Psychology. 2024 Dec; 59(6): 932-41. doi: 10.1002/ijop.13215.

[20] Ubago-Jimenez JL, Zurita-Ortega F, Ortega-Martin JL, Melguizo-Ibañez E. Impact of Emotional Intelligence and Academic Self-Concept on the Academic Performance of Educational Sciences Undergraduates. Heliyon. 2024 Apr; 10(8). doi: 10.1016/j.heliyon.2024.e29476.

[21] Iqbal J, Asghar MZ, Ashraf MA, Yi X. The Impacts of Emotional Intelligence on Students' Study Habits in Blended Learning Environments: The Mediating Role of Cognitive Engagement During COVID-19. Behavioral Sciences. 2022 Jan; 12(1): 14. doi: 10.3390/bs12010014.

[22] Wang Y, Xia M, Guo W, Xu F, Zhao Y. Academic Performance Under COVID-19: The Role of Online Learning Readiness and Emotional Competence. Current Psychology. 2023 Dec; 42(34): 30562-75. doi: 10.1007/s12144-022-02699-7.

[23] Emon MM, Siam SA, Siddique M. Exploring the Link Between Emotional Intelligence and Academic Performance among Bangladeshi Private University Students. Malaysian Mental Health Journal. 2023; 2(1): 26-8. doi: 10.26480/mmhj.01.2023.26.28.

[24] Megías-Robles A, Gutiérrez-Cobo MJ, Fernández-Berrocal P, Gómez-Leal R, Cabello R. The Development of Ability Emotional Intelligence During Adolescence. Personality and Individual Differences. 2024 Jul; 224: 112642. doi: 10.1016/j.paid.2024.112642.

DOI: https://doi.org/10.54393/pjhs.v7i2.2561

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Comparison between Lactobacillus Reuteri Probiotic in Addition to Standard Care versus Standard Care Alone in the Treatment of Infantile Colic

Shamaila Maqsood[1], Hina Naveed[2], Yusra Kafait[3], Samia Hafeez[1], Sidra Noor[1], Rehmana Waris[4] and Muhammad Ahsan[5*]

[1]Department of Pediatrics, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan
[2]Department of Pediatrics, Federal Government Polyclinic Hospital, Islamabad, Pakistan
[3]Department of Pediatrics, Divisional Headquarters Teaching Hospital, Mirpur, Pakistan
[4]Department of Pediatrics, Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad, Pakistan
[5]Department of Pediatrics, Nusrat Fateh Ali Khan Hospital, Faisalabad, Pakistan

ARTICLE INFO

Keywords:
Infantile Colic, *L. reuteri*, Probiotic, Abdominal Colic, Infant Crying

How to Cite:
Maqsood, S., Naveed, H., Kafait, Y., Hafeez, S., Noor, S., Waris, R., & Ahsan, M. (2026). Comparison between Lactobacillus Reuteri Probiotic in Addition to Standard Care versus Standard Care Alone in the Treatment of Infantile Colic: Lactobacillus Reuteri Probiotic in Addition to Standard Care in the Treatment of Infantile Colic. Pakistan Journal of Health Sciences, 7(2), 123-128. https://doi.org/10.54393/pjhs.v7i2.2561

***Corresponding Author:**
Muhammad Ahsan
Department of Pediatrics, Nusrat Fateh Ali Khan Hospital, Faisalabad, Pakistan
ahsanjahangir194@gmail.com

Received Date: 20th September, 2025
Revised Date: 30th December, 2025
Acceptance Date: 13th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Excessive crying is one of the most common problems in the first three months of life, accounting for nearly 20% of pediatric consultations. **Objectives:** To evaluate the effectiveness of *Lactobacillus reuteri* in infants with infantile colic compared with standard care alone. **Methods:** A prospective quasi-experimental study was used to enroll 172 infants (<13 weeks of age) with clinically diagnosed infantile colic who were enrolled. Group A received probiotic *L. reuteri* in addition to standard care, while Group B received standard care alone. Outcomes included mean daily crying time, crying episodes/week, and daily sleep duration, measured at baseline, days 7, 14, 21, and 28. Between-group comparisons were performed using the Mann–Whitney U test, and within-group changes were analyzed using the Friedman test. **Results:** Over 28 days, Group A showed greater improvement than Group B in reducing crying and increasing sleep. Daily crying decreased by −3.53 ± 1.05 hours in Group A vs. −1.79 ± 1.19 hours in Group B ($p<0.001$), weekly crying episodes by −3.60 ± 0.69 vs. −3.36 ± 0.97 ($p=0.041$), and daily sleep increased by 5.38 ± 2.08 hours vs. 2.80 ± 3.52 hours ($p<0.001$). **Conclusions:** *L. reuteri* supplementation in addition to standard care significantly reduced crying time and episodes, and improved sleep-in infants with colic compared to standard care alone.

INTRODUCTION

Excessive crying is the most common problem in the initial 3 months of infantile age. Nearly 20% of pediatric consultations by parents are for this reason. Although it is a self-limited problem, parents and caregivers face huge stress and anxiety due to this complaint [1]. Excessive crying can be attributed to various factors, including pain, hunger, discomfort, or the infant's need for emotional reassurance. Infantile colic is a common cause of excessive crying in infants, impacting 10-40% of this population. It is typically observed as early as 2 weeks of life and gradually diminishes by 6 months of age in infants. Both boys and girls are impacted in the same manner [2]. A healthy, well-nourished newborn under five months old suffering from fits of uncontrolled weeping is said to be suffering from infantile colic. Cry out loud for at least three hours every day, three times a week, for at least three weeks straight [3]. Infantile colic is a crying spell with no obvious etiology. Due to stress, parents use analgesics as

DOI: https://doi.org/10.54393/pjhs.v7i2.2561

well as sedative drugs to calm the infant, and sometimes this excessive and non-stop crying leads to shaken baby syndrome [4]. Very few (<5%) babies have an underlying organic cause of colic, e.g., lactose intolerance, constipation, or gastroesophageal reflux disease (GERD) [5]. Another school of thought postulates that colic is associated with increased peristaltic activity of the gut, supported by the fact that symptoms are relieved by the use of anticholinergic medications [6]. As large numbers of coliform bacteria are found in colicky babies, studies were conducted to try to modify the gut flora, and these studies have shown a positive impact in treating the symptoms of colic. Few measures can provide some degree of comfort, e.g., improve sleep hygiene and organize parents' and baby's routine [7], and use of fennel, chamomile, and peppermint [8].

Although extensive evidence is being gained in the world on the benefits of *L. reuteri* in the treatment of infantile colic, little local data is available in Pakistan. Practically all trials are initiated by Western populations, who have various feeding habits, access to healthcare, or gut microbiota profiles. This is the gap that restricts the development of evidence-based guidelines on the local level. Also, very limited research compared probiotic adjunct therapy to standard care only using longitudinal, multi-timepoint outcome measures. These gaps are addressed through this study as it provides strong local comparative data. This study aimed to evaluate the effectiveness of *Lactobacillus reuteri* in infants with infantile colic compared with standard care alone.

METHODS

This prospective quasi-experimental study aims to compare the efficacy of standard treatment with *Lactobacillus reuteri* for infantile colic conducted at Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU), Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, from January 2020 to June 2020. The study was approved by the ethical committee of the institute vide letter number F.1-1/2015/ERB/SZABMU/406. The sample size was calculated using the formula for comparing two means, with $\alpha = 0.05$, power = 80%, expected mean difference (Δ) = 58 minutes/day, and standard deviation (σ) = 135 minutes, based on Savino *et al.* This yielded 72 infants per group; allowing 20% for attrition, the final target was 86 per group (total n=172) [9]. Eligible participants were infants under 13 weeks old, breastfed or formula-fed, diagnosed with infantile colic, and meeting study criteria. Exclusions included infants under 2500 grams, those with failure to thrive, or with other medical conditions. Also excluded were infants and mothers who used **Lactobacillus reuteri** before the trial, infants starting solid foods, and those who received antibiotics in the last two weeks. Informed consent was provided by the parents. All the infants on probiotic *Lactobacillus reuteri*, along with the standard care, were enrolled in Group A (probiotic group), and all taking standard care alone in the form of conservative management in Group B (control group). Parents documented daily crying episodes and sleep duration in a provided diary. Follow-up occurred on days 7, 14, 21, and 28, with final assessments at day 28 when medication and diaries were returned. To address attrition, an additional 20% of participants were recruited. Effectiveness Definition: Treatment effectiveness was defined as a statistically significant improvement ($p \leq 0.05$) in at least two of the three primary outcomes (1) reduction in mean daily crying time, (2) reduction in mean weekly crying episodes, and (3) increase in mean daily sleep duration at day 28 compared with baseline, with greater improvement in the probiotic group than in the control group. Data analysis was performed using SPSS version 26.0. The Shapiro-Wilk test was used to test the normality of continuous variables. Since the majority of the variables were not normally distributed, the results were represented as median (interquartile range) of the baseline and follow-up measurements, as well as means with standard deviation of the change scores. The Mann-Whitney U test was used in between-group comparison, and the Friedman test was used in within-group differences over time. The Chi-square test was used to analyze categorical variables and was presented in the form of frequencies and percentages. The significance value of $p<0.05$ was taken as significant.

RESULTS

A little over half were aged 31–40 years (83 women, 53.5%), while 72 women (46.5%) were 20–30 years, with a mean age of 31.03 ± 5.89 years. Regarding BMI, 84 women (54.2%) had a normal BMI, 51 (32.9%) were overweight, and 20 (12.9%) were obese, giving a mean BMI of 25.31 ± 3.38 kg/m^2. Slightly more participants were multiparous (82, 52.9%) than nulliparous/primiparous (73, 47.1%). Education levels varied: 51 (32.9%) had secondary, 50 (32.2%) primary, 39 (25.2%) tertiary, and 15 (9.7%) no formal schooling. Socioeconomic status was predominantly low (80, 51.6%), followed by middle (52, 33.5%) and high (23, 14.9%). Residence was evenly distributed between urban (80, 51.6%) and rural (75, 48.4%). Only 1 woman (0.6%) reported smoking, while 154 (99.4%) were non-smokers. The average number of antenatal care (ANC) visits was 4.55 ± 2.27, and the mean gestational age at delivery was 33.88 ± 1.43 weeks, confirming the preterm status. All participants delivered preterm, confirming that the study population exclusively comprised women with preterm labor (Table 1).

DOI: https://doi.org/10.54393/pjhs.v7i2.2561

Table 1: The Baseline Measurements Data

Variables	Group A (Median [IQR])	Group B (Median [IQR])	p-value
Age (Weeks)	9.00 (6.00–10.00)	9.00 (7.00–10.00)	0.3311*
Crying Time (Hours) at Baseline	4.00 (4.00–5.00)	5.00 (4.00–5.00)	0.4298*
Crying Episodes/ Week at Baseline	5.00 (4.00–6.00)	5.00 (4.00–6.00)	0.0702*
Sleep (Hours/24h) at Baseline	11.00 (10.00–12.75)	11.00 (10.00–12.00)	0.4786*
Gender			
Male	47 (54.7%)	40 (46.5%)	0.2857**
Female	39 (45.3%)	46 (53.5%)	
Feeding			
Breast	47 (54.7%)	43 (50.0%)	0.7104**
Formula	24 (27.9%)	29 (33.7%)	
Mixed	15 (17.4%)	14 (16.3%)	

*Mann–Whitney U test. ** Chi-square test

The study compares the treatment outcomes between infants receiving *Lactobacillus reuteri* in addition to standard care (Group A) and those receiving standard care alone (Group B). At baseline, median crying time was similar between groups [4.00 (IQR: 4.00–5.00) vs. 5.00 (IQR: 4.00–5.00), p=0.430]. However, by day 7, Group A demonstrated a significant reduction in crying time compared to Group B [3.00 (IQR: 2.00–3.00) vs. 4.00 (IQR: 3.00–5.00), p<0.001], with this difference widening at day 14 [2.00 (IQR: 1.00–2.00) vs. 3.00 (IQR: 2.00–4.00), p<0.001], day 21 [1.00 (IQR: 1.00–2.00) vs. 3.00 (IQR: 3.00–4.00), p<0.001], and day 28 [1.00 (IQR: 1.00–1.00) vs. 3.00 (IQR: 2.00–4.00), p<0.001]. Within-group Friedman tests confirmed significant reductions over time in both groups (p<0.001). For crying episodes per week, baseline medians were comparable [5.00 (IQR: 4.00–6.00) in both groups, p=0.070], but Group A achieved significantly lower values from day 7 onward, with differences persisting through day 28 (all p≤0.002). Both groups showed significant reductions over time (p<0.001). Regarding sleep duration, no significant difference was observed at baseline [11.00 (IQR: 10.00–12.75) vs. 11.00 (IQR: 10.00–12.00), p=0.479]. From day 7 onwards, Group A demonstrated markedly greater increases in sleep hours compared to Group B, with median sleep at day 28 reaching 17.00 (IQR: 16.00–17.00) in Group A versus 13.50 (IQR: 12.00–16.00) in Group B (p<0.001). Within-group changes over time were significant for both groups (p<0.001). Mean change analysis from baseline to day 28 showed that Group A had a greater reduction in crying time (-3.53 ± 1.05 hours) compared to Group B (-1.79 ± 1.19 hours, p<0.001) and a greater increase in daily sleep (5.38 ± 2.08 hours vs. 2.80 ± 3.52 hours, p<0.001). The change in crying episodes per week was similar between groups (-3.60 ± 0.69 vs. -3.36 ± 0.97, p=0.567) (Table 2).

Table 2: Comparison between Lactobacillus reuteri Probiotic in Addition to Standard Care Versus Standard Care Alone in the Treatment of Infantile Colic

Outcomes	Time Point	Group A (Median [IQR])	Group B (Median [IQR])	Between Group	Within Group A	Within Group B
Crying Time (Hours)	Baseline	4.00 (4.00–5.00)	5.00 (4.00–5.00)	0.430	<0.001	<0.001
	Day 7	3.00 (2.00–3.00)	4.00 (3.00–5.00)	<0.001	<0.001	<0.001
	Day 14	2.00 (1.00–2.00)	3.00 (2.00–4.00)	<0.001	<0.001	<0.001
	Day 21	1.00 (1.00–2.00)	3.00 (3.00–4.00)	<0.001	<0.001	<0.001
	Day 28	1.00 (1.00–1.00)	3.00 (2.00–4.00)	<0.001	<0.001	<0.001
Crying Episodes/Week	Baseline	5.00 (4.00–6.00)	5.00 (4.00–6.00)	0.070	<0.001	<0.001
	Day 7	3.00 (3.00–4.00)	4.00 (3.25–5.00)	0.002	<0.001	<0.001
	Day 14	2.00 (2.00–3.00)	3.00 (2.00–3.00)	<0.001	<0.001	<0.001
	Day 21	1.00 (1.00–2.00)	2.00 (1.00–2.00)	<0.001	<0.001	<0.001
	Day 28	1.00 (1.00–1.00)	2.00 (1.00–2.00)	<0.001	<0.001	<0.001
Sleep (Hours/24h)	Baseline	11.00 (10.00–12.75)	11.00 (10.00–12.00)	0.479	<0.001	<0.001
	Day 7	12.00 (11.00–13.75)	11.00 (10.00–13.00)	<0.001	<0.001	<0.001
	Day 14	13.00 (12.00–14.00)	12.00 (10.00–12.00)	<0.001	<0.001	<0.001
	Day 21	14.00 (12.00–16.00)	12.00 (11.00–13.00)	<0.001	<0.001	<0.001
	Day 28	17.00 (16.00–17.00)	13.50 (12.00–16.00)	<0.001	<0.001	<0.001
Crying Time (Hours) Mean Change	Baseline to Day 28	-3.53 ± 1.05	-1.79 ± 1.19	<0.001	–	–
Crying Episodes/Week Mean Change	Baseline to Day 28	-3.60 ± 0.69	-3.36 ± 0.97	0.567	–	–
Sleep (Hours/24h) Mean Change	Baseline to Day 28	5.38 ± 2.08	2.80 ± 3.52	<0.001	–	–

Note: Values are presented as median (IQR). Between-group comparisons were performed using the Mann–Whitney U test. Within-group changes over time were analyzed using the Friedman test. A p-value < 0.05 was considered statistically significant.

DOI: https://doi.org/10.54393/pjhs.v7i2.2561

DISCUSSION

This study assessed the efficacy of *Lactobacillus reuteri* DSM 17938 in the management of infantile colic. At baseline, both treatment groups demonstrated comparable crying duration, crying episodes, and sleep patterns. By days 7, 14, 21, and 28, *L. reuteri*, in addition to standard care, significantly reduced crying time and crying episodes, while improving sleep duration, compared to standard care alone ($p<0.05$). At day 28, the mean crying-time reduction was -3.53 ± 1.05 hours in Group A versus -1.79 ± 1.19 hours in Group B ($p=0.000$), the mean crying-episode reduction was -3.60 ± 0.69 versus -3.36 ± 0.97 ($p=0.567$), and the mean increase in sleep duration was 5.38 ± 2.08 hours versus 2.80 ± 3.52 hours ($p=0.000$). These results indicate statistically significant changes as well as clinically significant improvements in symptom burden. According to a randomized controlled trial carried out by Jalal *et al.* in the Benazir Bhutto Hospital of Rawalpindi, probiotics that consisted of *L. reuteri* proved to significantly decrease infantile colic cases compared to simethicone [10]. It is also suggested by the Latin American Experts Group that *L. reuteri* DSM 17938 can be used in infantile colic [11]. During 28 days, Savino *et al.* randomly assigned 90 infants with colicky behavior who were breast-fed to either simethicone or *L. reuteri*. During day seven, the mean duration of crying in the probiotic and simethicone groups was 159 and 177 minutes, respectively. These values were 51 minutes and 145 minutes on day 28, and 95 percent of the probiotic group and 7 percent of the simethicone group improved [12]. Statistically significant differences are observed in our findings already on day 7 and throughout day 28, which is consistent with this temporal improvement. In comparison, the study conducted in the Department of Pediatrics of the University indicated that the enhanced parental knowledge of normal infant crying behavior can help to decrease the number of crying incidents as well, which prioritizes the role of non-pharmacologic and educational approaches, as well as therapeutic interventions [13]. Some other hypotheses suggest that alterations of faecal microbiota could be possible causes of infantile colic [8]. In that respect, lower faecal calprotectin concentrations have been noted in responders to *L. reuteri* treatment [14], which is in line with an anti-inflammatory effect, which is in line with our results of improvements in gastrointestinal symptoms and sleep duration. *L. reuteri* DSM 17938 has been the most widely researched strain in the management of infantile colic, and several randomized controlled trials have been performed in different settings. Szajewska *et al.* reported much better responder rates that were determined as a 50 percent decrease in daily crying time in the probiotic group at all time points ($p<0.05$) [15]. More responder rates were also reported in an Italian trial on days 7, 14, and 21 with microbiological evidence of higher faecal lactobacilli and lower *E. coli* [16]. Muller *et al.* showed that the probiotic group had less crying time and a shorter median crying period in contrast to the placebo group [2]. A study carried out in China also documented significant decreases in crying time by probiotics. Such uniform advantages in various settings prove the external validity of our findings [17]. These findings are further put into perspective through systematic reviews and meta-analyses. Schreck *et al.* found a pooled mean decrease in the duration of crying of about 56 minutes/day with a two-week favorable *L. reuteri* effect, with results meandering during the first week and reaching its peak in the third week- a nearly similar result to that in our trial [17]. Similar results were also found by Xu *et al.* with two and three-week benefits at six randomized trials [18]. Although no advantage was reported in a Canadian cohort at one month [19], Sung *et al.* reported that a subsequent meta-analysis of the same group reported consistent reductions in crying/fussing time in four randomized trials [20]. Variability could be attributed to dissimilarity in feeding condition, baseline symptom intensity, strain dosing, and methodology of analysis. The non-parametric analyses of our cohort established statistically significant between-group effects as well as significant within-group time effects, with both crying-time reduction and sleep gain by day 28 having clinically relevant magnitudes. The multifactorial effects of *L. reuteri* DSM 17938, such as improvement of gut microbial homeostasis through an increase in Lactobacilli colonization, inhibition of pathogenic *E. coli*, and minimization of intestinal inflammation, could explain the following benefits that were observed [16]. A reduction in the faecal calprotectin levels in the responders, as mentioned above [14], is an additional indicator of an anti-inflammatory effect. Also, the betterment of sleep patterns recorded here and in earlier studies [18] implies the possible regulation of the gut-brain axis. Clinically, the changes are meaningful, since they not only discuss infant distress, but also parental stress, difficulties feeding, and possible cessation of breastfeeding. Our study, especially the decrease in crying time by greater than 3.5 hours and increase in sleep by greater than 5 hours by day 28, is indicative of the ability of *L. reuteri* to be used as an adjunct in infantile colic, particularly in the first line.

This research has a number of limitations. The quasi-experimental non-randomized design does not make it possible to infer causation and can create selection bias. The single-center design limits generalizability. Parental diary reporting is associated with the possibility of recall bias. Follow up period of 28 days does not determine long-term outcomes and recurrence. It should be followed by

DOI: https://doi.org/10.54393/pjhs.v7i2.2561

future multicenter randomised controlled trials involving a longer follow-up, blinding, and objective biomarkers (e.g., fecal calprotectin, microbiome analysis). The priority should be put on the subgroup analysis based on feeding (breastfed vs. formula-fed). There is a need for health economic analyses to determine cost-effectiveness in low-resource environments.

CONCLUSIONS

Mean daily crying time and crying episodes per week were significantly reduced, and mean daily sleep duration was significantly improved at days 7, 14, 21, and 28 in infants receiving probiotic *L. reuteri* in addition to standard care compared with those receiving standard care alone. The probiotic therapy was well tolerated and demonstrated cost-effectiveness. Future studies with larger sample sizes, extended follow-up, and assessment of additional variables such as fecal calprotectin levels and gut microflora changes are recommended to further validate and elucidate these findings.

Authors' Contribution

Conceptualization: MA
Methodology: SM, SH, SN, RW
Formal analysis: HN, YK, RW, MA
Writing and Drafting: SM, SH, SN, MA
Review and Editing: SM, HN, YK, SH, SN, RW, MA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Ölmestig TK, Siersma V, Birkmose AR, Kragstrup J, Ertmann RK. Infant Crying Problems Related to Maternal Depressive and Anxiety Symptoms During Pregnancy: A Prospective Cohort Study. BioMed Central Pregnancy and Childbirth. 2021 Nov; 21(1): 777. doi: 10.1186/s12884-021-04252-z.

[2] Muller I, Ghio D, Mobey J, Jones H, Hornsey S, Dobson A *et al.* Parental Perceptions and Experiences of Infant Crying: A Systematic Review and Synthesis of Qualitative Research. Journal of Advanced Nursing. 2023 Feb; 79(2): 403-17. doi: 10.1111/jan.15492.

[3] Connor F, Salvatore S, D'auria E, Baldassarre ME, Acunzo M, Di Bella G *et al.* Cows' Milk Allergy-Associated Constipation: When to Look for It? A Narrative Review. Nutrients. 2022 Mar; 14(6): 1317. doi: 10.3390/nu14061317.

[4] Itzkowitz T. What is the Underlying Cause of Infantile Colic? The Science Journal of the Lander College of Arts and Sciences. 2021; 14(2): 34-7.

[5] Vandenplas Y, Kindt S, Salvatore S. Infant regurgitation and Pediatric Gastroesophageal Reflux Disease. In Pediatric Neurogastroenterology: Gastrointestinal Motility Disorders and Disorders of Gut Brain Interaction in Children. Cham: Springer International Publishing. 2023 Jan: 439-456. doi: 10.1007/978-3-031-15229-0_34.

[6] Banik SK, Zaman M, Karim MR, Rahman MM, Anam AN, Al Zami H *et al.* Efficacy of Lactobacillus reuteri in Improving Gut Barrier Function and Management of Infantile Colic. American Journal of Pediatrics. 2023; 9: 10-1648.

[7] Perry R, Hunt K, Ernst E. Nutritional Supplements and Other Complementary Medicines for Infantile Colic: A Systematic Review. Pediatrics. 2011 Apr; 127(4): 720-33. doi: 10.1542/peds.2010-2098.

[8] Hofman D, Kudla U, Miqdady M, Nguyen TV, Morán-Ramos S, Vandenplas Y. Faecal Microbiota in Infants and Young Children with Functional Gastrointestinal Disorders: A Systematic Review. Nutrients. 2022 Feb; 14(5): 974. doi: 10.3390/nu14050974.

[9] Savino F, Cordisco L, Tarasco V, Palumeri E, Calabrese R, Oggero R *et al.* Lactobacillus reuteri DSM 17938 in Infantile Colic: A Randomized, Double-Blind, Placebo-Controlled Trial. Pediatrics. 2010 Sep; 126(3): e526-33. doi: 10.1542/peds.2010-0433.

[10] Jalal MS, Mehdi SZ, Akber JU, Gowa MA, Lifschitz C. Infantile Colic: A Survey of Physicians in Pakistan. Pediatric Gastroenterology, Hepatology and Nutrition. 2024 May; 27(3): 186. doi: 10.5223/pghn.2024.27.3.186.

[11] Larrosa-Haro A, Abundis-Castro L, Contreras MB, Gallo MJ, Peña-Quintana L, Ferreira CT *et al.* Epidemiologic Trend of Pediatric Inflammatory Bowel Disease in Latin America: The Latin American Society for Pediatric Gastroenterology, Hepatology and Nutrition (LASPGHAN) Working Group. Revista de Gastroenterología de México (English Edition). 2021 Oct; 86(4): 328-34. doi: 10.1016/j.rgmxen.2021.07.004.

[12] Savino F, Pelle E, Palumeri E, Oggero R, Miniero R. Lactobacillus reuteri (American Type Culture Collection Strain 55730) versus Simethicone in the Treatment of Infantile Colic: A Prospective Randomized Study. Pediatrics. 2007 Jan; 119(1): e124-30. doi: 10.1542/peds.2006-1222.

[13] Augustin M, Licata-Dandel M, Breeman LD, Harrer M, Bilgin A, Wolke D *et al.* Effects of a mobile-based

DOI: https://doi.org/10.54393/pjhs.v7i2.2561

intervention for parents of children with crying, sleeping, and feeding problems: randomized controlled trial. Journal of Medical Internet Research: mHealth and uHealth. 2023 Mar; 11: e41804. doi: 10.2196/41804.

[14] Savino F, Garro M, Montanari P, Galliano I, Bergallo M. Crying Time and RORγ/FOXP3 Expression in Lactobacillus Reuteri DSM17938-Treated Infants with Colic: A Randomized Trial. The Journal of Pediatrics. 2018 Jan; 192: 171-7. doi: 10.1016/j.jpeds.2017.08.062.

[15] Szajewska H, Gyrczuk E, Horvath A. Lactobacillus reuteri DSM 17938 for he Management of Infantile Colic in Breastfed Infants: A Randomized, Double-Blind, Placebo-Controlled Trial. The Journal of Pediatrics. 2013 Feb; 162(2): 257-62. doi: 10.1016/j.jpeds.2012.08.004.

[16] Zermiani AP, de Paula AL, Miguel ER, Lopes LD, Santana ND, da Silva Santos T *et al.* Evidence of Lactobacillus reuteri to Reduce Colic in Breastfed Babies: Systematic Review and Meta-Analysis. Complementary Therapies in Medicine. 2021 Dec; 63: 102781. doi: 10.1016/j.ctim.2021.102781.

[17] Schreck Bird A, Gregory PJ, Jalloh MA, Risoldi Cochrane Z, Hein DJ. Probiotics for the Treatment of Infantile Colic: A Systematic Review. Journal of Pharmacy Practice. 2017 Jun; 30(3): 366-74. doi: 10.1177/0897190016634516.

[18] Xu M, Wang J, Wang N, Sun F, Wang L, Liu XH. The Efficacy and Safety of the Probiotic Bacterium Lactobacillus Reuteri DSM 17938 For Infantile Colic: A Meta-Analysis of Randomized Controlled Trials. PLOS One. 2015 Oct; 10(10): e0141445. doi: 10.1371/journal.pone.0141445.

[19] Basturk A. Investigation of the Effectiveness of Lactobacillus reuteri DSM 17938 in the Treatment of Infantile Colic: A Double-Blind Placebo-Controlled Randomized Study. Hong Kong Journal of Pediatrics (New Series). 2022 Jul; 27: 182-7.

[20] Sung V, D'Amico F, Cabana MD, Chau K, Koren G, Savino F et al. Lactobacillus reuteri to Treat Infant Colic: A Meta-Analysis. Pediatrics. 2018 Jan; 141(1): e20171811. doi: 10.1542/peds.2017-1811.

DOI: https://doi.org/10.54393/pjhs.v7i2.3283

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Etiological Profile of Epilepsy in Patients at a Tertiary Care Hospital: An Observational Study

Waleed Arshad[1*], Shahbaz Khan[1], Samahir Akram Nizamani[1], Abdul Hafeez Bughio[1] and Manzoor Ali Lakhair[1]

[1]Department of Neurology, Liaquat University of Medical and Health Sciences, Hospital, Jamshoro, Pakistan

ARTICLE INFO

Keywords:
Epilepsy, International League Against Epilepsy Classification, Electroencephalography, Magnetic Resonance Imaging

How to Cite:
Arshad, W., Khan, S., Nizamani, S. A., Bughio, A. H., & Lakhair, M. A. (2026). Etiological Profile of Epilepsy in Patients at a Tertiary Care Hospital: An Observational Study: Etiological Profile of Epilepsy in Patients at a Tertiary Care Hospital. Pakistan Journal of Health Sciences, 7(2), 129-135. https://doi.org/10.54393/pjhs.v7i2.3283

***Corresponding Author:**
Waleed Arshad
Department of Neurology, Liaquat University of Medical and Health Sciences, Hospital, Jamshoro, Pakistan
weed.ars2012@yahoo.com

Received Date: 23rd June, 2025
Revised Date: 19th January, 2026
Acceptance Date: 26th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Epilepsy has diverse etiologies that vary by age, gender, and region. Identifying the cause is essential for management and prognosis. **Objectives:** To determine the etiological profile of epilepsy in patients at a tertiary care hospital and assess associations with age and gender. **Methods:** This observational study was conducted in the Department of Neuro-medicine, Liaquat University of Medical and Health Sciences, Jamshoro, from March 15 to September 14, 2022. A total of 156 patients aged ≥18 years with epilepsy for over five years were enrolled by consecutive sampling. Those with acute symptomatic seizures or incomplete records were excluded. Etiologies were classified using International League Against Epilepsy 2017 criteria based on electroencephalography and magnetic resonance imaging. **Results:** A total of 156 adult epilepsy patients were included (mean age 54.7 ± 15.6 years; 101 male, 55 female). Acute ischemic stroke was the most common etiology, 74 (47.4%), followed by idiopathic epilepsy, 29 (18.6%), brain tumors, 15 (9.6%), traumatic brain injury, 13 (8.3%), intracerebral hemorrhage, 10 (6.4%), CNS infections, 8 (5.1%), and encephalitis, 11 (7.1%). A higher proportion of female was observed within the brain tumor and idiopathic epilepsy subgroups, 10 (66.7%) and 19 (65.5%), respectively ($p < 0.05$); however, these findings reflect distribution within the tertiary cohort and should not be interpreted as population-level risk. Insignificant associations were found between etiology and age group or epilepsy duration. **Conclusions:** Acute ischemic stroke was the leading cause of epilepsy, with significant gender differences for brain tumors and idiopathic epilepsy.

INTRODUCTION

Epilepsy is common in resource-limited regions of Pakistan, notably Khyber Pakhtunkhwa and younger male, with associations including parental consanguinity (42.8%), low socioeconomic status (88.6%), and urban residence; treatment non-compliance, deprivation, and seizure type predict poor therapy response [1]. A tertiary hospital study of Karachi reported 42% of seizures as secondary, primarily from neonatal encephalopathy (18.7%), head trauma (18.2%), and CNS infections (17.9%) [2]. Further research is needed to clarify epilepsy etiologies and seizure types in Pakistan. Data from the Emergency Department of Aga Khan University Hospital, Karachi, indicate that structural lesions account for 89.6% of new-onset seizures, whereas idiopathic causes comprise only 4%, emphasizing the need for locally developed guidelines to support emergency physicians in accurate diagnosis and effective management [3]. Consanguineous marriages, observed in approximately 63% of tribal societies in Pakistan, are strongly associated with an increased risk of epilepsy, with an odds ratio of 3.25 (95% CI: 2.35–4.51, $p<0.001$). One study found that 37.33% of patients had parents who were first cousins, with rates exceeding 60% in certain tribal areas of Khyber Pakhtunkhwa [4]. Although some data are available for

DOI: https://doi.org/10.54393/pjhs.v7i2.3283

children showing that 45.5% of refractory pediatric epilepsy cases have an undetermined cause and that the ketogenic diet, when started gradually, is a safe and effective treatment for Pakistani children, there is a lack of comprehensive data on the use and effectiveness of this therapy in adult patients [5]. A North Indian study reported that infections, malignancies, and metabolic causes are more prevalent in younger patients with new-onset seizures, whereas strokes predominate in individuals over 55 years, underscoring the importance of age-specific diagnostic and therapeutic strategies [6]. Status epilepticus is a severe neurological emergency with high morbidity and mortality, most common in young children and the elderly. In Pakistan, infections (17%) and trauma (11%) are the leading causes. In our setting, it is rare, predominantly convulsive, with no non-convulsive cases, highlighting the need for larger studies [7]. Epilepsy affects ~46 million people globally, with a higher incidence in low-income regions. A Karachi study found normal EEGs in two-thirds of pediatric patients and interictal epileptiform discharges in one-third, with generalized epilepsy more common in older children and focal in younger, highlighting EEG's diagnostic value and limitations [8]. Machine learning shows potential for predicting outcomes in drug-resistant epilepsy but is underutilized in Pakistan. Using clinical and demographic data, a support vector machine achieved 76.1% overall accuracy, 96.7% for temporal lobe, and 79.5% for extratemporal epilepsy, supporting supervised classification and feature selection to improve presurgical predictions [9]. Tertiary care hospitals play a key role in managing complex and drug-resistant epilepsy, offering advanced diagnostics such as MRI, PET, EEG, and genetic testing. Even in resource-limited settings, epilepsy-specific MRI and video-EEG are essential for accurate diagnosis, syndrome classification, lesion identification, and surgical candidate selection [10].

Although epilepsy is a significant burden in Pakistan, there is sparse local data that has been systematically used to describe the etiological spectrum of epilepsy with the updated ILAE 2017 classification. The majority of literature is based on outdated classifications that do not involve the use of advanced modalities of diagnosis, thus incomplete epidemiological profiling and non-optimal management plans. This study aims to assess the etiological picture of adult epilepsy at a tertiary care unit using the ILAE 2017 framework, evaluate the demographic correlations, and consider the new diagnostic tools to improve clinical decision-making and better resource allocation to the region.

METHODS

This analytical cross-sectional study was conducted in the Department of Neuro-medicine at Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, from March 15 to September 14, 2022, following ethical approval from the Institutional Review Board of LUMHS (Approval No. LUMHS/REC/-180). Using a non-probability consecutive sampling method, 156 patients were enrolled to assess the etiological spectrum of epilepsy. The sample size for this study was determined using the World Health Organization (WHO) sample size calculator. Based on a previously reported prevalence of encephalitis of 6.94% among epilepsy patients, a 4% margin of error, and a 95% confidence interval, the required sample size was calculated to be 156 participants. However, this sample size was deemed adequate to provide sufficient statistical power to analyze etiological factors within the study population [11]. Patients aged 18 years or older, of either gender, presenting to the Neuro-medicine outpatient department with a clinical diagnosis of epilepsy were enrolled after obtaining informed written consent. Inclusion criteria encompassed all adult epilepsy patients regardless of seizure duration, thereby including both newly diagnosed and chronic cases. Explicit exclusion criteria were applied to minimize bias and included patients presenting with acute symptomatic seizures, those with incomplete or missing medical records, and individuals unwilling to participate. Comprehensive demographic and clinical data were systematically collected for each participant. This included basic demographic variables such as age, gender, weight, and height. Seizure types were classified according to the International League Against Epilepsy (ILAE) 2017 criteria to ensure standardized diagnostic categorization. A thorough neurological examination was conducted to identify any focal neurological deficits or signs suggestive of underlying etiologies. Additionally, information on comorbid medical conditions was documented, given their potential impact on disease progression and management. Details regarding anti-seizure medication (ASM) regimens, including types and dosages, were recorded alongside the current seizure control status, defined by frequency and severity of episodes. Relevant patient history was also obtained, covering prior central nervous system infections, perinatal insults, traumatic head injuries, and family history of epilepsy, factors critical to understanding genetic and environmental contributions to epilepsy. All data were meticulously recorded using a structured proforma to maintain uniformity, completeness, and accuracy for subsequent analysis. All patients underwent CT (Toshiba, Canon) and epilepsy-specific MRI (1.5T, high-resolution T1/T2 sequences; 3T MRI), along with EEG and standard 12-

DOI: https://doi.org/10.54393/pjhs.v7i2.3283

lead digital ECG for seizure classification. CT scans were reviewed by the principal investigator and confirmed by a consultant radiologist. Etiologies were classified as hemorrhagic/ischemic stroke, CNS infections, neoplasms, metabolic, or idiopathic. Combining EEG, ECG, and imaging allowed comprehensive etiological profiling, with all data collected personally by the principal researcher under standardized protocols. Data analysis was performed using IBM SPSS Statistics Version 26.0. Categorical variables such as gender, etiological categories, and seizure types were summarized as frequencies and percentages. Data were stratified by age, gender, and epilepsy duration to examine associations with etiological patterns. Chi-square or Fisher's exact tests were used as appropriate, with a p-value<0.05 considered statistically significant.

RESULTS

The descriptive characteristics of 156 patients with epilepsy included in the study. The mean age of the cohort was 54.72 ± 15.60 years, with a predominance of male, 101(64.7%), compared to female, 55(35.3%). The average duration of epilepsy was 8.35 ± 2.49 years. Regarding etiological distribution, acute ischemic stroke was the most common cause, observed in 74 (47.4%), followed by central nervous system infections in 29 (18.6%), including tuberculous meningitis in 18 (10.9%) and encephalitis in 11 (7.1%). Hemorrhagic stroke was identified in 21 (13.5%), brain tumors in 15 (9.6%), and idiopathic epilepsy in 29 (18.6%). Structural causes, especially stroke, predominated in this adult epilepsy cohort, with notable contributions from infectious and idiopathic etiologies (Table 1).

Table 1: Descriptive Statistics of Epileptic Patients with Total Sample Size (n=156)

Variables	Mean ± SD, n (%)
Age Group	54.72 ± 15.60
Male	101 (64.7%)
Female	55 (35.3%)
Duration of Epilepsy	8.35 ± 2.49
Hemorrhagic Stroke	21 (13.5%)
Acute Ischemic Stroke	74 (47.4%)
Central Nervous System Infections	29 (18.6%)
Tuberculous Meningitis	18 (10.9%)
Encephalitis	11 (7.1%)
Brain Tumors	15 (9.6%)
Idiopathic	29 (18.6%)

Table 2: Descriptive Statistics of Epileptic Patients with Total Sample Size (n=156)

Etiological Factors of Epilepsy		Age Group (in years)		95% Confidence Interval for Mean 18 – 50		95% Confidence Interval for Mean>50		p-value
		18 – 50	>50	Lower Bound	Upper Bound	Lower Bound	Upper Bound	
Hemorrhagic Stroke	Yes	9 (42.9%)	12 (57.1%)	6.1	24.5	5.8	18.9	0.609
	No	50 (37.0%)	85 (63.0%)					
Acute Ischemic Stroke	Yes	30 (40.5%)	44 (59.5%)	38.1	63.5	35.5	55.3	0.506
	No	29 (35.4%)	53 (64.6%)					
Central Nervous System Infections	Yes	12 (41.4%)	17 (58.6%)	10.1	30.6	9.9	25.1	0.661
	No	47 (37.0%)	80 (63.0%)					
Tuberculous Meningitis	Yes	9 (50.0%)	9 (50.0%)	6.1	24.5	3.5	15.1	0.204
	No	48 (35.8%)	86 (64.2%)					
Encephalitis	Yes	2 (18.2%)	9 (81.8%)	0.0	8.0%	3.5	15.1	0.141
	No	57 (39.3%)	88 (60.7%)					
Brain Tumors	Yes	6 (40.0%)	9 (60.0%)	2.5	17.9	3.5	15.1	0.855
	No	53 (37.6%)	88 (62.4%)					
Idiopathic	Yes	7 (4.5%)	22 (14.1%)	3.6	20.1	14.4	31.0	0.092
	No	52 (33.3%)	75 (48.1%)					

Applied Chi-square and Fisher's Exact test

The distribution of epilepsy etiologies according to gender in the study cohort (n=156). Hemorrhagic stroke, acute ischemic stroke, central nervous system infections, tuberculous meningitis, and encephalitis showed no significant differences between male and female (p>0.05 for all). In contrast, brain tumors and idiopathic epilepsy demonstrated significant gender differences, with female accounting for a higher proportion in both categories: brain tumors: 66.7% female vs. 33.3% male (p=0.010), and idiopathic epilepsy: 12.2% female vs. 6.4% male (p<0.001). Most etiologies were similarly distributed by gender, with higher frequencies of brain tumors and idiopathic epilepsy among female (Table 3).

DOI: https://doi.org/10.54393/pjhs.v7i2.3283

Table 3: Stratification of Gender with Etiological Factors of Epilepsy (n=156)

Etiological Factors of Epilepsy		Gender		95% Confidence Interval for Mean Male		95% Confidence Interval for Mean Female		p-value
		Male	Female	Lower Bound	Upper Bound	Lower Bound	Upper Bound	
Hemorrhagic Stroke	Yes	13 (61.9%)	8 (38.1%)	6.4	19.4	5.2	23.9	0.770
	No	88 (65.2%)	47 (34.8%)					
Acute Ischemic Stroke	Yes	49 (66.2%)	25 (33.8%)	38.8	58.3	32.3	58.6	0.715
	No	52 (63.4%)	30 (36.6%)					
Central Nervous System Infections	Yes	15 (51.7%)	14 (48.3%)	7.9	21.8	13.9	37.0	0.104
	No	86 (67.7%)	41 (32.3%)					
Tuberculous Meningitis	Yes	14 (77.7%)	4 (22.3%)	7.1	20.6	0.4	14.1	0.398
	No	85 (63.4%)	49 (36.6%)					
Encephalitis	Yes	7 (63.6%)	4 (36.4%)	2.0	11.9	0.4	14.1	0.586
	No	94 (64.8%)	51 (35.2%)					
Brain Tumors	Yes	5 (33.3%)	10 (66.7%)	0.7	9.2	8.0	28.3	0.010
	No	96 (68.1%)	45 (31.9%)					
Idiopathic	Yes	10 (6.4%)	19 (12.2%)	4.1	15.7	21.9	47.0	<0.001
	No	91 (58.3%)	36 (23.1%)					

Applied Chi-square and Fisher's Exact test

The relationship between epilepsy duration and etiological factors in the study cohort (n=156), with durations categorized as 6–8 years and >8 years. Across all etiologies, including hemorrhagic stroke, acute ischemic stroke, central nervous system infections, tuberculous meningitis, encephalitis, brain tumors, and idiopathic epilepsy, no significant differences were observed between the two duration groups ($p>0.05$ for all). Etiological distribution was independent of epilepsy duration (Table 4).

Table 4: Stratification for Duration of Epilepsy with Etiological Factors of Epilepsy (n=156)

Etiological Factors of Epilepsy		Duration (in Years)		95% Confidence Interval for Mean 6 – 8		95% Confidence Interval for Mean >8		p-value
		6 – 8	>8	Lower Bound	Upper Bound	Lower Bound	Upper Bound	
Hemorrhagic Stroke	Yes	14 (66.7%)	7 (33.3%)	6.7	19.5	4.5	24.1	0.838
	No	93 (68.9%)	42 (31.1%)					
Acute Ischemic Stroke	Yes	49 (66.2%)	25 (33.8%)	36.4	55.3	37.0	65.0	0.544
	No	58 (70.7%)	24 (29.3%)					
Central Nervous System Infections	Yes	18 (62.1%)	11 (37.9%)	9.8	23.9	10.7	34.1	0.402
	No	89 (70.1%)	38 (29.9%)					
Tuberculous Meningitis	Yes	12 (66.6%)	6 (22.4%)	5.2	17.2	3.1	21.4	0.589
	No	93 (69.4%)	41 (30.6%)					
Encephalitis	Yes	6 (54.5%)	5 (45.5%)	1.3	9.9	1.7	18.6	0.236
	No	101 (69.7%)	44 (30.3%)					
Brain Tumors	Yes	11 (73.3%)	4 (26.7%)	4.6	16.0	0.5	15.8	0.463
	No	96 (68.1%)	45 (31.9%)					
Idiopathic	Yes	19 (12.2%)	10 (6.4%)	10.5	25.0	9.1	31.7	0.693
	No	88 (56.4%)	39 (25.0%)					

Applied Chi-square and Fisher's Exact test

DISCUSSION

This study characterized the etiological spectrum of adult epilepsy at a tertiary Pakistani hospital, identifying acute ischemic stroke as the leading cause, followed by idiopathic epilepsy and brain tumors. These results align with global trends recognizing cerebrovascular disease as a major contributor to adult-onset epilepsy, particularly in aging populations. Globally, stroke accounts for ~10% of epilepsy cases and up to 50% in adults >60 years. Hemorrhagic stroke, cortical involvement, and early seizures increase risk, with Select (AUC 0.77) and CAVE (AUC 0.81) showing good predictive accuracy [12]. In our cohort, acute ischemic stroke (47.4%) and intracerebral hemorrhage (6.4%) mirrored global trends, underscoring the need for stroke prevention, optimal management, and validated prediction tools. Meningiomas, common primary brain tumors, frequently cause seizures, with complete resection achieving up to 90% seizure freedom. Postoperative risk depends on histology, location, edema,

DOI: https://doi.org/10.54393/pjhs.v7i2.3283

recurrence, and complications, while long-term antiepileptic benefit is limited [13]. In our study, brain tumors caused 9.6% of cases, with a higher proportion of female observed within the brain tumor and idiopathic epilepsy subgroups (66.7% vs. 33.3%, p=0.010); however, these findings reflect distribution within the tertiary cohort and should not be interpreted as a higher population-level risk, highlighting the importance of surgical and risk-based management. A meta-analysis of 22 voxel-based morphometry studies involving 913 patients with idiopathic generalized epilepsy demonstrated increased cortical and decreased subcortical gray matter, indicative of thalamocortical network disruption [14]. In our cohort, idiopathic epilepsy accounted for 18.6% of cases and showed a higher proportion of female (p<0.001). However, this finding reflects the distribution within our tertiary care sample and should not be interpreted as indicating a higher population-level risk for female, while the normal conventional imaging in most cases is consistent with the absence of overt structural lesions in idiopathic epilepsy. A study of 198 patients with new-onset seizures reported that most were middle-aged (35–65 years, 44.4%) with a slight female predominance (55.1%), and structural brain lesions were the predominant etiology [15]. Similarly, in our cohort (mean age 54.72 ± 15.60 years; male-to-female ratio 2:1), acute ischemic stroke (47.4%) and brain tumors (9.6%) were the leading causes, reinforcing the impact of structural lesions in adult-onset epilepsy and the need for region-specific diagnostic and management approaches. A previous study of 996 patients reported primary seizures in 58% and secondary in 42%, with structural lesions including head trauma, tumors, and stroke predominating in adults, and generalized tonic–clonic seizures being most common [16]. Similarly, in our 156-patient cohort, acute ischemic stroke was the leading cause (47.4%), followed by idiopathic epilepsy (18.6%), brain tumors (9.6%), and traumatic brain injury (8.3%), with generalized seizures predominating, confirming the association of adult-onset epilepsy with structural brain lesions. In a retrospective study of 431 adult epilepsy patients at King Abdulaziz Medical City, generalized seizures were most common (25.3%), with structural etiologies predominating (42.9%), particularly stroke (24.3%) and tumors (23.8%), while 47.6% remained of unknown etiology [17]. In our 156-patient cohort, structural causes predominated acute ischemic stroke (47.4%), idiopathic epilepsy (18.6%), brain tumors (9.6%), and traumatic brain injury (8.3%), with more female in tumor-related and idiopathic cases, reflecting global trends and regional demographic variations. A retrospective review of 1,097 pediatric epilepsy patients at The Children's Hospital, Lahore (2016–2020), found afebrile (72.7%) and generalized seizures (49.8%) most common, with idiopathic (49.2%) and congenital (20.8%) etiologies; typical seizures lasted 1–3 minutes, with up-rolling eyes and frothing (34.9%) frequently observed [18]. In contrast, our adult cohort showed higher structural etiology prevalence of acute ischemic stroke (47.4%) and brain tumors (9.6%), with idiopathic epilepsy at 18.6%, highlighting age-related differences in etiology and seizure patterns. A 25-year retrospective study of 5,712 adult-onset epilepsy patients in China reported declining unknown etiologies, predominance of structural epilepsy, especially cerebrovascular in older adults, higher rates in male, and a recent rise in immune-related cases [19]. Similarly, our study found structural causes, particularly acute ischemic stroke (47.4%), as the most common, with idiopathic epilepsy and brain tumors more frequent in specific subgroups, highlighting age- and sex-related differences and the need for targeted diagnostics and management. This study has several limitations. The cross-sectional design precludes assessment of temporal or causal relationships, and observed associations reflect cohort distributions rather than independent risk factors. Multivariate analysis was not performed; therefore, associations across age and sex subgroups may be confounded by factors such as disease severity, comorbidities, or referral patterns. The single tertiary care–center setting limits generalizability and may overrepresent structural or severe epilepsy. Etiological subcategories, particularly central nervous system infections, were analyzed by case distribution rather than population prevalence; thus, subgroup proportions should not be interpreted as population-level risk [20].

Finally, limited access to advanced diagnostics (e.g., prolonged video-EEG, autoimmune, and genetic testing) may have led to under- or misclassification in some cases. Despite these limitations, the study provides valuable tertiary care–based insights into epilepsy etiology, highlighting the predominance of post-stroke and other structural causes. The findings underscore the need for integrated neurological follow-up for stroke survivors, improved diagnostic pathways to distinguish seizures from acute cerebrovascular events, and strengthened prevention strategies targeting cerebrovascular disease and central nervous system infections. Future multicenter, longitudinal studies with multivariate modeling and advanced diagnostics are warranted to identify independent predictors and support personalized epilepsy management. The study was a single tertiary center cross-sectional study, which is unable to cause causality, and results might be biased to structural or severe epilepsy as opposed to the general population. Case distribution was used to analyze etiological subgroups and, in particular,

DOI: https://doi.org/10.54393/pjhs.v7i2.3283

central nervous system infections; proportions cannot be used to denote risk at the population level. Out of disturbed diagnostics, it might have under- or misclassified certain types of epilepsy due to limited accessibility. Despite these drawbacks, the research offers good information on the pattern of adult epilepsy and the necessity of developing special diagnostics, prevention, and treatment measures.

CONCLUSIONS

Acute ischemic stroke was the leading cause of epilepsy in this cohort, with gender differences observed in brain tumor–related and idiopathic cases. These findings underscore the importance of systematic evaluation and region-specific management strategies, including timely neuroimaging and electrophysiological assessment, to guide targeted interventions, improve stroke prevention, and optimize epilepsy care.

Authors' Contribution

Conceptualization: WA, MAL
Methodology: WA, SK, MAL
Formal analysis: WA, SK, SAN, AHB, MAL
Writing and Drafting: WA, SK, SAN, AHB, MAL
Review and Editing: SK, SAN, AHB, WA, MAL

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Ullah S, Ali N, Khan A, Ali S, Nazish HR. The Epidemiological Characteristics of Epilepsy in the Province of Khyber Pakhtunkhwa, Pakistan. Frontiers in Neurology. 2018 Nov; 9: 845. doi: 10.3389/fneur.2018.00845.

[2] Jawaid W, Nisa Q, Umer SR, Barry SJ, Qureshi A, Shahbaz NN. Etiology and Types of Seizures in Patients Presenting to a Tertiary Care Hospital in Karachi: A Cross-Sectional Study. Cureus. 2020 Jul; 12(7). 1-10. doi: 10.7759/cureus.9194.

[3] Ali N, Dharamshi HA, Mustahsan S, Noorani S. Etiology and Outcomes of New Onset Seizure in Adult Patients: A Clinical Experience from the Emergency Department of a Tertiary Care Center. Pakistan Journal of Medical Sciences. 2022 May; 38(5): 1382. doi: 10.12669/pjms.38.5.4411.

[4] Badshah N, Ahmad S, Khan SH, Qureshi SA, Sarwar MT. Epilepsy in the Consanguineous Families at Tribal Society of Khyber Pakhtunkhwa, Pakistan. Journal of Medical Sciences. 2022 Apr; 30(1): 32-36. doi: 10.52764/jms.22.30.1.7.

[5] Anjum N, Zafar F, Yousuf M, Khattak ZU. Efficacy and Safety of the Ketogenic Diet Therapy in Pakistani Children with Refractory Epilepsy. Khyber Medical University Journal. 2023 Jun; 15(2): 111-115.

[6] Bhatia MS, Sharda SC, Yadav G, Mehta S, Attri R, Singla N. Etiology of New-Onset Seizures in Adult Patients of Different Age Groups Presenting to The Emergency Department in North India and Their Outcomes. Journal of Family Medicine and Primary Care. 2022 Nov; 11(11): 7129-7135. doi: 10.4103/jfmpc.jfmpc_730_22.

[7] Tabassum S, Soomro MH, Ali A, Ahmed I, Shafique S, Rahman M *et al.* The Status Epilepticus in Adults: Results from a Tertiary Care Teaching Hospital in Karachi, Pakistan. Bangladesh Journal of Medical Science. 2023 Jan; 22(1): 128-134. doi: 10.3329/bjms.v22i1.61861

[8] Hassan F, Ali S, Munir M, Masood A, Obaid MS, Baig RU *et al.* Assessment of Frequency of Electroencephalogram Findings in Children with Epilepsy in A Tertiary Care Hospital in Karachi, Pakistan: Frequency of Electroencephalogram Findings in Children with Epilepsy. Pakistan BioMedical Journal. 2022 Jun: 258-261. doi: 10.54393/pbmj.v5i6.565.

[9] Jourahmad Z, Habibabadi JM, Moein H, Basiratnia R, Geranqayeh AR, Ghidary SS *et al.* Machine Learning Techniques for Predicting the Short-Term Outcome of Resective Surgery in Lesional Drug-Resistant Epilepsy. arXiv preprint arXiv. 2023 Feb: 1-10.

[10] Asadi-Pooya AA, Damabi NM, Fazelian K, Moshfeghinia R, Niknam N. How to Successfully Establish an Epilepsy Care Center in Resource-Limited Countries: A Scoping Systematic Review. Seizure: European Journal of Epilepsy. 2023 Jul; 109: 92-96. doi: 10.1016/j.seizure.2023.06.001.

[11] Mahmoud MH, Awad EM, Mohamed AK, Shafik MA. Etiological Profile of New-Onset Seizures Among Adult Egyptians. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2021 Jul; 57(1): 95. doi: 10.1186/s41983-021-00349-6.

[12] Mafla-Mendoza AP, Paredes-Urbano ED, Gea-Izquierdo E. Risk Factors Associated with Epilepsy Related to Cerebrovascular Disease: A Systematic Review and Meta-Analysis. Neuropsychiatric Disease and Treatment. 2023 Dec: 2841-2856. doi: 10.2147/NDT.S439995.

[13] Masroor M, Bakhshi SK, Shamim MS. Seizure Outcomes After Meningioma Resection. The Journal of the Pakistan Medical Association. 2022 Apr; 72(4):

DOI: https://doi.org/10.54393/pjhs.v7i2.3283

776-778. doi: 10.47391/JPMA.22-31.

[14] Huang X, Mao L, Lin Q, Huang K, Li Y, Liu P *et al.* Voxel-Based Meta-Analysis of Gray Matter Abnormalities in Idiopathic Generalized Epilepsy. Cerebral Cortex. 2025 Aug; 35(8): 201. doi: 10.1093/cercor/bhaf201.

[15] Habib R, Haque MR, Khan MS, Alam D, Islam MR. Acute Symptomatic Seizures in Adults: A Study on Etiological Profile. Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders Medical Journal. 2022 May; 12(2): 99-105. doi: 10.3329/birdem.v12i2.59609.

[16] Masood R, Malik M, Rana MT, Habib S, Nawaz A, Habib T. Clinical Outcomes and Frequency of Electroencephalographic Abnormalities in Patients with First Unprovoked Seizure in a Tertiary Care Hospital. Pakistan Journal of Health Sciences. 2025 Jun; 6(6): 144-148.

[17] Makkawi S, Alshehri FS, Malaikah AA, Alghamdi AM, Al-Zahrani RM, Nahas RJ *et al.* Prevalence of Etiological Factors in Adult Patients with Epilepsy in a Tertiary Care Hospital in the Western Region of Saudi Arabia: A Cross-Sectional Study. Cureus. 2023 Jan; 15(1). doi: 10.7759/cureus.33301.

[18] Hameed AN, Nawaz MT, Hamza Khan MM, Tauqeer H, Angez M, Nazir Khan MM. Surveillance of Aetiologies, Clinical Presentation, and Most Common Types of Epilepsy Among Paediatric Patients at a Tertiary Care Hospital in Pakistan. The Journal of the Pakistan Medical Association. 2023 Mar; 73(3): 723-727. doi: 10.47391/JPMA.6200.

[19] Zhang X, Wang Z, Xiang F, Li Y, Shi X, Shao C *et al.* Etiologies of Patients with Adult-Onset Epilepsy Over the Past 25 Years: A Retrospective Study in China. BioMed Center Neurology. 2025 Dec; 25(1): 512. doi: 10.1186/s12883-025-04511-y.

[20] Beghi E, Giussani G, Sander JW, Perucca E, Hauser WA, Hesdorffer DC *et al.* The Epidemiology of Epilepsy: A Systematic Review of Population-Based Studies. Epilepsia. 2023; 64(2): 321-341.

DOI: https://doi.org/10.54393/pjhs.v7i2.3790

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Original Article

OPEN ACCESS

Efficacy of Long-Term Low-Dose Macrolide Therapy in Preventing Early Recurrence of Nasal Polyps after Endoscopic Sinus Surgery

Muhammad Shouzib Sultan[1*] and Waqas Javaid[1]

[1]Department of ENT, Fatima Jinnah Medical University, Sir Ganga Ram Hospital, Lahore, Pakistan

ARTICLE INFO

Keywords:
Nasal Polyps, Endoscopic Sinus Surgery, Macrolides, Lund-Kennedy, Lund-Mackay

How to Cite:
Sultan, M. S., & Javaid, W. (2026). Efficacy of Long-Term Low-Dose Macrolide Therapy in Preventing Early Recurrence of Nasal Polyps after Endoscopic Sinus Surgery: Long-Term Low-Dose Macrolides and Nasal Polyp Recurrence. Pakistan Journal of Health Sciences, 7(2), 136-141. https://doi.org/10.54393/pjhs.v7i2.3790

***Corresponding Author:**
Muhammad Shouzib Sultan
Department of ENT, Fatima Jinnah Medical University, Sir Ganga Ram Hospital, Lahore, Pakistan
dr.shouzib79@gmail.com

Received Date: 3rd January, 2026
Revised Date: 27th January, 2026
Acceptance Date: 19th February, 2026
Published Date: 28th February, 2026

ABSTRACT

Long-term low-dose macrolide therapy has been shown to reduce eosinophilic inflammation and delay early recurrence of nasal polyps following endoscopic sinus surgery (ESS). **Objective:** To compare the efficacy of long-term low-dose macrolide therapy in preventing early recurrence of nasal polyps after endoscopic sinus surgery. **Methods:** This randomized controlled trial was conducted in the Department of ENT, Sir Ganga Ram Hospital, Lahore, from October to December 2025. Male and female patients aged 15–75 years diagnosed with nasal polyps and undergoing ESS were included. Patients already receiving antibiotics or macrolides, those with multiple facial fractures, or those with neurological or psychological disorders were excluded. Preoperatively, Sino-Nasal Outcome Test (SNOT), Lund-Kennedy endoscopic score, and Lund-Mackay CT score were recorded. Postoperatively, Group A received clarithromycin 250 mg once daily for three months in addition to standard therapy, while Group B received standard postoperative treatment alone. Outcomes were reassessed at 8 and 12 weeks, and recurrence of nasal polyps was evaluated after three months. **Results:** Mean SNOT scores showed significant improvement in the macrolide group compared to controls at both 8 and 12 weeks ($p<0.05$). Similarly, Lund-Mackay and Lund-Kennedy scores demonstrated significantly greater reductions in the macrolide group than in the non-macrolide group ($p<0.05$). Recurrence of nasal polyps was observed in 12% of patients receiving macrolide therapy compared to 32% in the control group. **Conclusions:** Three-month low-dose clarithromycin therapy (250 mg/day) is a safe and effective adjunct to ESS, significantly improving clinical, endoscopic, and radiological outcomes while reducing early recurrence of nasal polyps.

INTRODUCTION

A chronic inflammatory disease that affects the sinuses and nasal canal, chronic rhinosinusitis affects 8% of Asians. Endoscopic sinus surgery plus typical post-operative medications, such as antibiotics, intranasal corticosteroids, mucolytic agents, oral hormones, and nasal irrigation, can cure chronic rhinosinusitis in 75% to 98% of cases; however, about 10% of patients still do not experience the desired clinical outcomes [1, 2]. Chronic rhinosinusitis has recently been treated with long-term, low-dose macrolide therapy [3]. Patients with other chronic inflammatory airway illnesses, including chronic rhinosinusitis without polyps, have reported the anti-inflammatory effects of macrolides, particularly clarithromycin. The literature contains conflicting views on the effectiveness of clarithromycin for individuals with chronic rhinosinusitis and sinonasal polyposis, and there are no national prospective studies evaluating the drug's efficacy in treating chronic rhinosinusitis within our population [4]. The absence of evidence in systematic reviews is reflected in the inconsistent guidelines about the inclusion of antibiotics in basic medical care. A fivefold difference in intervention rates can be explained by insufficient evidence to substantiate the role of surgery [5]. After endoscopic sinus surgery, "long-term" low-dose clarithromycin (250 mg/day) can reduce eosinophilic inflammation and stop nasal polyps from relapsing too

DOI: https://doi.org/10.54393/pjhs.v7i2.3790

soon [6, 7]. When compared to baseline, macrolide therapy can dramatically improve endoscopic and CT scores in patients with chronic rhinosinusitis. To verify the effectiveness and safety of macrolides in the treatment of chronic rhinosinusitis, further well-planned research is required [1]. One study in Iraq found that the Lund-Mackay score decreased from 20.53 ±2.16 to 5.90 ± 2.81 with macrolide, from 19.55 ± 3.14 to 8.45 ± 2.76 without macrolide ($p<0.05$), and the Lund-Kennedy score decreased from 18.13 ± 1.36 to 4.30 ± 0.65 with macrolide and from 17.52 ± 1.46 to 4.48 ± 0.79 without macrolide ($p>0.05$). These findings were reported in an Iraqi study [8]. With macrolide, regrowth is seen in 11% of cases, but 32% of cases without macrolide exhibit regrowth or recurrence of nasal polyps [9].

The purpose of this study was to compare the results of endoscopic sinus surgery and long-term low-dose macrolide therapy for nasal polyps. According to research, using low-dose macrolides over an extended period of time can lower the chance that nasal polyps will return following sinus surgery. There hasn't been any prior research in this area, and there isn't much local data in the literature to support our decision to add a macrolide for longer-term treatment. As a result, we intend to carry out this investigation. The study's findings will assist us in obtaining local magnitudes, which will enable us to apply the conclusions in a local context. This will enable us to enhance our procedures. Even after endoscopic surgery and conventional postoperative treatment, nasal polyp recurrence is still a serious clinical complication. Even though it is long-term and low doses of macrolide have demonstrated potential anti-inflammatory effects, the evidence on its effects in the prevention of postoperative polyp recurrence is inconsistent and limited, especially in local populations. The study aimed to compare the effectiveness of low-dose macrolide long-term treatment in preventing early recurrence of nasal polyps after endoscopic sinus surgery.

METHODS

The ENT Department at Sir Ganga Ram Hospital in Lahore conducted this randomized controlled experiment registered at clinicaltrials.gov (NCT07316959) from October to December 2025 after getting ethical approval (260/Proposal-ENT/ERC). A sample size of 100 cases, 50 in each group, was determined using the WHO calculator, with a 5% significance level, 80% study power, and the percentage of recurrence, which is 11% with macrolide and 32% without it, following endoscopic sinus surgery [9]. Both male and female patients between the ages of 15 and 75 who have been diagnosed with nasal polyps, a persistent swelling and inflammation of the nose brought on by chronic rhinosinusitis, are having endoscopic sinus surgery. Patients who were already taking antibiotics or macrolides, had multiple facial fractures, had ASA III or IV, or had neurological or psychological conditions were not included. One hundred patients who met the inclusion criteria were enrolled through the ENT wards following ethical review board permission. Written informed consent was obtained. Additional demographic data were recorded, including name, age, sex, duration of symptoms, domicile, socioeconomic level, history of diabetes, hypertension, smoking, allergic rhinitis, nasal polyps in the family history, and ASA status. Before surgery, the SNOT, Lund-Kennedy score, and Lund-Mackay score were recorded. The procedure's duration was recorded. Following surgery, patients were split into two groups at random using a lottery. For three months, patients in group A received Macrolide (clarithromycin 250 mg) once a day in addition to their usual prescription drugs. Following surgery, participants in group B received their usual prescriptions. Patients were evaluated for SNOT, Lund-Kennedy score, and Lund Mackay score at 8 and 12 weeks of therapy. Patients were also checked for nasal polyp recurrence after three months, if it was detected on a CT scan twelve weeks after surgery.

SPSS version 25.0 was used to examine the data that was gathered. The mean and standard deviation of quantitative factors, such as age, symptom duration, operative time, SNOT, Lund-Kennedy score, and Lund-Mackay score, were displayed. The frequency and percentage of qualitative characteristics, such as recurrence, gender, ASA, residence, socioeconomic position, and history (diabetes, hypertension, smoking, allergic rhinitis, and family history of nasal polyps), were displayed. The Lund-Kennedy, Lund-Mackay, and mean SNOT scores for both groups were compared using the t-test, and recurrence was evaluated using chi-square. A p-value significance level of ≤0.05 was used.

DOI: https://doi.org/10.54393/pjhs.v7i2.3790

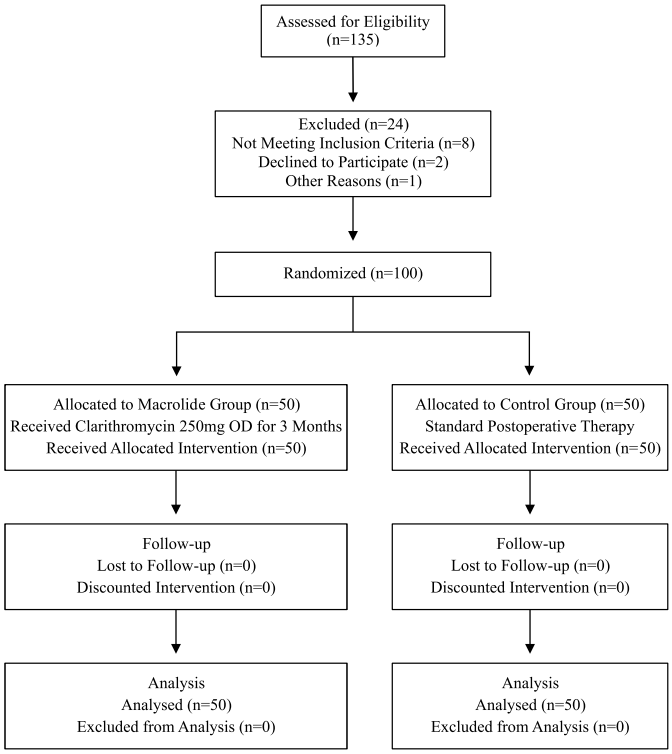

Figure 1: CONSORT Flow Diagram

RESULTS

This study involved 100 patients. In Group A, 50 patients (31 men and 19 women) with a mean age of 37.60 ± 13.18 years were examined. Group B consisted of 50 patients, with a mean age of 39.62±13.30 years, including 32 men and 18 women. The mean duration of symptoms in group A was 6.66 ± 1.99 weeks, and in group B was 6.70 ± 1.79 weeks. Mean operative time in group A was 34.48 ± 8.12 minutes, and in group B was 35.76 ± 9.38 minutes (Table 1).

Table 1: Distribution of Different Variables (n=100)

Variables	Group A (n=50), n (%)	Group B (n=50), n (%)
Age (Years)		
15-45	38 (76.0%)	33 (66.0%)
46-75	12 (24.0%)	17 (34.0%)
Gender		
Male	31 (62.0%)	32 (64.0%)
Female	19 (38.0%)	18 (36.0%)
Duration of symptoms (weeks)		
≤8	41 (82.0%)	42 (84.0%)
>8	09 (18.0%)	08 (16.0%)
ASA status		
I	27 (54.0%)	28 (56.0%)
II	23 (46.0%)	22 (44.0%)
Operative time (min)		
≤30	18 (36.0%)	18 (36.0%)
>30	32 (64.0%)	32 (64.0%)
SES		
Poor	14 (28.0%)	13 (26.0%)
Middle	28 (56.0%)	29 (58.0%)
Upper	08 (16.0%)	08 (16.0%)
Residence		
Rural	27 (54.0%)	25 (50.0%)
Urban	23 (46.0%)	25 (50.0%)
Hypertension		
Yes	11 (22.0%)	12 (24.0%)
No	39 (78.0%)	38 (76.0%)
Diabetes mellitus		
Yes	10 (20.0%)	11 (22.0%)
No	40 (80.0%)	39 (78.0%)
Smoking		
Yes	13 (26.0%)	18 (36.0%)
No	37 (74.0%)	32 (64.0%)
Allergic rhinitis		
Yes	08 (16.0%)	07 (14.0%)
No	42 (84.0%)	43 (86.0%)
Family h/o nasal polyp		
Yes	06 (12.0%)	06 (12.0%)
No	44 (88.0%)	44 (88.0%)

This study reported that the mean pre-operative SNOT score was 76.38 ± 5.00 and after 8 weeks and 12 weeks was 13.74 ± 1.65 and 9.72 ± 1.86 with macrolide treatment while from 77.95 ± 5.25, 20.80 ± 3.14 and 13.72 ± 1.95 without macrolide treatment ($p<0.05$), Lund-Mackay score was 20.08 ± 1.93, 5.88 ± 1.00 and 3.72 ± 0.81 with macrolide while 20.76 ± 1.46, 11.32 ± 0.96 and 7.86 ± 0.99 without macrolide ($p<0.05$) and Lund-Kennedy score was from 16.68 ± 1.41, 4.86 ± 1.11 and 2.74 ± 0.69 with macrolide and 16.54 ± 1.37, 11.38 ± 1.28 and 7.88 ± 0.90 without macrolide ($p<0.05$) (Table II).

Table 2: Comparison of the Outcome between Both Groups

Variables	Group A (n=50), Mean ± SD	Group B (n=50), Mean ± SD	p-value
Pre-Operative SNOT Score	76.38 ± 5.00	77.95 ± 5.25	0.128
After 8 Weeks SNOT Score	13.74 ± 1.65	20.80 ± 3.14	<0.001
After 12 Weeks SNOT Score	9.72 ± 1.86	13.72 ± 1.95	<0.001
Pre-Operative Lund-Kennedy Score	16.68 ± 1.41	16.54 ± 1.37	0.616
After 8 Weeks, Lund-Kennedy Score	4.86 ± 1.11	11.38 ± 1.28	<0.001
After 12 Weeks Lund-Kennedy Score	2.74 ± 0.69	7.88 ± 0.90	<0.001
Pre-Operative Lund-Mackay Score	20.08 ± 1.93	20.76 ± 1.46	0.049
After 8 Weeks, Lund-Mackay Score	5.88 ± 1.00	11.32 ± 0.96	<0.001
After 12 Weeks Lund-Mackay Score	3.72 ± 0.81	7.86 ± 0.99	<0.001

Recurrence was observed in 12% with macrolide, while 32% without macrolide, with statistically significant associations ($p=0.0158$) (Table3).

DOI: https://doi.org/10.54393/pjhs.v7i2.3790

Table 3: Comparison of the Recurrence between Both Groups

Resources	Group A (n=50), Frequency (%)	Group B (n=50), Frequency (%)	p-value
Yes	06 (12.0%)	16 (32.0%)	0.015
No	44 (88.0%)	34 (68.0%)	

DISCUSSION

Low-dose long-term (LDLT) macrolide therapy is a lengthier course of treatment with a lower dose than what is used to treat a bacterial infection that comes on suddenly. In 1984, LDLT erythromycin was used for the first time in Japan to treat patients with diffuse panbronchiolitis [10, 11]. Through a variety of mechanisms, macrolides' immunomodulatory and anti-inflammatory potencies, as well as their antibacterial qualities, are believed to be useful in controlling these disorders [12, 13]. According to this study, the mean pre-operative SNOT score was 76.38 ± 5.00, and the Lund Mackay score was 20.08 ± 1.93, 5.88 ± 1.00, and 3.72 ± 0.81 with macrolide and 20.76 ± 1.46, 11.32 ± 0.96, and 7.86 ± 0.99 without macrolide ($p<0.05$). The Lund-Kennedy score was 16.68 ± 1.41, 4.86 ± 1.11, and 2.74 ± 0.69 with macrolide and 16.54 ± 1.37, 11.38 ± 1.28, and 7.88 ± 0.90 without macrolide ($p<0.05$). Recurrence was seen in 32% of cases without macrolide and 12% of cases with it. One study in Iraq found that the Lund-Mackay score decreased from 20.53 ± 2.16 to 5.90 ± 2.81 with macrolide, from 19.55 ± 3.14 to 8.45 ± 2.76 without macrolide ($p<0.05$), and the Lund-Kennedy score decreased from 18.13 ± 1.36 to 4.30 ± 0.65 with macrolide and from 17.52 ± 1.46 to 4.48 ± 0.79 without macrolide ($p>0.05$). These findings were reported in an Iraqi study [8]. After receiving clarithromycin for 8–12 weeks, 40% of the 20 CRSwNP patients saw a reduction in the size of their nasal polyps and a notable decrease in the amount of IL-8 in their lavage fluid; the remaining 60% exhibited no change [14]. Eight weeks of 500 mg of clarithromycin before surgery cut down on the number of polyps that came back six and twelve months after surgery [15]. SNOT-20 scores of CRSwNP patients improved following eight weeks of steroid monotherapy and low-dose clarithromycin combination therapy [16]. With LDLT clarithromycin, 52 CRSwNP patients experienced a significant decrease in their SNOT-20 and Lund-Kennedy endoscopic score after 12 weeks [17]. Furthermore, compared to those who did not improve on SNOT-20, 54% (28 of 52) exhibited lower levels of total IgE. Three months of 150 mg roxithromycin treatment resulted in significant improvements in mucociliary transit time, nasal endoscopy results, and sinus nasal symptoms (SNOT- 20) in CRSsNP patients [18]. At three months, there were no significant differences between the two groups when looking at either the endoscopic results or the visual analogy ratings of symptoms. Clinical improvement was also observed in CRSsNP patients after 8 weeks of erythromycin treatment [19]. Apart from severe polyposis, LDLT azithromycin exhibited no significant differences between the treatment and placebo groups in a mixed cohort of CRSwNPs (52.0%) and CRSsNPs [20]. A biomarker analysis showed that the overall symptom score was a good sign for predicting which patients with CRS would need macrolide therapy following surgery [21]. In the Netherlands, a pragmatic, multicentre RCT comparing endoscopic sinus surgery + medication to medication alone in adults with chronic rhinosinusitis and nasal polyps has been published since the start of the MACRO Program. Additionally, the study demonstrated increased efficacy with surgery; however, the mean difference between groups in SNOT-22 at 6 months did not reach the minimal clinically significant difference. Patients who had not responded to proper medical therapy were also enrolled in the trial. Medical therapy is any medical intervention, without standardization, that the participant's otorhinolaryngologist deems appropriate, such as systemic antibiotics, intranasal corticosteroids, and systemic corticosteroids [22].

In spite of evidence that low-dose long-term macrolide treatment is associated with better symptom scores, endoscopic results, and lower recurrence rates, the small sample size, heterogeneity of disease phenotypes, and absence of follow-up limit the ability to make certain conclusions about the long-term effectiveness and safety. Large multicentric randomized trials with prolonged follow-up and the use of biomarkers to select patients in future investigations should define responders better and improve the use of postoperative macrolides with concerns of antimicrobial resistance.

CONCLUSIONS

Our study's findings supported the safety and effectiveness of a three-month low-dose (250 mg/day) clarithromycin treatment in preventing early recurrence of nasal polyps after endoscopic sinus surgery. This treatment was found to be substantially associated with an improvement in quality of life, as measured by SNOT-20, LMS, and LKS, and it can prevent an early recurrence of NP. Patient selection is essential to the successful administration of macrolide treatment in CRS. Particularly for CRS patients with comorbidities, our study advised using the macrolide at a low dose for three months after surgery.

DOI: https://doi.org/10.54393/pjhs.v7i2.3790

Authors' Contribution

Conceptualization: MSS
Methodology: MSS
Formal analysis: MSS, WJ
Writing and Drafting: WJ
Review and Editing: MSS, WJ

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Chen H, Zhou B, Huang Q, Li C, Wu Y, Huang Z *et al.* Efficacy and Safety of Long-Term Low-Dose Clarithromycin in Patients with Refractory Chronic Sinusitis After Endoscopic Sinus Surgery: A Prospective Clinical Trial. Ear, Nose, and Throat Journal. 2024 Jan; 103(1): 31-9. doi: 10.1177/01455613211032020.

[2] Loperfido A, Cavaliere C, Begvarfaj E, Ciofalo A, D'Erme G, De Vincentiis M *et al.* The Impact of Antibiotics and Steroids on the Nasal Microbiome in Patients with Chronic Rhinosinusitis: A Systematic Review According to Patient/Population, Intervention, Comparison, and Outcome Criteria. Journal of Personalized Medicine. 2023 Nov; 13(11): 1583. doi: 10.3390/jpm13111583.

[3] Wallwork B, Coman W, Mackay-Sim A, Greiff L, Cervin A. A Double-Blind, Randomized, Placebo-Controlled Trial of Macrolide in the Treatment of Chronic Rhinosinusitis. The Laryngoscope. 2006 Feb; 116(2): 189-193. doi: 10.1097/01.mlg.0000191560.53555.08.

[4] Bezerra TF, Pezato R, Barros PM, Coutinho LL, Costa LF, Pinna F *et al.* Prospective Evaluation of Clarithromycin in Recurrent Chronic Rhinosinusitis with Nasal Polyps. Brazilian Journal of Otorhinolaryngology. 2021 Jul; 87(3): 298-304. doi: 10.1016/j.bjorl.2019.09.008.

[5] Oakley GM, Harvey RJ, Lund VJ. The role of macrolides in chronic rhinosinusitis (CRSsNP and CRSwNP). Current allergy and asthma reports. 2017 May; 17(5): 30. doi: 10.1007/s11882-017-0696-z.

[6] Orlandi RR, Kingdom TT, Smith TL, Bleier B, DeConde A, Luong AU *et al.* International Consensus Statement on Allergy and Rhinology: Rhinosinusitis 2021. In International Forum of Allergy and Rhinology. 2021 Mar; 11(3):213-739.

[7] Mueller SK, Nocera AL, Dillon ST, Gu X, Wendler O, Otu HH *et al.* Noninvasive Exosomal Proteomic Biosignatures, Including Cystatin SN, Peroxiredoxin-5, And Glycoprotein VI, Accurately Predict Chronic Rhinosinusitis with Nasal Polyps. In the International Forum of Allergy and Rhinology. 2019 Feb; 9(2):177-186. doi: 10.1002/alr.22226.

[8] Perot BQ and Baban MI. The Role of the Macrolide in Preventing Recurrence of the Nasal Polyposis After Fess. Pakistan Journal of Medical & Health Sciences. 2021; 14.

[9] Lim YH, Kim JM, Hwang JY, Kwon TY, Kim YB, Kim SW. Effects of Low-Dose Long-Term Macrolide Therapy on the Postoperative Symptom Change, Mucociliary Clearance, and Polyp Regrowth. Journal of Rhinology. 2002: 47-51.

[10] Kricker JA, Page CP, Gardarsson FR, Baldursson O, Gudjonsson T, Parnham MJ. Nonantimicrobial Actions of Macrolides: Overview and Perspectives for Future Development. Pharmacological Reviews. 2021 Oct; 73(4): 1404-1433. doi: 10.1124/pharmrev.121.000300.

[11] Smith D, Du Rand IA, Addy C, Collyns T, Hart S, Mitchelmore P *et al.* British Thoracic Society Guideline for the use of Long-Term Macrolides in Adults with Respiratory Disease. Biomedical Journal Open Respiratory Research. 2020 Apr; 7(1): 1-6. doi: 10.1136/bmjresp-2019-000489.

[12] Undela K, Goldsmith L, Kew KM, Ferrara G. Macrolides Versus Placebo for Chronic Asthma. Cochrane Database of Systematic Reviews. 2021; 11: 1-97. doi: 10.1002/14651858.CD002997.pub5.

[13] Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S *et al.* European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. 2020 Feb;58(29): 1-484. doi: 10.4193/Rhin20.601.

[14] Ryu G, Lee E, Park SI, Park M, Hong SD, Jung Y *et al.* The Mechanism of Action and Clinical Efficacy of Low-Dose Long-Term Macrolide Therapy in Chronic Rhinosinusitis. International Journal of Molecular Sciences. 2023 May; 24(11): 9489. doi: 10.3390/ijms24119489.

[15] Seresirikachorn K, Chetthanon T, Suwansirisuk T, Aeumjaturapat S, Chusakul S, Kanjanaumporn J et al. Low-Dose Macrolides for Treating Pediatric Rhinosinusitis: A Retrospective Study and Literature Review. SAGE Open Medicine. 2020 Jun; 8: 1-7. doi: 10.1177/2050312120933642.

[16] Wu Y, Shi X, Ni S, Sun H. Efficacy of Clarithromycin Combined with Fluticasone Propionate on Nasal Function, Nasal Mucociliary Transport Function, and Serum Inflammatory Markers in Chronic

DOI: https://doi.org/10.54393/pjhs.v7i2.3790

Rhinosinusitis Patients After Functional Endoscopic Sinus Surgery. Ear, Nose & Throat Journal. 2024 Nov: 117. doi: 10.1177/01455613241294244.

[17] Lin CF, Wang MC, Merton AT, Ho NH, Wu PS, Hsu AT *et al.* Add-On Effect of Clarithromycin to Oral Steroids as Post-Operative Therapy for Chronic Rhinosinusitis with Nasal Polyps: A Randomised Controlled Trial. Rhinology. 2020 Dec; 58(6): 550-558.

[18] Seresirikachorn K. Predictive Factors for Identifying Macrolide Responders in Treating Chronic Rhinosinusitis. 2020: 1-69.

[19] Suzaki I. The Role of Macrolides in Chronic Rhinosinusitis and Nasal Polyps. Current Opinion in Allergy and Clinical Immunology. 2025 Feb; 25(1): 19-26. doi: 10.1097/ACI.0000000000001050.

[20] Videler WJ, Badia L, Harvey RJ, Gane S, Georgalas C, Van Der Meulen FW *et al.* Lack of Efficacy of Long-Term, Low-Dose Azithromycin in Chronic Rhinosinusitis: A Randomized Controlled Trial. Allergy. 2011 Nov; 66(11): 1457-1468. doi: 10.1111/j.1398-9995.2011.02693.x.

[21] Zeng M, Wang H, Liao B, Wang H, Long XB, Ma J *et al.* Clinical and Biological Markers Predict the Efficacy of Glucocorticoid-and Macrolide-Based Postoperative Therapy in Patients with Chronic Rhinosinusitis. American Journal of Rhinology and Allergy. 2021 Sep; 35(5): 596-606. doi: 10.1177/1945892420982236.

[22] Lourijsen ES, Reitsma S, Vleming M, Hannink G, Adriaensen GF, Cornet ME *et al.* Endoscopic Sinus Surgery with Medical Therapy Versus Medical Therapy for Chronic Rhinosinusitis with Nasal Polyps: A Multicentre, Randomised, Controlled Trial. The Lancet Respiratory Medicine. 2022 Apr; 10(4): 337-346. doi: 10.1016/S2213-2600(21)00457-4.

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Systemic Review

OPEN ACCESS

Physiological and Biochemical Impacts of Gestational Diabetes on Maternal and Fetal Health: A Systematic Review

Anjum Mahmood[1], Bibi Hajira Ishaq[2*], Maham Khalid[3], Sadaf Zahra[4], Qaiser Javed[5] and Azhar Ijaz[6]

[1]Department of Obstetrics and Gynecology, Pak International Medical College, Peshawar, Pakistan
[2]Department of Biochemistry, Khyber Medical College, Peshawar, Pakistan
[3]Department of Physiology, Rehman Medical College, Peshawar, Pakistan
[4]Department of Obstetrics and Gynecology, Pakistan Atomic Energy Commission General Hospital, Islamabad, Pakistan
[5]Department of Obstetrics and Gynecology, Loralai Medical College, Loralai, Pakistan
[6]Department of Physiology, Loralai Medical College, Loralai, Pakistan

ARTICLE INFO

Keywords:
Gestational Diabetes Mellitus, Inflammation, Oxidative Stress, Dyslipidemia, Adipokines, Fetal Macrosomia

How to Cite:
Mahmood, A., Ishaq, B. H., Khalid, M., Zahra, S., Javed, Q., & Ijaz, A. (2026). Physiological and Biochemical Impacts of Gestational Diabetes on Maternal and Fetal Health: A Systematic Review: Physiological and Biochemical Impacts of Gestational Diabetes on Maternal and Fetal Health. Pakistan Journal of Health Sciences, 7(2), 142-150. https://doi.org/10.54393/pjhs.v7i2.3607

***Corresponding Author:**
Bibi Hajira Ishaq
Department of Biochemistry, Khyber Medical College, Peshawar, Pakistan
hajirazahid.dr@gamil.com

Received Date: 17th November, 2025
Revised Date: 26th December, 2025
Acceptance Date: 8th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Gestational diabetes mellitus is increasingly recognized as more than a transient elevation of blood glucose during pregnancy. Evidence suggests that GDM represents a broader metabolic disturbance involving chronic low-grade inflammation, dyslipidemia, oxidative stress, endothelial dysfunction, and adipokine imbalance. These alterations appear to influence not only maternal metabolic health but also fetal growth and early developmental outcomes. **Objectives:** To synthesize recent evidence (2017–2024) on physiological and biochemical changes associated with GDM and to examine their implications for maternal and fetal health. **Methods:** A systematic literature search was conducted across PubMed, Scopus, Web of Science, and ScienceDirect in accordance with PRISMA 2020 guidelines. Original human studies comparing GDM and normoglycemic pregnancies were included if they assessed metabolic, inflammatory, oxidative, vascular, or endocrine biomarkers. Study quality was evaluated using the National Institutes of Health quality assessment tools for observational studies and the Cochrane Risk of Bias 2 tool for randomized trials. Due to heterogeneity in study design and outcome measures, findings were synthesized narratively. **Results:** Thirteen studies met the inclusion criteria. GDM was consistently associated with elevated inflammatory markers (hs-CRP, IL-6, IL-18), increased triglycerides, oxidative stress markers such as malondialdehyde, and reduced adiponectin and antioxidant enzymes. Maternal hypertriglyceridemia independently predicted fetal macrosomia, while elevated umbilical cord C-peptide reflected fetal hyperinsulinemia. Nutritional interventions, including DHA supplementation, showed favorable modulation of selected adipokines. **Conclusions:** The evidence supports GDM as a systemic metabolic disorder characterized by interconnected disturbances in glucose, lipid, inflammatory, and oxidative pathways, with important maternal and fetal implications.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a common pregnancy complication, affecting approximately 15% of pregnancies worldwide [1]. It was previously regarded as a transient state of mild hyperglycemia; however, accumulating evidence now characterizes GDM as a complex metabolic disorder involving insulin resistance, adipose tissue dysfunction, oxidative stress, and vascular alterations [2, 3]. This evolving understanding has blurred the distinction between pregnancy-specific metabolic disturbances and the early manifestation of chronic cardiometabolic disease [4]. Despite advances in pathophysiological insight, routine clinical assessment of GDM remains largely centered on glucose tolerance testing, often overlooking the contributory roles of lipid

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

dysregulation, inflammation, and oxidative imbalance [5, 6]. Such metabolic disturbances help explain adverse outcomes, including fetal macrosomia, neonatal hypoglycemia, and longer-term cardiometabolic risk, even among pregnancies with apparently adequate glycemic control. This gap highlights a delay in translating mechanistic knowledge into comprehensive clinical evaluation.

While numerous studies have explored glucose dysregulation in GDM, the broader metabolic disturbances such as lipid imbalance, oxidative stress, and inflammation are less consistently evaluated. Existing evidence is fragmented, with limited synthesis of how these factors contribute to complications. This systematic review aims to collate and critically appraise available literature on metabolic alterations in GDM, highlight gaps, and identify potential markers for improved clinical assessment and management.

METHODS

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [7]. Gestational diabetes mellitus (GDM) was defined as glucose intolerance with onset or first recognition during pregnancy, irrespective of severity, according to the American Diabetes Association diagnostic criteria [8]. A comprehensive literature search was performed across PubMed, Scopus, Web of Science, and ScienceDirect to identify studies published between 2017 and 2024 that examined physiological and biochemical alterations associated with GDM. The search strategy combined indexed terms and free-text keywords, including gestational diabetes mellitus, biochemical markers, inflammatory cytokines, oxidative stress, adipokines, maternal metabolism, fetal outcomes, and umbilical cord or fetal biomarkers, using Boolean operators (AND/OR) to optimize retrieval. A total of 570 records were identified from PubMed, Scopus, Web of Science, and ScienceDirect. After removal of duplicates and ineligible records (n = 130), 440 records were screened by title and abstract. Out of these, 380 records were excluded due to non-quantitative study design (n = 180), review or case-report format (n = 120), and irrelevant population or outcomes (n = 80). Fifty-eight full-text articles were assessed for eligibility, of which 45 were excluded for predefined reasons. Thirteen studies met the inclusion criteria and were included in the qualitative synthesis (Figure 1). Reference lists of relevant articles were also manually screened to identify additional eligible studies. Only original studies published in English and conducted on human participants were considered. Eligible study designs included cohort, case–control, cross-sectional, and randomized controlled trials that compared pregnancies affected by GDM with normoglycemic controls. Studies were required to report maternal, placental, fetal, or neonatal physiological or biochemical outcomes, including fetal or umbilical cord blood biomarkers (such as C-peptide) reflecting intrauterine metabolic exposure in GDM pregnancies. Reviews, meta-analyses, editorials, animal or in-vitro studies, conference abstracts, and studies lacking primary quantitative data were excluded. A minimum sample size threshold of 50 participants was applied to ensure analytical robustness; however, most included studies exceeded this threshold, with sample sizes generally above 100 participants. Study selection followed a two-stage screening process in accordance with PRISMA 2020. Two reviewers independently screened titles and abstracts, followed by full-text assessment of potentially eligible articles. Any disagreements were resolved through discussion and consensus. For randomized controlled trials, study selection and assessment considered intervention comparison outcome elements consistent with the PICO framework. In such trials, the population comprised pregnant women diagnosed with gestational diabetes mellitus and normoglycemic pregnant controls; the intervention included dietary, nutritional, or glycemic management strategies; comparators consisted of standard care or alternative interventions; and outcomes included maternal, fetal, or neonatal physiological and biochemical measures. For observational studies, eligibility was evaluated using predefined population, exposure, comparator, and outcome criteria. The population was defined as pregnant women diagnosed with gestational diabetes mellitus according to recognized diagnostic criteria, along with appropriate normoglycemic pregnant control groups. Where fetal or neonatal outcomes were assessed, the population also included offspring of mothers with GDM, provided that the reported biomarkers reflected intrauterine metabolic exposure. Exposure referred to the presence of GDM, while comparators were pregnancies without GDM, and outcomes included maternal or fetal physiological and biochemical markers. The PICO framework was not applied as the primary eligibility model because a substantial proportion of included studies were observational and biomarker-based, lacking a clearly defined intervention or interventional comparator. Data extraction was performed using a standardized form capturing study design, country, sample size, diagnostic criteria for GDM, gestational timing of biospecimen collection, measured physiological or biochemical markers, and reported maternal or fetal outcomes. Confounding factors were defined as variables associated with both GDM status and the outcomes of

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

interest that could distort observed associations if not adequately controlled. Common confounders included maternal age, pre-pregnancy body mass index, parity, gestational age at sampling, family history of diabetes, and other relevant clinical or lifestyle variables. Information on confounding variables adjusted for in individual studies was extracted and summarized in Table 1. Missing or unclear information was recorded as not reported. Control of confounding was assessed at the individual study level. Multivariable regression modeling, stratification, group matching, and restricted eligibility criteria were considered acceptable methods for confounding control. During data extraction, we specifically recorded whether reported associations were adjusted and which covariates were included. Studies reporting only unadjusted comparisons were interpreted with caution during qualitative synthesis. Quality assessment of observational studies was conducted using the National Institutes of Health (NIH) Quality Assessment Tool [9], for Observational Cohort and Cross-Sectional Studies, which evaluates study objectives, population selection, exposure and outcome measurement, control of confounding, and completeness of follow-up. Randomized controlled trials were assessed using the Cochrane Risk of Bias 2.0 (RoB 2) tool [10]. Risk-of-bias judgments were performed strictly according to the RoB-2 domain-level signaling-question algorithm and overall judgment criteria described in the Cochrane Handbook for Systematic Reviews of Interventions [11]. Studies were classified as low risk of bias when all five RoB-2 domains were judged as low risk; as some concerns when at least one domain raised some concerns but none were high risk; and as high risk when one or more domains were judged as high risk. The five domains assessed were the randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of the reported result. Studies were classified as low risk of bias when all key domains were adequately addressed, high risk when one or more critical domains showed methodological weakness, and some concerns when minor limitations were present, in accordance with NIH and Cochrane guidance [9, 10]. Due to substantial heterogeneity in study design, biomarker assays, outcome measures, and analytical approaches, meta-analysis was not undertaken. Instead, findings were synthesized qualitatively and organized into thematic domains encompassing maternal metabolic and inflammatory changes, fetal and neonatal biochemical outcomes, and overall methodological quality.

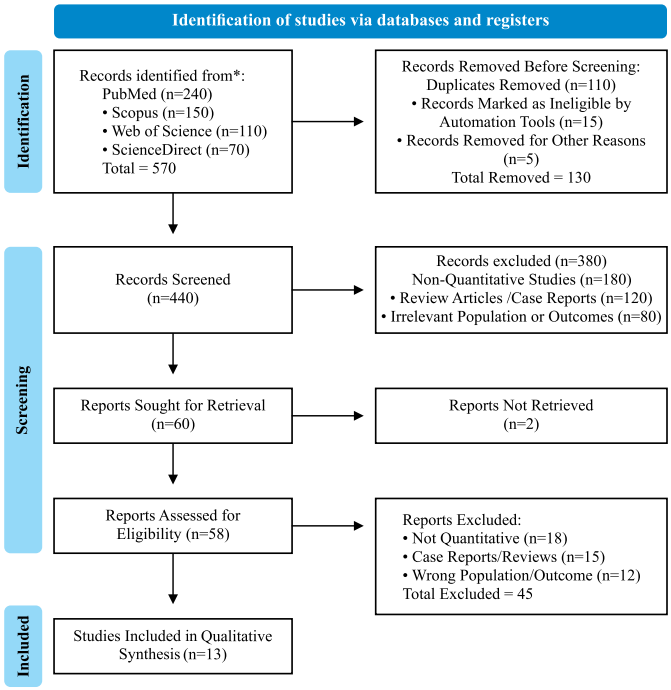

Figure 1: PRISMA flow chart for the study

RESULTS

The relationship between novel adipokines and insulin sensitivity has been evaluated in 18 human studies conducted across diverse populations and metabolic conditions. These studies cover a broad range of clinical contexts, including obesity, polycystic ovary syndrome, gestational diabetes mellitus, type 2 diabetes mellitus, metabolic syndrome, and pediatric populations, facilitating comparative evaluation of adipokine–insulin sensitivity relationships across diverse demographic groups. Omentin-1 and Nesfatin-1 were most frequently evaluated, followed by Chemerin and Visfatin, primarily in relation to HOMA-IR and fasting insulin indices. Across these heterogeneous populations, Omentin-1 showed the most consistent inverse association with insulin resistance, while Chemerin demonstrated the most reproducible positive association with insulin-resistant states, indicating stronger reliability across human studies. A consistent pattern was observed whereby lower levels of Omentin-1 or Nesfatin-1, and higher levels of Chemerin or Visfatin, clustered with obesity, prediabetes, diabetes, and related insulin-resistant conditions. In contrast, Nesfatin-1 and Visfatin showed greater variability across disease states, suggesting population- and stage-dependent effects (Table 1).

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

Table 1: Included Primary Studies (2017–2024): Biomarkers/Physiology in GDM and Maternal–Fetal Outcomes

Sr. No.	References	Design	Sample size (GDM / non-GDM)	Gestational Timing of Sampling	Key Biomarkers/ Physiology	Main Maternal–Fetal Outcomes	Covariates Explicitly Adjusted (Confounders)
1	[12]	Prospective Cohort	86 / 273	16–18 weeks	Ficolin-3, adiponectin (FAR)	FAR predicted later GDM	Age, BMI, gestational age
2	[13]	Nested Case–Control (Cohort-Based)	107 / 214	10–39 weeks	Adipokines (FABP4, chemerin, IL-6, leptin, adiponectin, etc.)	Adipokines improved GDM risk prediction	Age, pre-pregnancy BMI, parity, gestational week, family history of diabetes
3	[14]	Case–Control	110 / 100	24–28 weeks	Vitamin D, hs-CRP, Hcy, HOMA-IR	Lower Vit-D; higher inflammation in GDM	Group matching for age, BMI, parity
4	[15]	Cross-Sectional	NR	24–28 weeks	CRP/Albumin ratio	Higher CAR in GDM	NR (comparative analysis only)
5	[16]	Case–Control	NR	Late 2nd–3rd trimester	MDA, SOD, GSH	OS markers linked to adverse neonatal outcomes	NR (ROC-based models)
6	[17]	Case–Control (Cord Blood)	NR	At delivery	Cord C-peptide	Fetal hyperinsulinemia with GDM	NR
7	[18]	Retrospective Cohort	NR	At delivery	Cord C-peptide	Predicts neonatal hypoglycemia	NR
8	[19]	Rct	NR	Mid–late pregnancy; cord	DHA, cord adipokines	Favorable fetal adipokine profile	Maternal BMI, glycemia
9	[20]	Prospective Cohort	NR	24–28 weeks	TG, TG/HDL-C	TG predicts macrosomia	Regression models (limited covariates)
10	[21]	Case–Control	NR	24–28 weeks	hs-CRP, IL-6, IL-18	IL-18 correlated with dysglycemia	Age; BMI in selected models
11	[22]	Cross-Sectional	37 / 33	≥24 months postpartum	Flow-mediated dilation (FMD)	Persistent endothelial dysfunction	Restricted age; exclusion of smokers/ comorbidities
12	[23]	Case–Control	153 / 84	24–29 weeks	Chemerin, lipocalin-2, apelin	Adipokine dysregulation in GDM	NR
13	[24]	RCT	NR	At delivery	Cord leptin/adiponectin; ANGPTL4	Glycemic targets alter fetal profile	NR

NR' indicates that the study did not explicitly report statistical adjustment for confounding variables. Restricted eligibility refers to predefined inclusion/exclusion criteria used to minimize confounding.

Gestational diabetes mellitus was consistently associated with increased insulin resistance, inflammation, oxidative stress, endothelial dysfunction, and dysregulated adipokine profiles, supporting its characterization as a systemic metabolic disorder rather than isolated hyperglycemia. Multiple studies reported significantly elevated fasting glucose and HOMA-IR in women with GDM, alongside increased umbilical cord C-peptide levels, indicating fetal hyperinsulinemia and a close maternal–fetal metabolic link. Maternal hypertriglyceridemia was also identified as an independent predictor of fetal macrosomia, highlighting the role of lipid dysregulation beyond glucose-mediated effects. Inflammatory and oxidative markers, including hs-CRP, IL-6, IL-18, CRP/albumin ratio, and MDA, were consistently elevated, with evidence of persistent vascular impairment extending into the postpartum period. Collectively, these findings depict GDM as a complex metabolic cascade in which insulin resistance, lipid abnormalities, inflammation, oxidative stress, and hormonal disruption converge to influence maternal and fetal outcomes adversely (Table 2).

Table 2: Maternal Physiological and Biochemical Outcomes in Gestational Diabetes Mellitus (GDM)

Outcome Domain	Assay / Time Point	Direction vs Controls	Magnitude Summary	Adjustment Status	Notes On Heterogeneity	References
Glycemic / Insulin (HOMA-IR, fasting / OGTT glucose, insulin, C-peptide)	Fasting glucose, 75 g OGTT indices (24 – 28 w); cord C-peptide at delivery	↑ glycemia & ↑ HOMA -IR in GDM; ↑ cord C- peptide = fetal hyperinsulinemia	Moderate–large group differences; cord C-peptide markedly higher in GDM	Adjusted in Francis and Zhao; others unadjusted	GDM criteria and assay methods vary across studies	[21, 25]
Lipid (TG, HDL-C, LDL-C, NEFA)	Maternal fasting TG / HDL (24–36 w)	↑ maternal TG in GDM	Moderate ↑; TG linked to macrosomia and LGA	Unadjusted in most; Abdullah used regression	Timing and fasting status vary between studies	[20]

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

Inflammatory (CRP, IL-6, TNF-α, IL-18)	hs-CRP, IL-6 (24–28 w); CRP/Albumin ratio (1st–2nd trimester)	↑ hs-CRP and ↑ IL-6 / IL-18 in GDM; ↑ CAR in GDM	Small–moderate ↑ for CRP/IL-6; IL-18 strong ↑; CAR distinct difference	Zhao adjusted (age, BMI); Francis multi-adjusted	Inflammatory indices (CAR, NLR) and cytokine panels differ	[13, 25]
Oxidative / Endothelial (MDA, TAC, NO/ADMA, FMD)	MDA, SOD, GSH (late pregnancy); FMD ≥ 24 mo postpartum	↑ MDA; ↓ SOD/GSH in GDM; ↓ FMD in women with prior GDM	Moderate effect sizes; FMD ~3 % lower post-GDM ($p < 0.001$)	Wang used ROC models; Albayrak controlled for age and comorbid	Lab assays vary; FMD measured postpartum (legacy effect)	[16, 22]
Adipokines / Hormones (adiponectin, leptin, chemerin, FABP4, sOB-R, lipocalin-2, apelin, omentin-1, vaspin, RBP-4)	Serial sampling 10–39 w and at delivery (cord)	↓ adiponectin & sOB- R; ↑ leptin, FABP4, chemerin; ↑ lipocalin -2; apelin ↔ / variable	Consistent across cohorts; moderate to large effects for leptin, chemerin, and FABP4	Francis fully adjusted (age, BMI, parity, etc.); Mierzyński correlations;	Different assay kits & sampling windows (10–39 w); cohort vs case-control mix	[13, 23]
Placental Factors (PLGF, sFlt-1, PAPP-A)	Antenatal plasma/placenta	No data within 2017–2024 set	–	–	None of the included studies reported maternal placental angiogenic markers	–
Coagulation (fibrinogen, D-dimer)	Antenatal plasma	No data within 2017–2024 set	–	–	–	–
Dietary lipid intervention signal	Maternal DHA across gestation; cord adipokines at delivery	DHA ↔ / favorable shift in cord leptin/ adiponectin profile despite GDM	Small–moderate improvement in biomarker pattern	Xu adjusted (BMI, glycemia)	Intervention study; mechanistic evidence only	[19]

Fetal and neonatal outcomes closely reflected the maternal metabolic milieu, with dysglycemia, dyslipidemia, and inflammation influencing fetal growth, endocrine function, and early metabolic adaptation. Maternal hypertriglyceridemia showed an independent association with fetal macrosomia, indicating that lipid transfer across the placenta contributes to fetal adiposity beyond glucose-mediated effects. Elevated umbilical cord C-peptide levels in pregnancies complicated by GDM indicated fetal hyperinsulinemia and were predictive of neonatal hypoglycemia, supporting the Pedersen hypothesis. Dysregulated adipokines, characterized by low adiponectin and elevated leptin, FABP4, and chemerin, were associated with increased fetal adiposity and altered cord hormonal profiles, with evidence that looser maternal glycemic control exacerbated these changes. Collectively, oxidative stress, inflammation, and metabolic dysregulation appear to mediate a continuous maternal-fetal metabolic interaction that shapes fetal growth trajectories and may have lasting postnatal consequences (Table 3).

Table 3: Fetal/Neonatal Outcomes and Links to Maternal Biomarkers (Qualitative)

Outcome Category	Maternal Biomarker(S) and Timing	Association Direction (Materna → Fetal/Neonatal)	Effect Summary (Qualitative)	Adjustment Status	Notes on Heterogeneity	References
Fetal Overgrowth (Macrosomia/LGA)	Triglycerides (late 2nd–3rd tri); TG/HDL-C	↑ TG → ↑ macrosomia/LGA	Higher maternal TG independently predicts macrosomia among women with GDM	Adjusted logistic models	Fasting status and lipid panels vary; mostly late -gestation measures	[20]
Birthweight/ Adiposity (Cord Bio-Signatures)	Cord leptin, adiponectin; L/A ratio (at delivery)	↑ maternal glycemia /looser targets → ↑ cord L/A & leptin	Looser glycemic control is associated with higher cord L/A and endothelial gene expression shifts	Trial models (within-trial adjustment)	Intervention context: cord hormones reflec fetal fat mass	[24]
Birthweight/ Adiposity (Maternal Adipokines)	Adiponectin (↓) leptin (↑), FABP4 (↑), chemerin (↑) (10–39 w serial)	Adipokine profile consistent with ↑ fetal growth risk	Early/mid-pregnancy low adiponectin & high leptin/chemerin/ FABP4 associate with later GDM and pro-adiposity milieu	Multivariable models (age, BMI, parity, etc.)	Biomarker panels/ assays differ; multiethnic cohort	[13]

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

Neonatal Hypoglycemia	Cord C-peptide (delivery)	↑ C-peptide → ↑ hypoglycemia risk	Cord C-peptide strongly predicts early neonatal hypoglycemia in infants of GDM mothers	Multivariable models	Definitions and glucose thresholds vary by site	[18]
Fetal Hyperinsulinemia (Biochemical)	Maternal glycemia (24–28 w); metabolic control → Cord C-peptide	↑ maternal glycemia → ↑ cord C-peptide	Clear step-up of fetal C-peptide with maternal hyperglycemia/GDM	Regression models/ group comparisons	Cord sampling/assay platforms differ	[17]
Neonatal Neurodevelopment (Early)	Oxidative stress panel: MDA (↑), SOD (↓), GSH (↓)(late gestation)	↑ MDA / ↓ antioxidants → less favorable neurodevelopmental indices	OS markers associated with adverse perinatal outcomes and predicted poorer early neurodevelopment	ROC-based prediction; limited covariates	AMA population; follow-up timeframe is short	[16]
NICU/Perinatal Composite (Signal Via Inflammation)	Inflammatory cytokines: hs-CRP, IL-6, IL-18 (24–28 w)	↑ materna inflammation → adverse perinatal risk signal	Stronger IL-1 elevations track worse glycemic screens; perinatal links are indirect but biologically plausible	Adjusted for age (±BMI)	Cytokine panels and diagnostic thresholds vary	[21]
Placental–Endothelial Milieu (Mechanistic)	Maternal DHA across gestation; cord adipokines (delivery)	↑ maternal DHA → ↓ cord leptin / favorable L/A profile	DHA supplementation shifts cord biomarkers toward a less adipogenic profile	Trial models (BMI, glycemia)	Mechanistic RCT; not standard care	[19]
Fetal Vascular Function (Contextual)	Maternal vascular/ metabolic status (history of GDM)	Prior GDM → persistent maternal endothelial dysfunction	Postpartum ↓FMD suggests endothelial legacy; fetal linkage is indirect but supports milieu of risk	Restricted groups (age, comorbidities)	Postpartum measure (≥24 mo), not antenatal	[22]

Overall, the included studies demonstrated generally acceptable methodological quality, with most exhibiting low to moderate risk of bias based on the NIH Quality Assessment Tool and Cochrane RoB 2 criteria. Participant selection and exposure measurement were clearly described in several large cohort and randomized studies, particularly those by Francis *et al.* and Xu *et al.* which used standardized recruitment procedures and biomarker assays [13, 19]. Some limitations were observed in single-center or retrospective studies, where control for confounding variables such as maternal body mass index, parity, and gestational age was incomplete. Nevertheless, outcome measurements across studies were largely based on validated laboratory methods, with minimal evidence of missing data or selective reporting. Collectively, the low-to-moderate risk of bias supports the credibility of the observed associations between gestational diabetes, metabolic dysregulation, and adverse maternal–fetal outcomes, while underscoring the need for future multicenter studies with standardized adjustment strategies.

DISCUSSION

Gestational diabetes mellitus (GDM) has increasingly been recognized as a complex metabolic disorder rather than a transient disturbance of glucose homeostasis. The findings of this review consistently demonstrate that insulin resistance, dyslipidemia, inflammation, oxidative stress, endothelial dysfunction, and adipokine imbalance form an interconnected pathophysiological network in GDM [26]. These mechanisms appear to operate simultaneously and reinforce one another, supporting the concept that GDM represents a systemic metabolic condition with consequences extending beyond pregnancy [27, 28]. Lipid metabolism emerged as a key determinant of adverse fetal outcomes. Maternal hypertriglyceridemia and elevated triglyceride/HDL-C ratios were independently associated with fetal macrosomia, even after accounting for glycemic indices, highlighting the contribution of non-glucose substrates to fetal overgrowth [29]. These findings align with earlier evidence suggesting that reliance solely on glucose-based screening may underestimate fetal metabolic risk in GDM pregnancies [30, 31]. Placental transfer of lipids likely plays a substantial role in fetal adiposity, reinforcing the importance of dyslipidemia in maternal–fetal fuel dynamics. Inflammation and oxidative stress were also consistently implicated across studies.

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

Elevated inflammatory markers, including IL-6, IL-18, and CRP-based indices, reflect immune metabolic activation that may impair placental signaling and fetal metabolic programming [32]. Oxidative stress markers such as malondialdehyde, alongside reduced antioxidant capacity, were associated with endothelial dysfunction and adverse neonatal outcomes, including early neurodevelopmental vulnerability [33, 34]. These findings suggest that inflammatory and redox imbalance may act as mediators linking maternal metabolic stress to both vascular and developmental consequences. Adipokine dysregulation further underscores the systemic nature of GDM. Reduced adiponectin and increased levels of leptin, chemerin, and FABP4 were repeatedly associated with insulin resistance, inflammation, and increased fetal adiposity, independent of maternal body mass index [35, 36]. These alterations highlight the role of adipose tissue inflammation and endocrine dysfunction in shaping maternal and fetal metabolic phenotypes. Collectively, the evidence supports a unified metabolic cascade in which maternal insulin resistance, lipid abnormalities, inflammation, oxidative stress, and hormonal dysregulation converge to influence placental adaptation and fetal programming [37-39].

Most studies included in this review were cross-sectional or single-center, limiting causal inference and generalizability. Variability in biomarker measurement and lack of standardized panels across studies also constrain direct comparisons. Based on the reviewed evidence, future research should prioritize multicenter, longitudinal studies with standardized biomarker panels to clarify the independent and combined roles of glucose, lipids, inflammation, and oxidative stress in gestational diabetes mellitus. Integrating metabolic and inflammatory markers into clinical risk assessment may improve early identification of pregnancies at risk for adverse maternal-fetal outcomes.

CONCLUSIONS

This systematic review demonstrates that gestational diabetes mellitus is a multisystem metabolic disorder involving insulin resistance, dyslipidemia, inflammation, oxidative stress, adipokine imbalance, and vascular dysfunction. These maternal metabolic disturbances are closely linked to fetal consequences, including macrosomia, hyperinsulinemia, altered adipokine profiles, and metabolic vulnerability. Understanding GDM as a complex metabolic condition provides a stronger biological basis for interpreting maternal–fetal outcomes beyond glucose dysregulation alone.

Authors' Contribution

Conceptualization: AM
Methodology: BHI, MK, SZ, QJ
Formal analysis: AM
Writing and Drafting: AM, BHI, MK, SZ, QJ, AI
Review and Editing: AM, BHI, MK, SZ, QJ, AI

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Avilez RG, Ponti L, Gabini S, Camats S. Impact of Gestational Diabetes on Maternal and Fetal Health: Prevalence, Risks and Interdisciplinary Treatment. SCT Proceedings in Interdisciplinary Insights and Innovations. 2025; 3: 481. doi: 10.56294/piii2025481.

[2] Nakshine VS and Jogdand SD. A Comprehensive Review of Gestational Diabetes Mellitus: Impacts on Maternal Health, Fetal Development, Childhood Outcomes, and Long-Term Treatment Strategies. Cureus. 2023 Oct; 15(10). doi: 10.7759/cureus.47500.

[3] Ke JF, Liu S, Ge RL, Ma L, Li MF. Associations of Maternal Pre-Pregnancy BMI and Gestational Weight Gain with the Risks of Adverse Pregnancy Outcomes in Chinese Women with Gestational Diabetes Mellitus. BioMed Central Pregnancy and Childbirth. 2023 Jun; 23(1): 414. doi: 10.1186/s12884-023-05657-8.

[4] Zhang C and Catalano P. Screening for Gestational Diabetes. Journal of the American Medical Association. 2021 Aug 10; 326(6): 487-9. doi: 10.1001/jama.2021.12190.

[5] Al Bekai E, Beaini CE, Kalout K, Safieddine O, Semaan S, Sahyoun F *et al.* The Hidden Impact of Gestational Diabetes: Unveiling Offspring Complications and Long-Term Effects. Life. 2025 Mar; 15(3): 440. doi: 10.3390/life15030440.

[6] Kathuria K. Impact of Maternal Health and Disease on Neonatal Outcome. In Clinical Anesthesia for the Newborn and the Neonate. Singapore: Springer Nature Singapore. 2023: 11-27. doi: 10.1007/978-981-19-5458-0_2.

[7] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD *et al.* The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. British Medical Journal. 2021 Mar; 372.

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

[8] American Diabetes Association. Standards of Medical Care for Patients with Diabetes Mellitus. Diabetes Care. 2002 Jan; 25(suppl_1): s33-49. doi: 10.2337/diacare.25.2007.S33.

[9] Ma LL, Wang YY, Yang ZH, Huang D, Weng H, Zeng XT. Methodological Quality (Risk of Bias) Assessment Tools for Primary and Secondary Medical Studies: What Are They and Which Is Better? Military Medical Research. 2020 Feb; 7(1): 7. doi: 10.1186/s40779-020-00238-8.

[10] Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I *et al.* RoB 2: A Revised Tool for Assessing Risk of Bias in Randomized Trials. British Medical Journal. 2019 Aug; 366.

[11] Higgins JP and Green S. Cochrane Handbook for Systematic Reviews of Interventions. 2008. doi: 10.1002/9780470712184.

[12] Yuan XS, Shi H, Wang HY, Yu B, Jiang J. Ficolin-3/Adiponectin Ratio for the Prediction of Gestational Diabetes Mellitus in Pregnant Women. Journal of Diabetes Investigation. 2018 Mar; 9(2): 403-10. doi: 10.1111/jdi.12688.

[13] Francis EC, Li M, Hinkle SN, Cao Y, Chen J, Wu J et al. Adipokines in Early and Mid-Pregnancy and Subsequent Risk of Gestational Diabetes: A Longitudinal Study in a Multiracial Cohort. British Medical Journal Open Diabetes Research and Care. 2020 Aug; 8(1). doi: 10.1136/bmjdrc-2020-001333.

[14] Farkas A, Suranyi A, Kolcsar B, Gyurkovits Z, Kozinszky Z, Vari SG *et al.* Potential Glycobiomarkers in Maternal Obesity and Gestational Diabetes During Human Pregnancy. Journal of Clinical Medicine. 2025 Feb; 14(5): 1626. doi: 10.3390/jcm14051626.

[15] Ozdemir EU, Buyuk GN, Koc EM, Ipek G, Ozbebek UG, Gurun MA *et al.* Gestational Diabetes and C-Reactive Protein/Albumin Ratio in Pregnancy: A Prospective Study. Yonsei Medical Journal. 2024 May; 65(7): 413. doi: 10.3349/ymj.2023.0334.

[16] Wang Y, Fan Z, Ren J, Ma L. Changes in Oxidative Stress Markers in Pregnant Women of Advanced Maternal Age with Gestational Diabetes and Their Predictive Value for Neurodevelopmental Impact. Diabetes, Metabolic Syndrome and Obesity. 2024 Dec: 4003-12. doi: 10.2147/DMSO.S475385.

[17] Niknam A, Ramezani Tehrani F, Behboudi-Gandevani S, Rahmati M, Hedayati M *et al.* Umbilical Cord Blood Concentration of Connecting Peptide (C-Peptide) and Pregnancy Outcomes. BioMed Central Pregnancy and Childbirth. 2022 Oct; 22(1): 764. doi: 10.1186/s12884-022-05081-4.

[18] Saber AM, Mohamed MA, Sadek AA, Mahmoud RA. Role of Umbilical Cord C-Peptide Levels in Early Prediction of Hypoglycemia in Infants of Diabetic Mothers. BioMed Central Pediatrics. 2021 Feb; 21(1): 85. doi: 10.1186/s12887-021-02547-w.

[19] Xu YJ, Wang WJ, Zhang QY, Yang MN, Zhang L, He H *et al.* Docosahexaenoic Acid Supplementation in Gestational Diabetes Mellitus and Neonatal Metabolic Health Biomarkers. Frontiers in Nutrition. 2023 Mar; 10: 1089131. doi: 10.3389/fnut.2023.1089131.

[20] Abdullah K, Sweed M, Marmouch E, Ali M. Maternal Triglycerides Level as Predictor of Fetal Macrosomia in Pregnant Women with Gestational Diabetes Mellitus. Evidence-Based Women's Health Journal. 2023 May; 13(2): 192-9. doi: 10.21608/ebwhj.2023.190351.1233.

[21] Zhao X, Liu J, Shen L, Wang A, Wang R. Correlation Between Inflammatory Markers (hs-CRP, TNF-A, IL-1β, IL-6, IL-18), Glucose Intolerance, and Gestational Diabetes Mellitus in Pregnant Women. International Journal of Clinical and Experimental Medicine. 2018 Jan; 11(8): 8310-6.

[22] Albayrak Ö, Topçuoğlu MA. Evaluation of the Effects of Preeclampsia and Gestational Diabetes Mellitus on Endothelial Function. Bezmialem Science. 2024 Nov; 12(4): 456-462. doi: 10.14235/bas.galenos.2024.14880.

[23] Mierzyński R, Poniedziałek-Czajkowska E, Dłuski D, Kamiński M, Mierzyńska A, Leszczyńska-Gorzelak B. The Potential Role of Chemerin, Lipocalin 2, and Apelin in the Diagnosis and Pathophysiology of Gestational Diabetes Mellitus. Journal of Diabetes Research. 2021; 2021(1): 5547228. doi: 10.1155/2021/5547228.

[24] Popova P, Vasilyeva L, Tkachuck A, Puzanov M, Golovkin A, Bolotko Y *et al.* A Randomized, Controlled Study of Different Glycaemic Targets During Gestational Diabetes Treatment: Effect on the Level of Adipokines in Cord Blood and ANGPTL4 Expression in Human Umbilical Vein Endothelial Cells. International Journal of Endocrinology. 2018; 2018(1): 6481658. doi: 10.1155/2018/6481658.

[25] Zhang L, Yi H, Li J, Dong J. Correlation of Serum 25-Hydroxyvitamin-D3, Hs-CRP, And Homocysteine in Women with Gestational Diabetes Mellitus. Archives of Medical Science. 2021. doi: 10.5114/aoms/133347.

[26] Di Bernardo SC, Lava SA, Epure AM, Younes SE, Chiolero A, Sekarski N. Consequences of Gestational Diabetes Mellitus on Neonatal Cardiovascular Health: Mysweetheart Cohort Study. Pediatric Research. 2023 Jul; 94(1): 231-8. doi: 10.1038/s41390-022-02390-4.

[27] Jiménez-Osorio AS, Carreón-Torres E, Correa-Solís E, Ángel-García J, Arias-Rico J, Jiménez-Garza O *et*

DOI: https://doi.org/10.54393/pjhs.v7i2.3607

al. Inflammation and Oxidative Stress Induced by Obesity, Gestational Diabetes, and Preeclampsia in Pregnancy: Role of High-Density Lipoproteins as Vectors for Bioactive Compounds. Antioxidants. 2023 Oct; 12(10): 1894. doi: 10.3390/antiox12101894.

[28] Rathnayake H, Han L, da Silva Costa F, Paganoti C, Dyer B, Kundur A *et al.* Advancement in Predictive Biomarkers for Gestational Diabetes Mellitus Diagnosis and Related Outcomes: A Scoping Review. British Medical Journal Open. 2024 Dec; 14(12): e089937. doi: 10.1136/bmjopen-2024-089937.

[29] You Y, Hu H, Cao C, Han Y, Tang J, Zhao W. Association between the Triglyceride to High-Density Lipoprotein Cholesterol Ratio and the Risk of Gestational Diabetes Mellitus: A Second Analysis Based on Data from a Prospective Cohort Study. Frontiers In Endocrinology. 2023 Jul; 14: 1153072. doi: 10.3389/fendo.2023.1153072.

[30] Karcz K and Królak-Olejnik B. Impact of Gestational Diabetes Mellitus on Fetal Growth and Nutritional Status in Newborns. Nutrients. 2024 Nov; 16(23): 4093. doi: 10.3390/nu16234093.

[31] Sharma AK, Singh S, Singh H, Mahajan D, Kolli P, Mandadapu G *et al.* Deep Insight of the Pathophysiology of Gestational Diabetes Mellitus. Cells. 2022 Aug; 11(17): 2672. doi: 10.3390/cells11172672.

[32] Liu H, Zhang L, Cheng H, Chi P, Zhuang Y, Alifu X *et al.* The Associations of Maternal Liver Biomarkers in Early Pregnancy with the Risk of Gestational Diabetes Mellitus: A Prospective Cohort Study and Mendelian Randomization Analysis. Frontiers in Endocrinology. 2024 May; 15: 1396347. doi: 10.3389/fendo.2024.1396347.

[33] Davidov A, Razumnikova O, Bakaev M. Nature in the Heart and Mind of the Beholder: Psycho-Emotional and EEG Differences in Perception of Virtual Nature Due to Gender. Vision. 2023 Apr; 7(2): 30. doi: 10.3390/vision7020030.

[34] Karami M, Mousavi SH, Rafiee M, Heidari R, Shahrokhi SZ. Biochemical and Molecular Biomarkers: Unraveling Their Role in Gestational Diabetes Mellitus. Diabetology and Metabolic Syndrome. 2023 Jan; 15(1): 5. doi: 10.1186/s13098-023-00980-8.

[35] Sedgi FM, Hassani AH, Faghfouri AH, Gheibi S, Mohammadpour Y, Mokari-Yamchi A. Association between Oxidative Balance Score and Gestational Diabetes Mellitus Risk: A Case-Control Study. BioMed Central Endocrine Disorders. 2025 Dec; 25(1): 1-9. doi: 10.1186/s12902-025-02028-6.

[36] Kabbani N, Blüher M, Stepan H, Stumvoll M, Ebert T, Tönjes A *et al.* Adipokines in Pregnancy: A Systematic Review of Clinical Data. Biomedicines. 2023 May; 11(5): 1419. doi: 10.3390/biomedicines11051419.

[37] Akmalovna GI, Komilovna GK, Subanova GA, Orzijonovna NN, Sayfilloevna NN, Shopulatovna FO *et al.* Biochemical, Laboratory and Instrumental Diagnostic Indicators of Early Diagnosis of Women with Gestational Diabetes. Endocrine and Metabolic Science. 2025 Jun; 18: 100252. doi: 10.1016/j.endmts.2025.100252.

[38] Singh P, Elhaj DA, Ibrahim I, Abdullahi H, Al Khodor S. Maternal Microbiota and Gestational Diabetes: Impact on Infant Health. Journal of Translational Medicine. 2023 Jun; 21(1): 364. doi: 10.1186/s12967-023-04230-3.

[39] Zehravi M, Maqbool M, Ara I. Correlation between Obesity, Gestational Diabetes Mellitus, and Pregnancy Outcomes: An Overview. International Journal of Adolescent Medicine and Health. 2021 Dec; 33(6): 339-45. doi: 10.1515/ijamh-2021-0058.

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Systemic Review

OPEN ACCESS

Oxidative Stress and Lipid Peroxidation Markers in Obesity-Related Polycystic Ovary Syndrome and Menstrual Irregularities: A Systematic Review of Biochemical and Pharmacological Interventions

Shahnaz Fatima[1], Anum Saeedullah[2*], Anjum Mahmood[3], Mohammad Iqbal[4], Samina Firdous[3] and Umar Alim[5]

[1]Department of Pharmacology, Sahara Medical College, Narowal, Pakistan
[2]Department of Biochemistry, Northwest School of Medicine, Peshawar, Pakistan
[3]Department of Obstetrics and Gynecology, Pak International Medical College, Peshawar, Pakistan
[4]Department of Biochemistry, Muhammad College of Medicine, Peshawar, Pakistan
[5]Department of Pharmacology, Saidu Medical College, Swat, Pakistan

ARTICLE INFO

Keywords:
Polycystic Ovary Syndrome, Oxidative Stress, Lipid Peroxidation, Antioxidants, Obesity, Nutraceuticals, Menstrual Irregularity, Redox Balance

How to Cite:
Fatima, S., Saeedullah, A., Mahmood, A., Iqbal, M., Firdous, S., & Alim, U. (2026). Oxidative Stress and Lipid Peroxidation Markers in Obesity-Related Polycystic Ovary Syndrome and Menstrual Irregularities: A Systematic Review of Biochemical and Pharmacological Interventions: Oxidative Stress and Lipid Peroxidation Markers in Obesity-Related PCOS. Pakistan Journal of Health Sciences, 7(2), 151-160. https://doi.org/10.54393/pjhs.v7i2.3609

***Corresponding Author:**
Anum Saeedullah
Department of Biochemistry, Northwest School of Medicine, Peshawar, Pakistan
dranumsaeedullah@gmail.com

Received Date: 17th November, 2025
Revised Date: 20th December, 2025
Acceptance Date: 13th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Obesity in women with Polycystic Ovary Syndrome (PCOS) is strongly associated with oxidative stress and lipid peroxidation. Elevated reactive oxygen species and depleted antioxidant defenses contribute to menstrual dysfunction, insulin resistance, and impaired follicular quality. **Objective:** This review summarizes clinical evidence (2018-2024) on oxidative-stress and lipid-peroxidation markers in obesity-related PCOS and evaluates the effects of pharmacological and nutraceutical interventions targeting redox balance. **Methods:** Electronic searches of PubMed, Scopus, and Cochrane databases were conducted following PRISMA 2020 guidelines. Eligible studies included randomized controlled trials, case-control, and cross-sectional designs reporting oxidative or antioxidant biomarkers in human PCOS populations. Non-human studies and review articles were excluded. Extracted data included study design, biomarkers, interventions, and clinical outcomes. **Results:** Fifteen studies met the inclusion criteria. Observational data consistently showed elevated malondialdehyde (MDA) and reduced total antioxidant capacity (TAC), superoxide dismutase (SOD), and glutathione (GSH) in women with PCOS, with greater abnormalities in obese participants. Interventional trials demonstrated significant improvements in oxidative profiles following antioxidant supplementation, particularly probiotics, selenium, ellagic acid, oleoylethanolamide, and resveratrol, with partial recovery of menstrual, metabolic, and inflammatory parameters. **Conclusions:** Oxidative imbalance is a defining feature of obesity-related PCOS and appears to contribute to menstrual and metabolic dysfunction. Antioxidant-based interventions show promising benefits in restoring redox balance, especially among obese women. These findings support oxidative modulation as a relevant therapeutic target in PCOS management.

INTRODUCTION

Polycystic ovary syndrome (PCOS), affecting women of reproductive age, is a common endocrine and metabolic disorder, affecting 6-20 % of women globally [1]. Hyperandrogenism, ovulation, and polycystic ovarian morphology are how the condition manifests itself [2]. This disorder consists of insulin resistance, chronic low-grade inflammation, and lipid imbalance, in addition to obesity, which all increase the risks for diabetes, heart disease, and infertility over the long-term. Of these, obesity often occurs the most and is therefore a potential cause of oxidative stress and imbalance in hormones [3]. Excessive generation of reactive oxygen species leads to a state of oxidative stress. PCOS increases lipid peroxidation, which increases oxidative stress and raises MDA levels while

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

lowering total antioxidant capacity (TAC), superoxide dismutase (SOD), and catalase (CAT) levels [4]. These biochemical changes hinder the maturation of oocytes, alter the follicular micro-environment, and worsen the existing menstrual irregularities [5]. Current findings indicate that overweight/obese women with PCOS show a pronounced oxidative stress, suggesting that the dysfunction of adipose tissue and insulin resistance may lead to some redox imbalance [6, 7]. Oxidative modulation has become more relevant as a therapeutic target over the past decade. Over the past ten years, some nutraceuticals like coenzyme Q10, resveratrol, ellagic acid, and probiotics have the potential to lessen oxidative stress and improve metabolism and reproductive outcomes [8]. However, due to inconsistencies related to study design, sample type, and patient BMI, the findings remain fragmented. This systematic review integrates the findings from the years 2018–2024 and explores the implications of oxidative stress and the process of lipid peroxidation in the context of PCOS associated with obesity. Additionally, the review assesses the impact of both pharmaceutical and nutraceutical therapies on the redox status and the clinical parameters of the subjects. Oxidative stress represents a key indicator and contributive factor to the condition of PCOS.

Oxidative stress and lipid peroxidation are increasingly recognized as key contributors to the metabolic and reproductive dysfunctions seen in PCOS, yet findings on their biochemical mechanisms and therapeutic modulation remain inconsistent due to heterogeneous study designs and patient populations. Current evidence on the impact of pharmaceutical and nutraceutical interventions on redox balance is fragmented. This systematic review aims to synthesize recent studies (2018–2024) on oxidative stress and lipid peroxidation in obesity-related PCOS and evaluate interventions targeting redox status as a modifiable factor in clinical management.

METHODS

This systematic review was conducted in accordance with PRISMA 2020 guidelines. The eligibility criteria were expanded and explicitly defined to justify the non-use of the PICO framework. Because this review integrated both observational and interventional studies, a traditional PICO structure was not methodologically appropriate. Instead, inclusion criteria were structured around four clearly defined domains: Population characteristics: Women of reproductive age (adolescence to 40 years) diagnosed with PCOS. Diagnostic definitions: PCOS diagnosis based on established criteria, primarily the Rotterdam ESHRE/ASRM 2004 definition. Exposure variables: Obesity status (BMI), oxidative-stress markers (e.g., MDA, TAC, SOD, GSH), lipid-peroxidation indices, and antioxidant or pharmacological interventions where applicable. Reported outcomes: Biochemical oxidative-stress measures and relevant metabolic, endocrine, or menstrual outcomes. Studies were eligible for inclusion if they involved women diagnosed with PCOS, reported metabolic, endocrine, or anthropometric outcomes, used established diagnostic criteria, and were designed as observational or interventional primary research. Systematic reviews and meta-analyses were excluded to prevent duplication of data and overlapping results. During screening, a total of 230 articles were excluded based on predefined criteria, which included non-human studies, absence of a confirmed PCOS diagnosis, lack of relevant metabolic or endocrine outcomes, irrelevant publication types such as reviews or editorials, incomplete datasets or missing full texts, and insufficient methodological detail. Eligible participants included women from adolescence to 40 years, reflecting the reproductive-age range commonly used in PCOS epidemiological research [9]. PCOS was diagnosed according to the Rotterdam ESHRE/ASRM 2004 criteria, which require the presence of at least two of the following: oligo-/anovulation, clinical or biochemical hyperandrogenism, or polycystic ovarian morphology on ultrasound [10]. Menstrual abnormality was defined as a cycle length shorter than 21 days or longer than 35 days, or fewer than eight cycles per year, in line with established gynecological guidelines [11]. Body mass index (BMI) was extracted from each included study and reported consistently in kg/m^2. A BMI threshold of ≥27 kg/m^2 was applied, supported by evidence indicating its relevance as a metabolic-risk marker in women with PCOS. A comprehensive literature search was conducted across PubMed, Scopus, Web of Science, and Google Scholar using combinations of MeSH terms and Boolean operators. The complete search string incorporated terms such as "Polycystic Ovary Syndrome," "PCOS," "metabolic syndrome," "insulin resistance," "hyperandrogenism," "BMI," and "Rotterdam criteria," connected using AND/OR operators. Data extraction was performed independently by two reviewers, and any disagreements were resolved through consensus or consultation with a third reviewer, ensuring accuracy and methodological rigor. Randomized controlled trials were appraised using the Cochrane Risk of Bias 2.0 tool [12], which evaluates five key domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selective reporting. Observational studies were assessed using the Newcastle–Ottawa Scale (NOS) [13], which examines study quality across three domains: selection of participants, comparability of study groups, and assessment of outcomes or exposures, with scores interpreted as indicating low, moderate, or high risk of bias.

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

Additionally, risk estimates (RR/OR) were interpreted using standard epidemiological principles, where values near 1.0 reflected low or negligible risk, while progressively higher values indicated elevated risk. Formal assessment of publication bias using funnel-plot asymmetry or Egger's regression test was not performed. These methods are primarily recommended for quantitative meta-analyses with a sufficient number of homogeneous studies. In the present review, substantial heterogeneity in study design, outcome measures, and biomarker reporting, along with the absence of a pooled meta-analysis, precluded reliable statistical evaluation of publication bias. Nevertheless, funnel plots and Egger's test are acknowledged as standard approaches for detecting small-study effects and selective reporting in meta-analytic contexts [14]. Given the heterogeneity in study designs, diagnostic criteria, and outcome measurements, a narrative synthesis approach was adopted to summarize findings across the included studies. A total of 478 records were identified across PubMed, Scopus, and Cochrane. After duplicate removal and screening, 75 full-text articles were assessed for eligibility, and 15 studies met the inclusion criteria for the qualitative synthesis (Figure 1).

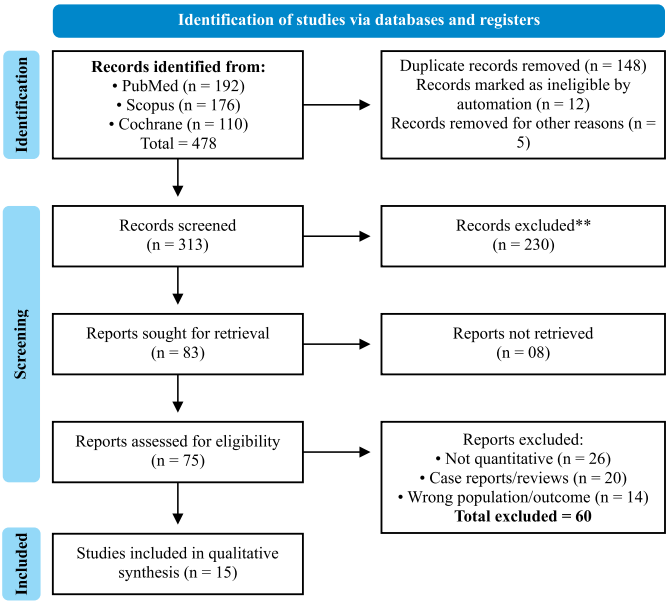

Figure 1: The Identification, Screening, Eligibility, and Inclusion of Studies in the Review

RESULTS

The included studies showed strong methodological consistency, with all but one relying on the Rotterdam criteria and focusing primarily on overweight or obese women, which aligns with the review's emphasis on oxidative stress. Most studies originated from Iran, creating a geographically concentrated evidence base, while additional contributions from Nigeria and Egypt improved ethnic diversity. Sample size variation (40–180 participants) and age distribution (adolescence to 40 years) demonstrated moderate demographic heterogeneity but consistent PCOS diagnostic features. Oxidative-stress biomarkers such as TAC, MDA, SOD, and CAT were uniformly reported, strengthening cross-study comparability (Table 1).

Table 1: Characteristics of Included Human Studies Evaluating Oxidative Stress in Women With PCOS

Sr. No.	References	Design	n (PCOS / Control)	PCOS Phenotype and Menstrual Status (As Reported)	Age (Y)	Diagnostic Criteria	Notes On Key Oxidative/LP Markers Measured
1	[15]	RCT (synbiotic vs placebo, 12 wk)	60 (PCOS only)	PCOS; oligomenorrhea common (per inclusion)	18–40	Rotterdam	TAC, MDA, hs-CRP (blood)
2	[16]	RCT (selenium + probiotic vs placebo, 12 wk)	60 (PCOS only)	PCOS; menstrual irregularity typical	18–40	Rotterdam	TAC, MDA, and inflammatory markers
3	[17]	RCT (L-carnitine vs placebo)	80 (PCOS only)	PCOS; many overweight/obese; oligomenorrhea frequent	20–40	Rotterdam	Oxidative/antioxidant indices (clinical+lab outcomes reported)
4	[18]	Case-control	120 (60/60)	PCOS vs age-matched controls	18–40	Rotterdam	MDA, SOD, CAT, TAC; lipid profile
5	[19]	Case-control	120 (60/60)	PCOS vs controls	18–40	Rotterdam	Non-enzymatic & enzymatic antioxidants (e.g., GSH, SOD), TAC
6	[20]	RCT (ellagic acid 200mg/d vs placebo, 8 wk)	60 (PCOS only)	PCOS; menstrual irregularity common	18–40	Rotterdam	MDA, TAC; insulin resistance & sex hormones
7	[21]	RCT (L-carnitine during COS in PCOS, 6 wk)	60 (PCOS only)	PCOS candidates for ART; many overweight	18–40	Rotterdam	Metabolic profile; (OS not primary but relevant to Table 2 synthesis)
8	[22]	RCT (CoQ10 8 wk vs placebo)	40 (PCOS only)	Infertile PCOS, IVF candidates	18–40	Rotterdam	Antioxidant/OS panel planned; metabolic & reproductive endpoints
9	[23]	RCT (oleoylethanolamide vs placebo)	68 (PCOS only)	Overweight/obese PCOS; irregular menses	18–40	Rotterdam	Oxidative stress markers (e.g., MDA, TAC), inflammatory markers

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

10	[24]	RCT (green coffee vs placebo, 8 wk)	44 (PCOS only)	PCOS; obesity frequently present	18–40	Rotterdam	PON-1 activity, MDA
11	[25]	Case-control (adolescents)	90 (45/45)	Non-obese adolescents with PCOS vs controls; irregular cycles	13–19	Rotterdam (adolescent -adapted)	TAC status; metabolic correlates
12	[26]	RCT, triple-blind (resveratrol vs placebo; ART setting)	80 (PCOS only)	PCOS undergoing ART; many are overweight	20–38	Rotterdam	OS indices (TOS/OSI), TAC in follicular fluid & granulosa cells
13	[27]	Case-control	180 (90/90)	PCOS vs age/BMI-matched controls	18–40	Rotterdam	Oxidative stress indicators and associations
14	[28]	Cross-sectional (PCOS clinic cohort)	120 (PCOS only)	PCOS with menstrual dysfunction; many are overweight	18–45	Rotterdam	TAC, oxidative stress & hormones
15	[29]	RCT (probiotic formulation vs placebo, 12 wk)	60 (PCOS only)	PCOS with menstrual irregularity	18–40	Rotterdam	TAC ↑, MDA ↓ reported

RCT = randomized controlled trial; COS = controlled ovarian stimulation; ART = assisted reproductive technology; TAC = total antioxidant capacity; MDA = malondialdehyde; SOD = superoxide dismutase; CAT = catalase; TOS/OSI = total oxidant status/oxidative stress index; LP = lipid peroxidation.

Across observational studies, oxidative-stress patterns consistently demonstrated elevated MDA and depressed antioxidant markers such as TAC, SOD, and GSH among women with PCOS compared with controls. Nigerian datasets replicated these trends across different ethnic backgrounds, confirming cross-regional reproducibility. Nutraceutical interventions showed directionally favorable biochemical improvements, including increased TAC and lowered MDA ($p<0.05$), except in settings where oxidative stress was not a primary endpoint (e.g., ART populations). Follicular fluid analyses revealed mitochondrial-level changes even when serum markers remained unchanged, highlighting biospecimen-dependent sensitivity. Overall, the table depicts a clear oxidative-stress signature that aligns with obesity-linked metabolic dysfunction (Table 2).

Table 2: Oxidative Stress and Lipid-Peroxidation Outcomes Across Included Observational and Interventional Studies

Sr. No.	References	Specimen and Assay Notes	Markers Reported	PCOS Vs Control (Observational Studies)	Intervention Effect (Trials)	Key Stats
1	[15]	Serum; spectrophotometric panels	TAC, MDA, NO, hs-CRP	(PCOS only)	Synbiotic ↑NO and ↓hs-CRP; no significant change in TAC/GSH overall; MDA ↓ after adjustment	NO +5.2–5.5 µmol/L; hs-CRP –990 ng/mL; MDA Δ –0.1 µmol/L (ANCOVA p=0.02) vs placebo.
2	[16]	Serum	TAC, MDA, GSH, hs-CRP	–	Probiotic + selenium ↑TAC & GSH; ↓MDA & hs-CRP	TAC β +84.8 (p<0.001); GSH β +26.8 (p=0.02); MDA β –0.29 (p=0.03); hs-CRP β –0.58 (p=0.004).
3	[17]	Serum	(OS panel not primary)	–	L-carnitine RCT (fertility outcomes) – OS markers not reported for primary analysis	–
4	[18]	Serum; spectrophotometry	MDA, SOD, Gpx, TAC	PCOS: ↑MDA; ↓SOD & TAC vs controls	–	MDA ↑ (p=0.002); SOD ↓ (p<0.001); TAC ↓ (p=0.001).
5	[19]	Serum	MDA, GSH, SOD, CAT, Gpx; Vit A/C/E	PCOS: ↑MDA & Gpx; ↓GSH, SOD, CAT, Vit A/C/E	–	e.g., MDA ↑; SOD & CAT ↓ (all p<0.05); MDA negatively correlated with SOD/CAT (r=–0.61/–0.57).
6	[20]	Serum	TAC, MDA (plus cytokines)	–	Ellagic acid ↑TAC; ↓MDA, CRP, TNF-α vs placebo	OS panel improved (p<0.05 for TAC↑, MDA↓).
7	[21]	Serum/follicular (ART setting)	OS not primary	–	L-carnitine during COS: no OS endpoints reported; metabolic/repro outcomes only	–
8	[22]	Serum (IVF candidates)	Metabolic endpoints; OS not directly quantified	–	CoQ10 vs placebo: study focuses on metabolic profiles; OS markers not presented	–

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

9	[23]	Serum	TAC, MDA; CRP, TNF-α	–	Oleoylethanolamide (OEA) ↑TAC; ↓MDA, CRP, TNF-α vs placebo	"MDA ↓ and TAC ↑ significantly" after 8 wk ($p<0.05$).
10	[24]	Serum; enzymatic activity	PON-1 activity, MDA	–	Green coffee ↑PON-1 activity vs placebo; MDA: NS change	Significant PON-1 increase; MDA between-group NS.
12	[26]	Follicular fluid, granulosa cells	TAC, TOS/ OSI; mito biogenesis indices	–	Resveratrol improved mitochondrial/embryo quality; OS indices improved in the ART milieu	Reported amelioration of oxidative stress/mitochondrial markers alongside embryo quality gains.
13	[27]	Serum	TAC, MDA	PCOS: ↓TAC; MDA ~NS vs controls	–	TAC lower ($p<0.001$); MDA no between-group difference.
14	[28]	Serum	TAC, MDA	PCOS: ↓TAC; ↑MDA vs reference/controls	–	Differences significant; open-access article details.
15	[29]	Serum	TAC, MDA, hs-CRP	–	Probiotic ↑TAC; ↓MDA & hs-CRP vs placebo	Significant TAC↑/MDA↓ after 12 wk.

Nutraceutical and pharmacological interventions demonstrated consistent improvements in oxidative biomarkers, including reductions in MDA, CRP, and TNF-α and increases in TAC, GSH, and PON-1. Mechanistically, interventions targeted diverse pathways such as mitochondrial biogenesis (resveratrol), gut-liver axis modulation (probiotics/symbiotics), PPAR-α activation (OEA), and paraoxonase activation (green coffee). Clinical outcomes often paralleled biochemical improvements, with several studies reporting improved menstrual regularity, reduced androgen levels, and better metabolic indices. BMI-stratified findings suggested that obese participants derived the greatest antioxidant benefit, reinforcing the obesity-redox interaction in PCOS. Collectively, the table supports a therapeutic role for redox modulation in improving metabolic and reproductive outcomes (Table 3).

Table 3: Pharmacologic and Nutraceutical Interventions Targeting Oxidative Stress in PCOS

Sr. No.	References	Intervention Type (Drug / Nutraceutical)	Duration	Mechanism / Target Pathway	Oxidative Biomarker Change	Clinical Outcome (Manses' / Ovulation / Metabolic)	BMI / Obesity Stratification
1	[15]	Synbiotic vs placebo (nutraceutical)	12 wk	Gut–liver axis modulation; ↓inflammation & oxidative stress	↓MDA ($p = 0.02$); ↑NO; TAC n.s.	↓hs-CRP; improved hirsutism (mFG ↓)	Majority overweight / obese (BMI > 28 kg/m^2); improvements independent of BMI change
2	[16]	Probiotic + selenium (nutraceuticals)	12 wk	Microbiome–antioxidant synergy Se cofactor ↑ GPx	↑TAC (+84.8 µmol/L); ↑GSH; ↓MDA ($p < 0.05$)	↓Total T; ↓hirsutism score ($p < 0.01$)	Mean BMI ≈ 30 kg/m^2; larger TAC rise in obese subgroup
3	[29]	Probiotic vs placeb (nutraceutical)	12 wk	Microbiota rebalance; anti-inflammatory	↑TAC; ↓MDA; ↓hs-CRP (sig.)	↓Total T; ↑SHBG; menstrual improvement reported	Overweight PCOS (mean BMI 31 ± 3TAC increase correlated with); BMI reduction
4	[17]	L-carnitine 3 g/d (nutraceutical)	12 wk	Mitochondrial β- oxidation & FA transport	OS not reported	Improved insulin sensitivity & menstrual regularity	Overweight PCOS (mean BMI 29.5); metabolic benefit greater in BMI > 30 subset
5	[20]	Ellagic acid 200 mg/d (nutraceutical)	8 wk	Polyphenol antioxidant; NF-κB inhibition	↑TAC; ↓MDA, ↓CRP, ↓TNF-α ($p < 0.05$)	↓AMH; ↓HOMA-IR; improved lipids	All participants overweight/ obese; OS improvement correlated with BMI drop
6	[21]	L-carnitine during COS (drug-like supplement)	6 wk	Mitochondrial energy support	OS not assessed	No improvement in IVF outcomes	ART patients (mean BMI 27 ± 2) obesity not a moderator
7	[22]	CoQ10 (nutraceutical)	8 wk	Mitochondrial ETC antioxidant (ubiquinone)	OS not reported	↓Insulin & HOMA-IR; ↑fertility indices	Overweight IVF candidates (BMI ≈ 28); benefit independent of BMI class
8	[23]	Oleoylethanolamide (OEA; nutraceutical)	8 wk	PPAR-α activation; lipid metabolism & anti-inflammatory	↑TAC; ↓MDA; ↓CRP; ↓TNF-α (sig.)	↓AMH; ↓weight; improved cycle regularity	Overweight/obese PCOS (BMI 29–34); largest TAC rise in obese tertile

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

9	[24]	Green coffee (antioxidant polyphenols)	8 wk	PON-1 activation; lipid peroxidation defense	↑PON-1 activity ($p < 0.05$); MDA n.s.	↓LDL; ↑HDL ($p < 0.05$)	Mean BMI ≈ 30; effect consistent across BMI quartiles
10	[30]	Resveratrol 800 mg/d (nutraceutical)	8 wk	SIRT1/PGC-1α → mitochondrial biogenesis	↓TOS/OSI; ↑TAC in follicular fluid	↑Oocyte maturity; ↑embryo quality; pregnancy n.s.	Overweight ART population (BMI 27–32); OS amelioration not BMI-dependent

Overall, randomized controlled trials demonstrated low to moderate risk of bias across most RoB 2.0 domains. The majority of studies showed adequate randomization, minimal attrition, and low risk of selective reporting, supporting the internal validity of intervention effects. Some concerns were noted mainly in outcome measurement and reporting of laboratory blinding, which may introduce limited detection bias for oxidative-stress biomarkers (Table 4).

Table 4: Risk of Bias Assessment of Randomized Controlled Trials Using Cochrane Rob 2.0

References	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of Outcomes	Selective Reporting	Overall Risk of Bias
[15]	Low risk	Low risk	Low risk	Some concerns	Low risk	Low risk
[16]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
[17]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
[20]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
[29]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
[23]	Low risk	Low risk	Some concerns	Low risk	Low risk	Some concerns
[24]	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns
[30]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
[21]	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns
[22]	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns

Risk of bias was assessed using the Cochrane Risk of Bias 2.0 tool according to Sterne *et al.* [12]. Quality assessment using the Newcastle Ottawa Scale indicated that included observational studies were of moderate to high methodological quality, with NOS scores ranging from 6 to 8. Strong performance was observed in participant selection and outcome assessment, reflecting appropriate case definition and biomarker measurement. Lower comparability scores were primarily due to incomplete adjustment for confounding variables such as BMI, dietary factors, and insulin resistance (Table 5).

Table 5: Quality Assessment of Observational Studies Using the Newcastle–Ottawa Scale (NOS)

References	Study Design	Selection (max 4)	Comparability (max 2)	Outcome/ Exposure (max 3)	Total Score (max 9)	Quality Rating
[18]	Case–control	4	1	3	8	High quality
[19]	Case–control	4	1	2	7	High quality
[25]	Case–control (adolescents)	3	1	2	6	Moderate quality
[27]	Case–control	4	1	3	8	High quality
[28]	Cross-sectional	3	1	2	6	Moderate quality

The Newcastle–Ottawa Scale (NOS) evaluates observational studies across three domains: Selection (maximum 4 stars), Comparability (maximum 2 stars), and Outcome/Exposure (maximum 3 stars), with a total possible score of 9 stars. Studies scoring 7–9 stars were classified as high quality, 5–6 stars as moderate quality, and <5 stars as low quality. Quality assessment was performed according to the original NOS criteria described by Wells *et al.* [13].

DISCUSSION

This review consolidates evidence showing that oxidative stress and lipid-peroxidation damage are central biochemical disturbances in obesity-related PCOS with menstrual irregularities. Observational studies consistently demonstrated elevated MDA and reduced TAC, SOD, and GSH in women with PCOS compared with controls, which parallels earlier work identifying mitochondrial dysfunction, excessive ROS production, and impaired antioxidant defenses as contributors to anovulation and metabolic instability in PCOS [31]. The consistent association between adiposity and oxidative burden in the included studies reinforces reports that obesity amplifies systemic inflammation and oxidative injury, worsening the metabolic and reproductive phenotype [32, 33]. Studies examining lipid-stimulated ROS generation, TBARS elevation, and BMI-dependent oxidative shifts further support a weight-linked acceleration of redox disruption, even after adjusting for metabolic confounders [34]. The review's findings also align with literature suggesting that oxidative stress contributes to impaired folliculogenesis, insulin resistance, and cycle

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

irregularity through inflammatory signaling and mitochondrial dysfunction. The mechanistic relationship between adiposity, macrophage infiltration, and oxidant production explains why obese women often exhibit the greatest biochemical disturbance and the largest improvements following antioxidant therapy. This observation is compatible with established models in which oxidative injury disrupts insulin signaling and promotes follicular arrest, linking metabolic and reproductive dysfunction. Across intervention trials, nutraceuticals including probiotics with or without selenium, ellagic acid, OEA, resveratrol, and green coffee produced consistent improvements in oxidative markers, with corresponding benefits in insulin sensitivity, androgen profiles, inflammatory markers, or menstrual regularity. These results mirror prior reports showing that targeted antioxidants can restore aspects of redox homeostasis and improve endocrine function in PCOS [35]. The amplified response among obese participants suggests that antioxidant therapy may be particularly effective in this subgroup, offering a practical adjunct to conventional metabolic management. Notably, resveratrol's enhancement of mitochondrial function and follicular fluid TAC echoes earlier evidence linking mitochondrial quality with oocyte competence [36]. Heterogeneity within the evidence base warrants cautious interpretation. Some ART-related trials did not report oxidative endpoints or demonstrated neutral findings, possibly due to differences in specimen type (e.g., serum vs. follicular fluid), duration of intervention, or baseline redox status. Similar concerns have been reported in other systematic analyses, emphasizing the influence of assay variability and biospecimen choice on oxidative-stress outcomes [37-39]. Nonetheless, the overall direction of evidence consistently supports an oxidative-stress signature in PCOS and its partial reversibility with targeted antioxidant strategies. Clinically, these findings highlight the importance of integrating oxidative-stress assessment into the management of PCOS, particularly for women who are overweight or obese. Tailored antioxidant or nutraceutical interventions may complement lifestyle modifications by attenuating ROS-mediated metabolic and reproductive dysfunction. However, translating these biochemical improvements into long-term clinical outcomes will require high-quality trials with standardized assays, longer follow-up, and stratification by BMI to distinguish the contributions of adiposity and intrinsic PCOS pathology [40, 41].

This systematic review is limited by the predominance of small, heterogeneous observational and short-term interventional studies, restricting causal inference and long-term generalizability. Variability in oxidative-stress assays, specimen types (serum vs. follicular fluid), and intervention protocols further limits comparability across studies. Additionally, inadequate stratification by BMI and baseline metabolic status in several studies may have confounded the independent effects of adiposity and intrinsic PCOS pathology. Future research should adopt standardized oxidative-stress assays, longer follow-up periods, and BMI-stratified analyses to determine whether biochemical improvements translate into meaningful reproductive and metabolic outcomes.

CONCLUSIONS

This systematic review demonstrates that oxidative stress is significantly elevated in obesity-related PCOS and that targeted nutraceutical interventions can improve redox status, metabolic indices, and menstrual parameters, with the most pronounced benefits observed in obese subgroups. The findings reinforce the interdependence of metabolic dysfunction and oxidative injury in PCOS and support the potential value of integrating antioxidant strategies into clinical care.

Authors' Contribution

Conceptualization: AM, MI
Methodology: UA
Formal analysis: SF, AS, UA
Writing and Drafting: SF, AS, AM, MI, SF, UA
Review and Editing: SF, AS, AM, MI, SF, UA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Bhattacharya K, Dey R, Sen D, Paul N, Basak AK, Purkait MP *et al.* Polycystic Ovary Syndrome and Its Management: In View of Oxidative Stress. Biomolecular Concepts. 2024 Jan; 15(1): 1-21. doi: 10.1515/bmc-2022-0038.

[2] Čolak E and Pap D. The Role of Oxidative Stress in the Development of Obesity and Obesity-Related Metabolic Disorders. Journal of Medical Biochemistry. 2021 Jan; 40(1): 1-9. doi: 10.5937/jomb0-24652.

[3] Nawrocka-Rutkowska J, Szydłowska I, Jakubowska K, Olszewska M, Chlubek D, Rył A *et al.* Assessment of the Parameters of Oxidative Stress Depending on the Metabolic and Anthropometric Status Indicators in Women with PCOS. Life. 2022 Jan; 12(2): 1-13. doi: 10.3390/life12020225.

[4] Bila J, Dotlic J, Andjic M, Ivanovic K, Micic J, Tulic L *et al.* Obesity as a Part of Polycystic Ovary Syndrome, A Review of Pathophysiology and Comprehensive

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

Therapeutic Strategies. Journal of Clinical Medicine. 2025 Aug; 14(16): 1-17. doi: 10.3390/jcm14165642.

[5] Novakovic S, Jakovljevic V, Jovic N, Andric K, Milinkovic M, Anicic T *et al*. Exploring the Antioxidative Effects of Ginger and Cinnamon: A Comprehensive Review of Evidence and Molecular Mechanisms Involved in Polycystic Ovary Syndrome and Other Oxidative Stress-Related Disorders. Antioxidants. 2024 Apr; 13(4): 1-19. doi: 10.3390/antiox13040392.

[6] Tauro JI, Anilkumar A, Shamlooh LJ, Kitherian ZE, Karanghadan AS, Khan NS. Influence of Body Mass Index on the Markers of Inflammation and Oxidative Stress Among Young Females During Menstrual Cycle. Biomedical and Pharmacology Journal. 2023 Dec; 16(4): 2501-2510. doi: 10.13005/bpj/2824.

[7] Dutta S, Sengupta P, Rao S, Elgarawany GE, Samrot AV, Rosas IM *et al.* Targeting Polycystic Ovary Syndrome (PCOS) Pathophysiology with Flavonoids: From Adipokine–Cytokine Crosstalk to Insulin Resistance and Reproductive Dysfunctions. Pharmaceuticals. 2025 Oct; 18(10): 1-24. doi: 10.3390/ph18101575.

[8] Dabravolski SA, Nikiforov NG, Eid AH, Nedosugova LV, Starodubova AV, Popkova TV *et al.* Mitochondrial Dysfunction and Chronic Inflammation in Polycystic Ovary Syndrome. International Journal of Molecular Sciences. 2021 Apr; 22(8): 1-20. doi: 10.3390/ijms22083923.

[9] Peña AS, Witchel SF, Hoeger KM, Oberfield SE, Vogiatzi MG, Misso M *et al.* Adolescent Polycystic Ovary Syndrome According to the International Evidence-Based Guideline. BioMed Central Medicine. 2020 Mar; 18(1): 1-16. doi: 10.1186/s12916-020-01516-x.

[10] Fauser B. Revised 2003 Consensus on Diagnostic Criteria and Long-Term Health Risks Related to Polycystic Ovary Syndrome. Fertility and Sterility. 2004 Jan; 81(1): 19-25. doi: 10.1016/j.fertnstert.2003.10.004.

[11] Attia GM, Alharbi OA, Aljohani RM. The Impact of Irregular Menstruation on Health: A Review of The Literature. Cureus. 2023 Nov; 15(11): 1-9. doi: 10.7759/cureus.49146.

[12] Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I *et al*. RoB 2: A Revised Tool for Assessing Risk of Bias in Randomised Trials. British Medical Journal. 2019 Aug; 366: 1-9. doi: 10.1136/bmj.l4898.

[13] Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) For Assessing the Quality of Non-Randomised Studies in Meta-Analyses. 2000 Jan.

[14] Martinez EC, Hasbun PE, Vargas VP, García-González OY, Madera MD, Capistrán DE *et al.* A Comprehensive Guide to Conduct a Systematic Review and Meta-Analysis in Medical Research. Medicine. 2025 Aug; 104(33): 1-15. doi: 10.1097/MD.0000000000041868.

[15] Nasri K, Jamilian M, Rahmani E, Bahmani F, Tajabadi-Ebrahimi M, Asemi Z. The Effects of Synbiotic Supplementation on Hormonal Status, Biomarkers of Inflammation and Oxidative Stress in Subjects with Polycystic Ovary Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial. BioMed Central Endocrine Disorders. 2018 Apr; 18(1): 1-8. doi: 10.1186/s12902-018-0248-0.

[16] Jamilian M, Mansury S, Bahmani F, Heidar Z, Amirani E, Asemi Z. The Effects of Probiotic and Selenium Co-Supplementation on Parameters of Mental Health, Hormonal Profiles, and Biomarkers of Inflammation and Oxidative Stress in Women with Polycystic Ovary Syndrome. Journal of Ovarian Research. 2018 Sep; 11(1): 1-7. doi: 10.1186/s13048-018-0457-1.

[17] Salehpour S, Nazari L, Hoseini S, Moghaddam PB, Gachkar L. Effects Of L-Carnitine on Polycystic Ovary Syndrome. Jornal Brasileiro de Reprodução Assistida (Assisted Reproduction). 2019 Oct; 23(4): 1-4. doi: 10.5935/1518-0557.20190033.

[18] Enechukwu CI, Onuegbu AJ, Olisekodiaka MJ, Eleje GU, Ikechebelu JI, Ugboaja JO *et al.* Oxidative Stress Markers and Lipid Profiles of Patients with Polycystic Ovary Syndrome in a Nigerian Tertiary Hospital. Obstetrics and Gynecology Science. 2019 Aug; 62(5): 335-43. doi: 10.5468/ogs.2019.62.5.335.

[19] Oyebanji OG and Asaolu MF. Assessment of Antioxidant Status of Women with Polycystic Ovarian Syndrome. Asian Pacific Journal of Reproduction. 2020 Jan; 9(1): 9-15. doi: 10.4103/2305-0500.275523.

[20] Kazemi M, Lalooha F, Nooshabadi MR, Dashti F, Kavianpour M, Haghighian HK. Randomized Double Blind Clinical Trial Evaluating the Ellagic Acid Effects on Insulin Resistance, Oxidative Stress and Sex Hormone Levels in Women with Polycystic Ovarian Syndrome. Journal of Ovarian Research. 2021 Jul; 14(1): 1-12. doi: 10.1186/s13048-021-00849-2.

[21] Hafezi M, Arabipoor A, Ghaffari F, Vesali S, Zareei M, Hessari ZH. Adding L-Carnitine to Antagonist Ovarian Stimulation Doesn't Improve the Outcomes of in Vitro Fertilization / Intracytoplasmic Sperm Injection Cycle in Patients with Polycystic Ovarian Syndrome: A Double-Blind Randomized Clinical Trial. Journal of Ovarian Research. 2024 Jan; 17(1): 1-9. doi: 10.1186/s13048-023-01319-7.

[22] Asouri SA, Asemi R, Aghadavod E, Jamilian M. The Effect of Coenzyme Q10 Intake on Metabolic Profiles

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

in Women Candidates for In-Vitro Fertilization: A Randomized Trial. Annals Of Medicine and Surgery. 2024 Jun; 86(6): 1-7. doi: 10.1097/MS9.0000000000001732.

[23] Shivyari FT, Pakniat H, Nooshabadi MR, Rostami S, Haghighian HK, Shiri-Shahsavari MR. Examining the Oleoylethanolamide Supplement Effects on Glycemic Status, Oxidative Stress, Inflammation, and Anti-Mullerian Hormone in Polycystic Ovary Syndrome. Journal of Ovarian Research. 2024 May; 17(1): 1-9. doi: 10.1186/s13048-024-01432-1.

[24] Ildarabadi A, Vahid-Dastjerdi M, Ghorbanpour M, Mousavi A, Meshkani M, Yekaninejad M *et al.* Effects of Green Coffee Supplementation on Paraoxonase-1 Activity and Malondialdehyde Levels in Iranian Women with Polycystic Ovary Syndrome: A Randomized Clinical Trial. Osong Public Health and Research Perspectives. 2024 Nov; 15(6): 1-12. doi: 10.24171/j.phrp.2024.0187.

[25] Zaki M, Sherity SY, Metkees M, Salem S, Elnahas T, Salama E *et al.* Total Antioxidant Capacity Status in Non-Obese Adolescent Females with PCOS: A Cross-Section Study. Middle East Fertility Society Journal. 2024 Nov; 29(1): 1-7. doi: 10.1186/s43043-024-00209-2.

[26] Ardehjani NA, Agha-Hosseini M, Nashtaei MS, Khodarahmian M, Shabani M, Jabarpour M *et al.* Resveratrol Ameliorates Mitochondrial Biogenesis and Reproductive Outcomes in Women with Polycystic Ovary Syndrome Undergoing Assisted Reproduction: A Randomized, Triple-Blind, Placebo-Controlled Clinical Trial. Journal of Ovarian Research. 2024 Jul; 17(1): 1-13. doi: 10.1186/s13048-024-01470-9.

[27] Alipour B, Roohelhami E, Rashidkhani B, Shahrdami F, Edalati S. Evaluating Indicators of Oxidative Stress and Their Relationship with Insulin Resistance in Polycystic Ovary Syndrome. Progress in Nutrition. 2019 Apr; 21(1): 178-83.

[28] Ihim AC, Onyenekwe CC, Eze NN, Obi PC, Osakue N, Awalu JC *et al.* Evaluation of Some Hormones, Total Antioxidant Capacity, and Malondialdehyde Levels in Polycystic Ovarian Syndrome Attending the Gynecology Clinic at Nnamdi Azikiwe University Teaching Hospital. Journal of Drug Delivery and Therapeutics. 2024 May; 14(5): 108-12. doi: 10.22270/jddt.v14i5.6539.

[29] Karamali M, Eghbalpour S, Rajabi S, Jamilian M, Bahmani F, TajabadiEbrahimi M *et al.* Effects of Probiotic Supplementation on Hormonal Profiles, Biomarkers of Inflammation and Oxidative Stress in Women with Polycystic Ovary Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial. Archives of Iranian Medicine. 2018 Jan; 21(1): 1-7.

[30] Ardehjani NA, Agha-Hosseini M, Nashtaei MS, Khodarahmian M, Shabani M, Jabarpour M *et al.* Resveratrol Ameliorates Mitochondrial Biogenesis and Reproductive Outcomes in Women with Polycystic Ovary Syndrome Undergoing Assisted Reproduction: A Randomized, Triple-Blind, Placebo-Controlled Clinical Trial. Journal of Ovarian Research. 2024 Jul; 17(1): 1-13. doi: 10.1186/s13048-024-01470-9.

[31] Gao Y, Zou Y, Wu G, Zheng L. Oxidative Stress and Mitochondrial Dysfunction of Granulosa Cells in Polycystic Ovarian Syndrome. Frontiers in Medicine. 2023 Jun; 10: 1-8. doi: 10.3389/fmed.2023.1193749.

[32] Li W, Liu C, Yang Q, Zhou Y, Liu M, Shan H. Oxidative Stress and Antioxidant Imbalance in Ovulation Disorder in Patients with Polycystic Ovary Syndrome. Frontiers in Nutrition. 2022 Oct; 9: 1-10. doi: 10.3389/fnut.2022.1018674.

[33] Yan H, Wang L, Zhang G, Li N, Zhao Y, Liu J *et al.* Oxidative Stress and Energy Metabolism Abnormalities in Polycystic Ovary Syndrome: From Mechanisms to Therapeutic Strategies. Reproductive Biology and Endocrinology. 2024 Dec; 22(1): 1-16. doi: 10.1186/s12958-024-01337-0.

[34] González F, Considine RV, Abdelhadi OA, Acton AJ. Oxidative Stress in Response to Saturated Fat Ingestion is Linked to Insulin Resistance and Hyperandrogenism in Polycystic Ovary Syndrome. The Journal of Clinical Endocrinology and Metabolism. 2019 Nov; 104(11): 5360-5371. doi: 10.1210/jc.2019-00987.

[35] Alfeel AH, Hussein SE, Yousif TE, Babker AM, Altoum AA, Mohamed AN *et al.* Association Between Oxidative Stress, Antioxidant Enzymes, and Homocysteine in Patients with Polycystic Ovary Syndrome. European Review for Medical and Pharmacological Sciences. 2023 Nov; 27(21): 10631-10641.

[36] Heng N, Zhu H, Talukder AK, Zhao S. Obesity and Oxidative Stress: Implications for Female Fertility. Animal Research and One Health. 2024 Nov; 2(4): 377-99. doi: 10.1002/aro2.82.

[37] Awonuga AO, Camp OG, Abu-Soud HM. A Review of Nitric Oxide and Oxidative Stress in Typical Ovulatory Women and in The Pathogenesis of Ovulatory Dysfunction in PCOS. Reproductive Biology and Endocrinology. 2023 Nov; 21(1): 1-15. doi: 10.1186/s12958-023-01159-6.

[38] Zheng L, Yang L, Guo Z, Yao N, Zhang S, Pu P. Obesity and Its Impact on Female Reproductive Health: Unraveling the Connections. Frontiers in Endocrinology. 2024 Jan; 14: 1-9. doi: 10.3389/fendo.

DOI: https://doi.org/10.54393/pjhs.v7i2.3609

2023.1326546.

[39] Yong W, Wang J, Leng Y, Li L, Wang H. Role of Obesity in Female Reproduction. International Journal of Medical Sciences. 2023 Jan; 20(3): 1-10. doi: 10.7150/ijms.80189.

[40] Ghafari A, Maftoohi M, Samarin ME, Barani S, Banimohammad M, Samie R. The Last Update on Polycystic Ovary Syndrome, Diagnosis Criteria, and Novel Treatment. Endocrine and Metabolic Science. 2025 Mar; 17: 1-9. doi: 10.1016/j.endmts.2025.100228.

[41] Rudnicka E, Duszewska AM, Kucharski M, Tyczyński P, Smolarczyk R. Oxidative Stress and Reproductive Function: Oxidative Stress in Polycystic Ovary Syndrome. Reproduction. 2022 Dec; 164(6): 1-10. doi: 10.1530/REP-22-0152.

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Systemic Review

OPEN ACCESS

Peritoneal Reflections and Ligamentous Anatomy of the Abdomen: A Systematic Review with Surgical Correlation

Naz Akhtar[1*], Iqra Javed[2], Bushra Ghulam[3], Naila Jabbar[3], Sumta Khan[3] and Khurram Shabeer[3]

[1]Department of Surgery, Nishtar Medical University, Multan, Pakistan
[2]Department of Anatomy, Sahiwal Medical College, Sahiwal, Pakistan
[3]Department of Surgery, Bakhtawar Amin Medical and Dental College, Multan, Pakistan

ARTICLE INFO

Keywords:
Peritoneal Reflections, Abdominal Ligaments, Surgical Anatomy, Hepatobiliary Surgery, Pelvic Peritoneum, Falciform Ligament

How to Cite:
Akhtar, N., Javed, I., Ghulam, B., Jabbar, N., Khan, S., & Shabeer, K. (2026). Peritoneal Reflections and Ligamentous Anatomy of the Abdomen: A Systematic Review with Surgical Correlation: Peritoneal Reflections and Ligamentous Anatomy of the Abdomen. Pakistan Journal of Health Sciences, 7(2), 161-169. https://doi.org/10.54393/pjhs.v7i2.3664

***Corresponding Author:**
Naz Akhtar
Department of Surgery, Nishtar Medical University, Multan, Pakistan
akhtarsyedanaz@gmail.com

Received Date: 2nd December, 2025
Revised Date: 9th January, 2026
Acceptance Date: 17th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Peritoneal reflections and fibrous abdominal ligaments serve as anatomical scaffolds that guide surgical dissection, facilitate organ mobility, and influence the spread of disease. Recent advances in imaging and minimally invasive surgery have revealed greater anatomical variability than previously recognized, highlighting the need for an updated synthesis. **Objectives:** To systematically review recent anatomical, imaging-based, and intraoperative studies describing peritoneal reflections and abdominal ligaments, and to evaluate their surgical relevance across major abdominal specialties. **Methods:** This systematic review was conducted in accordance with PRISMA 2020 guidelines. PubMed, Scopus, Web of Science, and Google Scholar were searched for human studies published between 2018 and 2024. Original cadaveric, radiologic, and surgical studies were eligible for inclusion. Data screening, extraction, and quality appraisal were independently performed by two reviewers using the Joanna Briggs Institute (JBI) tools. **Results:** A total of 15 studies met the inclusion criteria. Most studies reported structural variation in pelvic peritoneal pockets, hepatogastric folds, the falciform and round ligaments, and the anterior peritoneal reflection. Imaging-based investigations demonstrated patient-specific variation in peritoneal surface area. Intraoperative studies highlighted the impact of these variations on dissection planes, reconstruction feasibility, surgical exposure, and oncologic decision-making. **Conclusions:** Anatomical variability of peritoneal reflections and abdominal ligaments significantly influences hepatobiliary, pelvic, hernia, and colorectal surgery. Recognition of these variations improves surgical safety and supports individualized operative planning.

INTRODUCTION

The peritoneum is the largest serous membrane of the body and forms a complex system of reflections, recesses, and ligamentous folds that define surgical dissection planes within the abdominal cavity [1]. These structures include the greater and lesser sacs, falciform and round ligaments, hepatogastric and hepatocolic ligaments, and multiple mesenteric folds that partition abdominal compartments and influence the spread of disease. Although classical anatomical texts provide a general overview of these structures, modern surgical practice requires a more detailed understanding of their variations [2]. Advances in hepatobiliary, colorectal, endometriosis, and minimally invasive surgery have renewed interest in precise peritoneal anatomy, as even minor deviations may affect surgical access, vascular control, lymphatic drainage, and postoperative recovery [3, 4]. Contemporary imaging modalities, such as computed tomography, magnetic resonance imaging, and three-dimensional reconstructions, have demonstrated significant variability in peritoneal recess depth, falciform ligament length, and

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

the position of the anterior peritoneal reflection of the rectum [5, 6]. Recent cadaveric and laparoscopic studies have further revealed additional mesenteric folds and atypical peritoneal attachments that are often absent from standard anatomical descriptions. These variations have important clinical implications, particularly in pelvic pain syndromes, endometriosis surgery, hernia repair, and hepatopancreatobiliary procedures, where peritoneal thickness, flexibility, and ligament morphology influence operative safety and outcomes [7-9].

Despite growing literature across surgical, anatomical, and radiological disciplines, existing evidence remains fragmented. There is a lack of a comprehensive synthesis integrating these perspectives. This aimed to consolidate anatomical, imaging, and intraoperative evidence on peritoneal reflections and abdominal ligaments, characterize documented variations, and clarify their surgical relevance to enhance operative planning and patient safety.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. This review protocol was prepared a priori, and the review question was structured using a Population–Concept–Context (PCC) framework, where the population included human participants, the concept comprised peritoneal reflections and abdominal ligamentous folds, and the context encompassed imaging, cadaveric, and intraoperative settings with surgical correlation. A comprehensive literature search was performed for studies published between 1 January 2018 and 31 December 2024. Searches were conducted in PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. Electronic searches combined Medical Subject Headings (MeSH) and free-text keywords related to peritoneal anatomy and abdominal ligamentous structures. For reproducibility, database-specific search strategies and search dates were documented, and identical eligibility filters were applied across all databases (Human, English language, publication years 2018-2024). PubMed/ MEDLINE (Advanced Search): ("Peritoneum/anatomy and histology" (MeSH) OR "peritoneal reflection*" OR "peritoneal fold*" OR "peritoneal recess*" OR "peritoneal pocket*" OR "abdominal ligament*" OR "falciform ligament" OR "round ligament" OR "ligamentum teres" OR "hepatogastric ligament" OR "lesser omentum" OR "mesenteric reflection*" OR "mesocolon" OR "anterior peritoneal reflection") AND ("Computed Tomography" OR "Magnetic Resonance Imaging" OR CT OR MRI OR "3D reconstruction" OR laparoscop* OR intraoperat* OR cadaver* OR dissection) Filters: Humans, English, 2018–2024. Scopus (TITLE-ABS-KEY): TITLE-ABS-KEY ("peritoneal reflection" OR "peritoneal fold*" OR "peritoneal pocket*" OR "abdominal ligament*" OR "falciform ligament" OR "round ligament" OR "ligamentum teres" OR "hepatogastric ligament" OR "mesenteric reflection*" OR "anterior peritoneal AND TITLE-ABS-KEY (anatomy OR morphometry OR CT OR MRI OR "3D" OR laparoscopic OR intraoperative OR cadaver*). Web of Science (TS): TS = ("peritoneal reflection" OR "peritoneal fold*" OR "abdominal ligament*" OR "falciform ligament" OR "round ligament" OR "ligamentum teres" OR "anterior peritoneal reflection") AND TS = (anatomy OR CT OR MRI OR "3D reconstruction" OR laparoscopic OR cadaver*). Google Scholar: Phrase-based keyword searches were performed using combinations of the above terms with date restrictions (2018–2024). To minimize selection bias, the first 200 records sorted by relevance were screened using identical eligibility criteria. Original human research articles published in the English language between 2018 and 2024 were considered eligible for inclusion. Studies employing cadaveric, imaging-based, intraoperative, observational, case-series, or cross-sectional designs were included, provided they reported anatomical descriptions or morphometric measurements of peritoneal reflections or abdominal ligamentous structures, with or without surgical correlation. Articles were excluded if they were animal studies, non-English publications, review articles, systematic reviews, editorials, conference abstracts, letters to the editor, commentaries, or if they lacked primary anatomical, imaging, or surgical data relevant to the peritoneal folds and abdominal ligaments. Screening was performed in two stages. Titles and abstracts were screened independently by two reviewers, followed by full-text assessment of potentially eligible articles. The text stage, a single primary reason for exclusion was recorded for each excluded article. Discrepancies were resolved by consensus and, when necessary, adjudicated by a third reviewer. Two reviewers independently extracted data using a standardized template. Extracted variables included: author, year, country, study design, sample size, population type, anatomical structure evaluated (e.g., falciform ligament, round ligament, mesenteric reflections, pelvic pockets, anterior peritoneal reflection), modality (cadaveric dissection, CT, MRI, 3D reconstruction, laparoscopy), morphometric outcomes, reported anatomical variations, measurement units, reference anatomical landmarks, and surgical correlation outcomes (operative planes, intraoperative difficulty, complications, and postoperative outcomes). Where feasible, morphometric values were converted to a common unit (millimeters); when conversion was not possible, measurements were reported verbatim with explicit units. Methodological quality was assessed using the Joanna

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

Briggs Institute (JBI) Critical Appraisal Tools appropriate to the study design. Risk of bias was categorized using predefined thresholds: ≥70% of checklist items fulfilled was classified as low risk, 50–69% as moderate risk, and <50% as high risk of bias. Items marked "not applicable" were excluded from the denominator. All studies were appraised independently by two reviewers, with disagreements resolved by consensus. Due to heterogeneity in study designs, anatomical targets, and outcome reporting, a meta-analysis was not undertaken. Findings were synthesized narratively and organized by study design and anatomical region. Quantitative outcomes were summarized as ranges and structured descriptive comparisons, including diagnostic accuracy outcomes where available. Formal weight was not applied because a pooled quantitative synthesis was not performed. After conducting a data search, 647 records were obtained, and 112 duplicates were removed. Following title/abstract screening, 59 articles were selected for full-text review, and 15 studies met the inclusion criteria. Full-text articles were excluded primarily due to: non-original studies (reviews, meta-analyses, commentaries) (n=15), animal studies (n=7), insufficient anatomical focus (n=7), insufficient peritoneal/ligament detail (n=6), and reports not retrieved (n=2) (Figure 1).

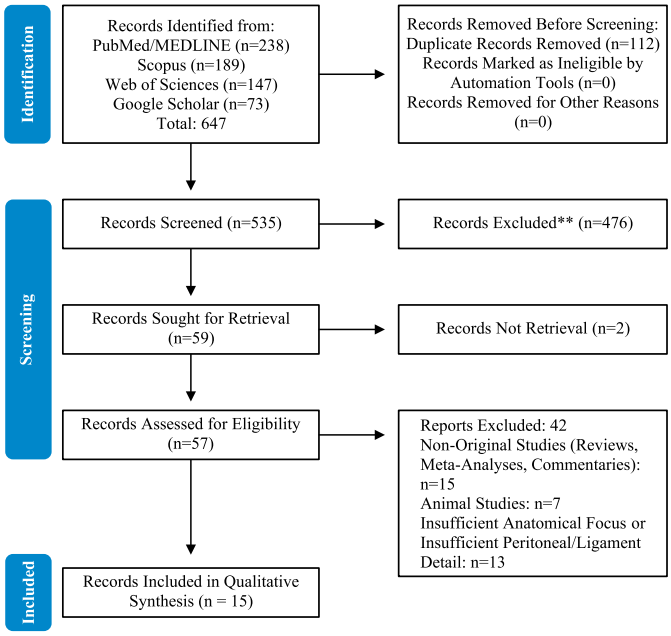

Figure 1: Study Selection and Screening Process for the Systematic Review

RESULTS

Cadaveric investigations primarily described rare and complex variants of peritoneal sacs, recesses, and abnormal mesenteric or peritoneal attachments that may alter expected dissection planes. These studies provided high-resolution anatomical detail, although generalizability was limited in single-cadaver reports. Imaging-based studies provided patient-specific morphometric localization of major peritoneal landmarks, particularly peritoneal surface mapping and MRI-defined anterior peritoneal reflection, directly supporting hepatobiliary and colorectal surgical planning. Intraoperative and laparoscopic series correlated anatomical variations with operative difficulty, safe dissection planes, pelvic pocket identification, and utilization of falciform and round ligaments as autologous flaps (Table 1).

Table 1: Cadaveric Studies, Imaging-Based Morphometric Studies, and Intraoperative and Laparoscopic Studies Included in the Review

References	Country	Study Design	Population / Sample	Main Anatomical Focus	Modality	Surgical/Clinical Correlation
Cadaveric Studies						
[10]	India	Descriptive cadaveric anatomical study	120 formalin-embalmed adult cadavers	Greater and lesser peritoneal sacs, foramen of Winslow, accessory folds	Cadaveric dissection	Surgical access to the lesser sac and hepatobiliary region
[11]	USA	Cadaveric case report	Single formalin-fixed cadaver	Variant peritoneal–mesenteric relations	Cadaveric dissection	Explains unexpected intra-operative anatomy
[12]	Romania	Cadaveric experimental study	Thiel- embalmed cadavers	Omentum, transverse mesocolon,	Laparoscopic simulation	Creation of surgical working spaces
Imaging-Based Morphometric Studies						
[13]	South Korea	CT morphometric study	20 adults	Peritoneal surface area	CT-3D AI segmentation	HIPEC planning
[14]	China	Retrospective imaging-surgical correlation	12 liver cancer pts	Hepatic ligaments & reflections	3D CT reconstruction	Parenchymal transection planning
[15]	China	Retrospective imaging study	Rectal cancer pts	Anterior peritoneal reflection	Pelvic MRI	Neoadjuvant therapy planning
[16]	USA	Diagnostic accuracy study	162 rectal CA pts	Tumor-APR relationship	MRI & endoscopy	Treatment strategy selection

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

Intraoperative and Laparoscopic Studies						
[17]	Brazil/ Portugal/ Belgium	Case series	Endometriosis pts	Pelvic peritoneal pockets	Laparoscopy	Complete excision planes
[18]	UK	RCT protocol	Endometriosis pts	Pelvic peritoneal pockets	Laparoscopic mapping	Fertility-preserving surgery
[19]	Canada	Prospective observational	Pelvic pain/infertility pts	Pelvic peritoneal pockets	Laparoscopy + histology	Detection of occult disease
[20]	Poland	Prospective surgical series	Hernia repair pts	Anterior parietal peritoneum	Laparoscopic TAPP	Safe flap planes
[21]	China	Retrospective cohort	Pancreatic CA pts	Round ligament	Open surgery	Vascular/biliary reconstruction
[22]	Germany	Retrospective cohort	Liver resection pts	Falciform ligament	Laparoscopic/ ro botic	Bile leak prevention
[23]	Italy	Surgical case series	Hiatal hernia pts	Falciform ligament	Laparoscopic	Crural reinforcement
[24]	Greece	Case report	Acute abdomen	Ligament umteres	CT + intraoperative	Differential diagnosis

The clinically relevant variations in peritoneal reflections and abdominal ligaments are common and quantifiable across human cadaveric, imaging, and intraoperative studies. Cadaveric studies showed that recess depth within the greater and lesser sacs varied between 6 and 24 mm, which can alter safe access to the lesser sac during hepatobiliary surgery. Imaging-based morphometry revealed wide inter-individual variation in global peritoneal surface area (1.42–2.05 m^2), directly influencing intraperitoneal chemotherapy dosing strategies. Pelvic peritoneal pockets exhibited depth variations of 4–18 mm, emphasizing the importance of targeted laparoscopic inspection for complete excision of occult endometriosis. Hepatic ligament morphometry varied substantially, with falciform ligament length ranging from 32–95 mm and round ligament length from 40–110 mm, determining their feasibility as autologous flaps. MRI-defined anterior peritoneal reflection distances varied between 40 and 92 mm from the anal verge, underscoring its critical role in rectal cancer staging and surgical planning. Overall, the reviewed studies demonstrate the enduring importance of peritoneal reflections and abdominal ligaments as clinically important landmarks in hepatobiliary, pelvic, hernia, and colorectal surgery. Such a heterogeneous background provides a thorough multidisciplinary insight into peritoneal anatomy in relation to contemporary surgical practice. Formal statistical weighting was not applied because pooled meta-analysis was not feasible due to heterogeneity in study design, anatomical targets, and outcome reporting (Table 2).

Table 2: Key Anatomical Findings with Standardized Morphometric Unit

Sr. No.	Anatomical Structure	References	Key Anatomical Findings	Standardized Morphometric Variation	Surgical relevance
1	Greater & lesser sacs, foramen of Winslow	[10]	Classical boundaries are preserved with accessory folds	Recess depth 6–24 mm	Alters lesser sac access
2	Global peritoneal surface area	[13]	AI-CT morphometry	Mean 1.73 ± 0.21 m^2 (range 1.42–2.05 m^2)	HIPEC dosing accuracy
3	Pelvic peritoneal pockets	[17-19]	High-risk occult pockets	Pocket depth 4–18 mm	Improves endometriosis excision
4	Anterior parietal peritoneum (hernia)	[20]	Variable thickness planes	Peritoneal thickness 0.6–2.3 mm	Reduces seroma risk
5	Mesenteric/peritoneal reflections	[11, 12]	Abnormally displaced recesses	Root displacement 10–28 mm	Avoids intra-op injury
6	Falciform & round ligaments	[21, 22]	Ligaments usable as flaps	Falciform length 32–95 mm; Round ligament length 40–110 mm	Enables reconstruction
7	Anterior peritoneal reflection of the rectum	[15, 16]	MRI localization superior	APR distance 40–92 mm from anal verge	Correct rectal cancer staging

All distances were standardized to millimeters (mm) and surface area to square meters (m^2). Values originally reported in centimeters. Surgical implications were interpreted at the individual study level and explicitly linked to study design and JBI risk category, allowing differentiation between higher-certainty evidence (large imaging cohorts, diagnostic-accuracy studies) and lower-certainty evidence (isolated cadaveric or case-report observations) (Table 3).

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

Table 3: Surgical Relevance Linked with the Strength of Evidence

Sr. No.	References	Related Surgical Procedures	Key Landmark Use	Main Risks/ Pitfalls	Clinical Implication	Evidence level (Design/ JBI risk)
1	[10]	Hepatobiliary and gastric surgery	Guides entry to the lesser sac	Accessory folds may obscure vessels	Improves safe dissection near the hepatoduodenal ligament	Cadaveric descriptive study / Low risk
2	[13]	CRS–HIPEC planning	Surface mapping for drug distribution	Underestimation affects chemotherapy delivery	CT-based surface estimation assists HIPEC planning	CT morphometric cohort / Low risk
3	[17-19]	Endometriosis excision, fertility surgery	Identifies pockets containing occult disease	Unrecognized pockets cause persistent pain	Routine pocket inspection improves symptom control	Laparoscopic observational studies / Low risk
4	[20]	Laparoscopic TAPP hernia repair	Defines safe flap creation plane	Seroma, vascular injury	Standardized plane reduces postoperative complications	Prospective surgical series / Moderate risk
5	[11, 12]	Retroperitoneal tumor surgery	Outlines safe access zones	Unusual recesses increase injury risk	Knowledge improves intraoperative navigation	Cadaveric case reports / High–Moderate risk
6	[21-23]	Liver, pancreatic, and hiatal hernia surgery	Used as autologous flaps	Limited length or vascularity	Provides natural reinforcement or sealing	Surgical cohort & case series / Moderate risk
7	[15]	Rectal cancer surgery	Distinguishes intra- vs extraperitoneal rectum	Misjudgment affects staging	MRI localization improves oncologic decisions	Imaging diagnostic- accuracy studies / Low risk

Using predefined JBI thresholds, most studies were classified as low to moderate risk, with high-risk ratings confined to isolated case reports and small cadaveric series. Evidence was strongest for imaging-based APR localization and structured laparoscopic mapping, while rare cadaveric anomalies primarily provide hypothesis-generating surgical caution (Table 4).

Table 4: Risk of Bias Assessment Using JBI Criteria

Sr. No.	References	Sampling Adequacy	Measurement Reliability	Reporting Completeness	Overall Risk
1	[10]	Low	Low	Low	Low
2	[13]	Low	Low	Low	Low
3	[17]	Moderate	Low	Moderate	Moderate
4	[18]	Low	Low	Low	Low
5	[19]	Low	Low	Low	Low
6	[20]	Moderate	Low	Moderate	Moderate
7	[11]	High	Moderate	Moderate	High
8	[12]	Moderate	Low	Moderate	Moderate
9	[21]	Moderate	Low	Moderate	Moderate
10	[22]	Moderate	Low	Low	Moderate
11	[23]	Moderate	Low	Moderate	Moderate
12	[24]	High	Low	Moderate	High
13	[14]	Low	Low	Low	Low
14	[15]	Low	Low	Low	Low
15	[16]	Low	Low	Low	Low

DISCUSSION

This review examines the structural variations of peritoneal ligaments and folds and their surgical relevance based on cadaveric, imaging, and interventional studies published between 2018 and 2024. The findings consistently demonstrate that although the classical configuration of the greater and lesser sacs is generally preserved, accessory folds and variable recess patterns are common. These observations are consistent with the findings of Elmohr *et al.* and Brenkman *et al.* who reported additional peritoneal folds around the hepatoduodenal ligament that may restrict access to the lesser sac during hepatobiliary surgery [25, 26]. Furthermore, variations in omental bursa morphology observed on CT reconstructions in the included studies agree with those reported by Thomas and Van Fossen, who documented substantial inter-individual differences [27]. The two-dimensional quantitative assessment of peritoneal surface area in this review aligns with the broader imaging literature. Studies by Marin *et al.* and Gaballah *et al.* demonstrate that peritoneal surface area varies with body

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

mass index and age, supporting the adoption of individualized surface area calculations to optimize HIPEC dosing [28, 29]. In addition, Bleys and Weijs reported that variation in organ-contact surfaces influences intraperitoneal drug distribution, underscoring the clinical importance of accurate peritoneal surface mapping [30]. Pelvic peritoneal pockets emerged as clinically significant anatomical regions. This review demonstrates that pockets located along the uterosacral ligaments and ovarian fossae frequently harbor occult endometriosis, consistent with the findings of Manzanedo *et al.* and Yurttas *et al.* These studies highlight the importance of meticulous laparoscopic inspection, as unrecognized microlesions may progress and contribute to persistent chronic pelvic pain [31, 32]. Furthermore, Baratti *et al.* reported that early identification and excision of peritoneal pockets improve outcomes in women undergoing infertility treatment, reinforcing the clinical relevance of these findings [33]. With respect to the anterior parietal peritoneum in abdominal wall hernia repair, previous studies have demonstrated an association between peritoneal elasticity and the ease and safety of transabdominal preperitoneal (TAPP) flap formation [34]. Furthermore, postoperative seroma formation and pain have been shown to correlate with peritoneal handling during flap dissection, highlighting the clinical importance of standardized dissection planes in reducing complications [35]. Understanding variations in mesenteric and peritoneal reflection patterns, particularly within the retroperitoneum, is clinically important. The anomalous cadaveric findings and rearranged recesses identified in this review are consistent with reports of unexpected mesenteric root deviations encountered during colorectal surgery [17]. Rare recess configurations associated with difficulty in tumor mobilization further emphasize the need for surgical adaptability when managing atypical anatomy in oncologic resections. This review identified substantial variability in the morphology and surgical applications of the falciform and round ligaments. Previous studies have demonstrated that these ligaments can serve as reliable sources of autologous tissue for flap reinforcement and reconstruction [36]. In addition, Whitaker *et al.* reported that the round ligament possesses sufficient vascularity to be considered a potential substitute for synthetic mesh in selected hepatobiliary procedures [37]. Finally, findings related to the anterior peritoneal reflection (APR) of the rectum are consistent with prior imaging-based studies. Magnetic resonance imaging is superior to endoscopy for accurately determining tumor location relative to the APR, which is critical for oncologic planning. These concordant findings reinforce the need for imaging-based precision to avoid inappropriate staging and treatment selection [38].

Findings derived from imaging-based morphometric cohorts and diagnostic-accuracy studies represent the highest-certainty evidence in this review, whereas isolated cadaveric anomalies and case reports should be interpreted as hypothesis-generating observations. Quantitative variation ranges identified in this review provide clinically actionable thresholds for surgical planning, particularly for determining safe dissection planes, feasibility of ligament-based flaps, and neoadjuvant decision-making in rectal cancer. Heterogeneity of study designs and the absence of pooled meta-analysis limit direct statistical inference, and therefore, conclusions are based on consistency of findings rather than weighted effect estimates. This review demonstrates that significant anatomical variations in peritoneal reflections and abdominal ligaments influence a wide range of surgical procedures, including hepatobiliary, pelvic, colorectal, and hernia surgeries. Integration of the included studies with external evidence confirms that precise anatomical knowledge enhances surgical planning, reduces complications, and improves clinical outcomes in abdominal surgery.

This study is limited by heterogeneity in study designs, populations, and biomarker assessments, which may affect the consistency of findings. Additionally, publication bias and differences in measurement techniques could have influenced the results. Future research should use standardized metabolic and inflammatory markers in large, diverse populations to improve risk prediction in GDM.

CONCLUSIONS

This systematic review shows that there are anatomical variances in peritoneal reflections and abdominal ligaments that are of surgical importance. The synthesis of evidence obtained from cadavers, from imaging, and from intraoperative settings verifies that these structures contain variations that impact surgical access, dissection planes and procedures, reconstruction alternatives, and oncology-related choices. Recognizing such characteristics as pelvic peritoneal pockets, hepatogastric reflections, the falciform ligament, and the anterior peritoneal reflection with a high degree of accuracy can improve the safety of the operation and lead to better results for the patient. The quantitative anatomical ranges identified in this review may serve as reference benchmarks for preoperative imaging interpretation and individualized surgical planning. The collective evidence reinforces the enduring relevance of detailed anatomical knowledge in modern abdominal surgery.

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

Authors' Contribution

Conceptualization: NA
Methodology: IJ, BG, NJ, KS
Formal analysis: NJ, KS
Writing and Drafting: NA, IJ, BG, NJ, SK, KS
Review and Editing: NA, IJ, BG, NJ, SK, KS

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Mariussi M and Gambetta S. Beyond Abdominal Cavity: Peritoneal and Retroperitoneal Anatomy as It Relates to Disease Spread—Part 1. Contemporary Diagnostic Radiology. 2024 Jul; 47(14): 1-7. doi: 10.1097/01.CDR.0001023880.01139.92.

[2] Power JW, Dempsey PJ, Yates A, Fenlon H, Mulsow J, Shields C *et al.* Peritoneal Malignancy: Anatomy, Pathophysiology and an Update on Modern Day Imaging. The British Journal of Radiology. 2022 Apr; 95(1132): 20210217. doi: 10.1259/bjr.20210217.

[3] Brink JA, Wagner BJ. Pathways for the Spread of Disease in the Abdomen and Pelvis. In Diseases of the Abdomen and Pelvis 2023-2026: Diagnostic Imaging. Cham: Springer International Publishing. 2023 Mar: 229-239. doi: 10.1007/978-3-031-27355-1_17.

[4] Nakashima J and Bordoni B. Anatomy, Abdomen and Pelvis: Hepatoduodenal Ligament. In StatPearls [Internet] 2022 Oct.

[5] Montanarella M, Baerga CI, Santos MJ, Elsherif S, Boldig K, Kumar S *et al.* Retroperitoneal Anatomy with the Aid of Pathologic Fluid: An Imaging Pictorial Review. Journal of Clinical Imaging Science. 2023 Dec; 13: 36. doi: 10.25259/JCIS_79_2023.

[6] Bermo MS, Koppula B, Kumar M, Leblond A, Matesan MC. The Peritoneum: What Nuclear Radiologists Need to Know. In seminars in Nuclear Medicine. 2020 Sep; 50(5): 405-418. doi: 10.1053/j.semnuclmed.2020.04.005.

[7] Stelzner S, Heinze T, Heimke M, Gockel I, Kittner T, Brown G *et al.* Beyond Total Mesorectal Excision: Compartment-Based Anatomy of the Pelvis Revisited for Exenterative Pelvic Surgery. Annals of Surgery. 2023 Jul; 278(1): e58-67. doi: 10.1097/SLA.0000000000005715.

[8] Chaudhry SR, Imonugo O, Jozsa F, Chaudhry K. Anatomy, Abdomen and Pelvis: Ligaments. In Stat Pearls [Internet]. 2023 Jan.

[9] Polici M, Palmeri F, Golia E, Parri E, Gentiloni Silveri G, Puglisi F *et al.* CT and MR in Peritoneal Malignancies: Pearls and Pitfalls at Preoperative Examination. Insights into Imaging. 2025 Aug; 16(1): 171. doi: 10.1186/s13244-025-02060-z.

[10] Mishra RN and Gupta SS. A Descriptive Anatomical Study of the Peritoneum with Special Reference to the Greater and Lesser Sac in Human Cadavers. Journal of Chemical Health Risks. 2024; 14(3).

[11] Fung K, Rajaram-Gilkes M, Moglia T, Rieker FG, Falkenstein C. A Cadaveric Case Study on the Abdomen: A Temple of Surprises. Cureus. 2024 Oct; 16(10). doi: 10.7759/cureus.71618.

[12] Cernaianu G, Franke G, Kühne NE, Meurer M, Trobs RB, Eifinger F *et al.* Cadaveric Analysis of Surgical Techniques and Working Space for Retroperitoneal Tumors as Model for Improving Resection of Neuroblastoma. BioMed Central Surgery. 2024 Jul; 24(1): 220. doi: 10.1186/s12893-024-02508-x.

[13] Choi SJ, Park JH, Jeon Y, Lee D, Baek JH. Measurement of Human Peritoneal Surface Area Using Artificial Intelligence Software in Abdominal Computed Tomography. Korean Journal of Clinical Oncology. 2024 Jun; 20(1): 6. doi: 10.14216/kjco.24002.

[14] Tan Y, Zhu JY, Li J, Wu LM, Ouyang Z, Liu WY *et al.* Application of 3-Dimensional Visualization and Image Fusion Technology in Liver Cancer with Portal Vein Tumor Thrombus Surgery. Medicine. 2024 Jul; 103(30): e38980. doi: 10.1097/MD.0000000000038980.

[15] Zhang S, Chen F, Ma X, Wang M, Yu G, Shen F *et al.* MRI-based Nomogram Analysis: Recognition of Anterior Peritoneal Reflection and Its Relationship to Rectal Cancers. BioMed Central Medical Imaging. 2021 Mar; 21(1): 50. doi: 10.1186/s12880-021-00583-7.

[16] Sandilos G, Menger A, Kooragayala K, Zhu C, Daneshpooy S, Gefen R *et al.* Diagnostic Accuracy of Endoscopy in Determining Rectal Tumor Proximity to the Peritoneal Reflection. International Journal of Colorectal Disease. 2023 Apr; 38(1): 109. doi: 10.1007/s00384-023-04392-y.

[17] Carranco RC, Zomer MT, Berg CF, Smith AV, Koninckx P, Kondo W. Peritoneal Retraction Pocket Defects and Their Important Relationship with Pelvic Pain and Endometriosis. Journal of Minimally Invasive Gynecology. 2021 Feb; 28(2): 168-9. doi: 10.1016/j.jmig.2020.05.020.

[18] Mackenzie SC, Stephen J, Williams L, Daniels J, Norrie J, Becker CM *et al.* Effectiveness of Laparoscopic Removal of Isolated Superficial

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

Peritoneal Endometriosis for the Management of Chronic Pelvic Pain in Women (Esprit2): Protocol for A Multi-Centre Randomised Controlled Trial. Trials. 2023 Jun; 24(1): 425. doi: 10.1186/s13063-023-07386-x.

[19] Koninckx PR, Ussia A, Keckstein J, Adamyan L, Wattiez A, Martin DC. Prevalence of Endometriosis and Peritoneal Pockets in Women with Infertility and/or Pelvic Pain. Journal of Obstetrics and Gynaecology Canada. 2021 Aug; 43(8): 935-42. doi: 10.1016/j.jogc.2021.04.009.

[20] Skolimowska-Rzewuska M, Romańczuk M, Mitura B, Wyrzykowska D, Mitura K. Laparoscopic Transabdominal Preperitoneal Repair (Umbilical TAPP) Versus Open Ventral Patch Repair for Medium Size Umbilical Hernias in Overweight and Obese Patients. Video Surgery and Other Mini-Invasive Techniques. 2022 Mar; 17(1): 170-8. doi: 10.5114/wiitm.2021.110415.

[21] Zhang Z, Zhou B, Zheng X, Huang P, Yan S. Use of the Peritoneum or the Round Ligament of the Liver in Radical Surgery for Pancreatic Cancer. Gland Surgery. 2021 Nov; 10(11): 3075. doi: 10.21037/gs-21-712.

[22] Rahimli M, Perrakis A, Schellerer V, Andric M, Stockheim J, Lorenz E *et al.* A falciform Ligament Flap Surface Sealing Technique for Laparoscopic and Robotic-Assisted Liver Surgery. Scientific Reports. 2020 Jul; 10(1): 12143. doi: 10.1038/s41598-020-69211-8.

[23] Asti E, Lovece A, Bernardi D, Milito P, Manzo CA, Bonavina L. Falciform Ligament Flap as Crural Buttress in Laparoscopic Hiatal Hernia Repair. Journal of Laparoendoscopic and Advanced Surgical Techniques. 2021 Jul; 31(7): 738-42. doi: 10.1089/lap.2021.0244.

[24] Bangeas P, Bitzika S, Loufopoulos P, Drevelegkas K, Papadopoulos VN. Infarcted Ligamentum Teres Hepatis Lipoma Mimicking Acute Abdomen in A Female Patient: A Case Report and Mini-Review of the Literature. Journal of Surgical Case Reports. 2020 Oct; 2020(10): rjaa391. doi: 10.1093/jscr/rjaa391.

[25] Elmohr MM, Blair KJ, Menias CO, Nada A, Shaaban AM, Sandrasegaran K *et al.* The Lesser Sac and Foramen of Winslow: Anatomy, Embryology, and CT Appearance of Pathologic Processes. American Journal of Roentgenology. 2020 Oct; 215(4): 843-51. doi: 10.2214/AJR.19.22749.

[26] Brenkman HJ, van der Wielen NI, Ruurda JP, van Leeuwen MS, Scheepers JJ, van der Peet DL *et al.* Surgical Anatomy of the Omental Bursa and the Stomach Based on A Minimally Invasive Approach: Different Approaches and Technical Steps to Resection and Lymphadenectomy. Journal of Thoracic Disease. 2017 Jul; 9(Suppl 8): S809. doi: 10.21037/jtd.2017.07.52.

[27] Thomas JM and Van Fossen K. Anatomy, Abdomen and Pelvis, Foramen of Winslow (Omental, Epiploic). 2025 Dec.

[28] Marin BG, Aghagoli G, Hu SL, Massoud CM, Robinson-Bostom L. Calciphylaxis and Kidney Disease: A Review. American Journal of Kidney Diseases. 2023 Feb; 81(2): 232-9. doi: 10.1053/j.ajkd.2022.06.011.

[29] Gaballah AH, Algazzar M, Kazi IA, Badawy M, Guys NP, Mohamed EA *et al.* The Peritoneum: Anatomy, Pathologic Findings, and Patterns of Disease Spread. Radiographics. 2024 Aug; 44(8): e230216. doi: 10.1148/rg.230216.

[30] Bleys RL and Weijs TJ. Surgical Anatomy of the Stomach and the Omental Bursa. InAtlas of Minimally Invasive Techniques in Upper Gastrointestinal Surgery. Cham: Springer International Publishing. 2021 Feb: 201-206. doi: 10.1007/978-3-030-55176-6_25.

[31] Manzanedo I, Pereira F, Cascales-Campos P, Muñoz-Casares C, Asensio E, Torres-Melero J *et al.* Treatment of Peritoneal Surface Malignancies by Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in Spain: Results of the National Registry of the Spanish Group of Peritoneal Oncologic Surgery (REGECOP). Journal of Clinical Medicine. 2023 May; 12(11): 3774. doi: 10.3390/jcm12113774.

[32] Yurttas C, Hoffmann G, Tolios A, Haen SP, Schwab M, Koenigsrainer I *et al.* Systematic Review of Variations in Hyperthermic Intraperitoneal Chemotherapy (HIPEC) For Peritoneal Metastasis from Colorectal Cancer. Journal of Clinical Medicine. 2018 Dec; 7(12): 567. doi: 10.3390/jcm7120567.

[33] Baratti D, Kusamura S, Iusco D, Bonomi S, Grassi A, Virzì S *et al.* Postoperative Complications After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy Affect Long-Term Outcome of Patients with Peritoneal Metastases from Colorectal Cancer: A Two-Center Study Of 101 Patients. Diseases of the Colon and Rectum. 2014 Jul; 57(7): 858-68. doi: 10.1097/DCR.0000000000000149.

[34] Ilnitsky S, Abu Rafea B, Vilos AG, Vilos GA. Pelvic Peritoneal Pockets: Distribution, Histopathology, and Clinical Significance. Journal of Obstetrics and Gynaecology Canada. 2019 Sep; 41(1251): 10-16. doi: 10.1016/j.jogc.2018.05.016.

DOI: https://doi.org/10.54393/pjhs.v7i2.3664

[35] Gortazar de Las Casas S, Pascual Miguelañez I, Spagnolo E, Álvarez-Gallego M, López Carrasco A, Carbonell López M *et al.* Quality of Life and Low Anterior Resection Syndrome Before and After Deep Endometriosis Surgery. Langenbeck's Archives of Surgery. 2022 Dec; 407(8): 3671-9. doi: 10.1007/s 00423-022-02705-3.

[36] Gawron I, Derbisz K, Jach R, Trojnarska D, Milian-Ciesielska K, Pietrus M. Pelvic Peritoneal Endometriosis Is Linked to the Endometrial Inflammatory Profile: A Prospective Cohort Study. BioMed Central Women's Health. 2025 Mar; 25(1): 94. doi: 10.1186/s12905-025-03632-3.

[37] Whitaker LH, Doust A, Stephen J, Norrie J, Cooper K, Daniels J *et al.* Laparoscopic Treatment of Isolated Superficial Peritoneal Endometriosis for Managing Chronic Pelvic Pain in Women: Study Protocol for a Randomised Controlled Feasibility Trial (ESPriT1). Pilot and Feasibility Studies. 2021 Jan; 7(1): 19. doi: 10.1186/s40814-020-00740-9.

[38] Koninckx PR, Ussia A, Adamyan L, Tahlak M, Keckstein J, Martin DC. The Epidemiology of Endometriosis Is Poorly Known as the Pathophysiology and Diagnosis Are Unclear. Best Practice and Research Clinical Obstetrics and Gynaecology. 2021 Mar; 71: 14-26. doi: 10.1016/j. bpobgyn.2020.08.005.

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Systemic Review

OPEN ACCESS

Iron Supplementation in the Prevention and Treatment of Iron Deficiency Anemia in Children Under Five: A Systematic Review

Tujza Tahir[1], Uzma Bari[1*], Fatima Tuz Zahra[1], Hafsa Tariq[2], Faisal Hussain[3] and Muhammad Iqbal[4]

[1]Department of Pediatric Medicine, The Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad, Pakistan
[2]Department of Pathology, Pak International Medical College, Peshawar, Pakistan
[3]Department of Pediatric Medicine, Combined Military Hospital, Peshawar, Pakistan
[4]Department of Biochemistry, Muhammad College of Medicine, Peshawar, Pakistan

ARTICLE INFO

Keywords:
Iron Supplementation, Iron Deficiency Anemia, Children Under Five, Micronutrient Powders, Oral Iron Therapy, Public Health Nutrition

How to Cite:
Tahir, T., Bari, U., Zahra, F. T., Tariq, H., Hussain, F., & Iqbal, M. (2026). Iron Supplementation in the Prevention and Treatment of Iron Deficiency Anemia in Children Under Five: A Systematic Review: Iron Supplementation in the Prevention and Treatment of Iron Deficiency Anemia . Pakistan Journal of Health Sciences, 7(2), 170-178. https://doi.org/10.54393/pjhs.v7i2.3735

Corresponding Author:
Uzma Bari
Department of Pediatric Medicine, The Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad, Pakistan
ridaundleeb@gmail.com

Received Date: 29th November, 2025
Revised Date: 6th January, 2026
Acceptance Date: 14th January, 2026
Published Date: 28th February, 2026

ABSTRACT

Iron deficiency anemia (IDA) is a public health issue in children under 5 years of age, mostly in low and middle-income countries. Iron supplements are given for preventing or treating iron deficiency. **Objectives:** To systematically evaluate the effectiveness, safety considerations, and implementation characteristics of iron supplementation strategies used for the prevention and treatment of iron deficiency anemia among children under five years of age. **Methods:** An electronic literature search was performed in PubMed, Scopus, and Cochrane Library for any studies written in English and published between 2019 and 2024. Primary human research of any type assessing iron supplementation in children aged 0-59 months was encompassed. This excluded systematic reviews, meta-analyses, case reports, and animal studies. The study selection was in accordance with PRISMA 2020. The synthesis of the data was conducted narratively, and the risk of bias was assessed using the RoB-2 and Joanna Briggs Institute tools. **Results:** A total of 15 studies reported significant improvements in hemoglobin levels and iron status after iron supplementation, using either oral ferrous preparations or iron-containing micronutrient powders. Prevention measures reduced the rate of anemia, and treatment supplementation successfully corrected known IDA. High anemia burden, inconsistent adherence to supplementation, and dietary iron deficit were observed in observational studies. **Conclusions:** Iron supplementation remains an effective approach for preventing and treating iron deficiency anemia in children. Optimizing program delivery, adherence, and safety monitoring is essential to maximize benefits, particularly in resource-limited settings.

INTRODUCTION

Iron deficiency anemia is among the most widespread nutritional illnesses that impacts children below the age of five years all over the world, and has been a leading cause of childhood morbidity and poor development [1]. The young children are especially susceptible because of the rapid growth, higher iron demands, and lack of bioavailable iron in the food. The situation is further worsened in the low- and middle-income nations by food insecurity, frequent infections, and insufficient health services [2, 3]. Iron supplementation is commonly used in early childhood to address low iron stores and reduce the risk of anemia. Widespread strategies are oral iron preparations, as well as the iron-containing multi-micronutrient powders administered via community and healthcare settings [4]. Although their earlier-evidence has demonstrated their hematologic benefits, adherence, safety in high-infection settings, and inconsistent program effectiveness have raised concerns necessitating a new assessment [5]. Over

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

the past few years, several clinical trials and community-based interventions, as well as observational studies, have been published, which represent a further development in terms of supplementation approaches and implementation settings[6, 7].

Results, however, are mixed, and evidence that is specific to children below the age of five has not continuously been synthesized without statistical pooling.The systematic review aimed to systematically evaluate the effectiveness, safety considerations, and implementation characteristics of iron supplementation strategies used for the prevention and treatment of iron deficiency anemia among children under five years of age.

METHODS

The systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines 2020 [8]. The search strategy, screening, and data extraction were pre-determined by a structured protocol. The purpose of the review was to single out the research that assessed iron supplementation as a measure to prevent and treat iron deficiency anemia in children below the age of five years. Studies were located by searching major biomedical databases, namely 'PubMed, Scopus, and the Cochrane Library', which located the appropriate studies released no earlier than January 2019 and no later than December 2024. The search was narrowed down to the English language and human subjects. The combinations of the terms were used as keywords and Medical Subject Headings (MeSH). "Iron supplementation", "iron deficiency anemia", "micronutrient powder", "ferrous sulfate", "anemia prevention", "children under five", and related synonyms. An example search syntax for PubMed was: ("iron supplementation" OR "micronutrient powder" OR "ferrous sulfate") AND ("iron deficiency anemia" OR "anemia") AND ("child" OR "children" OR "infant" OR "under five"). All search results were exported into EndNote for deduplication. Eligibility of studies was determined using predefined inclusion criteria. Population: Children aged under five years (0–59 months). Intervention: Iron supplementation in any form (e.g., oral iron preparations, micronutrient powders with iron). Outcomes: Studies reporting at least one relevant hematological outcome (e.g., hemoglobin, ferritin, anemia prevalence). Types of studies: Original human studies employing experimental or observational designs, including randomized and non-randomized approaches, were considered. Time frame: Published between 2019 and 2024, in English. Exclusion Criteria: Systematic reviews, meta-analyses, case reports, case series, editorials, and animal or in-vitro studies. Studies not reporting anemia or iron-related outcomes. Studies where the under-five subgroup data could not be extracted separately. All records found were put into EndNote, and duplication was eliminated. Title and abstract screening were conducted by two reviewers against the eligibility criteria. All the potentially relevant articles were retrieved and evaluated to determine eligibility. Where discrepancies arose, these discrepancies were fixed by discussion or referring to a third reviewer. The PRISMA 2020 flow chart was made to record the selection procedure. PRISMA 2020 flow diagram illustrating the identification, screening, eligibility assessment, and inclusion of studies for the systematic review focusing on the use of iron supplements to improve iron status and anemia-related outcomes in children younger than five years. A total of 716 records were identified through database searches, and 15 studies met the inclusion criteria and were included in the qualitative synthesis(Figure 1).

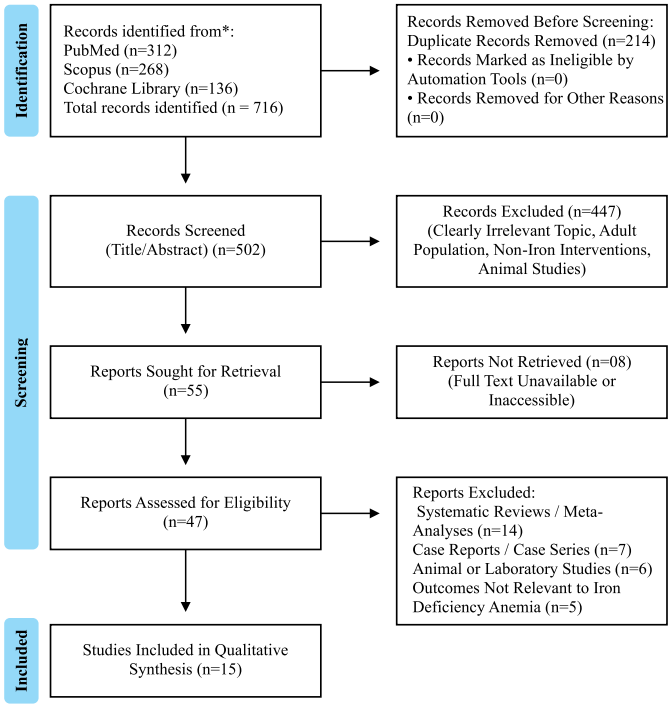

Figure 1: Process of Study Selection

Each of the included studies provided the following data on the standardized data extraction form: author(s), publication date, country or setting of the study and its design, population characteristics, type and duration of iron intervention, comparator, and key outcomes (e.g., changes in hemoglobin, anemia prevalence). In case of observational studies, exposure and key findings concerning iron supplementation or other determinants associated with the same were extracted. The methodological quality of randomized controlled trials was evaluated by the Cochrane Risk of Bias tool version 2 (RoB-2) [9, 10]. To conduct non-randomized intervention and quasi-experimental studies, the Joanna Briggs Institute (JBI) critical appraisal checklist was employed [11]. The JBI

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

analytical cross-sectional checklist was used to evaluate Cross-sectional studies. Two reviewers independently assessed risk of bias, and a consensus was reached by discussing. Since the study designs, interventions, and outcomes were heterogeneous, a narrative synthesis was used. The grouping of studies was based on the type of intervention and study design. Results were described descriptively without meta-analysis. Observational studies were provided individually as contextual evidence and implementation evidence.

RESULTS

The evidence on iron supplementation in children under 5 years between 2019 and 2024 comes from South Asia, Africa, the Middle East, and the Americas. Most intervention studies were randomized controlled trials, and cross-sectional designs provided evidence related to the context of interventions and implementation. Most interventions were with micronutrient powders or oral ferrous sulfate used preventively and/or therapeutically. The various studies differed in duration, delivery platforms, and baseline anemia status that were clinically heterogeneous in accordance with real-world settings relevant to public health (Table 1).

Table 1: Characteristics of Included Studies (2019–2024)

References	Country	Design	Population (Under-5)	Intervention (Iron Strategy)	Comparator	Key Outcomes Reported
[12]	Arusha District Tanzania	Trial (frequency comparison)	Children 6–59 months	Micronutrient powder (iron-containing) with different dosing frequencies	Alternate frequency arms	Anemia/iron status indicators
[13]	Gaza Strip Clinics (UNRWA)	RCT (parallel)	Healthy infants 6 months (followed by 12 months)	MNP Iron-containing MNP administered thrice weekly with standard supplementation	National supplement alone	Growth + anemia/ iron indicators
[14]	NR	Open-label therapeutic trial	Young children with mild to moderate IDA (young age group)	Ferrous sulfate oral solution	No parallel comparator (single-arm)	Hb response, safety, acceptability
[15]	Rural Bangladesh	Individually randomized, placebo-controlled trial	Infants/young children (under-2 at start)	Iron syrup OR iron-containing MNPs (3 months)	Placebo control	Anemia prevalence, iron status, safety outcomes
[16]	US	RCT	Infants/young children (includes 6–23 months)	MNP point-of-use fortification	Placebo	Anemia + iron deficiency outcomes
[5]	Brazil	Randomized clinical trial	Children 6–48 months	MNP fortification	Comparator arm (as per trial design)	Iron deficiency/ iron markers; anemia outcomes
[17]	Pakistan (Community-Based)	Non-randomized community trial	Children 6–23 months	Lipid-based supplementary food with micronutrients (iron-containing)	Control group	Hb, micronutrient status, growth indicators
[18]	Pakistan (Community Setting)	Community intervention study	Children 24–59 months	MNP supplementation (1 year)	Control/ comparison group	Hb/anemia + micronutrient status + growth
[19]	Bangladesh (Sub-Study Within Trial)	Randomized trial sub-study	Young children (trial infants; under-5)	Iron syrup vs iron-containing MNP	Placebo	Neurocognitive/ brain activity + trial outcomes
[20]	Rural Bangladesh	RCT (microbiome analysis within trial)	Infants (under-2 at start)	Iron and iron-containing MNPs (3 months)	Placebo	Gut microbiome safety signals + follow-up
[21]	Multi-Site (I.E., Kampala and Fort Portal, Uganda)	Masked randomized placebo trial	Infants between 6 and 23 months of age and ≥24 months (includes under-5)	Ferrous sulfate tablets (dose by age band)	Placebo	Safety/efficacy outcomes (anemia/ iron indicators)
[22]	Pakistan (Multan)	RCT	Children with IDA (age NR in abstract snippet)	Ferrous sulfate + vitamin C vs ferrous sulfate alone	Active comparator	Hb/iron response as per trial outcomes
[23]	Ethiopia (Survey-Based)	Cross-sectional	Infants 6–23 months	Exposure: received MNP	Not applicable	Prevalence + predictors of MNP use
[24]	Ethiopia (Hospital-Based)	Cross-sectional	Children 6–59 months	Exposure includes supplementation variables (as reported)	Not applicable	Anemia prevalence + associated factors

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

[25]	Ethiopia	Cross-sectional (secondary analysis)	Children 6–59 months	Exposure: iron-related feeding/ supplement variables	Not applicable	Iron-related consumption patterns

Intervention trials showed that children under-five who received micronutrient powders or oral ferrous sulphate had improved hemoglobin and iron status and decreased risk of iron deficiency. The use of micronutrient powders and oral ferrous sulfate was effective in the prevention of anemia, while treatment improved hemoglobin recovery of children with developed iron deficiency anemia. Some research shows positive knock-on effects on growth and neurodevelopment. The evaluation of safety and specific effects of various formulations has been highly inconsistent. The direction of effect for some results in some trials differed, but overall, the direction of effect for iron either with micronutrient powders or oral was markedly favourable (Table 2).

Table 2: Summary of Main Findings from Intervention Trials (2019–2024)

References	Prevention or Treatment Focus	Main Outcomes Assessed	Direction of Effect (As Reported)	Descriptive Summary of Findings
[12]	Prevention	Hemoglobin, iron status	Improved	Different dosing frequencies of iron-containing MNPs were associated with improvements in hemoglobin and iron status indicators among children aged 6–59 months.
[13]	Prevention	Growth, anemia, and iron indicators	Improved	Long-term MNP supplementation alongside routine care resulted in reduced anemia risk and improved iron indicators, with additional positive effects on growth.
[14]	Treatment (IDA)	Hemoglobin response, safety	Improved	Ferrous sulfate oral solution led to clinically meaningful hemoglobin improvement and was generally well tolerated in young children with mild to moderate IDA.
[15]	Prevention / Early-Life Risk	Anemia prevalence, iron status, safety	Mixed	Iron syrup and iron-containing MNPs improved anemia and iron status, while also highlighting formulation-specific safety considerations in high-infection settings.
[16]	Prevention	Anemia, iron deficiency	Improved	Point-of-use MNP fortification reduced anemia and iron deficiency and was associated with improved expressive language development.
[5]	Prevention/Treatment	Iron deficiency markers, anemia	Improved	MNP fortification demonstrated beneficial effects on iron deficiency and anemia outcomes in Brazilian children under five.
[17]	Prevention	Hemoglobin, micronutrients, and growth	Improved	Iron-containing supplementary food improved hemoglobin levels and plasma micronutrient concentrations, with concurrent improvements in growth indicators.
[18]	Prevention (Long-Term)	Hemoglobin, micronutrients, and growth	Improved	One-year MNP supplementation was associated with sustained improvements in hemoglobin, micronutrient status, and growth among children aged 24–59 months.
[19]	Prevention (Substudy)	Neurocognitive markers, iron exposure	Physiologic change	Iron syrup and iron-containing MNPs altered resting brain activity patterns, suggesting potential neurodevelopmental relevance alongside hematologic effects.
[21]	Treatment	Safety and efficacy (Hb/iron)	Improved	Daily ferrous sulfate supplementation for three months improved anemia indicators under controlled safety monitoring in a vulnerable pediatric population.
[22]	Treatment (IDA)	Hemoglobin, iron response	No added benefit	The addition of vitamin C to ferrous sulfate did not demonstrate a clear advantage over ferrous sulfate monotherapy in improving hematologic outcomes.

Observational studies do not provide effect estimates, but important contextual information. The high prevalence of anemia in children under-five is reinforced by widespread variation in the use of micronutrient powder and consumption of iron-rich foods. Consistent predictors of use were socioeconomic position, maternal education, and access to health services. Moreover, they did not allow us to infer causality, but this study highlights significant implementation challenges that can affect the iron supplementation (Table 3).

Table 3: Findings from Observational Studies (Contextual and Implementation Evidence)

References	Study Focus	Population	Key Outcomes	Main Findings
[23]	MNP Program Coverage	Infants 6–23 months	Prevalence, predictors	MNP consumption varied widely, with maternal education, health-service contact, and household factors influencing uptake.

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

[24]	Anemia Burden and Correlates	Children 6–59 months	Anemia prevalence	High anemia prevalence was observed, with nutritional and health-related factors, including supplementation variables, associated with anemia status.
[25]	Dietary Iron Exposure	Children 6–59 months	Iron-rich food intake	Consumption of iron-rich foods was suboptimal and socially patterned, highlighting dietary gaps that may limit the effectiveness of supplementation programs.

A review of the risk-of-bias for RCTs indicates that overall, 8 of 10 RCTs had a low risk of bias. Moreover, we demonstrated that the domains concerned with outcome measures and completeness of data were at low risk. The assessment of the RCTs and evaluations showed high and moderate risk for the other two domain areas. Nonetheless, the other ROBINS-I evaluated the non-randomized studies and the community-based intervention studies. The lack of allocation concealment and potential made their moderate to high risk of bias (Table 4).

Table 4: Risk of Bias Assessment of Intervention Trials (RoB-2 / JBI) F

References	Study Design	Assessment Framework	Allocation Process	Adherence to Assigned Intervention	Completeness of Outcome Data	Outcome Assessment	Reporting Transparency	Overall Methodological Concern
[12]	Frequency-Based Intervention Study	JBI Critical Appraisal Tool for Quasi- Experimental Studies	Minor Concerns	Minimal Concern	Minimal Concern	Minimal Concern	Minor Concerns	Moderate Concern
[13]	Randomized Intervention Study	Cochrane Risk Assessment Framework (RoB-2)	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern
[14]	Non-Masked Intervention Study	JBI Critical Appraisal Tool for Quasi-Experimental Studies	Major Concerns	Minor Concerns	Minimal Concern	Minimal Concern	Minor Concerns	Major Concern
[15]	Randomized Intervention with Placebo Comparator	Cochrane Risk Assessment Framework (RoB-2)	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern
[16]	Randomized Intervention Study	Cochrane Risk Assessment Framework (RoB-2)	Minimal Concern	Minimal Concern	Minor Concerns	Minimal Concern	Minimal Concern	Minimal Concern
[5]	Randomized Intervention Study	Cochrane Risk Assessment Framework (RoB-2)	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minor Concerns	Minimal Concern
[17]	Non-Randomized Intervention Study	JBI Critical Appraisal Tool for Quasi-Experimental Studies	Major Concerns	Minor Concerns	Minor Concerns	Minimal Concern	Minor Concerns	Moderate to High Concern
[18]	Community-Based Intervention Study	JBI Critical Appraisal Tool for Quasi-Experimental Studies	Major Concerns	Minor Concerns	Minor Concerns	Minimal Concern	Minor Concerns	Moderate to High Concern
[19]	Nested Analysis within a Randomized Study	Cochrane Risk Assessment Framework (RoB-2)	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minor Concerns	Minimal Concern
[20]	Randomized Intervention Study	Cochrane Risk Assessment Framework (RoB-2)	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern
[21]	Masked Randomized Intervention	Cochrane Risk Assessment Framework (RoB-2)	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern	Minimal Concern
[22]	Randomized Intervention Study	Cochrane Risk Assessment Framework (RoB-2)	Minor Concerns	Minimal Concern	Minimal Concern	Minimal Concern	Minor Concerns	Moderate Concern

Every study that was observed showed an underlying moderate risk of bias, which is mainly due to selection bias and residual confounding. Hospital-based research had an increased risk because of poor generalizability, whereas national survey research had strong sampling designs. Statistical analysis and measurement areas were usually satisfactory in studies. Such results confirm the applicability of observational evidence to contextual interpretation and not causal patterns (Table 5).

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

Table 5: Methodological Appraisal of Observational Studies

References	Study Design	Appraisal Framework	Participant Selection	Exposure and Outcome Assessment	Control of Confounding	Analytical Approach	Overall Methodological Concern
[23]	Cross-Sectional Survey	JBI Analytical Appraisal Checklist	Minor Concerns	Minimal Concern	Moderate Concern	Minimal Concern	Moderate Concern
[24]	Hospital-Based Cross-Sectional Study	JBI Analytical Appraisal Checklist	Major Concerns	Minimal Concern	Moderate Concern	Minimal Concern	Moderate to Great Concern
[25]	National Survey Secondary Analysis	JBI Analytical Appraisal Checklist	Minor Concerns	Minimal Concern	Moderate Concern	Minimal Concern	Moderate Concern

The methodological quality of observational studies was evaluated using the Joanna Briggs Institute analytical appraisal framework. Assessment focused on participant selection procedures, accuracy of exposure and outcome measurement, handling of potential confounding factors, and adequacy of analytical methods. Terminology was adapted to reflect levels of methodological concern rather than categorical bias labels.

DISCUSSION

This systematic review states that iron supplementation is an effective intervention for iron deficiency anemia (IDA) in children under age 5, in line with the existing evidence on hematologic benefits. Prophylactic use of micronutrient powders (MNPs) containing iron and operative use of oral preparations of iron remained consistently beneficial in enhancing hemoglobin and iron status in a variety of environments. The results are in line with the larger clinical evidence, such as large syntheses of the effects of iron supplementation in children's populations [4, 26]. Iron supplementation is not only beneficial at raising hemoglobin but also helps to lower the general prevalence of anemia in high-burden areas, which can be concluded from the systematic evidence [27]. Most of the previous systematic reviews and meta-analyses integrate various outcomes of trials, but one can point out that the similarity of benefit can be observed even when the schedules of interventions differ [28, 29]. MNPs' preventive supplementation was successful in diverse demographic backgrounds, yet programmatic receipt and compliance are important issues of practical effectiveness. The recent meta-analyses have associated a low dietary diversity and micronutrient sources with increased odds of anemia among young children, which highlights the necessity of implementing combined nutrition interventions in addition to supplementation [30]. Oral iron is still a first-line form of treatment, therapeutically. New formulations, including liposomal iron, have the potential to be better tolerated and can have a beneficial effect on developmental outcomes, so that areas of further clinical research are possible [31]. Similarly, there is also evidence of alternate-day supplementation as a measure to enhance iron absorption and possibly lower the side effects, which would fine-tune dosing strategies in young children [32]. Although the hematologic effects remain consistent, the results are not always positive. There is some evidence that low-dose iron supplementation in healthy, low-risk infants does not significantly prevent anemia or improve development [33].

These results indicate that the strategy of supplementation should be specific to the risk population profiles, and not applied universally in low-impact situations. This subtlety is significant when making policy recommendations in an environment where anemia prevalence in the baseline differs. Safety is also one of the issues to consider, as it is a high burden in terms of infectious diseases in places where iron may affect gut bacteria or have endemic interactions with other infections. Literature indicates the possible measurable microbiome responses to iron supplementation, which should be monitored in program roll-outs [34]. It has been observed that anemia is very prevalent in most under-five populations, and predominantly where the intake of iron through the diet and dietary diversity is low [35]. These results support the need to consider iron supplementation with comprehensive approaches to nutrition in general and dietary enhancement and maternal education, in particular. Community-based supplementation models are promising in the context of Pakistan, but need a stricter assessment to accommodate confounding. The implementation research is required to learn how to integrate the iron supplementation with the regular child-health services most successfully, and also to control the dietary determinants and infection prevention.

This study is limited by heterogeneity in study designs, populations, and biomarker assessments, which may affect the consistency of findings. Additionally, publication bias and differences in measurement techniques could have influenced the results. Further studies are needed on standardized outcome measures, longer follow-up of developmental outcomes, and the relative effectiveness of newer iron preparations. Also, program evaluation research involving a combination of supplementation with diet and health system strengthening can give an insight into the sustainable control of anemia.

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

CONCLUSIONS

This systematic review indicates that iron supplementation remains an effective strategy for both the prevention and treatment of iron deficiency anemia in children under five years of age. Evidence from recent trials demonstrates consistent improvements in hemoglobin and iron status with the use of oral iron preparations and iron-containing micronutrient powders. Preventive interventions appear beneficial at the community level, while therapeutic supplementation effectively corrects established anemia when adherence is ensured. However, variability in program implementation, safety monitoring, and baseline nutritional status influences observed outcomes. Observational evidence highlights persistent anemia burden and suboptimal dietary iron intake, underscoring the need for integrated nutrition approaches. Future research should prioritize context-specific implementation studies and standardized outcome reporting to inform sustainable child health policies, particularly in low-resource settings such as Pakistan.

Authors' Contribution

Conceptualization: UB
Methodology: UB, HT, FH
Formal analysis: UB
Writing and Drafting: TT, UB, FTZ, HT, FH, MI
Review and Editing: TT, UB, FTZ, HT, FH, MI

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Iolascon A, Andolfo I, Russo R, Sanchez M, Busti F, Swinkels D *et al.* Recommendations for Diagnosis, Treatment, and Prevention of Iron Deficiency and Iron Deficiency Anemia. Hemasphere. 2024 Jul; 8(7): e108. doi: 10.1002/hem3.108.

[2] Sundararajan S and Rabe H. Prevention of Iron Deficiency Anemia in Infants and Toddlers. Pediatric Research. 2021 Jan; 89(1): 63-73. doi: 10.1038/s41390-020-0907-5.

[3] Kyei-Arthur F, Aballo J, Mahama AB, Adu-Afarwuah S. Infant and Young Child Feeding Practices Among Mothers in the Pilot Micronutrient Powder Initiative in Four Geographically and Ethnically Diverse Districts in Ghana. Plos One. 2024 Aug; 19(8): e0307961. doi: 10.1371/journal.pone.0307961.

[4] Andersen CT, Marsden DM, Duggan CP, Liu E, Mozaffarian D, Fawzi WW. Oral Iron Supplementation and Anemia in Children According to Schedule, Duration, Dose and Cosupplementation: A Systematic Review and Meta-Analysis of 129 Randomized Trials. British Medical Journal Global Health. 2023 Feb; 8(2). doi: 10.1136/bmjgh-2022-010745.

[5] Machado MM, Lopes MD, Schincaglia RM, da Costa PS, Coelho AS, Hadler MC. Effect of Fortification with Multiple Micronutrient Powder on the Prevention and Treatment of Iron Deficiency and Anemia in Brazilian Children: A Randomized Clinical Trial. Nutrients. 2021 Jun; 13(7): 2160. doi: 10.3390/nu13072160.

[6] Nicholson WK, Silverstein M, Wong JB, Chelmow D, Coker TR, Davis EM *et al.* Screening and Supplementation for Iron Deficiency and Iron Deficiency Anemia During Pregnancy: US Preventive Services Task Force Recommendation Statement. Journal of the American Medical Association. 2024 Sep; 332(11): 906-13. doi: 10.1001/jama.2024.15196.

[7] Arulparithi CS, Arunbabu T, Manjani S. Iron Preparations in the Management of Iron Deficiency Anemia in Infants and Children: A Systematic Review and Meta-Analysis. Indian Pediatrics. 2023 Sep; 60(9): 752-8. doi: 10.1007/s13312-023-2991-6.

[8] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD *et al.* The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. British Medical Journal. 2021 Mar; 372.

[9] Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP *et al.* Updated Guidance for Trusted Systematic Reviews: A New Edition of the Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Database of Systematic Reviews. 2019 Oct; 2019(10): ED000142. doi: 10.1002/14651858.Ed000142.

[10] Munn Z, Stone JC, Aromataris E, Klugar M, Sears K, Leonardi-Bee J *et al.* Assessing the Risk of Bias of Quantitative Analytical Studies: Introducing the Vision for Critical Appraisal Within JBI Systematic Reviews. Joanna Briggs Institute Evidence Synthesis. 2023 Mar; 21(3): 467-71. doi: 10.11124/JBIES-22-00224.

[11] Barker TH, Stone JC, Sears K, Klugar M, Leonardi-Bee J, Tufanaru C *et al.* Revising the JBI Quantitative Critical Appraisal Tools to Improve Their Applicability: An Overview of Methods and the Development Process. Joanna Briggs Institute Evidence Synthesis. 2023 Mar; 21(3): 478-93. doi: 10.11124/JBIES-22-00125.

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

[12] Kejo D, Petrucka P, Martin H, Mosha TC, Kimanya ME. Efficacy of Different Doses of Multiple Micronutrient Powder on Haemoglobin Concentration in Children Aged 6–59 Months in Arusha District. Scientifica. 2019; 2019(1): 8979456. doi: 10.1155/2019/8979456.

[13] Albelbeisi A, Shariff ZM, Mun CY, Rahman HA, Abed Y. Multiple Micronutrient Supplementation Improves Growth and Reduces the Risk of Anemia Among Infants in Gaza Strip, Palestine: A Prospective Randomized Community Trial. Nutrition Journal. 2020 Dec; 19(1): 133. doi: 10.1186/s12937-020-00652-7.

[14] Pachuta Węgier L, Kubiak M, Liebert A, Clavel T, Montagne A, Stennevin A *et al.* Ferrous Sulfate Oral Solution in Young Children with Iron Deficiency Anemia: An Open-Label Trial of Efficacy, Safety, and Acceptability. Pediatrics International. 2020 Jul; 62(7): 820-7. doi: 10.1111/ped.14237.

[15] Pasricha SR, Hasan MI, Braat S, Larson LM, Tipu SM, Hossain SJ *et al.* Benefits and Risks of Iron Interventions in Infants in Rural Bangladesh. New England Journal of Medicine. 2021 Sep; 385(11): 982-95. doi: 10.1056/NEJMoa2034187.

[16] Black MM, Fernandez-Rao S, Nair KM, Balakrishna N, Tilton N, Radhakrishna KV *et al.* A Randomized Multiple Micronutrient Powder Point-of-Use Fortification Trial Implemented in Indian Preschools Increases Expressive Language and Reduces Anemia and Iron Deficiency. The Journal of Nutrition. 2021 Jul; 151(7): 2029-42. doi: 10.1093/jn/nxab066.

[17] Khan A, Ul-Haq Z, Fazid S, Fatima S, Muhammad N, Ahmed J *et al.* Effectiveness of Locally Produced Ready-To-Use Supplementary Food on Hemoglobin, Anthropometrics, and Plasma Micronutrient Concentrations of 6 To 23-Month-Old Children: A Non-Randomized Community-Based Trial from Pakistan. Frontiers in Nutrition. 2023 Jul; 10: 1176778. doi: 10.3389/fnut.2023.1176778.

[18] Khan A, Ul-Haq Z, Fatima S, Ahmed J, Alobaid HM, Fazid S *et al.* Long-Term Impact of Multiple Micronutrient Supplementation on Micronutrient Status, Hemoglobin Level, and Growth in Children 24 To 59 Months of Age: A Non-Randomized Community-Based Trial from Pakistan. Nutrients. 2023 Mar; 15(7): 1690. doi: 10.3390/nu15071690.

[19] Larson LM, Feuerriegel D, Hasan MI, Braat S, Jin J, Tipu SM *et al.* Supplementation with Iron Syrup or Iron-Containing Multiple Micronutrient Powders Alters Resting Brain Activity in Bangladeshi Children. The Journal of Nutrition. 2023 Jan; 153(1): 352-63. doi: 10.1016/j.tjnut.2022.12.026.

[20] Baldi A, Braat S, Hasan MI, Bennett C, Barrios M, Jones N *et al.* Effects of Iron Supplements and Iron-Containing Micronutrient Powders on the Gut Microbiome in Bangladeshi Infants: A Randomized Controlled Trial. Nature Communications. 2024 Oct; 15(1): 8640. doi: 10.1038/s41467-024-53013-x.

[21] Frosch AE, Musiime V, Staley C, Conroy AL, Rutebarika D, Ategeka G *et al.* Safety and Efficacy of Iron Supplementation with 3 Months of Daily Ferrous Sulphate in Children Living with HIV and Mild-To-Moderate Anemia in Uganda: A Double-Blind, Randomized, Placebo-Controlled Trial. The Lancet HIV. 2024 Nov; 11(11): e727-35. doi: 10.1016/S2352-3018(24)00238-8.

[22] Naz N, Zafar Q, Jaffar, M, Khan K, Ibrahim M, Batool S. Comparative Efficacy of Ferrous Sulphate Monotherapy Versus Combination Therapy with Vitamin C in Pediatric Iron Deficiency Anemia: A Randomized Controlled Trial. Biological and Clinical Sciences Research Journal. 2024; 5(1). doi: 10.54112/bcsrj.v2024i1.843.

[23] Terefe B and Chekole B. Prevalence of Multiple Micronutrient Powders Consumption and Its Determinants Among 6-To 23-Month-Old Children in East Africa: A Mixed Effect Analysis Using the Recent Population-Based Cross-Sectional National Health Survey. BioMed Central Nutrition. 2024 May; 10(1): 79. doi: 10.1186/s40795-024-00888-0.

[24] Hailu MK, Wudu MA, Gebriye DB, Birhanu TA, Bekalu YE. Prevalence of Anemia and its associated factors among 6–59 months age children visiting public hospitals at Afar Region, Northeast Ethiopia: a hospital-based cross-sectional study. BioMed Central Pediatrics. 2024 Sep; 24(1): 589. doi: 10.1186/s12887-024-05078-2.

[25] Beressa G, Desta F, Lencha B, Sahiledengle B, Atlaw D, Gomora D *et al.* Iron-Rich Food Consumption and Predictors among Children Aged 6–59 Months Old in Ethiopia: A Multilevel Complex Sample Analysis of the Ethiopian Mini-Demographic and Health Survey 2019 Data. Plos One. 2024 Jun; 19(6): e0305046. doi: 10.1371/journal.pone.0305046.

[26] Rehman T, Agrawal R, Ahamed F, Das S, Mitra S, Kumar D *et al.* Optimal Dose and Duration of Iron Supplementation for Treating Iron Deficiency Anemia in Children and Adolescents: A Systematic Review and Meta-Analysis. Plos One. 2025 Feb; 20(2): e0319068. doi: 10.1371/journal.pone.0319068.

[27] Leung AK, Lam JM, Wong AH, Hon KL, Li X. Iron Deficiency Anemia: An Updated Review. Current Pediatric Reviews. 2024 Aug; 20(3): 339-56. doi: 10.2174/1573396320666230727102042.

DOI: https://doi.org/10.54393/pjhs.v7i2.3735

[28] Gedfie S, Getawa S, Melku M. Prevalence and Associated Factors of Iron Deficiency and Iron Deficiency Anemia among Under-5 Children: A Systematic Review and Meta-Analysis. Global Pediatric Health. 2022 Jul; 9: 2333794X221110860. doi: 10.1177/2333794X221110860.

[29] Gutema BT, Sorrie MB, Megersa ND, Yesera GE, Yeshitila YG, Pauwels NS *et al.* Effects of Iron Supplementation on Cognitive Development in School-Age Children: Systematic Review and Meta-Analysis. Plos One. 2023 Jun; 18(6): e0287703. doi: 10.1371/journal.pone.0287703.

[30] Li H, Moosavian SP, Ghanbari N, Mirlohi SH, Rahimlou M. Association of Dietary Diversity and Odds of Anemia in Children and Adolescents: A Systematic Review and Meta-Analysis of Observational Studies. BMC Nutrition. 2025 Apr; 11(1): 83. doi: 10.1186/s40795-025-01069-3.

[31] Bahbah WA, Omar ZA, El-Shafie AM, Mahrous KS, El Zefzaf HM. Interventional Impact of Liposomal Iron on Iron-Deficient Children's Developmental Outcome: Randomized, Double-Blind, Placebo-Controlled Trial. Pediatric Research. 2025 Jun: 1-2. doi: 10.1038/s41390-025-04204-9.

[32] Dhanvijay AD, Patidar V, Singh J, Kumar S, Mudgal SK, Varikasuvu SR *et al.* Efficacy of Daily Versus Alternate Day Oral Iron Supplementation for Management of Anaemia among the General Population: A Systematic Review and Meta-Analysis. BioMed Central Pharmacology and Toxicology. 2025 Aug; 26(1): 152. doi: 10.1186/s40360-025-00984-2.

[33] Svensson L, Chmielewski G, Czyżewska E, Domellöf M, Konarska Z, Pieścik-Lech M *et al.* Effect of Low-Dose Iron Supplementation on Early Development in Breastfed Infants: A Randomized Clinical Trial. Journal of the American Medical Association Pediatrics. 2024 Jul; 178(7): 649-56. doi: 10.1001/jamapediatrics.2024.1095.

[34] Andersen CT, Marsden DM, Duggan CP, Liu E, Mozaffarian D, Fawzi WW. Oral Iron Supplementation and Anemia in Children According to Schedule, Duration, Dose, and Cosupplementation: A Systematic Review and Meta-Analysis of 129 Randomized Trials. British Medical Journal Global Health. 2023 Feb; 8(2). doi: 10.1136/bmjgh-2022-010745.

[35] Dessie G, Li J, Nghiem S, Doan T. Prevalence and Determinants of Stunting-Anemia and Wasting-Anemia Comorbidities and Micronutrient Deficiencies in Children Under 5 in the Least-Developed Countries: A Systematic Review and Meta-Analysis. Nutrition Reviews. 2025 Feb; 83(2): e178-94. doi: 10.1093/nutrit/nuae063.

DOI: https://doi.org/10.54393/pjhs.v7i2.3636

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 02 (February 2026)

Case Series

OPEN ACCESS

Effect of Percutaneous-Nephrolithotomy on Renal Function Tests and Hemoglobin Levels in the Early Postoperative Period at 24 Hours and 21st Day

Saddam Hussain[1], Muhammad Saleem[1], Farhan Ahmad[1*], Malik Furqan Mahmood[1] and Muhammad Nasir Jamil[1]

[1]Department of Urology, Ayub Teaching Hospital, Abbottabad, Pakistan

ARTICLE INFO

Keywords:
Percutaneous Nephrolithotomy, Renal Function Tests, eGFR, Hemoglobin

How to Cite:
Hussain, S., Saleem, M., Ahmad, F., Mahmood, M. F., & Jamil, M. N. (2026). Effect of Percutaneous-Nephrolithotomy on Renal Function Tests and Hemoglobin Levels in the Early Postoperative Period at 24 Hours and 21st Day: PNCL on Renal Function Tests and Hb Levels in the Early Postoperative Period. Pakistan Journal of Health Sciences, 7(2), 179-183. https://doi.org/10.54393/pjhs.v7i2.3636

***Corresponding Author:**
Farhan Ahmad
Department of Urology, Ayub Teaching Hospital, Abbottabad, Pakistan
farhan.ahmad978@gmail.com

Received Date: 1st December, 2025
Revised Date: 6th January, 2026
Acceptance Date: 14th January, 2026
Published Date: 28th February, 2026

ABSTRACT

The impact of percutaneous nephrolithotomy (PCNL) on renal function tests (RFTs) and hemoglobin (Hb) levels remains debated. Early postoperative changes may indicate transient renal dysfunction and hematological shifts. **Objectives:** To evaluate measurable changes in serum creatinine, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), and hemoglobin (Hb) following PCNL at 24 hours and 21 days post-procedure. **Methods:** A detailed case series was conducted at the Department of Urology, Ayub Teaching Hospital, Abbottabad, for exactly three months (2nd August to November 2025). During consecutive sampling, 68 patients aged 18-65 years, ASA Class I-II, subjected to PCNL were included. Renal functions were assessed using eGFR (MDRD formula), while Hb was measured at baseline, 24 hours, and 21 days postoperatively. Repeated-measures ANOVA was performed to analyze within-subject comparisons, while chi-square tests were used for categorical variables. **Results:** Both eGFR and Hb showed significant declines at 24 hours post-PCNL (64.8 ± 12.9 ml/min/1.73m^2 and 12.4 ± 2.2 g/dL, respectively; $p<0.001$ vs. baseline). By day 21, partial recovery (eGFR 69.7 ± 13.1; Hb 13.4 ± 1.9) was noted, showing significantly lower values compared to preoperative levels ($p<0.001$). Higher eGFR and Hb values were observed in younger patients (18–35 years) across all time points ($p<0.05$). **Conclusions:** PCNL produces an initial decline in renal function and hemoglobin levels, with partial recovery by three weeks. Postoperative fluctuations are significantly influenced by age, emphasizing the need for close monitoring in younger patients.

INTRODUCTION

Renal stone disease affects 2–20% of the global population and shows a rising trend in adults. The presence of urinary tract stones causing renal impairment varies depending on the obstruction or infection status. The link between stone formation and chronic conditions such as metabolic syndrome, diabetes, and hypertension has been studied to devise treatment strategies for urinary stones, aiming to restore kidney function. Minimally invasive surgical approaches are recommended over traditional open surgeries due to their milder impact on kidney function [1]. Kidney stones that tend to grow or persist for over two years are associated with a high risk of recurrence or urinary tract infections, followed by obstruction, bleeding, or persistent pain, and thus require active intervention. Careful evaluation of renal function is required in such cases. Patients with recurrent stone episodes, coexisting medical conditions, infections, and urinary blockage leading to renal insufficiency are influenced by several factors. High-risk individuals are screened for renal function tests to ensure optimal treatment planning. Retrograde intrarenal surgery (RIRS) and miniaturized percutaneous nephrolithotomy (mini-PCNL) are proven to be effective and safe treatment options among minimally invasive procedures [2, 3]. Individuals with moderate to

DOI: https://doi.org/10.54393/pjhs.v7i2.3636

large upper urinary tract stones are commonly directed to PCNL. Despite being less invasive than open surgery, PCNL is still associated with significant pain and potential complications, including bleeding, infections, and damage to nearby organs. Postoperative discomfort and hemoglobin loss vary according to patient-specific factors such as BMI, stone size, and stone location. Procedural modifications, such as the use of balloon or Amplatz™ dilators, help reduce blood loss and pain by minimizing operative time, implementing staged procedures for extensive stone burdens, and using ultrasound-guided access [4]. Renal function tests (RFTs), including blood urea nitrogen (BUN) and serum creatinine, are considered key indicators of kidney health. The impact of surgery on renal function is determined by assessing RFTs after PCNL, which helps detect complications at an early stage, such as acute kidney injury (AKI) [5]. Hemoglobin (Hb) levels are tracked to assess blood oxygenation and potential hemorrhage after surgery. Regular hematological evaluations reinforce the correlation between surgical blood loss and compensatory physiological responses [6]. Glomerular filtration rate (GFR) shows a fluctuating pattern similar to serum creatinine, with a notable postoperative decline and subsequent recovery. For example, Hosseini et al. reported a mean preoperative GFR of 74.89 mL/min, dropping to 64.04 mL/min at 48 hours and recovering to 69.54 mL/min at 72 hours ($p<0.0001$). A significant reduction in hemoglobin levels following PCNL was also reported, with average preoperative Hb at 15.06 ± 0.87 g/dL, dropping to 13.09 ± 1.06 g/dL post-surgery ($p<0.0005$) [6]. Early diagnosis of kidney function fluctuations or hemoglobin decline may help minimize potential complications and ensure smoother recovery.

This study aims to evaluate measurable changes in RFTs (serum creatinine, BUN, eGFR) and Hb following PCNL, particularly at 24 hours and 21 days post-procedure.

METHODS

A descriptive case series was conducted at the Department of Urology, Ayub Teaching Hospital, Abbottabad, over a period of three months (2nd August to November 2025) after approval of the synopsis. The study was conducted following approval from the Ethical Committee of Ayub Teaching Hospital, Abbottabad (Approval Code/Ref.No.RC-EA-2025/003). The sample size for the study was determined using the WHO sample size calculator to be 68 patients. The sample size was calculated to achieve 80% statistical power at a significance level of 0.05, based on the assumed effect size derived from prior studies. The calculation considered the mean postoperative hemoglobin level of 13.09 ± 1.06 g/dL for this study [7]. A non-probability consecutive sampling technique was utilized, acknowledging potential selection bias but chosen for feasibility in a tertiary care setting. All cases of either gender, ranging in age from 18 to 65 years, who underwent PCNL and were ASA Class I or II were included. Exclusion criteria included smokers, ASA Class III–IV, and those with a history of more than one percutaneous intervention or taking drugs that affect hemodynamics or electrolyte balance. A total of 68 patients were selected based on inclusion criteria, with each participant providing informed written consent. Demographic profile, including registration number, age, gender, BMI category, and place of residence, was recorded. Preoperative assessment included urine culture and analysis (with antibiotics prescribed for urinary infections), serum biochemistry and electrolyte evaluations (creatinine, urea, sodium, potassium, chloride), coagulation profile (prothrombin time, partial thromboplastin time), viral hepatitis markers (HBsAg, HBcAb, HCVAb), complete blood count, and body weight measurement. Non-contrast CT scans and kidney, ureter, and bladder imaging were performed for all patients. General anesthesia was given to perform the tubeless PCNL technique. A 4–5 Fr ureteral catheter was placed and positioned. The target calyx was punctured with a guide wire under fluoroscopic guidance. Tract dilation was carried out in a single step using Amplatz dilatators. A pneumatic lithotripter (LithoCrack, Sp. Swiss-Germany) with continuous saline irrigation was used to remove the stone, aided by placement of the Amplatz sheath. An additional access site was created for residual stones >2 cm. Shock wave lithotripsy (SWL) was performed for residual stones <2 cm. Ureteral and Foley catheters were removed between 12 and 24 hours postoperatively. Glomerular filtration rate (GFR) and hemoglobin levels were observed at baseline, 24 hours, and 21 days post-surgery. GFR was calculated using the simplified MDRD equation: eGFR (ml/min/1.73m^2) = 186 × [Scr]^–1.154 × [Age]^–0.203 × [0.742 if female] × [1.21 if black]. SPSS version 26 was used for analysis. Normality was tested with the Shapiro–Wilk test (results reported: GFR and Hb were normally distributed, $p>0.05$). Mean ± SD were computed for numerical variables (age, surgery duration, GFR, Hb). Frequencies and percentages were used for categorical variables (gender, side, BMI). Repeated-measures ANOVA was applied for within-subject comparisons across time points (pre-op, 24h, 21d). Stratification was performed by age, gender, side, and BMI. For comparisons across more than two groups (e.g., age categories), ANOVA was consistently used instead of independent t-tests. A p-value≤0.05 was considered statistically significant.

DOI: https://doi.org/10.54393/pjhs.v7i2.3636

RESULTS

The mean age was 40.52 ± 13.74 years. Most were male (78.3%, n=54) compared to females (20.3%, n=14). BMI distribution: 2.9% underweight (n=2), 23.2% normal (n=16), 42% overweight (n=29), and 30.4% obese (n=21). All this descriptive analysis is summarized in table 1.

Table 1: Descriptive Statistics of the Study Group

Variables	Frequency (%), Mean ± SD
Age	40.52 ± 13.74
Gender	
Male	54 (78.3%)
Female	14 (20.3%)
BMI Category	
Underweight	2 (2.9%)
Normal	16 (23.2%)
Overweight	29 (42%)
Obese	21 (30.4%)

The GFR means with ranges in preop, 24 hours postop, and 21 days post op period were: 74 .76 (59 – 98), 64.79 (52–87), and 69.66 (54 – 93), respectively. Similarly, the HB level means with ranges in preop, 24 hours postop, and 21-day postop were: 14.5 (10 – 18), 12.38 (8 – 17), and 13.38 (9 - 17), respectively. Following PCNL, both GFR and Hb showed a significant decline at 24 hours (GFR: 64.79 ± 12.9, Hb: 12.38 ± 2.17; p<0.001 vs. pre-op). Partial recovery was observed by day 21 (GFR: 69.66 ± 13.1, Hb: 13.38 ± 1.85), though values remained significantly lower than baseline (p<0.001). Repeated-measures ANOVA confirmed significant time effects (p<0.001), as summarized in table 2.

Table 2: Comparison of Trends of GFR and Hb Trends Following PCNL

Variables	Time point	Mean ± SD	Pairwise p-value vs Pre-op	Pairwise p-value vs 24h post-op	ANOVA (p-value)
GFR	Pre-op	74.76 ± 11.05	–	–	0.19 (<0.001)
	24hr post-op	64.79 ± 10.92	<0.001	–	
	21day post-op	69.66 ± 11.11	<0.001	<0.001	
Hb	Pre-Op	14.5 ± 1.72	–	–	0.15 (<0.001)
	24hr post-op	12.38 ± 2.17	<0.001	–	
	21day post-op	13.38 ± 1.85	<0.001	<0.001	

In this study, GFR changes after PCNL were more marked in the younger age group 18–35 years: they had higher GFR at all time points (pre-op: 82.04, 24hr: 71.12, 21day: 77.29) in comparison to the older groups, and this was statistically significant (p<0.001). But gender and BMI didn't show any significant difference in GFR values: male and female had similar GFR (pre-op 74.90 vs 74.21, p=0.79, 21day postop 69.4 vs 70.64, p=0.65), and the BMI groups too demonstrated quite comparable values (pre-op range 71.50 to 76.28, p=0.76, 21-day range 67.75 to 71.09, p=0.75). So only age was associated with statistically significant GFR fluctuation, as shown in table 3.

Table 3: Association of Demographic Features with the GFR Fluctuations

Variables	Time point	GFR (Mean ± SD)	F (p-value)
Age (18-35: 36-50: 51-65)	Pre-op	82.04 ± 18.42: 71.56 ± 16.67: 69.95 ± 15.01	20.8 (<0.001)
	24 Hours Post-Op	71.12 ± 16.81: 62.30 ± 16.35: 60.28 ± 15.64	19.18 (<0.001)
	21 Days Post-Op	77.29 ± 18.30: 66.52 ± 17.56: 64.38 ± 15.51	20.80 (<0.001)
Gender (Male: Female)	Pre-Op	74.90 ± 18.78: 74.21 ± 18.82	0.069 (0.79)
	24 Hours Post-Op	64.57 ± 17.81: 65.64 ± 18.20	0.204 (0.65)
	21 Days Post-Op	69.40 ± 19.00: 70.64 ± 20.19	0.198 (0.65)
BMI Category (Underweight: Normal: Overweight: Obesity)	Pre-Op	71.50 ± 27.67: 73.75 ± 15.36: 74.44 ± 17.80: 76.28 ± 21.33	0.380 (0.76)
	24 Hours Post-Op	63.50 ± 22.02: 63.43 ± 15.75: 65.03 ± 17.19: 65.61 ± 19.96	0.255 (0.85)
	21 Days Post-Op	69.00 ± 26.97: 67.75 ± 16.34: 69.72 ± 19.36: 71.09 ± 20.52	0.394 (0.75)

The Hb level change after PCNL was higher in the young age group. Age 18–35 had higher Hb at all time (pre-op 15.25, 24hr 13.29, 21day 14.00) than older groups, and this difference was significant (p=0.01, 0.03, 0.05). But gender didn't show any difference: male and female almost had similar readings (pre-op 14.51 vs 14.42, p=0.86, 21day postop 13.37 vs 13.42, p=0.91). Also, BMI groups had similar Hb values (pre-op range 14.00 to 14.81, p=0.63, 21day postop 12.0 to 13.56, p=0.65). So only age was related to Hb fluctuation, as shown in table 4.

Table 4: Association of Demographic Features with the Hb Fluctuations

Variables	Time point	GFR (Mean ± SD)	F (p-value)
Age (18-35: 36-50: 51-65)	Pre-op	15.25 ± 1.39: 14.39 ± 1.69: 13.76 ± 1.81	4.71 (0.01)
	24 Hours Post-Op	13.29 ± 1.98: 12.00 ± 2.13: 11.76 ± 2.16	3.57 (0.03)
	21 Days Post-Op	14.00 ± 1.50: 13.39 ± 1.90: 12.66 ± 1.98	3.08 (0.05)
Gender (Male: Female)	Pre-Op	14.51 ± 1.75: 14.42 ± 1.65: 14.50 ± 1.72	0.03 (0.86)
	24 Hours Post-Op	12.37 ± 2.15: 12.42 ± 2.31: 12.3 ± 2.17	0.00 (0.93)

DOI: https://doi.org/10.54393/pjhs.v7i2.3636

	21 Days Post-Op	13.37 ± 1.92: 13.42 ± 1.60: 13.38 ± 1.85	0.01 (0.91)
BMI Category (Underweight: Normal: Overweight: Obesity)	Pre-Op	14.00 ± 2.82: 14.81 ± 1.10: 14.62 ± 1.95: 14.14 ± 1.74	0.56 (0.63)
	24 Hours Post-Op	10.50 ± 3.53: 12.62 ±1.50: 12.51 ± 2.47: 12.19 ± 2.11	0.64 (0.58)
	21 Days Post-Op	12.00 ± 2.82: 13.56 ± 1.15: 13.51 ± 1.95: 13.19 ± 2.11	0.53 (0.65)

DISCUSSION

This study reinforces evidence that PCNL exerts a measurable impact on renal function and hematological parameters. The decline in GFR and Hb at 24 hours postoperatively is consistent with prior studies reporting transient renal impairment and blood loss [7, 8]. Mean GFR dropped from baseline (74.89 mL/min) to 64.79 mL/min at 24 hours, with partial recovery to 69.66 mL/min by day 21. This trajectory resembles findings by Ran *et al.* [9]. Younger patients demonstrated higher baseline and recovery values, supporting better renal reserve. Hemoglobin declined from 14.51 g/dL to 12.38 g/dL, consistent with intraoperative blood loss [8]. Partial recovery by day 21 (13.38 g/dL) reflected compensatory hematopoiesis. Age was the only significant factor influencing both GFR and Hb. Gender and BMI showed no significant associations. These findings align with long-term studies on mini-PCNL and RIRS [10]. Best practices to minimize trauma and bleeding include tubeless PCNL with Amplatz dilators and pneumatic lithotripsy [11–14]. Vigilant postoperative monitoring of RFTs and Hb is essential to detect early complications [15-20].

The study's sample size was relatively small, and follow-up was limited to 21 days, restricting assessment of long-term renal recovery. Additionally, factors such as intraoperative blood loss, stone size, and comorbidities were not fully controlled. Future studies should include larger cohorts with extended follow-up to evaluate long-term renal function and hematological recovery after PCNL.

CONCLUSIONS

PCNL is associated with a measurable decline in renal function (GFR) and hemoglobin levels within 24 hours, with partial recovery by 21 days. Age significantly influences recovery patterns, while gender and BMI do not. These findings highlight the importance of age-based risk stratification and close postoperative monitoring.

Authors' Contribution

Conceptualization: SH
Methodology: SH, MS, MFM, MNJ
Formal analysis: FA
Writing and Drafting: SH, MS, FA, MFM, MNJ
Review and Editing: SH, MS, FA, MFM, MNJ

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Şahan M, Aydın ME, Yarımoğlu S, Koraş Ö, Polat S, Gokalp F *et al.* Early and Late Effects of Percutaneous Nephrolithotomy on Renal Functions According to Basal Renal Function Reserve. Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Dergisi. 2022; 17(1): 115-20. doi: 10.17517/ksutfd.861872.

[2] Jung JH, Yoo S, Park J, Cho MC, Son H, Jeong H *et al.* Postoperative Renal Functional Changes Assessed by 99mtc-DTPA Scintigraphy and Predictive Factors After Miniaturized Percutaneous Nephrolithotomy and Retrograde Intrarenal Surgery: An Observational 1-Year Follow-Up Study. Investigative and Clinical Urology. 2020 Jan; 61(1): 59-66. doi: 10.4111/icu.2020.61.1.59.

[3] Wishahi M, El Feel A, Elkhouly A, Fahmy A, Roshdy M, Elbaz AG et al. Concerns About Stone Free Rate and Procedure Events of Percutaneous Nephrolithotripsy (PCNL) for 2–4 Cm Kidney Stones by Standard-PCNL Vs Mini-PCNL-Comparative Randomized Study. BioMed Central Urology. 2023 May; 23(1): 96. doi: 10.1186/s12894-023-01270-1.

[4] Jamil S and Ather MH. The Impact of Post-PCNL Tube Type on Blood Loss and Postoperative Pain. Pakistan Journal of Medical Sciences. 2020 Mar; 36(3): 402. doi: 10.12669/pjms.36.3.1558.

[5] Thakur A, Sharma AP, Devana SK, Parmar KM, Mavuduru RS, Bora GS *et al.* Does Miniaturization Actually Decrease Bleeding After Percutaneous Nephrolithotomy? A Single-Center Randomized Trial. Journal of Endourology. 2021 Apr; 35(4): 451-6. doi: 10.1089/end.2020.0533.

[6] Paymannejad S, Dehghani M, Dehkordi RJ, Taheri S, Shamlou F, Salehi H *et al.* Prevalence of Acute Kidney Injury Following Percutaneous Nephrolithotomy. Journal of Research in Medical Sciences. 2024 Mar; 29(1): 17. doi: 10.4103/jrms.jrms_317_23.

[7] Hosseini SR, Mohseni MG, Roshan H, Alizadeh F. Effect of Tubeless Percutaneous Nephrolithotomy on Early Renal Function: Does It Deteriorate?

DOI: https://doi.org/10.54393/pjhs.v7i2.3636

Advanced Biomedical Research. 2015 Jan; 4(1): 190. doi: 10.4103/2277-9175.166144.

[8] Kulkarni CR, Shivde SR, Date JA, Valsangkar RS. Do Changes Occur in Hemodynamic Parameters, Hemogram, Renal Function and Serum Electrolytes during Percutaneous Nephrolithotomy? Its Correlation with Irrigation Fluid and Intravenous Fluid. Open Journal of Urology. 2022 Jan; 12(1): 57-68. doi: 10.4236/oju.2022.121006.

[9] Ran R, Zhang R, Xie Y, Yin Z. Decreased Hemoglobin as a Quantifiable Indicator of Renal Arterial Embolization in Post-Percutaneous Nephrolithotomy Hemorrhage. Urolithiasis. 2021 Apr; 49(2): 137-43. doi: 10.1007/s00240-020-01206-6.

[10] Eksi M, Ozlu DN, Kargi T, Yavuzsan AH, Haciislamoglu A, Karadag S *et al.* Pre-Operative Parameters Predicting Hemoglobin Decline Related to Percutaneous Nephrolithotomy. Sisli Etfal Hastan Tip Bul. 2022 Mar; 56(1): 70-6. doi: 10.14744/SEMB.2021.21284.

[11] Lee H, Sharapatov Y, Park H, Castillo CJ, Alharthi M, Zogan M *et al.* An Observational 3-Year Follow-Up Study for Postoperative Renal Function Changes Assessed by 99 Mtc-DTPA Scintigraphy and Predictive Factors After Miniaturized Percutaneous Nephrolithotomy and Retrograde Intrarenal Surgery. BioMed Central Urology. 2025 Apr; 25(1): 108. doi: 10.1186/s12894-025-01761-3.

[12] Wilhelm K, Hein S, Kunath F, Schoenthaler M, Schmidt S. Totally Tubeless, Tubeless, and Tubed Percutaneous Nephrolithotomy for Treating Kidney Stones. Cochrane Database of Systematic Reviews. 2023 Jul.

[13] Türk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M *et al.* EAU Guidelines on Interventional Treatment for Urolithiasis. European Urology. 2016 Mar; 69(3): 475-82. doi: 10.1016/j.eururo.2015.07.041.

[14] Moe OW. Kidney Stones: Pathophysiology and Medical Management. The Lancet. 2006 Jan; 367(9507): 333-44. doi: 10.1016/S0140-6736(06)68071-9.

[15] Setthawong V, Srisubat A, Potisat S, Lojanapiwat B, Pattanittum P. Extracorporeal Shock Wave Lithotripsy (ESWL) Versus Percutaneous Nephrolithotomy (PCNL) or Retrograde Intrarenal Surgery (RIRS) For Kidney Stones. Cochrane Database of Systematic Reviews. 2023 Aug. doi: 10.1002/14651858.CD007044.pub4.

[16] Akman T, Binbay M, Tekinarslan E, Ozkuvanci U, Kezer C, Erbin A *et al.* Outcomes of Percutaneous Nephrolithotomy in Patients with Solitary Kidneys: A Single-Center Experience. Urology. 2011 Aug; 78(2): 272-6. doi: 10.1016/j.urology.2010.12.029.

[17] Kukreja R, Desai M, Patel S, Bapat S, Desai M. First Prize: Factors Affecting Blood Loss During Percutaneous Nephrolithotomy: Prospective Study. Journal of Endourology. 2004 Oct; 18(8): 715-22. doi: 10.1089/end.2004.18.715.

[18] Talyshinskii A, Tzelves L, Juliebø-Jones P, Hameed BZ, Sharapatov Y, Traxer O *et al.* The Evolution of Percutaneous Nephrolithotripsy–An Overview from European Association of Urology Endourology Section. Journal of Endourology. 2025 May. doi: 10.1089/end.2024.0910.

[19] Seitz C, Desai M, Häcker A, Hakenberg OW, Liatsikos E, Nagele U, Tolley D. Incidence, Prevention, and Management of Complications Following Percutaneous Nephrolitholapaxy. European Urology. 2012 Jan; 61(1): 146-58. doi: 10.1016/j.eururo.2011.09.016.

[20] Zhou G, Zhou Y, Chen R, Wang D, Zhou S, Zhong J et al. The Influencing Factors of Infectious Complications After Percutaneous Nephrolithotomy: A Systematic Review and Meta-Analysis. Urolithiasis. 2022 Dec; 51(1): 17. doi: 10.1007/s00240-022-01376-5.