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Editorial **Open Access**

Artificial Intelligence in Medical Writing – Understanding the Fine Line Between Assistance and Academic Misconduct

Iqbal Hussain Udaipurwala

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The explosion of artificial intelligence (AI) in biomedical research and clinical documentation heralds a new era in medical writing.[1,2,3] AI-driven tools, predominantly large language models (LLMs) like ChatGPT, GPT-4, DeepSeek, Scholar GPT and other natural language processing systems, have introduced unprecedented efficiency in generating, translating, summarizing, and editing medical content. Its significant capability to evaluate huge amount of data allows it to recapitulate medical text with great rationality and precision. The user-friendly interface of these LLMs have made it an ideal mean for medical and scinetific writing.[4] However, guidelines for AI bots are still under development, growth of Chat-GPT has surpassed its preliminary anticipations.[5] The newest version, GPT-5, exceeds ChatGPT in terms of innovative reasoning, text handling capability and image analysis, it even shows a higher level of creativity. These capabilities of AI bots raise pressing questions around fairness, equity, bias, authorship, and ethical implications of using AI in medical writing. Its fair use promise enhanced productivity and accessibility, while unfair use has risk of misinformation, academic misconduct and systemic bias replication. Its fair use can support human authorship, promote inclusivity and improve clarity without replacing critical thinking or scholarly rigor. Fair use of AI in medical writing may include language assistance for non-native speakers, manuscript formatting or grammar check, summarizing data-heavy report, automated translation and plagiarism detection. Conversely, unfair application may involve ghost-writing the entire manuscript, fabricating citations, bypassing peer review via AI-written submissions, misinformation propagation and biased amplification from training data. Such uses of AI will categorically undermine transparency, accountability, and trust in medical literature.

AI does not meet the criteria for authorship under the International Committee of Medical Journal Editors (ICMJE) guidelines. It cannot take responsibility for the integrity or accuracy of a study. From a legal point of view, AI has no status of a human being, making humans as the definitive duty conveyers. Unless AI contribution is disclosed, editorial board cannot assess whether scientific standards were met, leading to possible misconduct. Journals must enforce policies requiring transparency about AI tool usage, akin to declaring statistical software. There is a risk of unintentional plagiarism with the use of AI, as it creates manuscript based on the available facts and it may duplicate the same with different words and phrases. Medical and scientific literature often contains complex and context-specific material, which can be misinterpreted by LLMs leading to misinformation that can potentially dangerous in patient care and scientific understanding.[6] There is an in-built risk that investigators may depend on AI tools too much, weakening critical human judgment, which is essential to genuine and sometimes life-threatening medical discourse. Another important and pressing concern in the use of AI-generated medical writing is algorithmic bias. Training data, often sourced from western population which may fail to represent global health diversity, thereby encoding systemic inequalities. LLMs are also notorious for fabricating content that appears plausible but is false and it may include fake references, misquoted studies and invalid statistics. ChatGPT frequently creates citations to journals that did not exist in reality. In medical context, these inaccuracies could mislead practitioners or influence research directions based on invalid claims. If authors rely solely on AI without proper vetting, erroneous statements may be peer-reviewed and published, leading to downstream harms. Thus, mandatory verification of all AI-generated outputs is crucial for scientific validity. AI enables researchers from low-resource settings to meet publication standards and express complex ideas. On the other hand, access to premium AI tools is often gated behind paywalls or language barriers. If only elite institutions afford the best AI support, disparities in publication rates and visibility may widen. For AI to be used fairly, global access equity is essential, including open-source tools and multilingual capacities.[3]

Despite the amazing accomplishments of AI, there is still substantial hesitation regarding objectivity and prejudice in the field of medicine.[7] It is the topic of widespread research and discussion for the last many years in medical and health sciences.[8,9,10] AI tools trained on clinical data pose additional concerns regarding patient privacy issues.[11] It may gather and store information including medical and personal sensitive data that can be used later on in content generation.

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Transparency in the usage of clinical information is very crucial and patient must be informed that his data could be used in AI bot.[12] Further patient must have chance to offer informed consent with strong and reasonable privacy policy. Moreover, copyright infringement emerges when AI reproduces protected text verbatim. Journals must define permissible boundaries and require authors to affirm that content does not violate patient rights. Peer review process is also not immune to AI transformation, as AI-assisted reviewers can expedite checks but at the same time pose risk of automation bias, lacking clinical nuance and bypassing plagiarism detection. As AI continue to reshape our technological landscape in medical writing, we should prepare ourselves to proactively face this challenge. To uphold fair usage and prevent misuse, the following policy measures are recommended:

- Ø Mandatory disclosure: Journals should require explicit declarations of any AI tool usage during submission, including its role, clearly mentioning the level of AI involvement ranging from proofreading to finally full manuscript writing. Secondly, also require to mention the human involvement throughout manuscript preparation including formatting, proofreading, revising, editing and authenticating AI generated information. Lastly also provide details about the AI tool used with name of software and version used etc. as we do for using statistical software.
- Ø Prohibited uses: Total AI authorship or citation generation should be explicitly disallowed without human verification.
- Ø AI Authorship Ban: AI systems must not be credited as authors.
- Ø Audit trails: Tools used must offer version tracking for accountability.
- Ø Bias auditing: Require authors to confirm that no bias was introduced through AI tool use.
- Ø Improve collaboration with AI developers, journal editors and researchers to formulate policies the can cater the need of all stakeholders. In addition, regularly assess the influence of AI on value and prejudices in medical writing as this utility is continuously evolving.
- Ø Training and education: Universities should integrate AI ethics into medical research curricula.
- Ø Global accessibility: Encourage open-source, equitable AI tool dissemination.

To conclude, artificial intelligence is neither inherently fair nor unfair, it reflects the intentions, inputs, and structures created by humans. In medical writing, its potential is immense enabling multilingual authorship, reducing clerical burden, and improving readability. Without ethical guidelines and critical oversight, AI risks eroding the trust and rigor of medical writing. As we stand at a technological inflection point, the medical research community must collaboratively define what constitutes responsible AI use. This means building policies, tools, and cultures that harness AI's strengths while safeguarding the integrity of medical knowledge. The future of medical writing depends not on AI's capability but on our accountability.

Authors Contribution:
Iqbal Hussain Udaipurwala: Conception, writing, literature search, proof reading

REFERENCES

1. Wang C, Liu S, Yang H, Guo J, Wu Y, Liu J. Ethical Considerations of Using ChatGPT in Health Care. J Med Internet Res. 2023; 25: e48009. https://www.jmir.org/2023/1/e48009. DOI: 10.2196/48009.
2. Filippi CG, Stein JM, Wang Z, Bakas S, Liu Y, Chang PD, Lui Y, Hess C, Barboriak DP, Flanders AE, Wintermark M, Zaharchuk G, Wu O. Ethical Considerations and Fairness in the Use of Artificial Intelligence for Neuroradiology. AJNR Am J Neuroradiol. 2023; 44(11): 1242-1248. doi: 10.3174/ajnr.A7963.
3. Grzybowski A, Jin K, Wu H. Challenges of artificial intelligence in medicine and dermatology. Clin Dermatol. 2024; 42(3): 210-215. doi: 10.1016/j.clindermatol.2023.12.013.
4. Anders BA. Is using ChatGPT cheating, plagiarism, both, neither, or forward thinking? Patterns (N Y). 2023; 4(3): 100694. doi: 10.1016/j.patter.2023.100694.
5. Liebrenz M, Schleifer R, Buadze A, Bhugra D, Smith A. Generating scholarly content with ChatGPT: ethical challenges for medical publishing. Lancet Digit Health. 2023; 5(3): e105-e106. doi: 10.1016/S2589-7500(23)00019-5.
6. Hryciw BN, Seely AJE, Kyeremanteng K. Guiding principles and proposed classification system for the responsible adoption of artificial intelligence in scientific writing in medicine. Front Artif Intell. 2023; 6: 1283353. doi: 10.3389/frai.2023.1283353.
7. Yang Y, Lin M, Zhao H, Peng Y, Huang F, Lu Z. A survey of recent methods for addressing AI fairness and bias in biomedicine. J Biomed Inform. 2024; 154: 104646. doi: 10.1016/j.jbi.2024.104646.
8. Hanna MG, Pantanowitz L, Jackson B, Palmer O, Visweswaran S, Pantanowitz J, Deebajah M, Rashidi HH. Ethical and Bias Considerations in Artificial Intelligence/Machine Learning. Mod Pathol. 2025; 38(3): 100686. doi: 10.1016/j. modpat. 2024.100686.
9. Jeyaraman M, Ramasubramanian S, Balaji S, Jeyaraman N, Nallakumarasamy A, Sharma S. ChatGPT in action: Harnessing artificial intelligence potential and addressing ethical challenges in medicine, education, and scientific research. World J Methodol. 2023; 13(4): 170-178. doi: 10.5662/wjm.v13.i4.170.
10. Collins GS, Dhiman P, Andaur Navarro CL, et al. Protocol for development of a reporting guideline (TRIPOD-AI) and risk of bias tool (PROBAST-AI) for diagnostic and prognostic prediction model studies based on artificial intelligence. BMJ Open, 2021; 11: e048008. doi: 10.1136/bmjopen-2020-048008.
11. Naik N, Hameed BMZ, Shetty DK, Swain D, Shah M, Paul R, Aggarwal K, Ibrahim S, Patil V, Smriti K, Shetty S, Rai BP, Chlosta P, Somani BK. Legal and Ethical Consideration in Artificial Intelligence in Healthcare: Who Takes Responsibility? Front Surg. 2022; 9: 862322. doi: 10.3389/fsurg.2022.862322.
12. El Emam K, Jonker E, Arbuckle L, Malin B. A systematic review of re-identification attacks on health data. PLoS One. 2011; 6(12): e28071. doi: 10.1371/journal.pone.0028071.

Original Article **Open Access**

Comparison between Creation of Pneumoperitoneum by Open Technique and Closed Technique

Amjad Gul, Zaki Hussain Salamat, Inshal Jawed, M. Najam Shabbir, Muhammad Umair, Zaffar Abbas

ABSTRACT:

Objectives: Compare closed (Veress needle) and open (trocar) techniques for pneumoperitoneum in laparoscopic procedures regarding access time, complication rates, and patient outcomes.

Study Design and Setting: 99 patients undergoing laparoscopic procedures were divided into two groups. Group A (closed technique with a veress needle) included 43 patients, and Group B (open technique using a trocar) included 56 patients. The main outcome was access time (minutes), and secondary outcomes included complications like gas leaks, organ injury, vascular injury, hematomas, and site infections. This design intended to compare the efficacy and safety of both techniques.

Methodology: Total of 99 patients were included: 43 in Group A (closed method) and 56 in Group B (open method). The primary outcome was access time, while secondary outcomes included complications such as gas leaks, organ injury, vascular injury, hematomas, and site infections. Statistical analysis was conducted to compare the two techniques.

Results: Access time was significantly longer in the open method group (7.88 ± 2.76 vs. 6.25 ± 2.55 min, p = 0.03). Open method was associated with a higher incidence of gas leaks (25% vs 7%, p = 0.029), vascular injury (16% vs 2%, p = 0.04), and site infections (25% vs 7%, p = 0.029). No significant difference was observed in organ injuries.

Conclusions: Closed method is more efficient and associated with fewer complications in low-risk cases. Open technique remains a viable alternative for patients with prior abdominal surgery or a higher risk of complications. Individualized patient assessment is essential for selecting optimal approach.

Keywords: Laparoscopy, Pneumoperitoneum, Prospective Complications, Trocar

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INTRODUCTION

Laparoscopic surgery would be impossible without the establishment of a pneumoperitoneum, which provides the necessary space for visualization of the abdominal cavity and the manipulation of instruments. Insufflation of gas, usually carbon dioxide (CO2), in a controlled manner, elevates the abdominal wall and genetically strains the peritoneal cavity, allowing access to internal structures. Pneumoperitoneum can be achieved with two main methods: the closed method performed traditionally with a veress needle and the open method done generally with a Hasson trocar. Though these techniques are a mainstay of laparoscopic effectiveness and safety, they each have pros and cons, which have been thoroughly investigated and discussed in the surgical literature.

A closed method is usually chosen due to its simplicity and speed. It consists of placing a Veress needle in the abdominal cavity and insufflating CO2 to obtain the necessary insufflation. This method is generally faster, which can be critical in time-critical scenarios. It has hazards, however. Not only does it cause harm to underlying structures, especially in patients with previous abdominal surgeries,[1] but it also increases future complications such as obesity and malformations. Surgery technique choice surgical forum

is one of the chief worries using this closed method.[2] This contrasts with the open method, which takes longer but is safer for patients with these risk factors. The operation starts with a small incision made in the abdominal wall, after which, under direct vision, the trocar is inserted. This approach is preferred, especially in high-risk patients, for closed technique complications such as bowel or vascular injury.[3]

The closed method is used for most laparoscopic surgery, but the open procedure remains superior in specific patient populations. For example, people with a history of abdominal surgery who make adhesions are in increased danger of damaging themselves during the closed system and so want an open approach.[4] Moreover, research has shown that in some high-risk groups, open surgery reduces complications as compared with the laparoscopic approach. These include obese patients (BMI = 35) or those who have had previous abdominal wall reconstruction surgery.[5]

The contention between the two strategies is primarily over the balance of quickness and risk of complication. However, two studies found that the closed method, despite its shorter time in surgery, actually led to more complications, including bowel perforation and injury to blood vessels.[6] On the other hand, while the open technique requires more time for each operation, it is safer in certain situations. Still, it has dangers. For instance, two may become infected at any wound site on your body; the positioning may bring on a hernia after the incision.[7] For this reason, the choice of methods is typically detective in nature: it depends on the surgeon's judgment, the medical histories of his patients, and peculiar developments that may occur in a given surgical case.

Although several studies have compared the safety, effectiveness, and outcome of these open and closed pneumoperitoneum methods, the findings are divergent, which justifies further investigation.[3, 5] There were advantages to the open method as it required a smaller incision, was less invasive for high-risk patients and was overall safer.[8] However, heterogeneous patient selection and outcome measures limit direct comparisons. This research compares locked (Veress needle) and open (trocar) entry in a laparoscopic procedure based on fundamental quantitative indicators in the postoperative process (time access (min), complications, end results). These findings would help optimize patient management and surgical decision-making, contributing to the conduct of safer procedures. An academic session emphasized clinical decision-making, which is thus expected to be one outcome.

Recent studies emphasize that low-pressure pneumoperitoneum can accelerate postoperative recovery and lessen pain compared to standard pressures.[9] In addition, pulmonary recruitment maneuvers at the end of surgery reduce residual pneumoperitoneum and shoulder pain.[10] These findings can be used to emphasize the need to optimize pneumoperitoneum techniques to achieve maximal benefits from minimally invasive procedures.

METHODOLOGY

This study was performed in a tertiary care hospital with 99 patients undergoing laparoscopic surgeries from October 2024 to February 2025. The primary aim was to compare two commonly used methods for establishing pneumoperitoneum during laparoscopic surgery, closed technique (using Veress needle) and open technique (with trocar in another hand). Patients were randomly allocated to either group according to the method for creating pneumoperitoneum: Group A (Veress needle/closed technique) had 43 patients, and Group B (the open method) had 56 participants.

The study followed the principles of the Declaration of Helsinki.[12] All participants provided written informed consent and the study was approved by the hospital's Institutional Review Board (ERC/2024/SURG/III dated 21 October 2024), in accordance with standards of accepted medical ethics.

The sample size was calculated based on previous research outputs, which compared access time for open and closed methods for creating pneumoperitoneum.[1, 2] The undermentioned formula was used to compare two means:

$$n = \frac{[(\frac{Z\alpha}{2} + Z\beta)^2 * 2 * \alpha^2]}{d^2}$$

Where:

- $Z\alpha/2 = 1.96$ (for á = 0.05, two-tailed)
- $Z\beta = 0.84$ (for 80% power)
- $\sigma = 2.7$ (pooled standard deviation estimated from previous studies)
- $d = 1.63$ (expected difference in access time between groups)

This calculation resulted in a minimum sample size of 43 patients per group. Assuming a possible 15% dropout rate, we planned to enroll at least 99 patients (50 for each group) for this investigation.

The study included patients aged 18-70 years, planned for elective laparoscopic procedures such as cholecystectomy, appendectomy, or hernia who and gave formalized written consent for participation in the study. These criteria guaranteed that there were suitable candidates for laparoscopic procedures in which both pneumoperitoneum techniques could be conducted safely.[3, 4]

Patients were excluded from the study included those patients who have an absolute contraindication for pneumoperitoneum, such as, widespread abdominal adhesions, history of multiple abdominal surgeries at high complications, severe cardiovascular or respiratory disease contraindicating pneumoperitoneum.[5, 6] The above exclusion criteria were developed to reduce the risk of complications and provide an

opportunity for patient safety during the study.[11, 12]

Data was methodically collected. Age, sex, body mass index (BMI), and any comorbidities (e.g., prior surgery, diabetes, cardiovascular disease, etc.) were taken down from each patient. These are all important data for adjusting to differences in the basic situation of the groups.[2, 5] Regarding procedure time, time was noted in minutes for each of the two groups being studied, from the first incision until the target intra-abdominal pressure was achieved. One of the most important parameters for determining how efficient every technique is.[6] Complications were documented and categorized into several categories, including gas leaks, organ injuries, vascular injuries hematomas, and site infections. SPSS version 25 (IBM Corp) was used for data analysis, a statistical method for assessing access time and complications (primary outcomes).

Regarding Access Time two independent cohorts have been studied for comparative analysis of pneumoperitoneum time between the two groups (guided vs blind pneumoperitoneum) using an independent Student's t-test. The means of the two independent groups can be compared for normally distributed data using the t-test. Levene's test for equality of variances was used to check that the variances fulfilled the assumptions of the t-test.[9] Moreover, the incidence of complications was compared between two groups using Fisher's Exact test, which is suitable in the presence of small sample sizes and categorical data. This test provides a correct calculation technique for the significance of complication rates when closed versus open surgery methods are being debated.[4, 11] All tests were done two-tailed for significance at $p < 0.05$. Multivariate analysis well as there - also was with adjustments for possible confounders, including BMI and previous abdominal surgery history.[1, 3]

RESULTS:

Both cohorts were comparable in demographic variables, including age, gender distribution, and BMI category (Table 1). The mean age of patients in Group A (closed method) was 36 ± 13.78 years, while for Group B (open method), it was 33.5 ± 12.23 years, with no significant age difference between the two groups. The comparable age distribution indicates that age-related factors were unlikely to have impacted surgical outcomes. Furthermore, the two groups were well-matched for BMI and gender, reducing the risk of confounding from these variables in our results. This demographic matching suggests that confounding factors such as age, gender, and BMI were adequately normalized, underlying that the differences in surgical outcomes could be isolated using the different pneumoperitoneum methods.Complication rates were reported in the two groups (Table 3). The difference between closed and open-tech cigarettes in the occurrence of these complications is significant.

The incidence of gas leaks was 1.5 times larger in Group B (open-open method) than in Group A (closed-closed method), with 14 patients having gas leaks versus three patients in Group A, $p = 0.029$. This aligns with countless reports on the conventional (open) method getting air leaks more readily than the closed method closed by a programmed needle. One explanation is that it is necessary to pass the trocar entranceway, which may harm wires around the balloon or not close corners of a pneumoperitoneal apparatus adequately.[8, 9] On the other hand, because a Veress needle is used in the closed scar-free puncture method, complications arising from peritoneal access are fewer than for the open method.

More vascular injuries were observed in Group B (open method) than in Group A. Nine (16%) of the Group B patients had vascular injuries in particular, whereas there was only one case of a patient (2%) in Group A who experienced vascular injury ($p = 0.04$). At the start of open-method abdominal surgery, the trocar penetration can result in trauma to large blood vessels in the abdominal wall, and the incidence of vascular injuries has been reported as frequent.[5] By comparison, a low frequency of vascular injuries has been associated with the closed method: The Veress needle technique is often done under controlled conditions that reduce the chance of injuring large blood vessels.[7]

Patients in Group B (open method) had a significantly higher rate of site infection (14 patients, 25%) than in Group A (closed method; 3, 7%) ($p = 0.029$). This observation aligns with the available literature, which shows that the open method is subjected to post-operative infections due to its greater invasiveness, with more extensive incisions and greater exposure to external contaminants, such as trocars placed into the abdomen.[1] In addition, although site infections were found in both groups, the higher prevalence in Group B reflects the need for strict aseptic techniques in laparoscopic procedures, especially in open pneumoperitoneum patients.[9]

No significant difference was observed in statistics between the two groups regarding complication rate (Table 3). Organ injury was found in two patients (5 %) of Group A and four patients (7 %) of Group B. Hematomas were found in one patient (2 %) of Group A and two patients (4 %) of Group B. Although these complications were rare in both groups, their similar incidences rule out pneumoperitoneum technique as a significant cause of these postoperative occurrences.[3,11]

Summary of Key Findings: In conclusion, our results showed that our access time is significantly shorter in the closed method (Veress needle) pneumoperitoneum than in the open method (trocar) in laparoscopic surgery. The closed approach also had significantly fewer gas leaks and vascular injuries. However, the open approach had a higher rate of site infections. These results offer important information regarding the safety and efficacy of both of these techniques and may

influence clinical decision-making, especially within populations of patients at increased risk for complications, including prior abdominal surgery or obesity.[6]

DISCUSSION:

Based on previous research, the closed method of creating a pneumoperitoneum was shown to shorten the times needed for access points, which reduced anesthesia duration, shortened the overall time of operation and improved recovery as well.[3, 6] This method also encountered fewer complications, such as gas leaks and vascular injury, which are critical points for patient security. Gas leaks can affect vision and movement, while vascular injuries cause severe bleeding and require additional medical care.[2, 15] The closed method is undoubtedly less of an ordeal than the open approach. Previous research showed that this method produces a pneumoperitoneum more efficiently and safely.[8, 9]

Despite these benefits, this study does recognize the constraint of the closed technique. It may be more favorable to use the open method in specific clinical contexts, given the decrease in the incidence of organ injury in the closed group. Patients who have had previous abdominal surgeries, adhesions, or other anatomical changes, for example, are at increased risk of injury using the closed approach, especially if they have either dense scar tissue or altered anatomy that may challenge appropriately directing the Veress needle.[5, 16] For these high-risk cases, although access time and complication rate were longer than usual, the open method could be a safer alternative, which directly observed the abdominal cavity and reduced the risk of inadvertent injury.[3, 17] For example, populations such as patients who have had multiple laparotomies and patients with a history of peritoneal disease may be better suited to the open method since this can allow for safer trocar placement and a reduced risk of bowel or vascular injury.[2, 13]

However, the higher site infection rate among the open group should also be interpreted cautiously. The open technique may have a more invasive effect: larger incisions and the abdominal cavity are much more exposed to external contamination.[10, 18] When the surgical field is more exposed, the risk of picking up the infection is higher because this can enable the entry of bacteria into the operative field. Although the closed method is less harmful and probably has fewer infections, the infection risk does not depend only on the method of pneumoperitonization. While the biofilm's nature affects infection severity, aseptic technique, prophylactic antibiotics, and patient factors (immune status and comorbidities) are critical to infection outcome.[19]

Results from this study are similar to previous studies regarding the trade-off between the closed and open methods. Agarwal et al. (2023) emphasized the time efficacy of the closed technique but also suggested that the open approach may be safer in high-risk patients, particularly those with a history of prior abdominal operations.[2] The closed method is generally faster and associated with fewer complications. However, the open method may be safer in specific patient populations. These studies propose that the technique of choice should be patient-specific and tailored to the patient's history and risk factors.[2] The open versus closed method debate continues, and although the scale appears to lean toward the closed method with faster time to intervention and decreased complications, the open method proves to be a powerful device in the specific clinical setting, particularly in patients at greater risk for intra-abdominal injury or who lack a safe, closed approach for some other reason.[6, 21]

The results of our study have important clinical consequences for the practice of laparoscopic surgery. The difference in

Table 01**:** Demographic variables of the patients in each group.

Variables		**Group A: Veress Needle (N=43)**		**Group B: Open Method (N= 56)**	
		Mean ± SD	**Count (%)**	**Mean ± SD**	**Count (%)**
Age (years)		36 ± 13.78	-	33.5 ± 12.23	-
Gender	Female	-	16 (35)	-	30 (65)
	Male	-	27 (51)	-	26 (49)
Body Mass Index	Greater than 25	-	17 (39)	-	27 (61)
	Less than 25	-	26 (47)	-	29 (53)

Table 02: Time for the creation of pneumoperitoneum in each group.

Access time (minutes)	*Group A: Closed method (N = 43)*	*Group B: Open method (N = 56)*	*P value**
1–5	*24*	*15*	-
6–10	*15*	*39*	-
>10	*4*	*2*	-
Mean access time	*6.25 ± 2.55*	*7.88 ± 2.76*	*0.03*

*Values are significant when p-value <0.05

access time detected in closed (6.25 ± 2.55 min) compared to open (7.88 ± 2.76 min) methods has an important efficiency advantage that could manifest in decreased anesthesia exposure and enhanced operating room throughput. The findings are consistent with Madhok et al. (2022), who underscored that even small gains in time in high-volume surgical centers significantly boost resource utilization.[6] Our findings for the closed method group (7% vs. 25%, p = 0.029) with greatly decreased gas leak rates are consistent with observations by Naqvi et al (2024), who reported that with stable pneumoperitoneum, operative field visualization is improved and surgical precision optimized.[8] The significant difference in vascular injury rates (2% for closed method versus 16% for open method, p=0.04) is particularly striking. It compares to the work of Martínez-Hoed et al. (2021), who found similar advantages in the closed technique.[3] Our site infection findings' clinical significance (7% closed vs. 25% open, p=0.029) is evident from the Garteiz-Martínez et al (2021) study identifying entry technique as a contributing factor to postoperative infection risk.[10] Although our research reinforces the closed approach in routine cases, it also recognizes the ongoing significance of the open technique in certain high-risk situations, especially for abdominal surgery or adhesions, as pointed out by Agarwal et al. (2023).[2] This highlights the need for individualist techniques, such as choosing a specific patient risk profile rather than using a particular protocol for everyone, in favor of a personalized surgical approach, as described by Patel et al. (2022).[5]

Finally, this study adds novelty to the ongoing debate to determine the best approach for establishing pneumoperitoneum during laparoscopic surgery. Although access time and complication rates are considerably improved with the closed method, especially for low-risk patients, the open method is still relevant for high-risk patients. For instance, additional research should assess and narrow down the parameters and define the basis for selecting the technique as per each patient.[9, 22]

Various limitations of our study should be taken into account in the interpretation of its results. Naqvi et al. (2016) noted the inherent limits of a single-center design, which might not apply to other health systems with dissimilar levels of surgical expertise and experience in minimally invasive surgeries.[8] Although sufficiently large to detect differences in primary outcomes and common complications, our sample size was likely small for rare but major adverse events, as the same limitation was noted by Liu et al. (2024) in other comparative studies.[11] Despite our best attempts at standardization, the operators' variability and effects on outcomes may be a confounding factor identified in comparisons of surgical technique by Luketina et al. (2021).[12] Focusing as we do on immediate and short-term outcomes, our study may miss late complications like trocar site hernias or adhesion-related problems that Jimenez-Santana et al. (2024) considered important when considering a comprehensive surgical outcome.[22] Lack of standardized patient-reported outcomes, including postoperative pain scores and satisfaction assessment is another limitation since such indicators are an important source of complementary data.[9] Even after attempts at randomization, subtle selection biases might have affected technique choice in some cases, especially where a patient had challenging anatomical features – one of the methodological challenges highlighted by Kim et al. 2021 in comparative surgical studies.[1] Future research should attempt to overcome these limitations in larger, multicenter randomized controlled trials with long-term follow-up and comprehensive outcome evaluations reported by Delia et al. (2021) in their review of surgical research methodology.[21]

CONCLUSION:

The closed technique (C) is traditionally performed using a Veress needle. It provides significantly shorter access time than the open technique (Op), thus decreasing anesthesia and surgical time. Our results show that the closed technique offers much shorter access time than the open technique (6.25 ± 2.55 min versus 7.88 ± 2.76 min), hence reduced anesthesia time and total operation time.

Further, the closed method was linked to lower complication rates, especially the gas leaks (7% as compared to 25%), vascular injuries (2% as compared to 16%), and site infections (7% as compared to 25%). The declined incidence of complications implies that the closed technique is more efficient and less dangerous for patients who have not undergone abdominal surgery, contributing to tissue integrity maintenance and faster recovery.

However, since it operates longer and has higher complication rates, the open approach is a useful alternative to specific patient groups. For patients who have had abdominal surgeries, adhesions, obesity, or abdominal wall disorders, the open method will provide direct vision that may avoid potential organ injuries. The direct visual access offered by the open technique may be life-saving for high-risk cases in which blind needle insertion may be a problem.

The individualized patient understanding and evaluation used in the selection of the optimal approach of pneumoperitoneum highlights the study. Despite the closed method's superiority for everyday low-risk cases, the open method remains relevant to patients with complex surgical histories and anatomical predicaments.

Further validation of these findings would be possible with future studies with large multi-center studies, varying patient populations, and long-term follow-up. Further, exploring patient-specific risk factors can also result in a more specific set of recommendations on the choice of technique, which can contribute to greater effectiveness in the surgical process and improved safety in laparoscopic procedures.

LIMITATIONS

Being a single tertiary care hospital study may limit the generalizability of these findings. Pump-related complications also may be underreported because the sample size may not have had enough statistical power to detect differences in less common complications. The findings of this study may be confirmed by future studies with larger cohorts and multi-center data.[3, 1]

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REFERENCES:

1. Kim W-J, Lim T-W, Park P-J, Choi S-B, Kim W-B. Safety and feasibility of pure laparoscopic extended cholecystectomy: comparison with the open technique in a propensity analysis at a single center. Surgical Endoscopy. 2021:1-7. https://doi.org/10.1007/s00464-020-08112-3
2. Agarwal PK, Golmei J, Goyal R, Maurya AP. Comparison between closed and open methods for creating pneumoperitoneum in laparoscopic cholecystectomy. Cureus. 2023;15(3). DOI: 10.7759/cureus.35991
3. Martínez-Hoed J, Bonafe-Diana S, Bueno-Lledó J. A systematic review of the use of progressive preoperative pneumoperitoneum since its inception. Hernia. 2021:1-16. https://doi.org/10.1007/s10029-020-02247-x
4. Bada-Bosch I, Escolino M, De Agustín JC, Esposito C. Pediatric inguinal hernia repair, laparoscopic versus open approach: a systematic review and meta-analysis of the last 10-year evidence. Journal of Laparoendoscopic & Advanced Surgical Techniques. 2022;32(5):583-94. https://doi. org/10.1089/lap.2021.0690
5. Patel K, Shergill S, Vadivelu N, Rajput K. Analgesia for gynecologic oncologic surgeries: a narrative review. Current Pain and Headache Reports. 2022;26(1):1-13. https://doi.org/10.1007/s11916-022-00998-z
6. Madhok B, Nanayakkara K, Mahawar K. Safety considerations in laparoscopic surgery: a narrative review. World journal of gastrointestinal endoscopy. 2022;14(1):1. doi:10.4253/wjge.v14.i1.1
7. Ietto G, Amico F, Pettinato G, Iori V, Carcano G. Laparoscopy in emergency: why not? Advantages of laparoscopy in major emergency: a review. Life. 2021;11(9):917. https://doi.org/10.3390/life11090917
8. Naqvi AZ, Balasubaramaniam V, Raza W, Rai L, Whiteley GS. Systematic review on techniques for the creation of pneumoperitoneum in laparoscopic surgeries. Asian Journal of Medical Sciences. 2024;15(5):253-9. DOI: 10.3126/ajms.v15i5.62482
9. Moro ET, Pinto PC, Neto AJ, Hilkner AL, Salvador LF, da Silva BR, et al. Quality of recovery in patients under low-or standard-pressure pneumoperitoneum. A randomised controlled trial. Acta Anaesthesiologica Scandinavica. 2021;65(9):1240-7. https://doi.org/10.1111/aas.13938
10. Garteiz-Martínez D, Rodríguez-Ayala E, Weber-Sánchez A, Bravo-Torreblanca C, Carbó-Romano R. Pulmonary recruitment can reduce residual pneumoperitoneum and shoulder pain in conventional laparoscopic procedures: results of a randomized controlled trial. Surgical Endoscopy. 2021;35:4143-52. https://doi.org/10.1007/s00464-020-07881-1
11. Liu S, Chi J, Cao H, Zhou X, Ma Q, Yang Y, et al. Massive subcutaneous emphysema and bilateral tension pneumothorax following laparoscopic inguinal hernia repair under general anesthesia: A case report. Heliyon. 2024;10(16). DOI:10.1016/j.heliyon.2024.e36005
12. Luketina R, Luketina TL, Antoniou SA, Köhler G, Könneker S, Manzenreiter L, et al. Prospective randomized controlled trial on comparison of standard CO 2 pressure pneumoperitoneum insufflator versus AirSeal®. Surgical endoscopy. 2021;35:3670-8. https://doi.org/10.1007/s00464-020-07846-4
13. Farda W, Tani MK, Manning RG, Fahmi MS, Barai N. Laparoscopic cholecystectomy: review of 1430 cases in cure international hospital, kabul, Afghanistan. BMC surgery. 2021;21:1-8. https://doi.org/10.1186/s12893-021-01342-9
14. Liang H, Ganji N, Alganabi M, Zhu H. Evidence-based advances in minimally invasive surgery in infants with congenital gastrointestinal anomalies: a narrative review. Translational Pediatrics. 2024;13(5):791. doi:10.21037/tp-23-611
15. Mohamed Ea, Ibrahim Ab, Mashal Ah. Clip Application Versus Harmonic Scalpel in Sealing and Division of the Appendicular Stump during Laparoscopic Appendectomy in Children. The Medical Journal of Cairo University. 2024;91(12):1289-300. DOI:10.21608/mjcu.2024.342718
16. Huang T. Purpose: As depression in patients with pelvic inflammatory diseases (PID) has. Women in Obstetrics and Gynecology. 2023;16648714:247. DOI:10.3389/fmed. 2022.926351
17. Morozov K, Morozova O, Severgina L, Marchuk T, Morozov D. Scientific Publications Experimental Surgery. 2021. DOI:https://dx.doi.org/10.18484/2305-0047.2021.2.137
18. Joelson AM, Shen B. Salvage Endoscopy in the Management of Acute Lower Gastrointestinal Endoscopy-Associated Complications. Corrective Endoscopy and Surgery in Inflammatory Bowel and Colorectal Diseases-E-Book: Advanced Management of Complications. 2024:165. https://doi.org/10.1016/B978-0-323-83439-1.00011-1
19. Di Carlo A, Gunder M, Doria C. Surgical Management of Pancreatic Adenocarcinoma. Hepato-Pancreato-Biliary Malignancies: Diagnosis and Treatment in the 21st Century: Springer; 2022. p. 557-68. https://doi.org/10.1007/978-3-030-41683-6_52
20. Rim CM, Verghese ST, Kane TD. Minimally Invasive Versus Open Surgical Approaches in Children: Pros/Cons. Anesthetic Management in Pediatric General Surgery: Evolving and Current Concepts. 2021:129-39. https://doi.org/10.1007/978-3-030-72551-8_8

21. Delia C-G, Hübner M, Mohammad A, Aditi B, Wim C, Olivier G, et al. Primary and metastatic peritoneal surface malignancies (Primer). Nature Reviews: Disease Primers. 2021;7(1). DOI:10.1038/s41572-021-00326-6

22. Jimenez-Santana JD, Díaz-Cambronero O, Schultz MJ, Mazzinari G. Current Concepts in Intraoperative Ventilation during Anesthesia for Laparoscopic and Robot–Assisted Surgery–a Narrative Review. Current Anesthesiology Reports. 2024;14(4):534-50. https://doi.org/10.1007/s40140-024-00648-7

23. Anita Kottapalli B, Megha Gangadhar B, Ven Kottapalli M. A Novel Treatment Approach to Treatment-Resistant, Recurrent Clostridioides difficile. 2022. DOI:10.1159/000527854

Original Article **Open Access**

Comparison of Empagliflozin-Linagliptin with Empagliflozin- Metformin Combination Therapy in Assessing Cardiovascular Profile and Anemia in Type 2 Diabetic Patients

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ABSTRACT

Objective: This study aimed to compare the effects of empagliflozin-metformin versus empagliflozin- linagliptin combination therapy on cardiovascular parameters and anemia in patients with type 2 diabetes mellitus (T2DM).

Study Design and setting: An analytical study was conducted over 12 weeks at National Medical Centre Hospital, Karachi.

Methodology: T2DM patients were randomly assigned to either the Empagliflozin 12. 5 mg with Metformin 500mg or Empagliflozin 10mg with Linagliptin 5mg. Clinical assessments were conducted at baseline Week 0, 4, and 12, focusing on C-reactive protein levels, blood pressure, temperature, heart rate, respiratory rate, ECG findings, hemoglobin levels, BMI, and glycated hemoglobin (HbA1c) and cardiac examination was performed in all visits. Descriptive statistics were used to compare outcomes between the groups.

Results: The comparative analysis of empagliflozin–metformin (EM) and empagliflozin–linagliptin (EL) regimens demonstrated notable differences in outcomes. HbA1c decreased significantly in both groups, but the EL group showed a greater reduction by week 12 ($p = 0.021$, OR = 1.65, 95% CI: 1.05–2.58). BMI declined in both arms, but intergroup difference was not statistically significant ($p = 0.078$). CRP levels dropped more in the EL group, reaching statistical significance ($p = 0.037$, OR = 1.43, 95% CI: 1.01–2.11). Cardiovascular parameters, including systolic BP ($p = 0.116$) and diastolic BP ($p = 0.098$), remained stable, showing no significant differences. ECG (QTc interval) changes were also nonsignificant ($p = 0.316$). Hemoglobin levels showed no significant difference between groups at week 12 ($p = 0.212$). Overall, both regimens were effective and cardiovascularly safe, though EL provided superior benefits in glycemic control (HbA1c, $p = 0.021$) and anti-inflammatory effect (CRP, $p = 0.037$).

Conclusion: The combination of empagliflozin with either metformin or linagliptin proved to be effective treatment with cardiovascular safety. The combination of empagliflozin with linagliptin showed enhanced reductions of CRP markers and comparative better hemoglobin as empagliflozin with metformin significantly raised anemia possibilities.

Keywords: Blood Pressure, Cardiovascular Diseases, C-Reactive Protein, Diabetes Mellitus, Empagliflozin, Linagliptin, Metformin

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INTRODUCTION

Type 2 Diabetes mellitus (T2DM) is a metabolic disease that includes insulin resistance combined with hyperglycemia. This may lead to many aliments including cardiac impairment.[1] Persistent high blood sugar levels, evident in T2DM, has a significant impact on the pathogenesis and the development of atherosclerosis which is the main cause of cardiovascular disease. High blood glucose levels also have a direct effect on the endothelial cells that line the blood vessels and make these dysfunctional. This damage together with further rise in oxidative stress and pro-inflammatory cytokine activity in the body provides a conducive place for the formation of plaques on the arterial walls. These cause the arteries to narrow gradually and disrupts proper blood flow which may lead to hypertension, coronary artery disease, myocardial infarction, heart failure, and stroke.[2,3]

Moreover, T2DM has been linked to diabetic cardiomyopathy.

This condition, effectively, impairs the myocardial relaxation and contraction and contributes to the development of heart failure. Also, insulin resistance, which is characteristic of T2DM, increases the levels of triglycerides and decreases the levels of HDL cholesterol and causes obesity localized in the abdomen. These changes compound the consequences on cardiovascular risk. Hence, proper control of many factors including blood glucose levels, lipids, and blood pressure are key in managing the risk of cardiovascular diseases among T2DM patients.[4]

Thus, cardiovascular diseases are contributing to the high mortality rate among patients with T2DM, and proper and efficient glycemic control is essential. Besides glycemic control, there are other specific cardinal intervention measures for the patient to adopt with the aim of preventing long-term end-organ damage. Among them, oral antidiabetic drugs (OADs) are a critical part in this management strategy. The management aims at achieving and maintaining near-normal blood glucose levels because these two kinds of complications lie at opposite poles: microvascular compounding of nephropathy, neuropathy, and retinopathy and macrovascular such as heart diseases and stoke. OADs act by decreasing the glycemic index, increasing the biosynthesis of insulin, decreasing gluconeogenesis, or stimulating diabetic glycosuria.[5]

Moreover, some of the newer class of OADs that has been classified as SGLT2 inhibitors and DPP-4 inhibitors have extra advantages aside from glucose reduction, which includes cardio and renal protection. Besides, they are not only effective for regulating blood glucose but also useful for prevention of other conditions frequently observed in patients with T2D.[6] Empagliflozin, metformin, and linagliptin represent commonly prescribed OADs which studies

have thoroughly evaluated regarding their impact on glucose levels.[7] Whereas, study needs additional exploration regarding the effects of these combinations on cardiovascular parameters.[8]

The cardiovascular disease risk level in T2DM patients is two to four times greater than in people without diabetes.[9] Three primary factors which contribute to cardiovascular problems in diabetes include persistent inflammation and dysfunction of endothelial cells and abnormal fat metabolism.[10] Measures of C-reactive protein (CRP) serve as an essential marker of systemic inflammation because elevated levels show a direct link to increased atherosclerosis risk together with myocardial infarction and stroke.[11] The assessment of CRP variations after different antidiabetic treatments becomes essential to determine cardiovascular effects.

Studies show that empagliflozin as a sodium-glucose cotransporter-2 inhibitor (SGLT2) brings substantial cardiovascular benefits to patients.[12] Linagliptin, a dipeptidyl peptidase-4 (DPP- 4) inhibitor, improves glycemic control by enhancing incretin hormone activity, leading to increased insulin secretion and suppressed glucagon release.[13] Whereas, metformin, a first- line biguanide antidiabetic agent, acts by reducing hepatic glucose production, increasing insulin sensitivity, and promoting weight loss.[14] Hence, given the significant impact of T2DM treatment, this study aimed to compare the effects of empagliflozin-metformin versus empagliflozin-linagliptin combination therapy in terms of cardiovascular profile.

METHODOLOGY:

It was a comparative analysis involving 200 participants with type 2 diabetes mellitus conducted over 12 weeks (January 2022–June 2022) to compare the difference in clinical parameters between two treatment interventions. The patients were selected in two equal arms (the Empagliflozin-Linagliptin (EL) and Empagliflozin-Metformin (EM) arms) through simple randomization, which was a computer-generated simple randomization, whereby one arm (n=100) received Empagliflozin-Linagliptin (EL) while the other arm (n=100) received Empagliflozin-Metformin (EM). All recruited participants had high HbA1c and BMI baseline. Patients who had cardiovascular diseases, acute infections or other metabolic disorders were not included.

The research was ethically endorsed by the Institutional Ethical Review Committee (ERC) of Bahria University (ERB no: 105/2022 ; Date:) and signed informed consent was obtained to all the participants. The ethical standards were maintained.

Sample size estimation: OpenEpi (Version 3.01) was used to compare two proportions, and statistical tools to calculate the sample size were used, with a confidence level of 95 and power of 80. They assumed that 25 percent of the patients in the treatment arm (EL group) would have desired outcome (HbA1c

< 7.0), which was 10 percent in the control arm (EM group). With these assumptions, it was predicted that the difference in proportions would be 15%. The equation to estimate a sample size in OpenEpi has the formula:

n=(P1?P2)2[(Z1?á/22P(1?P)+Z1?âP1(1?P1)+P2(1?P2))]2

On these assumptions, the sample size needed per group was estimated to be 91. The sample size was adjusted to include 100 participants in each arm to facilitate the representation of the possible dropouts and the resultant number of 200 participants.

The assessment examined both subjective symptoms and objective markers of cardiovascular performance and metabolic status together with inflammatory response indicators across all phases of testing. The study measured the inflammatory marker C-reactive protein (CRP) as well as blood pressure along with heart rate and respiratory rate and electrocardiogram (ECG) findings and results from cardiac examinations. Other metabolic parameters include hemoglobin levels, BMI, and glycated hemoglobin (HbA1c)

levels.

With standardized equipment, patients ECG results were evaluated by technician, which included the examination of cardiac rhythm patterns combined with QT intervals and essential cardiac information. Sphygmomanometer measurement of blood pressure and pulse rate monitoring techniques provided additional safety measures in this analysis. Moreover, others included respiratory rates through observational techniques while laboratory testing determined both the hemoglobin and HbA1c levels. The BMI determined through height and weight measurements at every assessment point. The effects and side effects of both the groups were also assessed.

The analysis of data was done with the SPSS version 22. As normally distributed, used descriptive statistics (T-Test) to evaluate how CRP levels together with cardiovascular function and metabolic indicators and clinical symptoms changed across the 12-week period. Results were compared between Empagliflozin-Metformin administration and Empagliflozin- Linagliptin administration to determine their therapeutic equivalence.

RESULTS:

The participants in the Empagliflozin-Metformin combination therapy started with a HbA1c value of 7.9% which decreased to 7.6% during Week 12. Both groups reported improvements in HbA1c levels yet the Empagliflozin-Linagliptin patients showed consistently better results since their baseline of 7.4% fell to 6.6% in comparison to 7.9% to 7.6% for Empagliflozin- Metformin patients. The BMI levels decreased across both treatment groups. The patients in the Empagliflozin-Metformin group had baseline BMI levels at 27.0 kg/m² while those in the Empagliflozin-Linagliptin group started with 28.9 kg/m². The patients in both groups experienced BMI reductions with results showing 26.0 kg/m² in the Empagliflozin-Metformin group while the Empagliflozin-Linagliptin group recorded 28.0 kg/m² at Week 12. HbA1c quantity reduced similarly between initial measurements and final testing periods (Table 1).

The study started with Empagliflozin-Metformin patients showing C-reactive protein (CRP) at

0.35 mg/dl and Empagliflozin-Linagliptin patients with 0.40 mg/dl and gradually decreasing more in linagliptin group. Glycemia measurements showed steady decreases until the end of study when patients from both groups maintained 0.30 mg/dl and 0.26 mg/dl respectively at Week 12. The blood pressure readings started at 126/95 mmHg for the Empagliflozin- Metformin group yet 125/93 mmHg for the Empagliflozin-Linagliptin group. The results showed blood pressure decreased to 118/90 mmHg in both groups as well as 120/90 mmHg. All patients maintained stable body temperature levels since no participant experienced fever during the experimentation period (Table 2).

The heart rate levels diminished steadily in each treatment group throughout the study. The patients in the Empagliflozin-Metformin group started with an initial heart rate of 87 bpm while patients in the Empagliflozin-Linagliptin group began with 75 bpm. By Week 12, it had dropped to 68 bpm and 65 bpm, respectively. Similarly, the respiratory rate, which started at 14 and 15 breaths per minute, respectively, declined to 12 and 14 breaths per minute by Week 12. Electrocardiogram (ECG) findings remained unchanged throughout the study, indicating a heart rate of 80 bpm, sinus rhythm, a normal cardiac axis, normal P waves, no pathological Q waves, normal and narrow QRS complexes, no ST segment changes, and T wave inversion in leads aVR, V1-V2, and lead III. The QT interval was 420 milliseconds, with a corrected QT interval of 430 milliseconds in both groups.

No episodes of orthopnea, shortness of breath, tachypnea, dyspnea, chest pain, heart palpitations, tiredness, nausea, dizziness, fatigue, or fainting were reported in either group at any point. Cardiac examination consistently revealed normal S1 and S2 heart sounds with a regular rate and rhythm in all participants. Hemoglobin levels showed a slight decline over time in the Empagliflozin-Metformin group, it was 12.3 g/dL at baseline, decreasing to 11.9 g/dL by week 12, whereas in the Empagliflozin-Linagliptin group, it remained stable at approximately 14.0 g/dL throughout the study.

At last, the study compared Empagliflozin-Metformin and Empagliflozin-Linagliptin in 12 weeks, demonstrating the HbA1c and CRP after treatment, adjusted with age, gender, and BMI in logistic regression, which proved the efficacy of treatment and the treatment equity. (Table 3)

DISCUSSION

This study evaluated the cardiovascular safety in type 2 diabetes mellitus (T2DM) patients treated with empagliflozin-linagliptin versus empagliflozin-metformin combination therapy over a 12-weeks period. The findings demonstrated that while both regimens were cardio vascularly safe, the empagliflozin-linagliptin combination resulted in a greater reduction in C- reactive protein (CRP) levels and better perservance of hemoglobin levels., whereas the empagliflozin-metformin group showed higher anemia incidence probably due to metformin- associated vitamin B12 deficiency.

Both treatment groups experienced a decline in HbA1c levels, indicating effective glycemic control. However, the empagliflozin-linagliptin group showed a greater reduction (from 7.4% to 6.6%) compared to the empagliflozin-metformin group (from 7.9% to 7.6%). Linagliptin enhances incretin hormone activity, leading to more sustained insulin secretion and reduced glucagon release, which could explain the superior HbA1c reduction in this group.[14]

BMI reduction was greater in the empagliflozin-metformin group (27.0 kg/m² to 26.0 kg/m²) compared to the

Table 1. Comparison of Clinical and Metabolic Parameters Between Empagliflozin– Metformin and Empagliflozin–Linagliptin Groups at Baseline and Week 12

Parameter	Time point	Empagliflozin–Metformin (Mean ± SD)	Empagliflozin–Linagliptin (Mean ± SD)	p- value*
HbA1c (%)	Baseline	7.9 ± 0.4	7.4 ± 0.3	0.042*
	Week 12	7.6 ± 0.3	6.6 ± 0.2	0.018*
BMI (kg/m²)	Baseline	27.0 ± 1.5	28.9 ± 1.6	0.036*
	Week 12	26.0 ± 1.3	28.0 ± 1.4	0.041*
CRP (mg/dL)	Baseline	0.35 ± 0.05	0.40 ± 0.06	0.071
	Week 12	0.30 ± 0.04	0.26 ± 0.05	0.039*
Systolic BP (mmHg)	Baseline	126 ± 5	125 ± 4	0.521
	Week 12	118 ± 4	120 ± 5	0.283
Diastolic BP (mmHg)	Baseline	95 ± 3	93 ± 3	0.108
	Week 12	90 ± 2	90 ± 2	0.911
Body Temp (°C)	All points	36.8 ± 0.3	36.9 ± 0.3	NS

Table 2. Comparison of CRP Levels (mg/dL) in Each Treatment Group Using Paired t-Test

Group	Baseline (Mean ± SD)	Week 12 (Mean ± SD)	Mean Difference	*t* value	p-value
Empagliflozin– Metformin	0.35 ± 0.05	0.30 ± 0.04	–0.05	2.41	0.024*
Empagliflozin– Linagliptin	0.40 ± 0.06	0.26 ± 0.05	–0.14	4.92	<0.001*

Table 3. Comparison of Clinical, Metabolic, and Cardiovascular Parameters between Groups

Parameter	Time point	Group A (Empa+Met) Mean ± SD	Group B (Empa+Lina) Mean ± SD	p-value (T-test)	Adjusted OR (95% CI)*
HbA1c (%)	Baseline	8.9 ± 0.6	8.8 ± 0.7	0.412	–
	Week 4	8.1 ± 0.5	8.3 ± 0.6	0.058	1.12 (0.71–1.84)
	Week 12	7.2 ± 0.4	7.5 ± 0.5	0.021*	1.65 (1.05–2.58)*
BMI (kg/m²)	Baseline	30.2 ± 2.4	30.0 ± 2.6	0.612	–
	Week 12	28.6 ± 2.1	29.2 ± 2.3	0.078	1.24 (0.81–1.97)
CRP (mg/L)	Baseline	4.8 ± 1.2	4.7 ± 1.3	0.734	–
	Week 12	3.1 ± 1.0	3.6 ± 1.1	0.037*	1.43 (1.01–2.11)*
Systolic BP (mmHg)	Baseline	136 ± 12	135 ± 11	0.538	–
	Week 12	128 ± 10	130 ± 11	0.116	1.09 (0.72–1.65)
Diastolic BP (mmHg)	Baseline	86 ± 8	85 ± 9	0.671	–
	Week 12	80 ± 7	82 ± 8	0.098	1.18 (0.79–1.77)
ECG (QTc interval, ms)	Baseline	430 ± 18	432 ± 19	0.482	–
	Week 12	427 ± 16	429 ± 17	0.316	1.07 (0.68–1.62)
Hemoglobin (g/dL)	Baseline	13.5 ± 1.1	13.4 ± 1.0	0.624	–
	Week 12	13.8 ± 1.2	13.6 ± 1.1	0.212	1.11 (0.74–1.65)

empagliflozin-linagliptin group (28.9 kg/m² to 28.0 kg/m²). This aligns with previous studies showing that metformin induces mild weight loss through improved insulin sensitivity, reduced hepatic glucose production, and appetite suppression.[15]

Empagliflozin leads to weight reduction through urine glucose elimination followed by sodium loss which results in typical 1-2 kg weight loss during twelve weeks.[16]

The inflammatory marker CRP has essential roles in monitoring cardiovascular risks pertaining to diabetes-related complications because of persistent low-level inflammation.[13] Treated patients with empagliflozin and linagliptin shown larger decrease in CRP concentrations than those who added empagliflozin to metformin therapy. The patients taking empagliflozin and linagliptin showed CRP results dropping from 0.40 mg/dL to 0.26 mg/dL whereas patients receiving empagliflozin with metformin went from 0.35 mg/dL to 0.30 mg/dL. The findings suggest that linagliptin delivers

added anti-inflammatory effects through its actions on inflammatory pathways and oxidative stress mechanisms.[17] The data indicates that DPP-4 inhibitors suppress systemic inflammation independently of glucose management therefore leading to improved cardiovascular results.[17]

The study participants showed constant blood pressure measurements in addition to maintaining stable heart rate results and normal ECG results throughout the study period.

Empagliflozin alongside other SGLT2 inhibitor medications lowers blood pressure through mechanisms that enhance natriuresis and diuresis with arterial stiffness reduction effects.[18, 19] The patients given metformin and empagliflozin started with blood pressure levels of 126/95 mmHg and patients given linagliptin and empagliflozin had an initial reading of 125/93 mmHg but both groups demonstrated blood pressure reductions to 118/90 mmHg and 120/90 mmHg respectively after 12 weeks. The study backs previous studies showing SGLT2 inhibitors produce blood pressure reduction while avoiding reflex tachycardic effects.[19]

Measurement of ECG results across the entire study period indicated normal findings with no detected arrhythmias while also showing no QT prolongation alongside no evidence of ischemic changes in both treatment groups. Multiple prior studies have confirmed that empagliflozin along with linagliptin avoid escalating cardiovascular hazards.[19]

Hemoglobin levels demonstrated an essential distinction between treatment groups as empagliflozin combined with metformin use caused a larger decrease from 12.3 g/dL to 11.9 g/dL compared to 14.0 g/dL to 14.3 g/dL in the empagliflozin-linagliptin group. The use of metformin consistently leads to vitamin B12 deficiency which results in megaloblastic anemia and neurological problems.[20] Vitamin B12 absorption decreases inside the intestines due to metformin treatment and the duration of treatment presents a risk of deterioration.[21] This study demonstrates that patients undergoing metformin therapy experience elevated anemia risk making routine testing of hemoglobin and vitamin B12 essential for patients utilizing metformin long-term.

Study suggests that linagliptin evades disrupting vitamin B12 absorption and indications show it benefits erythropoiesis. This study confirmed findings which showed the empagliflozin- linagliptin combination both maintained stable and sometimes improved hemoglobin measurements. Relief from inflammatory processes and oxidative stress presents as a possible mechanism which helps prevent anemia development in diabetic patients. However, the study's limitation includes a small sample, and a short follow-up period.

CONCLUSION:

Cardiovascular safety exists between empagliflozin-metformin and empagliflozin-linagliptin but empagliflozin-linagliptin had superior effectiveness in CRP reduction and maintained stable hemoglobin levels compared to empagliflozin-metformin group.

CONFLICT OF INTEREST

There is no conflict of interest in this study

LIMITATIONS

Two minor limitations are the use of self-report symptoms which can cause some recall bias and a relatively short follow up of 12 weeks which restricts a long-term outcome assessment.

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Authors Contribution:
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Muhammad Sajid Abbas Jaffri: Overall review
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REFERENCES

1. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. International journal of molecular sciences. 2020 Aug 30;21(17):6275.
2. Ye J, Li L, Wang M, Ma Q, Tian Y, Zhang Q, Liu J, Li B, Zhang B, Liu H, Sun G. Diabetes mellitus promotes the development of atherosclerosis: the role of NLRP3. Frontiers in immunology. 2022 Jun 29;13:900254. Diabetes mellitus promotes the development of atherosclerosis: the role of NLRP3. Frontiers in immunology
3. Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. Canadian Journal of Cardiology. 2018 May 1;34(5):575-84. DOI: 10.1016/j.cjca.2017.12.005
4. Radzioch E, D¹bek B, Balcerczyk-Lis M, Fr¹k W, Fularski P, M³ynarska E, Rysz J, Franczyk B. Diabetic cardiomyopathy—from basics through diagnosis to treatment. Biomedicines. 2024 Mar 29;12(4):765.
5. Ma CX, Ma XN, Guan CH, Li YD, Mauricio D, Fu SB. Cardiovascular disease in type 2 diabetes mellitus: progress toward personalized management. Cardiovascular diabetology. 2022 May 14;21(1):74.
6. Feingold KR. Oral and injectable (non-insulin) pharmacological agents for the treatment of type 2 diabetes. Endotext [Internet]. 2024 Sep 11.
7. Tinahones FJ, Gallwitz B, Nordaby M, Götz S, Maldonado-Lutomirsky M, Woerle HJ, Broedl UC. Linagliptin as add-on to empagliflozin and metformin in patients with type 2 diabetes: two 24-week randomized, double-blind, double-dummy, parallel-group trials. Diabetes, Obesity and Metabolism. 2017 Feb;19(2):266-74. doi: 10.1111/dom.12814.Epub 2016 Nov 24

8. Bae JH, Park EG, Kim S, Kim SG, Hahn S, Kim NH. Comparative renal effects of dipeptidyl peptidase-4 inhibitors and sodium-glucose cotransporter 2 inhibitors on individual outcomes in patients with type 2 diabetes: a systematic review and network meta-analysis. Endocrinology and Metabolism. 2021 Mar 31;36(2):388-400. doi: 10.3803/EnM.2020.912. Epub 2021 Mar 31.

9. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A, del Cañizo-Gómez FJ. Type 2 diabetes and cardiovascular disease: have all risk factors the same strength?. World journal of diabetes. 2014 Aug 15;5(4):444. doi: 10.4239/wjd.v5.i4.444

10. Li Y, Liu Y, Liu S, Gao M, Wang W, Chen K, Huang L, Liu Y. Diabetic vascular diseases: molecular mechanisms and therapeutic strategies. Signal transduction and targeted therapy. 2023 Apr 10;8(1):152. DOI: 10.1038/s41392-023-01400-z

11. Amezcua-Castillo E, González-Pacheco H, Sáenz-San Martín A, Méndez-Ocampo P, Gutierrez-Moctezuma I, Massó F, Sierra-Lara D, Springall R, Rodríguez E, Arias-Mendoza A, Amezcua-Guerra LM. C-reactive protein: the quintessential marker of systemic inflammation in coronary artery disease—advancing toward precision medicine. Biomedicines. 2023 Sep 2;11(9):2444. doi: 10.3390/biomedicines11092444

12. Anker SD, Butler J, Filippatos G, Khan MS, Marx N, Lam CS, Schnaidt S, Ofstad AP, Brueckmann M, Jamal W, Bocchi EA. Effect of empagliflozin on cardiovascular and renal outcomes in patients with heart failure by baseline diabetes status: results from the EMPEROR-reduced trial. Circulation. 2021 Jan 26;143(4):337-49.

13. Kabil MF, Lababidi JM, Azzazy HM. Linagliptin: A comprehensive profile. Profiles of Drug Substances, Excipients, and Related Methodology. 2025 Jan 23;50:97. DOI:10.1016/bs.podrm.2024.10.001.

14. Hostalek U, Campbell I. Metformin for diabetes prevention: update of the evidence base. Current medical research and opinion. 2021 Oct 3;37(10):1705-17. doi: 10.1080/03007995.2021.1955667

15. Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin. Diabetologia. 2017 Sep;60(9):1577-85. doi: 10.1007/s00125-017-4342-z

16. EMPA-Kidney Collaborative Group. Empagliflozin in patients with chronic kidney disease. New England Journal of Medicine. 2023 Jan 12;388(2):117-27. doi: 10.1056/NEJMoa2204233

17. Xie D, Wang Q, Huang W, Zhao L. Dipeptidyl-peptidase-4 inhibitors have anti-inflammatory effects in patients with type 2 diabetes. European Journal of Clinical Pharmacology. 2023 Oct;79(10):1291-301. doi: 10.1007/s00228-023-03541-0

18. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New england journal of medicine. 2015 Nov 26;373(22):2117-28. DOI: 10.1056/ NEJMoa1504720

19. Rosenstock J, Kahn SE, Johansen OE, Zinman B, Espeland MA, Woerle HJ, Pfarr E, Keller A, Mattheus M, Baanstra D, Meinicke T. Effect of linagliptin vs glimepiride on major adverse cardiovascular outcomes in patients with type 2 diabetes: the CAROLINA randomized clinical trial. Jama. 2019 Sep 24;322(12):1155-66. doi: 10.1001/jama.2019.13772

20. Li YR, Tsai SS, Chen DY, Chen ST, Sun JH, Chang HY, Liou MJ, Chen TH. Linagliptin and cardiovascular outcomes in type 2 diabetes after acute coronary syndrome or acute ischemic stroke. Cardiovascular Diabetology. 2018 Jan 4;17(1):2. doi: 10.1186/s12933-017-0655-y

21. Infante M, Leoni M, Caprio M, Fabbri A. Long-term metformin therapy and vitamin B12 deficiency: an association to bear in mind. World journal of diabetes. 2021 Jul 15;12(7):916. doi: 10.4239/wjd.v12.i7.916.

Original Article **Open Access**

Assessment of Anterior Maxillary Bone Thickness and Cemento Enamel junction–Crest Distance Using Cone Beam Computed Tomography

Amna Amjad, Sajjad Hussain, Midhat Ahmed, Mahgul Nasr Aheer, Ayesha Shahid, Minhal Amjad

ABSTRACT

Objective: To evaluate and compare thickness of palatal and labial bone, along with the cementoenamel junction (CEJ) – bone crest distance of anterior maxillary teeth using cone-beam computed tomography (CBCT) technique.

Methods: This study is a retrospective cross-sectional study including 140 CBCT scans fulfilling the inclusion criteria. For each pair of anterior maxillary teeth, the thickness of palatal and facial bones was taken at three points along with distance between CEJ and bony crest. To ensure validity and reliability of measurements, single operator performed and recorded the measurements for each included CBCT scan.

Results: The mean age calculated from 140 CBCT scans was 34.84±8.0 years (age range 15-55 years), out of which there were 76 (54.3%) and 63 (45.0%) males and females, respectively. Most of the mean values at each measurement point of palatal and facial bone thickness were similar for both right and left teeth. Significant differences were noted in mean values among gender. For males, most of these values were higher as compared to the females. In terms of age, some values correlated positively with age including palatal thickness of CI and LI, while some correlated negatively with age including labial thickness of CI and LI.

Conclusion: The bone measurements significantly differed among males and females, and varied across age as well. The bone thickness measurements vary across populations therefore it is vital to know the anatomical bone dimensions in anterior maxilla for optimal 3-dimensional placement of the implant.

KEYWORDS: Maxilla, cuspid, incisor, cone - beam computed tomography, dental implants

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INTRODUCTION

In dental practice, implant placement is the most frequently performed procedures for replacement of lost teeth. Success in implant dentistry is highly dependent on proper planning, particularly anterior maxillary region, which is important in esthetics.[1] A detailed understanding the anatomy of alveolar bone, especially the facial and palatal bone plates, is essential for achieving favorable functional and esthetic outcomes.[2] Long-term success of implants is determined not only by osseointegration but also by the harmonious relationship between the implant, surrounding soft tissues, and underlying bone. Soft tissue recession, bone resorption, and poor esthetics may result from inadequate planning and insufficient bone volume. This is especially critical for maxilla, where the facial bone is often thin and highly susceptible to resorption.[3]

Tooth extraction is followed by predictable alveolar bone remodeling, regardless of whether the implant is placed immediately or in a delayed fashion. Studies show that bone resorption, particularly of the facial plate, occurs mostly within the first 3–6 months post-extraction.[4] The width of facial bone before extraction is a key determinant of the extent of resorption. Literature proposed that a facial bone width of at least 2 mm is critical for preserving vertical ridge height and minimizing soft tissue changes post-implant.[5]

The width of facial and palatal bone also influences the regenerative potential and the likelihood of achieving optimal esthetic outcomes. Thin facial bone is associated with higher risks of mucosal depression, appearance of implant threads, and compromised esthetics. Therefore, assessing the dimensions of alveolar bone is crucial during planning, especially in esthetically sensitive zones.[6-7]

Furthermore, the morphology of the anterior maxilla often varies among individuals, and it is influenced by several biological factors, including genetic predisposition, periodontal health, and history of trauma or disease. These factors may lead to asymmetries or inconsistencies in bone thickness, which can significantly influence the clinical approach. A comprehensive radiographic evaluation before implant surgery is, therefore, indispensable.

Cone-beam computed tomography (CBCT) has emerged as reference standard for three-dimensional imaging in implant dentistry. It offers high resolution, multiplanar views, and relatively low radiation exposure.[8] CBCT allows accurate measurement of bone width at coronal, middle, and apical levels on both the labial and palatal sides, as well as the distance between CEJ to bony-crest. These parameters are vital for deciding on immediate implant placement, guided surgery, and the need for bone augmentation.[9] Numerous studies have examined these bone parameters across different populations, reporting considerable variations by ethnicity, gender, and age. For instance, some studies found that males tend to have thicker facial bone than females, while others reported no significant gender-based differences.[10-11] However, much of the existing literature originates from developed countries, with limited data available from developing regions such as South Asia.

Understanding variations in labial and palatal bone thickness, as well as CEJ-to-crest distances at mid-facial, mesial, and distal sites, can help practitioners plan implants more precisely and avoid complications. Moreover, such data can serve as a foundational reference for developing population specific protocols, enhancing educational curricula in dental institutions, and improving patient counseling regarding surgical risks and esthetic expectations. This retrospective study aimed to evaluate facial and palatal bone thickness around maxillary CI, LI, and canines using CBCT scans. Additionally, it measured the vertical distance between CEJ and crest at three locations (mid-facial, mesial, and distal) to assess bone levels. Comparisons were also made based on gender, age, and side to identify any anatomical variations within the Pakistani population. The findings are expected to contribute valuable local data for implant treatment planning and surgical decision-making.

METHODOLOGY

A retrospective cross-sectional study was carried out at Department of Prosthodontics of Rawal Institute of Health Sciences, reviewing the records of dental patients who underwent CBCT scans from Jan 2023 to Dec 2024. Ethical approval for this study was attained from the Ethics Committee of Rawal Institute of Health Sciences (Approval no: RIHS/IRB/D/24/004). The CBCT scans of patients with normal dentition or minor dental problems, taken for various clinical reasons including extractions, impacted teeth, orthodontic assessments or implant planning were screened for inclusion in the study. Properly exposed CBCT volumes with good contrast images, patient age more than 20 years, presence of six anterior maxillary teeth were included in the study. History of dental pathologies, oral lesions, gingival disease, evidence of periodontal bone loss, crowed teeth hindering the bone measurements or patients who underwent orthodontic treatment were excluded from the study. A total of 140 CBCT scans were included, all performed and reported by qualified operators using the CS9300 system (Carestream Health Inc., Paris, France).

The measurements were taken using SIMPLANT Pro 17 software (Materialise Dental, Leuven, Belgium). The thickness of palatal and facial bone plates was measured in facio-palatal direction at right angle to the elongated axis of the root, as directed in previous studies. For each tooth, the width of facial wall and palatal wall was measured three points including the coronal third which is the thickest part of the bone within approximately 3 mm from the crest, middle third and the apical third of the root. Using the same three points, the palatal wall thickness was measured as well. In addition, the distance from CEJ to alveolar crest was measured at mesial, distal, and mid-facial sites. Each set of measurement was taken for three pairs of teeth including right and left CI, LI and canines.

In order to ensure validity of measurements, single operator took all the measurements from the scans. The data was managed and organized by using the IBM SPSS software (version 29.0). Normality of data was assessed using histograms and Q–Q plots. means and standard deviations were reported for all bone measurements. In order to compare the mean measurements between right and left pair of teeth, we used paired-samples T-test, while to compare the mean measurements between gender we used independent-samples T-test. Age was correlated with mean measurements using the Pearson's correlation test. The p-value =0.05 was considered significant.

RESULTS

140 subjects were included in the study, CBT volumes were measured for each enrolled participant. The mean age was 34.84±8.0 years (minimum age 15 years and maximum age 55 years). The study population comprised of 76 (54.3%) males and 63 (45.0%) females. Table 1 provides mean, minimum and maximum values of each tooth for various point measurements.

The point measurements were compared for each right and left tooth respectively using the paired samples T-test as

shown in table 2. Most of the measurements were alike for both right and left teeth where the p-values were not significant, while on the contrary some mean point measurements were not alike for right and left teeth shown by significant differences in the means. This might be due to slight variations in taking the measurements.

The measurements were compared between gender, most of the mean values were similar for both gender and p-values were not found significant. While significant

Table 1: Minimum, Maximum and mean value of all measurements taken for each tooth in millimeters

Tooth	Measurement points	Minimum	Maximum	Mean	SD
Right CI	Labial coronal 3rd	0.40	1.61	0.81	0.28
	Labial middle 3rd	0.24	1.72	0.81	0.27
	Labial apical 3rd	0.45	2.00	0.95	0.36
	Palatal coronal 3rd	0.85	3.05	1.60	0.51
	Palatal middle 3rd	1.41	5.40	3.03	0.89
	Palatal apical 3rd	1.79	9.50	5.06	1.74
	CEJ to mid-crest	0.57	6.83	2.83	0.92
Right LI	Labial coronal 3rd	0.00	1.44	0.76	0.32
	Labial middle 3rd	0.00	1.70	0.75	0.38
	Labial apical 3rd	0.00	1.70	0.73	0.41
	Palatal coronal 3rd	0.72	2.42	1.56	0.46
	Palatal middle 3rd	1.26	5.73	2.98	0.98
	Palatal apical 3rd	2.00	8.90	4.71	1.59
	CEJ to mid-crest	0.72	5.53	2.22	0.85
Right Canine	Labial coronal 3rd	0.00	1.79	1.08	0.43
	Labial middle 3rd	0.00	1.79	0.96	0.42
	Labial apical 3rd	0.00	2.00	0.88	0.49
	Palatal coronal 3rd	1.23	4.11	2.15	0.61
	Palatal middle 3rd	1.71	4.44	3.07	0.50
	Palatal apical 3rd	2.43	9.10	4.21	1.24
	CEJ to mid-crest	1.08	5.34	2.33	0.96
Left Canine	Labial coronal 3rd	0.00	1.83	0.99	0.32
	Labial middle 3rd	0.00	2.78	0.91	0.41
	Labial apical 3rd	0.00	3.33	1.00	0.49
	Palatal coronal 3rd	1.08	3.13	2.21	0.56
	Palatal middle 3rd	1.30	5.95	3.14	0.65
	Palatal apical 3rd	2.04	8.77	4.31	1.28
	CEJ to mid-crest	0.88	5.26	2.27	0.89
Left CI	Labial coronal 3rd	0.00	1.50	0.86	0.29
	Labial middle 3rd	0.00	1.44	0.84	0.30
	Labial apical 3rd	0.00	1.81	0.99	0.44
	Palatal coronal 3rd	0.89	3.05	1.77	0.49
	Palatal middle 3rd	1.51	6.72	3.27	1.01
	Palatal apical 3rd	2.00	10.43	4.75	1.62
	CEJ to mid-crest	0.69	5.57	2.20	0.94
Left LI	Labial coronal 3rd	0.00	2.61	0.85	0.41
	Labial middle 3rd	0.00	2.78	0.81	0.43
	Labial apical 3rd	0.00	2.61	0.81	0.45
	Palatal coronal 3rd	0.82	3.05	1.59	0.45
	Palatal middle 3rd	1.33	5.56	3.00	0.95
	Palatal apical 3rd	1.84	8.13	4.43	1.34
	CEJ to mid-crest	0.65	4.95	2.13	0.84

CI=central incisor, LI=lateral incisor

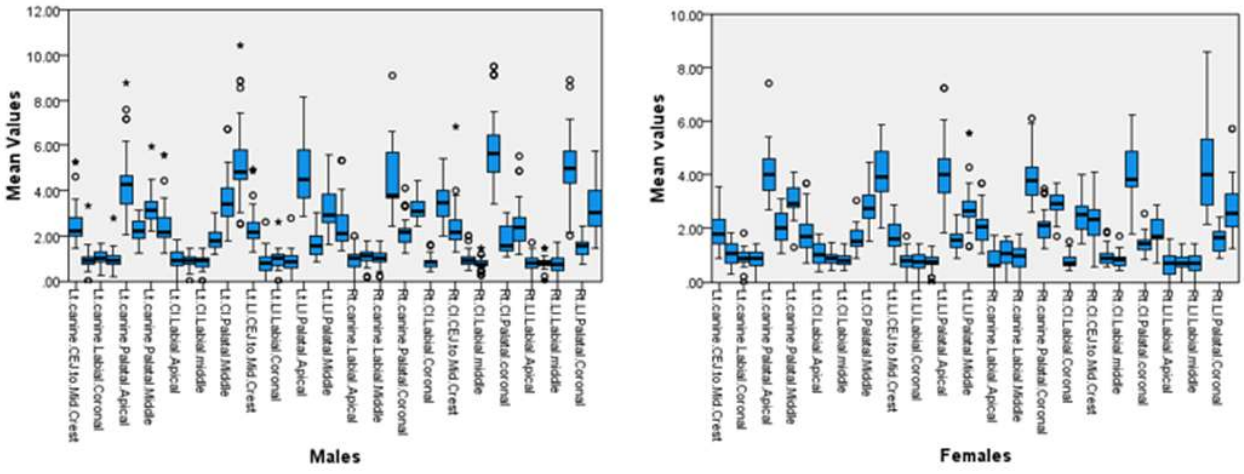
differences were found for right CI palatal coronal 3rd (p<0.001), palatal middle 3rd (p<0.001), palatal apical 3rd (p<0.001); left CI palatal coronal 3rd (p<0.001), palatal middle 3rd (p<0.001), palatal apical 3rd (p<0.001), CEJ to mid-crest (p<0.001); left LI labial coronal 3rd (p=0.003), palatal middle 3rd (p=0.033), palatal apical 3rd (p=0.008), CEJ to mid-crest (p<0.001); right LI palatal apical 3rd (p=0.015), CEJ-to mid-crest (p<0.001); right canine palatal middle (p=0.004), palatal apical (p=0.013), CEF to mid-crest (p0.010); and left canine CEJ to mid-crest (p=0.001). All the mean values were higher among males as compared to the females as shown in figure 1.

The study population age was correlated with the point measurements for each tooth and some significant relationships were observed. There was a negative correlation found between age and right CI labial coronal 3rd (r=-0.216, p=0.010), left CI labial apical 3rd (r=-0.183, p=0.030), left LI labial coronal 3rd (r=-0.238, p=0.005), right LI labial middle 3rd (r=-0.239, p=0.004), left LI labial middle 3rd (r=-0.187, p=0.027), left LI labial apical 3rd (r=-0.193, p=0.022) which means lower values were noted with increasing age. While on the other hand, a positive correlation was found between age and left CI palatal apical 3rd (r=0.0272, p=0.001),

Table 2: Point dimensions for right and left teeth (mm)

Tooth	Measurement point	Overall	Right side	Left side	p
CI	Labial coronal 3rd	0.84±0.24	0.815±0.28	0.86±0.29	0.045
	Labial middle 3rd	0.83±0.25	0.81±0.27	0.84±0.30	0.147
	Labial apical 3rd	0.97±0.33	0.95±0.36	0.99±0.44	0.250
	Palatal coronal 3rd	1.68±0.42	1.60±0.51	1.77±0.49	<0.001
	Palatal middle 3rd	3.15±0.85	3.03±0.89	3.27±1.01	0.001
	Palatal apical 3rd	4.91±1.58	5.06±1.74	4.75±1.6	0.002
	CEJ to mid-crest	2.29±0.76	2.38±0.92	2.20±0.94	0.046
LI	Labial coronal 3rd	0.80±0.33	0.76±0.32	0.85±0.41	0.001
	Labial middle 3rd	0.78±0.38	0.75±0.38	0.81±0.43	0.021
	Labial apical 3rd	0.77±0.39	0.73±0.41	0.81±0.45	0.022
	Palatal coronal 3rd	1.57±0.37	1.56±0.46	1.59±0.45	0.524
	Palatal middle 3rd	0.78±0.38	2.98±0.98	3.00±0.95	0.788
	Palatal apical 3rd	4.57±1.33	4.71±1.59	4.43±1.34	0.009
	CEJ to mid-crest	2.17±0.80	2.22±0.85	2.13±0.84	0.059
Canine	Labial coronal 3rd	1.03±0.33	1.08±0.43	0.99±0.32	0.005
	Labial middle 3rd	0.93±0.37	0.96±0.42	0.91±0.41	0.096
	Labial apical 3rd	0.94±0.43	0.88±0.49	1.00±0.49	0.003
	Palatal coronal 3rd	2.18±0.54	2.15±0.61	2.21±0.56	0.138
	Palatal middle 3rd	3.11±0.46	3.07±0.50	3.14±0.65	0.242
	Palatal apical 3rd	4.26±1.14	4.21±1.24	4.31±1.28	0.289
	CEJ to mid-crest	2.30±0.86	2.33±0.96	2.27±0.86	0.215

Figure 1: Comparison of mean point measurements of each tooth among males and females



right LI palatal middle 3rd (r=0.293, p<0.001), left LI palatal middle (r=0.193, p=0.022), right LI palatal apical 3rd (r=0.303, p<0.001), left LI palatal apical (r=0.213, p=0.011), right LI CEJ to mid-crest (r=0.236, p=0.005), right canine palatal middle 3rd (r=0.267, p=0.001), left canine palatal middle 3rd (r=0.293, p<0.001), right canine palatal apical 3rd (r=0.319, p<0.001), left canine palatal apical 3rd (r=0.220, p=0.009), right canine CEJ to mid-crest (r=0.266, p=0.001) and left canine CEJ to mid-crest (r=0.209, p=0.013) which means these measurements increased with increase in age.

DISCUSSION

We examined 140 CBCT scans retrospectively to examine mean bone width of anterior maxillary teeth at various positions. In current study, the mean thickness of labial coronal 3rd was reported to be 0.84 mm for CI, 0.80 mm for LI and 1.03 mm for canines. In current study, the mean thickness of palatal coronal 3rd was reported to be1.68 mm, 1.57 mm and 2.18 mm respectively for CI, LI and canines. The current study reported 2.29 mm, 2.17 mm and 2.30 mm mean distance between CEJ to mid bony-crest for CI, LI and canines, respectively.

In a retrospective study including 156, 149 and 152 CI, LI and canines, respectively Rojo-Sanchis J et al,[12] reported relationship between CEJ to mid bony-crest distance, facial and alveolar bone at anterior maxillary teeth. The authors reported that the facial bone thickness was significantly higher for all the teeth as compared to other measurements, while an inverse relationship was noted between CEJ to mid-bony crest distance and bone thickness measured at all points. The mean width reported for CI, LI and canines are reported to be similar as in present study i.e., 0.79 mm, 0.7 mm and 0.89 mm respectively. In a systematic review reported by Rojo-Sanchis J et al,[13] in 2022, included 17,321 teeth to analyse pooled mean facial alveolar bone thickness of =1 mm in maxillary incisors and canines. Thinner facial bone was associated with age, females and Asian population. The CEJ-bone crest distance averaged 2–2.5 mm, with greater distances observed in males. The findings stated were quite similar to those reported in current study where males are found to have higher bone thickness and younger age group.

Soumya P et al,[14] conducted a research study in Nigeria to report bone thickness at five predefined points and CEJ-crest distances in their local populations. The author found that facial bone over healthy maxillary anterior teeth was very thin (<2 mm at all levels), with 0.5–1 mm at the crest and 1–2 mm at the apex, labio-palatal width at the apex averaged around 7 mm. It was concluded that frequent fenestrations and dehiscence highlight the need for thorough bone evaluation before implant placement. Dominial M et al,[15] conducted CBCT scans of hundred young adults to evaluate the bone deficiencies on the basis of bone thickness and distance measurements. The authors reported that in 91% of the healthy young adults there was at least one bone defect observed, where think alveolar bone was most prevalent. The mean thickness values reported by the author are somewhat lower than the mean values reported in current study, that can be due to variations in study population characteristics. The authors concluded that high prevalence of bone problems highlight the value of understanding the structure of anterior maxillary and other facial bones in order to properly plan for dental implants and procedures.

A study by Lee JE et al,[16] from Korea included twenty participants who underwent CBCT scans to evaluate the structure of anterior maxilla. The authors reported that most Korean participants had labial bony wall width <2 mm at 3 and 5 mm apical to the CEJ in CI and LI, while palatal thickness was generally >2 mm. Males had significantly thicker labial bone than females at these levels. These findings highlight the importance of CBCT-based preoperative assessment for safe extraction or implant placement in anterior regions. Saglikli A et al,[17] retrospectively evaluated hundred and four randomly chosen CBCT scans to examine the width of anterior teeth. The mean widths were reported to be 1.13 mm for CI, 1.22 mm canines and 1.04 mm for LI, with age and bone width negatively related, also lesser width was noticed amongst females. These findings are quite similar to what was reported in current study in terms of relationships, while the mean thickness is slightly lower in our study. A study from Saudia Arabia, conducted by Sheerah H et al,[18] evaluated the bone profile of anterior maxillary teeth using four hundred and ninety CBCT scans of adults, out of which 186 were included in analysis. The authors reported mean thickness values that are quite similar to what were reported in current study. The facial bone thickness varied significantly among anterior teeth, with males showing greater thickness and bone height than females. Facial plate height increased with age, emphasizing the importance of considering age and gender in anterior maxillary treatment planning.

The findings from the present study support the notion that comprehensive evaluation of alveolar bone characteristics is critical in treatment planning for implants in the esthetic zone. One of the significant clinical implications of this study is the identification of areas with inadequate bone volume, which may necessitate ridge augmentation or use of shorter and narrower implants. Additionally, the differences observed in bone parameters by gender and age emphasize the need for individualized treatment protocols. Younger patients, due to having thicker facial bone, may have a higher success rate for immediate implant placement, whereas older individuals may benefit from bone grafting procedures.[19] Moreover, gender-based differences highlight the need for greater caution in planning implants for females, especially when esthetics is a priority.

In terms of surgical protocols, understanding bone thickness at various levels (coronal, middle, and apical) helps determine

flap designs, implant angulation, and the choice of implant system.[20] For example, in sites with less than 1 mm of facial bone, a flapless approach might increase the risk of bone loss, thus favoring open flap surgery with simultaneous grafting. Furthermore, the correlation between CEJ-to-crest distance and facial bone thickness suggests that bone remodeling after tooth extraction may follow predictable patterns, aiding clinicians in anticipating and mitigating resorptive changes.

Comparative data from this study also help in forming region-specific guidelines for implantology in the South Asian context. Given the lack of large-scale data from Pakistan and neighboring countries, the current findings provide a foundation for future prospective studies that could incorporate a wider demographic representation and explore additional parameters such as bone density, vascularization, and soft tissue biotype.

Finally, the reliance on CBCT as the diagnostic tool highlights its irreplaceable role in preoperative assessment. With 3D visualization and precise measurements, CBCT ensures that no critical anatomical variations are overlooked. However, its accessibility and cost may limit its use in routine dental practices across developing countries. Thus, these findings also call for policy-level considerations on improving access to advanced imaging technologies in dental healthcare. Our study highlights the frequent need for soft and hard tissue augmentation to ensure optimal implant aesthetics and long-term outcomes in the aesthetic zone.

CONCLUSION

The bone measurements significantly differed among males and females, and varied across age as well. The bone thickness measurements vary across populations therefore it is vital to know the anatomical bone dimensions in anterior maxilla for optimal 3-dimensional placement of the implant. This can help the clinicians place implants in more appropriate and esthetic positions, enhancing their longevity as well.

LIMITATIONS

The limitations include retrospective design, limited sample size that was based on availability of CBCT scans in the institute, and limited time and resources. It is recommended that large prospective studies including study sample from diverse population can provide better estimated of anterior maxilla morphology in our local population.

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REFERENCES

1. Jayachandran S, Walmsley AD, Hill K. Challenges in dental implant provision and its management in general dental practice. Journal of Dentistry. 2020 Aug 1;99:103414. DOI: https://doi.org/10.1016/j.jdent.2020.103414
2. Kim S, Kim SG. Advancements in alveolar bone grafting and ridge preservation: a narrative review on materials, techniques, and clinical outcomes. Maxillofacial Plastic and Reconstructive Surgery. 2024 Apr 16;46(1):14. DOI: https://doi.org/10.1186/s40902-024-00425-w
3. Silviana NM. Alveolar bone thickness around anterior teeth in different classifications of malocclusion: A systematic review. Ins Dent J. 2022 May 28;11(1):41-53. DOI: 10.18196/di.v10i1.12884
4. Couso-Queiruga E, Stuhr S, Tattan M, Chambrone L, Avila-Ortiz G. Post-extraction dimensional changes: a systematic review and meta-analysis. Journal of Clinical Periodontology. 2021 Jan;48(1):127-45. DOI: https://doi.org/10.1111/jcpe.13390
5. Albeshri S, Greenstein G. Significance of Facial Bone Thickness After Dental Implantations in Healed Ridges: A Literature Review. Compendium of Continuing Education in Dentistry (15488578). 2021 Oct 1;42(9). ISSN: 1548-8578
6. Ramanauskaite A, Sader R. Esthetic complications in implant dentistry. Periodontology 2000. 2022 Feb;88(1):73-85. DOI: https://doi.org/10.1111/prd.12412
7. Chackartchi T, Romanos GE, Sculean A. Soft tissue-related complications and management around dental implants. Periodontology 2000. 2019 Oct;81(1):124-38. DOI: https://doi.org/10.1111/prd.12287
8. Jain S, Choudhary K, Nagi R, Shukla S, Kaur N, Grover D. New evolution of cone-beam computed tomography in dentistry: Combining digital technologies. Imaging science in dentistry. 2019 Sep 24;49(3):179. DOI: https://doi.org/10.5624/isd.2019.49.3.179
9. Rojo-Sanchis J, Peñarrocha-Oltra D, Peñarrocha-Diago M, Zaragozí-Alonso R, Viña-Almunia J. Relation between the distance from the cementoenamel junction to the bone crest and the thickness of the facial bone in anterior maxillary teeth: A cross-sectional tomographic study. Medicina Oral, Patología Oral y Cirugía Bucal. 2019 May;24(3):e409. DOI: 10.4317/medoral.22802
10. Tsigarida A, Toscano J, de Brito Bezerra B, Geminiani A, Barmak AB, Caton J, Papaspyridakos P, Chochlidakis K. Buccal bone thickness of maxillary anterior teeth: A systematic review and meta-analysis. Journal of clinical periodontology. 2020 Nov;47(11):1326-43. DOI: https://doi.org/10.1111 /jcpe.13347
11. Arango E, Plaza-Ruíz SP, Barrero I, Villegas C. Age differences in relation to bone thickness and length of the zygomatic process of the maxilla, infrazygomatic crest, and buccal shelf area. American Journal of Orthodontics and Dentofacial Orthopedics. 2022 Apr 1;161(4):510-8. DOI: https://doi.org/10.1016/j.ajodo.2020.09.038
12. Srebrzyñska-Witek A, Koszowski R, Ró¿y³o-Kalinowska I, Piskórz M. CBCT for estimation of the cemento-enamel junction and crestal bone of anterior teeth. Open Medicine. 2020 Aug 3;15(1):774-81. DOI: doi.org/10.1515/med-2020-0211

13. Rojo-Sanchis J, Soto-Peñaloza D, Peñarrocha-Oltra D, Peñarrocha-Diago M, Viña-Almunia J. Facial alveolar bone thickness and modifying factors of anterior maxillary teeth: a systematic review and meta-analysis of cone-beam computed tomography studies. BMC Oral Health. 2021 Dec;21:1-7. DOI: https://doi.org/10.1186/s12903-021-01495-2

14. Soumya P, Chappidi V, Koppolu P, Pathakota KR. Evaluation of facial and palatal alveolar bone thickness and sagittal root position of maxillary anterior teeth on cone beam computerized tomograms. Nigerian Journal of Clinical Practice. 2021 Mar 1;24(3):329-34. DOI: 10.4103/njcp.njcp_318_20

15. Dominiak M, Hnitecka S, Olchowy C, Olchowy A, Gedrange T. Analysis of alveolar ridge width in an area of central lower incisor using cone-beam computed tomography in vivo. Annals of Anatomy-Anatomischer Anzeiger. 2021 Jul 1;236:151699. DOI: https://doi.org/10.1016/j.aanat.2021.151699

16. Lee JE, Jung CY, Kim Y, Kook YA, Ko Y, Park JB. Analysis of alveolar bone morphology of the maxillary central and lateral incisors with normal occlusion. Medicina. 2019 Sep 3;55(9):565. DOI: https://doi.org/10.3390/medicina55090565

17. Saðlýklý A, Ýpek F. Evaluation of the buccal bone thickness in the anterior maxillary region using cone-beam computed tomography. International Dental Research. 2023 Oct 15;13(S1):1-0. DOI: https://doi.org/10.5577 /idr.2023. vol13. S1.1

18. Sheerah H, Othman B, Jaafar A, Alsharif A. Alveolar bone plate measurements of maxillary anterior teeth: A retrospective Cone Beam Computed Tomography study, AlMadianh, Saudi Arabia. The Saudi dental journal. 2019 Oct 1;31(4):437-44. DOI: https://doi.org/10.1016/j.sdentj.2019.04.007

19. Le LN, Tan LT, Tran DT, Nguyen TT. A Comprehensive Study on Dentogingival Dimensions in the Maxillary Anterior Region with CBCT Imaging. The Open Dentistry Journal. 2025 Apr 23;19(1). DOI: 10.2174/0118742106377293250414102239

20. Ahmed AS, Ali BJ, Hassan BK, Sabah Mohammad A. The Estimation of Cementoenamel Junction Crestal Bone Distance in Mandibular Anterior Teeth. Clinical, Cosmetic and Investigational Dentistry. 2025 Dec 31:13-20. DOI: https://doi.org/10.2147/CCIDE.S492129

Original Article **Open Access**

Comparative Cross-Sectional Study Evaluating the Efficacy and Safety of Sublingual Misoprostol versus Intravaginal Dinoprostone for Labor Induction

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ABSTRACT

Objective: The investigation aimed to evaluate the effectiveness and safety of sublingual misoprostol compared with intravaginal dinoprostone for labor induction at Maroof International Hospital.

Study Design and Setting: A comparative cross-sectional study was carried out in the Obstetrics Department, Maroof International Hospital from 1 August 2023 to 30 September 2024, including 219 pregnant women aged between 18 and 40 years and gestation periods ranging from 37 to 42 weeks.

Methodology: Participants were randomly allocated to receive either sublingual misoprostol (50 mcg every 4 hours, up to 6 doses) or intravaginal dinoprostone (3 mg every 6 hours). The study assessed the interval between induction and delivery, delivery method, induction failure, and adverse consequences including gastrointestinal problems and fetal distress. Data analysis was conducted utilizing SPSS, with a significance threshold established at $p < 0.05$.

Results: Misoprostol markedly decreased the induction-to-delivery interval (8.4 vs. 10.2 hours, $p < 0.05$). Nonetheless, it was linked to an increased incidence of cesarean sections (12.5% compared to 5%), predominantly attributable to fetal discomfort. Misoprostol also elevated the occurrence of nausea and vomiting in comparison to dinoprostone.

Conclusion: Sublingual misoprostol reduced induction-to-delivery time but increased adverse effects and cesarean sections. Misoprostol for labor induction requires careful monitoring to balance efficacy and safety.

Keywords: Cesarean Section, Dinoprostone, Fetal Distress, Labor Induction, Misoprostol, Pregnancy

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INTRODUCTION

Labor induction, a procedure originating in the time of Hippocrates, has seen considerable evolution throughout the years. Initially, techniques like as breast stimulation and mechanical cervical ripening were employed.[1] Advancements in medicine and obstetrics have refined the methods of labor induction, customizing them to enhance results for both women and newborns. The escalation in labor induction rates is mostly ascribed to the growth in advanced mother age and the growing incidence of maternal comorbidities, including hypertension and diabetes.[2] Various pharmacological and mechanical techniques are employed to induce and enhance uterine contractions and facilitate cervical ripening, aiming to optimize outcomes for both the mother and the fetus.[3] The increasing accessibility of antenatal surveillance and monitoring has resulted in a diminished threshold for labor induction, as its safety has been extensively validated, notably through studies such as the ARRIVE trial (2018), which compared induction to expectant management in low-risk pregnancies and revealed advantageous outcomes for induction.[4] Consequently, the practice of labor induction has grown prevalent in contemporary obstetric treatment. Labor induction techniques are designed to induce and enhance uterine contractions, as well as promote cervical

softening to enable a successful vaginal birth.[5] Intravaginal dinoprostone and sublingual misoprostol are the most often utilized medicines, each with distinct advantages and limits. Misoprostol, a synthetic derivative of prostaglandin E1, is esteemed for its efficacy in producing uterine contractions and facilitating cervical ripening. Misoprostol has gained favor in labor induction procedures due to its quick beginning of action and convenience of administration, especially in its sublingual form.[6]

Nonetheless, although it is efficacious, it is concomitantly linked to adverse effects, such as gastrointestinal disorders, uterine hyperstimulation, and fetal distress, which raise concerns over its application.[7] Conversely, dinoprostone, a naturally occurring prostaglandin E2, has historically been the agent of choice for cervical ripening and labor induction owing to its demonstrated safety and effectiveness.[8] Dinoprostone is typically administered intravaginally, and though it is generally regarded as safe, it too has potential side effects, including uterine hyperstimulation and fever.[9] Notwithstanding these apprehensions, dinoprostone continues to be extensively utilized in clinical practice, especially for individuals deemed at elevated risk due to prior health issues. Its established safety profile and effectiveness render it a popular option in handling such patients, when meticulous monitoring is crucial to mitigate any consequences.[10] Furthermore, labor induction procedures might differ markedly among distinct healthcare environments, necessitating an analysis of outcomes in diverse circumstances. Pakistan possesses a distinctive healthcare landscape marked by constrained resources, heterogeneous populations, and uneven degrees of healthcare accessibility. The efficacy of labor induction drugs may be affected by these elements; therefore, it is essential to comprehend the performance of misoprostol and dinoprostone within private healthcare environments in Pakistan.[11] Prior research has investigated the benefits and drawbacks of misoprostol and dinoprostone in various contexts; nevertheless, a significant portion of the existing studies concentrates on wider, global populations. Data regarding the utilization of these drugs in Pakistan is limited. The absence of dependable local data highlights the necessity for targeted research on the safety and effectiveness of misoprostol and dinoprostone within the private hospital context in Pakistan.[12] This study aimed to compare the effectiveness and safety of sublingual misoprostol with intravaginal dinoprostone for labor induction in a private hospital setting in Pakistan, which may enhance patient outcomes and provide valuable information for clinical practice.

METHODOLOGY

This study aimed to assess and contrast the safety and efficacy of two prevalent labor induction methods sublingual misoprostol and intravaginal dinoprostone in actual clinical environments. The research was performed in the Obstetrics Department at Maroof International Hospital in Islamabad, Pakistan, spanning 14 months from 1-August-2023, to 30-September -2024. Ethical approval for the study was granted by the hospital's Institutional Review Board (IRB) (Ref: RD 2023-10, dated 26-July-2023). All participants provided written informed consent prior to inclusion in the study.

The research comprised women aged 18 to 40 years with full-term singleton pregnancies in the vertex position, who were considered appropriate candidates for labor induction. The exclusion criteria included breech or atypical fetal presentations, fetal malformations, a history of uterine surgery, and women who declined participation throughout the research period. The inclusion and exclusion criteria were meticulously selected to provide a representative sample of pregnant women appropriate for labor induction in practical clinical environments.[13]

Participants were randomized into two groups using a simple randomization method. The ultimate analysis comprised 219 women from an original cohort of 270 recruited. Following the application of exclusion criteria, 120 women were administered sublingual misoprostol (50 mcg every 4 hours, up to 6 doses), whereas 99 women got intravaginal dinoprostone (3 mg every 6 hours), as determined by the attending obstetrician's clinical discretion. The primary outcomes were induction-to-delivery interval and mode of delivery (vaginal or cesarean).

The secondary outcomes included induction failure, maternal adverse effects (nausea, vomiting, gastrointestinal discomfort), and fetal distress. The subjects were not matched by age, parity, or Bishop Score, as the study sought to represent authentic therapeutic practice without artificial modifications.

The sample size was determined via the Raosoft sample size calculator (Raosoft, Inc., Seattle, WA, USA). Given an estimated population of 270, a confidence level of 95%, and a margin of error of 5%, the advised sample size was a minimum of 200 participants (100 per group) to identify statistically significant differences between the two groups in critical outcomes such as induction-to-delivery time, cesarean section rates, and incidence of side effects.[14] During the labor phase, essential data were gathered, encompassing the duration from induction to birth, the mode of delivery (vaginal or cesarean), and any difficulties, including fetal distress or emergency cesarean sections. Adverse symptoms, including nausea and emesis, were also documented. Data were gathered via the patients' electronic medical records and portable maternity notes, so assuring consistency and precision in the data collecting method. Statistical analysis was carried out in SPSS using the independent samples t-test and chi-square test, with a p-value of < 0.05 was considered statistically significant.

The study was executed in strict accordance with ethical norms, and all participants were apprised of the study's objectives and methodologies. Informed written permission

was acquired from all participants prior to their inclusion in the study, in compliance with ethical standards and institutional review board regulations.

RESULTS

A total of 219 patients were included in this study, with 120 patients receiving misoprostol and 99 patients receiving dinoprostone for labor induction. The analysis focused on the failure rate of induction, the induction-to-delivery interval, the rate of cesarean sections for fetal distress, and the reasons for induction. Below are the detailed findings.

The failure rates of labor induction were compared between misoprostol and dinoprostone. The results indicated that 15% of the patients who received misoprostol failed to induce labor as compared to 10% of patients that received dinoprostone. The failure rates were calculated and a chi-square test was used to determine if this difference was statistically significant. Although the failure rate was greater for misoprostol (15%) than for dinoprostone (10%), this difference was not considered statistically significant ($\div^2$ = 0.78, p = 0.38). Therefore, it would appear that both medications were similarly effective for labor induction in this study.

The average time from induction to delivery with misoprostol (8.4 hours) was significantly shorter than with dinoprostone (10.2 hours). An independent samples t-test confirmed this was statistically significant (t = -3.12, p = 0.002) indicating that misoprostol resulted in a faster labor induction than dinoprostone in this study.

Compared to the dinoprostone group (5%), the misoprostol group had a higher rate of cesarean sections performed because of fetal distress (12.5%). This result showed a marginally significant difference according to the chi-square test.

The incidence of cesarean sections due to fetal distress was higher in the misoprostol group (12.5%) compared to the dinoprostone group (5%). While this difference showed marginal statistical significance ($\div^2$ = 3.85, p = 0.05), further investigation is required to establish a definitive association between misoprostol administration and increased risk of fetal distress. Post-term pregnancy was the most frequent cause of induction, accounting for 40.4% of cases in the dinoprostone group and 41.6% of cases in the misoprostol group. The second most frequent indication in both groups was hypertension, which was marginally more common in the misoprostol group (25% vs. 20.2%).

With minor variations in the frequency of additional indications for labor induction, the two medications were mainly used for post-term pregnancy and hypertension. The reason for induction varied by drug, reflecting clinical preferences and patient characteristics.

In conclusion, misoprostol and dinoprostone had comparable failure rates; however, misoprostol was linked to a quicker induction-to-delivery period. Misoprostol also had a higher, though borderline significant, rate of cesarean sections for fetal distress. The primary reasons for induction in both groups were post-term pregnancy and hypertension. These results can aid in clinical decision-making, balancing the need for faster induction with potential risks of complications such as fetal distress.

DISCUSSION

In our study, misoprostol reduced the induction-to-delivery interval, but dinoprostone demonstrated greater safety with a lower incidence of maternal or newborn complications and cesarean deliveries. Despite misoprostol's greater incidence of side effects compared to dinoprostone, such as gastrointestinal complications and fetal distress, it is more cost-effective and simpler to administer for labor induction in our locality.

Misoprostol (PGE1) and dinoprostone (PGE2) are extensively utilized medicines for the induction of labor. These drugs primarily function by facilitating cervical ripening and stimulating myometrial contractions, hence playing a crucial role in human parturition.[15] Misoprostol, due to its cost-effectiveness, accessibility, and versatility in administration

Table 1: Comparison of Labor Induction Outcomes between Misoprostol and Dinoprostone

Values	Misoprostol	Dinoprostone
Total Patients	120	99
Failed Induction (N)	18	10
Failed Induction (%)	15%	10%
Average Interval (Hours)	8.4	10.2
Minimum Interval (Hours)	3	4
Maximum Interval (Hours)	18	20
C-Sections for Fetal Distress (N)	15	5
C-Sections for Fetal Distress (%)	12.5%	5%

Table 2: Reasons for Induction

Reason for Induction	Misoprostol (N)	Misoprostol (%)	Dinoprostone (N)	Dinoprostone (%)
Post-term pregnancy	50	41.6%	40	40.4%
Hypertension	30	25%	20	20.2%
Premature rupture of membranes	20	16.6%	10	10.1%
Fetal growth restriction	10	8.3%	15	15.1%
Other	10	8.3%	14	14.2%

routes, has demonstrated favorable outcomes in labor induction. Nonetheless, it is linked to a marginally elevated occurrence of fetal discomfort and gastrointestinal problems relative to dinoprostone, which is often delivered via the vaginal route. Nonetheless, dinoprostone demonstrates outcomes similar to misoprostol for induction-to-delivery duration, while exhibiting fewer adverse effects.[16]

The outcomes of our investigation corroborate these observations. Our findings indicate that misoprostol is linked to a markedly reduced induction-to-delivery interval (8.4 hours) in contrast to dinoprostone (10.2 hours), corroborating existing research that demonstrates misoprostol's efficacy in expediting labor.[17] Nonetheless, this benefit was accompanied by an increased occurrence of cesarean sections resulting from fetal distress (12.5%) in contrast to dinoprostone (5%). These findings correspond with a research done in Pakistan that compared misoprostol to PGE2 agents, revealing that misoprostol resulted in shorter induction-to-delivery intervals but was linked to increased adverse effects, including uterine hyperstimulation and fetal distress.[4,18]

Consistent with our data, a randomized controlled trial (RCT) performed in a Pakistani hospital, which compared misoprostol with dinoprostone in patients experiencing pre-labor rupture of membranes, revealed that the induction-to-delivery delay was reduced in the misoprostol cohort. The research further observed an elevated incidence of cesarean deliveries due to fetal distress in the misoprostol cohort, corroborating the results of our investigation.[19] Our study indicates that misoprostol is an effective and safe method for labor induction, however it is associated with a higher incidence of unfavorable outcomes compared to dinoprostone.

Our findings corroborate the conclusions of a comprehensive review and meta-analysis of eight randomized controlled trials involving 1,807 individuals, which determined that misoprostol is a safe and effective alternative to dinoprostone for facilitating vaginal delivery at term. The meta-analysis validated the shortened induction-to-delivery delay with misoprostol, aligning with our study's findings, which demonstrated that misoprostol considerably decreased the time to delivery in comparison to dinoprostone.[20]

Moreover, the results of our investigation aligned with an extensive review of randomized controlled trials concerning third-trimester induction, which included 31 active interventions. The research indicated that low-dose oral misoprostol exhibited the least likelihood of cesarean sections, while also noting that vaginal and buccal/sublingual misoprostol correlated with elevated rates of uterine hyperstimulation, a result consistent with our study's outcomes.[21] Our study noted a greater prevalence of uterine hyperstimulation in the misoprostol cohort compared to the dinoprostone group, indicating that the risk of adverse effects is a significant consideration when using misoprostol for labor induction.

A multi-center randomized controlled trial done at four university hospitals revealed that the cesarean section rate in the misoprostol group was 22.1%, in contrast to 19.9% in the dinoprostone group, with the misoprostol group exhibiting a considerably greater rate of vaginal deliveries within 24 hours (59.3% vs. 45.7%).[22] This study has some limitations. The study was conducted at a single facility, limiting the generalizability of the findings to other settings, particularly those with diverse healthcare systems. The study failed to control for variables that may influence the outcomes, such as maternal comorbidities or variations in therapy techniques, hence introducing confounding factors. The observational nature of the study indicates that randomization was impractical, resulting in potential bias. To corroborate these findings, more research with larger, multi-center designs and more robust controls is necessary.

CONCLUSION

When comparing misoprostol and dinoprostone, both demonstrated similar failure rates for labor induction, with misoprostol having a significant decrease in induction-to-delivery time. However, there was a concern of a higher, clinically borderline significant rate of c-sections for fetal distress associated with misoprostol that should be viewed cautiously in clinical practice. This data supports induction methods being individualized based on the degree to which rapid access to delivery is valuable against the risk of harm to the fetus.

LIMITATION

This study's findings should be interpreted with caution because it was conducted at a single center, limiting generalizability, and followed an observational, non-randomized design in which treatment choice depended on the attending obstetrician, introducing potential selection bias. Important confounding factors such as maternal age, parity, Bishop score, and comorbidities were not controlled or matched, and reliance on routinely recorded clinical data may have led to information bias. Although the sample size was adequate for primary outcomes, it may not have been large enough to detect differences in rare maternal or neonatal complications, further constraining the strength of the conclusions.

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REFERENCES

1. Patabendige M, Rolnik DL, Li W, Weeks AD, Mol BW. How labor induction methods have evolved throughout history, from the Egyptian era to the present day: evolution, effectiveness, and safety. American journal of obstetrics & gynecology MFM. 2024;7(1):101515. https://doi.org/10.1016/j.ajogmf.2024.101515
2. Lewis S, Zhao Z, Schorn M. Elective induction of labor or expectant management: outcomes among nulliparous women with uncomplicated pregnancies. Journal of Midwifery & Women's Health. 2022 Mar;67(2):170-7. https://doi.org/10.1111/jmwh.13313
3. Polónia-Valente R, Costa S, Coimbra C, Xavier J, Figueiredo R, Ferraz T, et al. Labor induction with a combined method (pharmacologic and mechanical): a randomized controlled trial. Journal of Gynecology Obstetrics and Human Reproduction. 2023;52(9):102649. https://doi.org/10.1016/j.jogoh.2023.102649
4. Lakho N, Hyder M, Ashraf T, Khan S, Kumar A, Jabbar M, et al. Efficacy and safety of misoprostol compared with dinoprostone for labor induction at term: an updated systematic review and meta-analysis of randomized controlled trials. Frontiers in Medicine. 2024;11:1459793. https://doi.org/10.3389/fmed.2024.1459793
5. Taliento C, Manservigi M, Tormen M, Cappadona R, Piccolotti I, Salvioli S, Scutiero G, Greco P. Safety of misoprostol vs dinoprostone for induction of labor: A systematic review and meta-analysis. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2023 Oct 1;289:108-28. https://doi.org/10.3109/14767058.2015.1046828
6. Di Tommaso M, Pellegrini R, Ammar O, Lecis S, Huri M, Facchinetti F. Safety of the use of dinoprostone gel and vaginal insert for induction of labor: A multicenter retrospective cohort study. International Journal of Gynecology & Obstetrics. 2025;168(3):1039-46. https://doi.org/10.1002/ijgo.15952
7. Ahn H. Imaging in Acute Obstetric Conditions: A Pictorial Essay. Korean Journal of Radiology. 2025;26. https://doi.org/10.3348/kjr.2025.0037
8. Chaudhary S, Anjum HH, Khan MU, Khurram A, Nazim U, Dar MM. A Systematic Review On Complications of Intrahepatic Cholestasis of Pregnancy. Pakistan Journal of Medical & Health Sciences. 2022 Dec 20;16(10):894-. https://doi.org/10.53350/pjmhs221610894
9. Galan HL, Huguelet T, editors. Emergencies in Obstetrics and Gynecology, an Issue of Obstetrics and Gynecology Clinics, E-Book: Emergencies in Obstetrics and Gynecology, an Issue of Obstetrics and Gynecology Clinics, E-Book. Elsevier Health Sciences; 2022 Sep 21. https://books.google.com.pk/books?hl=en&lr=&id=mPSKEAAAQBAJ&oi=fnd&pg=PP1&dq=Sullivan+C,+et+al.+Sublingual+Misoprostol+for+Labor+Induction.+Am+J+Obstet+Gynecol.+2017%3B+216(1):+5662.&ots=tCYimyjNai&sig=0U17pZQIBUlDvllgIq4YvVlQXV8&redir_esc=y#v=onepage&q&f=false
10. Chua JYX, Choolani M, Lalor JG, Yi H, Chong YS, Shorey S. Perceptions of healthcare professionals regarding labour induction and augmentation: A qualitative systematic review. Women and Birth. 2024;37(1):79-87. https://doi.org/10.1016/j.wombi.2023.09.003
11. Ansar H. Framing Misoprostol Programs in Pakistan Within a Postcolonial Context: The Ohio State University; 2022. http://rave.ohiolink.edu/etdc/view?acc_num=osu1650561525188022
12. Israr M, Noor-e-Marfa Amin TM, Khan SY, Basit A. Contemporary-Issues-in-Health Contemporary Issues in Health: AJPO Journals USA LLC; 2023. https://books.google.com.pk/books?hl=en&lr=&id=FKLUEAAAQBAJ&oi=fnd&pg=PA4&dq=Israr+M,+Noor-e-Marfa+Amin+TM,+Khan+SY,+Basit+A.+Contemporary-Issues-in-Health+Contemporary+ Issues+in+Health:+AJPO+Journals+USA+LLC%3 B+2023&ots=0 sKIMDpSKI&sig=Xl60QL8tW5RlBV0BlydDt-RpEfk&redir_esc=y#v=onepage& q&f=false
13. Ratiu O, Ratiu D, Mallmann P, Di Liberto A, Ertan AK, Morgenstern B, Mallmann MR, Ludwig S, Gruettner B, Eichler C, Thangarajah F. Oral Misoprostol for the Induction of Labor: Comparison of Different Dosage Schemes With Respect to Maternal and Fetal Outcome in Patients Beyond 34 Weeks of Pregnancy. in vivo. 2022 May 1;36(3):1285-9.DOI: https://doi.org/10.21873/invivo.12828
14. Ramadan M, Bashour G, Eldokmery E, Alkhawajah A, Alsalhi K, Badr Y, et al. The efficacy and safety of oral and vaginal misoprostol versus dinoprostone on women experiencing labor: A systematic review and updated meta-analysis of 53 randomized controlled trials. Medicine. 2024;103(40):e39861. https://doi.org/10.1097/MD.0000000000039861
15. Young DC, Delaney T, Armson BA, Fanning C. Oral misoprostol, low dose vaginal misoprostol, and vaginal dinoprostone for labor induction: Randomized controlled trial. PloS one. 2020;15(1):e0227245. DOI: 10.1097/MD. 0000000000039861
16. Chang TA, Li YR, Ding DC. Oxytocin and vaginal dinoprostone in labor induction: A systematic review and meta-analysis. International Journal of Gynecology & Obstetrics. 2024;166(2):626-38. https://doi.org/10.1002/ijgo.15443
17. Huang H, Ding G, Li M, Deng Y, Cheng Y, Jin H. Menopause and stress urinary incontinence: the risk factors of stress urinary incontinence in perimenopausal and postmenopausal women. Journal of Obstetrics and Gynaecology Research. 2023;49(10):2509-18. https://doi.org/10.1111/jog.15742
18. Fatima T, Jabeen F, Mukhtar B. Effectiveness of oral PGE1 Versus Intracervical PGE2 in induction of labor. Journal of The Society of Obstetricians and Gynaecologists of Pakistan. 2024;14(1):11-5. https://jsogp.net/index.php/ jsogp/article/view/679 /831
19. Mukherjee S, Valson H, Balaji K. A study of effect of oral PGE1 and cervical PGE2 on induction of labor and mode of delivery. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2018 Jun 1;7(6):2161. DOI:10.18203/2320-1770.ijrcog20181995
20. Psyche V. Category–Sexual Health and Contraception. 2021. https://doi.org/10.1016/j.whi.2020.10.003
21. Mendez-Figueroa H, Bicocca MJ, Gupta M, Wagner SM, Chauhan SP. Labor induction with prostaglandin E1 versus E2: a comparison of outcomes. Journal of Perinatology. 2021;41(4):726-35. DOI https://doi.org/10.1038/s41372-020-00888-5
22. Curtis KM. US selected practice recommendations for contraceptive use, 2024. MMWR Recommendationsand Reports.2024;73.https://www.cdc.gov/mmwr/volumes/73/rr/rr7303a1.htm?scid=rr7303a1w

Original Article **Open Access**

Clinical Evaluation of injectable Mitomycin-C in Trabeculectomy for Glaucoma Patients

Mehvash Hussain, Sania Ishaque, Fizzah Farooq, Muhamamd Muneer Quraishy

ABSTRACT

Objective: To evaluate the efficacy of injectable Mitomycin-C (MMC) administered at the bleb site during trabeculectomy in patients with glaucoma.

Study Design and Setting: This cross-sectional study was conducted at the Department of Ophthalmology, Unit-1, Dow Medical College, Dr. Ruth K. M. Pfau Civil Hospital Karachi, and SMBB Trauma Centre from January to June 2022.

Methodology: Data were obtained through non-probability consecutive sampling. After obtaining informed consent, patients meeting the diagnostic criteria and undergoing trabeculectomy were enrolled. Demographic data, including age, gender, and eye laterality, were recorded. Efficacy was defined as a postoperative intraocular pressure (IOP) reduction of more than 30% compared to preoperative values. Ophthalmic examinations included visual acuity, refraction, slit-lamp biomicroscopy, gonioscopy, and IOP measurement. The effect of MMC across different subgroups was analyzed using an independent t-test, with a p-value =0.05 considered statistically significant.

Results: A total of 62 patients underwent trabeculectomy with injectable MMC. The mean preoperative IOP was 32.81 ± 13.13 mmHg, while the mean postoperative IOP at one month was 13.88 ± 5.90 mmHg, indicating a significant reduction (p = 0.01). Over 30% IOP reduction was achieved in the majority of cases. Only five patients developed postoperative complications, including fibrosis and flat blebs.

Conclusion: Injectable Mitomycin-C is an effective adjunctive therapy in trabeculectomy, significantly lowering intraocular pressure and enhancing surgical success while minimizing postoperative scarring and surgical failure.

Key Words: Efficacy, Glaucoma, Intraocular Pressure (IOP), Mitomycin C and Trabeculectomy

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INTRODUCTION

Glaucoma is a specific type of optic neuropathy which is defined by visual field loss, optic disc damage, and typically but not always increased IOP. Glaucoma has been a major cause of deterioration of vision especially in the developed world. Refractory glaucoma refers to glaucoma that is resistant to conventional treatment. In Karachi, Pakistan estimated 9.6% of the population have a confirmed diagnosis of glaucoma[1]. Globally, glaucoma is estimated to impact 79.6 million people till 2020.[2] Trabeculectomy is a type of filtration surgery commonly performed to reduce intraocular pressure (IOP) in glaucoma patients. It establishes an alternative pathway for aqueous fluid to drain into the subconjunctival space.[3] It is commonly believed that vision can be maintained in glaucomatous eyes if eye pressure is kept below the level at which injury to the optic nerve has previously taken place. In the past, the success rate of this surgery was restricted due to postoperative fibroblast proliferation and scarring of the filtering bleb. Various adjunctive modifications, including antimetabolites like MMC and anti-VEGF agents, have been utilized to prevent scarring.[4]

Trabeculectomy is a surgical procedure used to treat glaucoma by creating an additional channel for the filtration of aqueous humor. The success of this procedure relies heavily on the natural ocular wound healing response. Research has shown that the inhibition of fibroblast proliferation is crucial for successful filtering surgery.[5]

Mitomycin C (MMC) is an anticancer agent obtained from the soil bacterium *Streptomyces caespitosus* that acts as a

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Deoxyribonucleic acid cross-linker and leads to inhibition the cascade of fibroblast growth.[6] Mitomycin C is an antiproliferative agent that has been widely used as an adjunct in trabeculectomy surgery. By inhibiting fibroblast proliferation, Mitomycin C helps to prevent scarring and promote the formation of a functional filtering bleb.[7] Mitomycin C is commonly used in trabeculectomy to minimize episcleral fibrosis in post-operative period and prevent failure of bleb caused by scarring during the healing of wound.[8] Mitomycin C enhances the outcomes of glaucoma filtration surgery (trabeculectomy) by ensuring effective long-term intraocular pressure (IOP) control. Mitomycin C has been proven to optimize the success rate of trabeculectomy in patients with refractory glaucoma, particularly those with: African ancestry, uveitis and congenital glaucoma.[9] While Mitomycin C is an effective adjunct in trabeculectomy, its use can be associated with complications such as: thin-walled blebs, bleb leaks and scleromalacia.[10] Therefore, careful consideration of Mitomycin C dosage and exposure time is essential to minimize the likelihood of experiencing adverse effects.

Mitomycin-C is applied to the tissues using surgical sponges during the procedure, but alternate method of application is also used in which Mitomycin C can be given in injectable form.

Mitomycin C is applied using a sponge, which is soaked in the medication and placed on the eye in subconjunctival space for 5 minutes. Both the dose and time for sponge can be altered. Hence, this method is still widely used, but it can be associated with issues like: varying concentrations and sizes of sponges[11], inconsistent dosing, increased risk of complications and difficulty in determining the exact amount of medication delivered.

Injectable Mitomycin C is a relatively new approach that offers a more precise and controlled delivery of the medication. It also proves to assist in better IOP control and lesser surgical complication. Injectable method involves injecting Mitomycin C directly into the subconjunctival space, allowing for: precise dosing and reduced risk of overdose[11], targeted delivery to the specific area of the eye and reduced risk of complications associated with sponge application.[12]

Mitomycin C injectible is prepared with dilution in dose of 0.1ml of 0.2mg/ml MMC with 0.1 ml of 1% lidocaine. Subtenon injection of Mytomycin C hydro dissects the conjunctiva off the sclera, aiding in flap dissection[11].

Qualitative and quantitative analysis using optical coherence tomography (OCT) revealed blebs arising after MMC enhanced trabeculectomy had optimal functionality, characterized by a low reflectivity index and a cystoid pattern. Conversely, trabeculectomies performed without MMC exhibited mixed OCT patterns (layered or diffuse), which correlated with high infrared reflectivity and reduced functionality.

Rationale of this study is that injectable Mitomycin C is alternate method which is less time consuming, easier to inject in the desired tissue and can be spread to make a uniform bleb. Dose of MMC used is less than sponge method resulting in less harm to the adjacent tissues due to controlled delivery.

METHODOLOGY

A cross-sectional study was undertaken within the facility of Department of Ophthalmology and Visual Sciences, Dr Ruth K.M.Pfau, Civil Hospital Karachi, Shaheed Mohtarrma Benazir Bhutto (SMBB) Trauma Center, Dow Univeristy of Health Sciences (DUHS), Karachi. Study period was from January 2022 to June 2022. Ethical approval for the study was granted by the Institutional Review Board (IRB) of Dow University of Health Sciences (IRB/DUHS/Approval /2022/2118). All participants were provided with written consent to get it signed before registering in the research study process. Confidentiality of the data of participants was ensured. Men and women aged 20–70 years with primary or secondary glaucoma were included if they were scheduled for trabeculectomy (alone or with cataract surgery), especially if they were not taking medicines regularly or wanted surgery only to control eye pressure. Patients were not included if they had other health problems like asthma, high blood pressure, or diabetes, if they had eye surgery for reasons other than glaucoma, or if they had previous glaucoma operations such as valve, shunt, or goniotomy procedures.

Sample size of this study was determined using open EPI sample size calculator. Taking treatment success rate of trabeculectomy augmented with MMC reported to be 78.7% according to study by Qin ZX et al, margin of error 5%, confidence level 95%, sample size was calculated to be 65. Hence we enrolled 62 patients for our study.[13]

Non probability consecutive sampling was taken into account. Patients were usually diagnosed in out patient department (OPD) where they were assessed for screening of glaucoma. Later gonioscopy was done in investigation room. They were booked for surgery. After the pre requisite pre op assessment of lab tests apart from ocular assessment they were given a date for augmented trabeculectomy. Pre op lab tests included complete blood count (CBC), blood pressure monitoring, random blood sugar (RBS) and screening for viral markers (Hepatitis B and Hepatitis C). All participants had to go through extensive and crisp ophthalmic assessments of vision, refraction, slit lamp bio microscopy, gonioscopy, IOP measurement using applanation tonometry and fundoscopy. All surgeries were performed by a single experienced surgeon in the same surgical center under topical anesthesia to rule out surgeon factor. Several steps were ensured to improve the effectiveness of the surgical procedure. In order to avoid the leakage to the surface, incision for trabeculectomy was made small. A blunt 30-gauge cannula

was advanced 7 to 8 mm from the limbus and the MMC solution was delivered subconjunctivally in a calculated dose on 0.2mg/ml, behind the intended site of the surgical flap. The conjunctival entry site was delicately compressed using a surgical sponge (free of MMC) to prevent any escape of the injected MMC. Afterwards, the blunt cannula was removed and a sponge soaked in normal saline was used to spread the solution more widely over the area. The conjunctival periotomy was then completed. Hemostasis was achieved with bipolar cautery. Generous irrigation with balanced salt solution was followed by.

Trabeculectomy was carried out using the standard technique. A 3 × 3 mm scleral flap was outlined with a diamond knife preset to a depth of 300 ìm. Dissection of the partial-thickness scleral flap was performed using a 57 blade. A paracentesis was made in the temporal cornea using a 1-mm side-port blade. A sclerotomy was created with a Kelly punch, followed by the formation of a peripheral iridectomy using DeWecker scissors. The scleral flap was then secured in position with two fixed 10-0 nylon sutures (non-releasable) at its corners.

Balanced salt solution was introduced into the anterior chamber, and the surgeon confirmed flow through the trabeculectomy site using surgical sponges. If the flow appeared excessive, additional sutures were applied. Once a satisfactory flow was established and the anterior chamber remained stable, the conjunctiva was closed with a continuous 9-0 nylon suture on a vascular needle. At the end of the procedure, the conjunctival incision was carefully inspected to ensure it was watertight.

Patients were followed in out patient department a day after surgery for assessment. In the post op assessment intraocular pressure was measured weekly, after 15 days and then after one month for final outcome. Pre operatively intraocular pressure was recorded. While taking IOP each time several precautionary measures were taken. Intraocular pressure was taken after instilling anesthetic drops (lignocaine) and waiting for 1-2 min for the effect of anesthesia to start. Fluorescein strip was used to stain cornea and intraocular pressure measured under blue cobalt filter. It was ensured that pupil is not dilated. Each time same consultant took intraocular pressure so that extend of compression while place applanation prism was homogenous. A total of three readings were taken on different intervals and mean calculated. This is a universally accepted criterion of measuring to eliminate any human error on part of patient and consultant both. Excessive pressure, squeezing and abnormal tear film can change the values in one reading A reduction of more than 30% between preoperative and postoperative intraocular pressure was defined as efficacy as proven by study by Do JL et al which concluded mean change of pre and post operative intraocular pressure of greater than 30% after use of mitomycin-C as effective success measurement tool.[14]

The mean preoperative intraocular pressure (IOP) in this study was 32.81±13.13mmHg, while the mean postoperative IOP at one month after surgery was 13.88±5.90mmHg. The p-value was 0.01, as shown in Table 1. Stratification of gender concerning efficacy showed that among males, 40 (70.2%) achieved efficacy, while 1 (20%) did not. Among females, 17 (29.8%) achieved efficacy, whereas 4 (80%) did not. The p-value was 0.04, as tabulated in Table 2

Stratification of age in relation to efficacy revealed that 21 patients (36.8%) in the 20-45 years age group and 36 patients (63.2%) in the 46-70 years age group achieved efficacy. In contrast, 3 patients (60%) in the 20-45 years age group and 2 patients (40%) in the 46-70 years age group did not achieve

Figure-1: Efficacy Distribution (n=62)

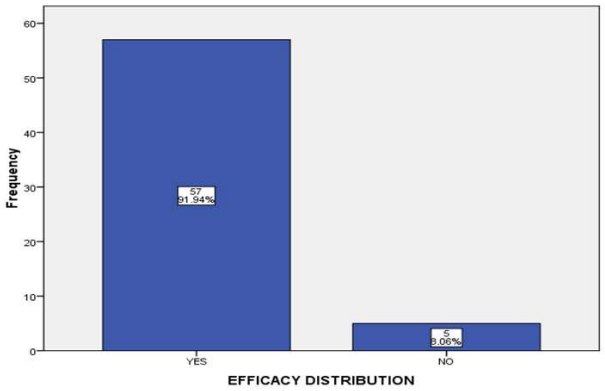

Table-1 : Mean Preoperative And Postoperative Intraocular Pressure (N=62)

Intra ocular pressure at 1 week		
Pre- Operative IOP	Post-Operative IOP	p-Value
25.1±10.34	19.78±6.20	0.32
Intra ocular pressure at 2 weeks (mmHg)		
28.1±9.19	16.42±10.2	0.01
Intra ocular pressure at 1 month (mmHg)		
32.81±13.13	13.88±5.90	0.01

Table-2: Efficacy According To Gender

GENDER	**EFFICACY**		**TOTAL**
	YES	NO	
MALE	40 (70.2%)	01 (20%)	41 (66.1%)
FEMALE	17 (29.8%)	04 (80%)	21 (33.9%)
TOTAL	57 (100%)	05 (100%)	62 (100%)
p-VALUE	0.04		

Table-3: Efficacy According To Age Groups (n=62)

AGE	**EFFICACY**		**TOTAL**
	YES	NO	
20-45	21 (36.8%)	03 (60%)	24 (38.7%)
46-70	36 (63.2%)	02 (40%)	38 (61.3%)
TOTAL	57 (100%)	05 (100%)	62 (100%)
p-VALUE	0.28		

efficacy. P-value was 0.28. Results of stratification according to age groups are tabulated in Table 3. Stratification of laterality in reference to efficacy showed that among patients with right eye involvement, 34 (59.6%) achieved efficacy, while 2 (40%) did not. In contrast, among those with left eye involvement, 23 (40.4%) achieved efficacy, whereas 3 (60%) did no. P-value was 0.34.

further stratification was also for outcome efficacy in relation to the socio economic status, concluding that no statistical significance was found as p value = 0.76. Amongst the 5 patients which didn't achieve efficacy 2 patients (3.2%) had flat, a-vascularized bleb and hence were kept on anti-glaucoma drugs for 2 months with close monitoring. Plan for re surgery will be done in future. 2 patients(3.2%) reported to have fibrosis while one patient had siedel test positive on the first post op day. He/she was taken to operation theater the very next day and sutures applied to re secure the bleb. Stratification via t-test showed no significant result for complications as p value of greater than 0.05 was noted.

DISCUSSION

Our study showed that overall efficacy of pre and post op Intra ocular pressure was 91.9%. Multiple clinical trials and research studies have validated the efficacy and safety of mitomycin-C application in sponge soaked and place at the scleral site rather than the injectable form during trabeculectomy. Hence there is shortage of comparative literature especially locally.

et al conducted a retrospective study on 35 and 36 eyes of angle closure and open angle glaucoma respectively that underwent trabeculectomy.[15] Our study evaluated prospectively on a similar comparative sample size of 62 eyes in total.

A study conducted in San Diego, USA, compared sub conjunctival mitomycin C with direct scleral mitomycin C application.[14] The mean age reported was 69.9 ± 13.4 years in the injection group. Results of our study concluded that mean age of inectable group was reported to be 55.14±8.49 years. The comaprison of both studies showed roughly equal mean age in years.

A comprehensive Cochrane review by Wilkins et al., analyzing 11 clinical studies with a total of 698 patients, demonstrated that Mitomycin-C significantly lowers the risk of surgical failure in both primary trabeculectomy and in eyes considered at high. [16] Research on primary trabeculectomy using low-dose MMC showed that intraocular pressure (IOP) remained at or below 15 mmHg in greater than 80% of patients after one year and in 60% after six years. This study followed patient for 12 months. While our study followed patients with post op Intra ocular pressure after only one month of surgery hence results cannot be comparable.

Lester M et al in his study, discussing post operative intraocular pressure after subconjunctival mitomycin-C injecting in non penetrating glaucoma surgeries, concluded that average intraocular pressure before the application of mitomycin-C injections was 17 ± 6.6 mmHg while post operatively intraocular pressure after injectable mitomycin-C after 6 month was 13.9 ± 2.9 mmHg.[17] In our study the mean post operative intraocular pressure came out to be 13.88±5.90 mmHg. This is quiet close to the earlier discussed study.

Annen DJ et al conducted a retroepcetive pilot study that included a majority of high-risk patients reported 84% achievement rate at a one-year follow-up when low dose injectable mitomycin-C of 0.2 mg/mL was applied for five minutes.[18] While our study reported that 57 (91.1%) patients acheived >30% efficacy within 1 month using 0.2mg/ml injectable mitomycin-C. Annen and Stürmer, who used the same mitomycin-C concentration for one minute, found that 88% of cases maintained an intraocular pressure below 21 mmHg after about a year, with 8.8% of cases exhibiting an avascular bleb. Hence the dose of this study was same as the inectable dose that we used and our study results showed avascular bleb in 3.2%.

Singh et al analyzed a consecutive series of 20 eyes that underwent trabeculectomy with intraoperative application of 0.02 mg/mL mitomycin-C, reporting an overall success rate of 85%.[19] Among these cases, two experienced recurrent leaks, while another two developed scleral necrosis, resulting in ciliary body exposure. The authors warned that although rare, such complications can still arise even with lower mitomycin-C doses. They recommended that using reduced mitomycin-C concentrations or placing mitomycin-C in the Sub-Tenon's space without the need for scleral dissection could help mitigate the risk of scleral necrosis. Similarily 2 (3.2%) of our patients had fibrosis and 1 (1.6%) had bleb leak with the adjunctive use of 0.2mg/ml injectable mitomycin-C.

There are other studies too that reported complications with the use of mitomycin C in injectable form. Akova YA et al documented incidence of scleromalacia in two pediatric patients treated with 0.4 mg/cc mitomycin-C for five minutes.[20] Likewise, Fourman described a group of five patients who experienced scleritis within 3 to 24 weeks after receiving mitomycin-C during inferior trabeculectomy.[21] These complications were not found in our study.

Choosing mitomycin injection during trabeculectomy allows ophthalmologists to accurately determine the exact amount of antimetabolite delivered to the surgical site, ensuring consistent dosing for each patient. Additionally, intraoperative injections offer the benefit of broader mitomycin distribution through subconjunctival dissipation, resulting in a wider area of application. There were few shortcomings of our study. Our study is single centered with a smaller sample size. We looked for a single drug augmented in

trabeculectomy with a shorter post op assessment of only 1 month. Hence, a multi centered study of a larger population is a necessity in future to interpret surgical complications on a broader aspect. There is also a need of studies to comapare effectiveness of mitomycin with other drugs like 5-fluorouracil that can be augmented in tabeculectomy too. Evaluation of productiveness of standardized pre-configured kits of mitomycin formulations, such as Mitosol is a necessity of future.

LIMITATIONS

There were few shortcomings of our study. Our study is single centered with a smaller sample size. We looked for a single drug augmented in trabeculectomy with a shorter post op assessment of only 1 month. Hence, a multi centered study of a larger population is a necessity in future to interpret surgical complications on a broader aspect. There is also a need of studies to comapare effectiveness of mitomycin with other drugs like 5-fluorouracil that can be augmented in tabeculectomy too. Evaluation of productiveness of standardized pre-configured kits of mitomycin formulations, such as Mitosol is a necessity of future.

CONCLUSIONS

Our study results concluded suggest that the augmentation of injectable Mitomycin-C during trabeculectomy is required for improving surgical outcomes. It enhances the bleb survival and provides better intraocular pressure control, reducing the risk of surgical failure. Injectable Mitomycin-C form also allows for more uniform drug distribution, potentially minimizing complications compared to traditional sponge-applied methods.

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REFERENCES

1. Nawab A, Sheikh J, Alam S, Kamali B. Tackling the Silent Thief of Sight: Assessing Glaucoma Awareness, Knowledge, and Risk of Prevalence in Karachi. Pakistan Journal of Public Health. 2024 Mar 29;14(1):47-50. https://doi.org/10.32413/pjph.v14i1.680
2. Abdelkareem HA. Relationship between Glaucoma Severity, Vision-related Quality of Life and Perceived Wellbeing among Older Adults. Damanhour Scientific Nursing Journal. 2024 Dec 1;2(4):114-33. http://dx.doi.org/10.21608/dsnj.2025.334093.1043
3. Theventhiran AB, Kim G, Yao W. Fornix-based versus limbal-based conjunctival trabeculectomy flaps for glaucoma. Cochrane Database of Systematic Reviews. 2021(8). https://doi.org/10.1002/14651858.CD009380.pub2
4. Dave B, Patel M, Suresh S, Ginjupalli M, Surya A, Albdour M, Kooner KS. Wound Modulations in Glaucoma Surgery: A Systematic Review. Bioengineering. 2024 Apr 30;11(5):446. https://doi.org/10.3390/bioengineering11050446
5. Shao CG, Sinha NR, Mohan RR, Webel AD. Novel therapies for the prevention of fibrosis in glaucoma filtration surgery. Biomedicines. 2023 Feb 21;11(3):657. https://doi.org/10.3390/biomedicines11030657
6. Baindara P, Mandal SM. Bacteria and bacterial anticancer agents as a promising alternative for cancer therapeutics. Biochimie. 2020 Oct 1;177:164-89. https://doi.org/10.1016/j.biochi.2020.07.020
7. Sacchi M, Tomaselli D, Ruggeri ML, Aiello FB, Sabella P, Dore S, Pinna A, Mastropasqua R, Nubile M, Agnifili L. Fighting Bleb Fibrosis After Glaucoma Surgery: Updated Focus on Key Players and Novel Targets for Therapy. International Journal of Molecular Sciences. 2025 Mar 5;26(5):2327. https://doi.org/10.3390/ijms26052327
8. Azhany Y, Siti-Fairuz MY, Ahmad A, Yusuf WN, Hou LJ, Liza-Sharmini AT, Hamzah JC. Modulation Agents of Wound Healing in Ocular Surgeries. Malaysian Journal of Medicine and Health Sciences. 2024 Jan 1;20(1):293-303. https://doi.org/10.47836/mjmhs.20.1.37
9. Mamidipaka A, Shi A, Addis V, He J, Lee R, Di Rosa I, Salowe R, Ying GS, O'Brien J. Outcomes of Trabeculectomy and Predictors of Success in Patients of African Ancestry With Primary Open Angle Glaucoma. Journal of Glaucoma. 2025 Feb 1;34(2):127-35. http://dx.doi.org/10.1097/IJG.0000000000002503
10. Kavitha S, Tejaswini SU, Venkatesh R, Zebardast N. Wound modulation in glaucoma surgery: The role of anti-scarring agents. Indian Journal of Ophthalmology. 2024 Mar 1;72(3):320-7. http://dx.doi.org/10.4103/IJO.IJO_2013_23
11. Maheshwari D, Pillai MR, Hm P, Kader MA, Rengappa R, Pawar N. Long-term safety and efficacy of injection mitomycin C (MMC) versus sponge application in trabeculectomies. European Journal of Ophthalmology. 2024 Aug 2:11206721241266981. https://doi.org/10.1177/ 11206721241266
12. Zheng J, Zhang A. Efficacy and safety of intraoperative injection of mitomycin C during trabeculectomy: a systematic review and meta-analysis. International Ophthalmology. 2024 Sep 6;44(1):372. https://link.springer.com/article/10.1007/s10792-024-03291-7

13. Qin ZX, Ying X, Han Q, et al. Outcomes and risk factors for failure of trabeculectomy in glaucomatous patients in Southwest China: a 325 eyes analysis. Int J Ophthalmol. 2023;16(3):367–374. https://pmc.ncbi.nlm.nih. gov/articles/PMC10009591/

14. Do JL, Xu BY, Wong B, Camp A, Ngai P, Long C, Proudfoot J, Moghimi S, Yan D, Welsbie DS, Weinreb RN. A randomized controlled trial comparing subconjunctival injection to direct scleral application of mitomycin C in trabeculectomy. American journal of ophthalmology. 2020 Dec 1;220:45-52. https://doi.org/ 10.1016/j.ajo.2020.07.002

15. Quist MS, Brown N, Bicket AK, Herndon LW. The Short-term Effect of Subtenon Sponge Application Versus Subtenon Irrigation of mitomycin-C on the outcomes of trabeculectomy with express glaucoma filtration device: a randomized trial .J. Glaucoma. 2018 Feb;27(2):148-56. http://dx.doi.org/10.1097/IJG.0000000000000830

16. Wilkins M, Indar A, Wormald R. Intra-operative mitomycin C for glaucoma surgery [review] Cochrane Database Syst Rev. 2005;4:CD002897. https://pubmed.ncbi.nlm.nih.gov/16235305/

17. Iester M, Ravinet E, Mermoud A. Postoperative subconjunctival mitomycin-C injection after non-penetrating glaucoma surgery. Journal of ocular pharmacology and therapeutics. 2002 Aug 1;18(4):307-12. https://doi.org/10.1089/1080768026021847

18. Annen DJ, Stürmer J. Follow-up of a pilot study of trabeculectomy with low dosage mitomycin C (0.2 mg/mL for 1 minute). Independent evaluation of a retrospective nonrandomized study. Klin Monbl Augenheilkd. 1995;206(5):300–302. German. https://doi.org/10.1055/s-2008-1035446

19. Singh J, O'Brien C, Chawla HB. Success rate and complications of intraoperative 0.2 mg/mL mitomycin C in trabeculectomy surgery. Eye (Lond) 1995;9(Pt 4):460–466. http://dx.doi.org/10.1038/eye.1995.107

20. Akova YA, Koç F, Yalvaç I, Duman S. Scleromalacia following trabeculectomy with intraoperative mitomycin C. Eur J Ophthalmol. 1999;9(1):63–65. http://dx.doi.org/10.1177/112067219900900110

21. Fourman S. Scleritis after glaucoma filtering surgery with mitomycin C. Ophthalmology. 1995;102(10):1569–1571. https://doi.org/10.1016/S0161-6420(95)30829-9

Original Article **Open Access**

Use of Dexmedetomidine as adjunct with Bupivacaine in TAP block for postoperative pain relief in patients undergoing laparoscopic cholecystectomy

Meamoona Shabbir, Ayesha, Atif Nazir, Mahnoor Nasir, Tanzeela Iram, Sidra Shabbir

ABSTRACT:

Objective: To analyze adjunct effect of Dexmedetomidine along with Bupivacain in TAP block for postoperative analgesia in laparoscopic cholecystectomy.

Study Design and Setting: Prospective interventional study was conducted 1st September 2022 to 31st January 2023 at Anesthesia department of PAF Hospital Islamabad, affiliated with Air University.

Methodology: A total of 60 patients undergoing elective laparoscopic cholecystectomy between age 18 to 60 years were included. Patients having hypertension, heart disease, diabetes were excluded. Group A patients were given TAP block using 10ml 0.25 % Bupivacaine on each side.Group B patients were given 10ml of 0.25% Bupivacaine with injection Dexmedetomidine 0.5 µg/kg in divided dose on each side under ultrasound guidance. Patients were followed for postoperative pain in first 24 hours.

Results: Data was analyzed on SPSS 25.Mean ± SD of pain score on VAS was 6.54 ± 1.98 versus 3.54 ± 1.87 at 4 hours (p value =0.0001) , 5.51 ± 1.16 versus 2.89 ± 1.65 at 8 hours (p value=0.0001) , 4.89 ± 1.11 versus 2.13 ± 1.25 at 12 hours (p value=0.0001) ,4.47 ± 1.07 versus 1.63 ± 0.85 at 24 hours (p value=0.0001) in group A and B respectively. Stratification was done with age, gender, ASA status and duration of surgery .Results of study were not affected by these factors.

Conclusion: Dexmedetomidine when added as an adjunct to Bupivacaine is better than Bupivacaine alone in TAP block for postoperative analgesia after laparoscopic cholecystectomy.

Keywords: Dexmedetomidine, laparoscopic cholecystectomy, transverses abdominas plane block

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INTRODUCTION:

Laparoscopic cholecystectomy was introduced four decades back and with the passage of time it has replaced traditional open cholecystectomy.[1] The benefits of laparoscopic cholecystectomy include shorter surgical time and hospital stay, less blood loss and early mobilization. However in 6-8 % of patients complications are still prevalent.[2] The most common complication reported after laparoscopic cholecystectomy is postoperative pain. Moderate to severe pain is reported in first 24 hours. The pathophysiology of postoperative pain involves visceral pain due to gas insufflations.[3] Postoperative pain is the most common cause of readmission in hospital after discharge. If left untreated it may lead to development of chronic postsurgical pain.[4] Review of literature showed multiple modalities for managing postoperative pain after cholecystectomy. Laproscopy using three ports, creating pneumoperitonium with low pressure, extraction of umbilical port, irrigation of abdominal cavity with saline at the end of procedure and ensuring maximum aspiration of pneumoperitonium are key surgical factors that can help to minimize postoperative pain.

Pharmacological agents used to treat postoperative pain include NSAIDS, steroids, COX 2 inhibitors, dexamethasone

and local anesthetic infiltration at port side. However, none of them proved to be 100% effective. Intravenous Ketamine, Opioids and preoperative Pregabalin have got a moderate to high quality evidence in comparison to other intravenous analgesics. Most common used drugs for postoperative pain are opioids. However both systemic and neuraxial opioid administration are associated with frequent dose dependent adverse effects including nausea, vomiting, pruritus, sedation, respiratory depression and hyperalgesia. [5] Apart from traditional intravenous analgesics various nerve blocks are also being practiced.TAP block introduced in 2001 involves injection of local anesthetic in triangle of petit between internal oblique and transverses abdominus muscle. Initially it was done by blind landmark technique till 2007, when it was attempted under ultrasound guidance with more success rate reported than blind technique. In ultrasound guided approach, neurovascular fascial plane was identified and drug was injected in this plane to block the dermatomal afferents of T7-11 intercostal nerves, T12 subcostal nerve, ilioinguinal and iliohypogastric nerves and cutaneous branches of L1-3 nerves. These nerves give sensation to the anterior and lateral abdominal wall as well as the parietal peritoneum.[5]

The TAP block can be used for postoperative analgesia management in open and laparoscopic abdominal surgeries as well as inpatient and outpatient surgical procedures. TAP block may be performed unilaterally, left or right sided in specific procedures. Unilateral blocks are preferred in cholecystectomy, appendectomy, nephrectomy, renal transplants, while bilateral TAP blocks are used in midline and transverse abdominal incisions, such as umbilical or ventral hernia repair, cesarean deliveries, hysterectomy, and prostatectomy.TAP blocks are part of multimodal pain management for abdominal surgeries which adds analgesic benefit to the patients by reducing postoperative opioid requirements. Pain relief with TAP block has been found to be superior as compare to infiltration of local anesthetics.[6] Although it can be done at anytime during surgery, the use of preoperative TAP block was associated with decreased intraoperative opiate use during minimally invasive cholecystectomy.[7] The TAP block aims to provide sensory blockage of the anterior abdominal wall and generally does not affect visceral pain.[8] Various approaches used for TAP block includes posterior, sub costal and rectus sheath approach.[9] Since local anesthetics have got short half life, different adjuvants have been practiced to enhance quality and duration of local anesthetics.[10] Dexmedetomidine is one of the most commonly used adjuvant in nerve blocks. It is highly selective alpha 2 agonist with sedative, analgesic and sympatholytic properties. It has got both central and peripheral mediated action. In nerve blocks its mode of action involves vasoconstriction at the site of injection, hence causing delay in absorption of drug and prolongs its action. Moreover it acts directly on peripheral nerves to enhance both duration and quality of block. The rationale of this trial is to evaluate role of dexmedetomidine as adjuvant in TAP block in addition to bupivacaine so as to enhance effect of bupivacaine in terms of pain relief. Since limited data is available at national level, results of this trial will help us to improvise perioperative analgesia management in laparoscopic cholecystectomy in our population using recent modalities of ultrasonography.

METHODOLOGY:

This prospective interventional study was done in Anesthesia department of PAF hospital(affiliated with Air University) over a period of 5 months from 1st September 2022 to 31st January 2023 after taking ethical committee approval dated 10th June 2022 (IRB No CPSP/REU/ANS-2019-137-2237) . Sample size was calculated with following assumptions (power of significance=5%, Power of test = 90% , Test value of population mean = 4.58 , Anticipated Population mean = 1.808 , Population SD = 0.64 [11]) sample size comes out to be 60 (30 patients in each group A and B).Patients with age 18-60 years, ASA [12] status I-II, undergoing elective laparoscopic cholecystectomy were included in this study. Patients with history of hypertension, ischemic heart disease, diabetes and those who were converted to open cholecystectomy were excluded from this trial.[11] Our hypothesis was addition of dexmedetomidine to bupivacain in TAP block improves postoperative analgesic effect as compared to bupivacain alone.All patients included in this study were recruited from operation theatre of PAF Hospital Islamabad. A detailed history and examination was done lab investigations including blood CP, BSR, LFTs, PT, APTT, ECG were checked. An informed written consent was taken from patients. Patients were divided into two groups A and B by random allocation by table of random numbers. Patients were premedicated with injection Midazolam 2 mg intravenously, injection Ondansetron 4mg. Induction of anesthesia was done with injection Propofol 2mg/kg and injection Atracurium 0.5 mg/kg. Patients were ventilated for 3 minutes after induction and intubated with endotracheal tube (ETT) of appropriate size. Vitals were monitored. Anesthesia was maintained with 100% oxygen and 1.2% Isoflurane. Lateral approach for TAP block was selected.Linear probe of ultrasonography was placed in axial plane midway between subcostral margin and iliac crest in midaxillary line. Three layers of abdominal wall muscles named external oblique, internal oblique and transverses abdominus were visualized. Facial plane between internal oblique muscle and transverses abdominus was identified. Using 25 G spinal needle, needle was inserted in midaxillary line and needle tip was advanced into fascial plane between internal oblique and transverses abdominus muscle. After negative aspiration for blood , drug was injected under ultrasound guidance visualizing sausage formation in the targeted fascial plane. Group A was given 10ml of 0.25% Bupivacain in TAP block [13] on each side at end of procedure

before extubation. Group B was given 10ml of 0.25%Bupivacaine along with Dexmedetomidine 0.5µg/kg in divided doses under ultrasound guidance. Both injections were prefilled under aseptic conditions and person who was performing TAP block was blinded to study. At the end of procedure residual neuromuscular blockade was reversed with injection Neostigmine 0.04mg/kg. Patients were extubated and shifted to post anesthesia care unit with stable vitals. Patients were followed in postoperative period for intensity of postoperative pain on visual analog scale [14] where patients were asked to mark their pain on a scale with scoring 0-10, value of 0 being no pain at all and 10 being worst and intolerable pain. Pain scoring was done 4 hourly postoperatively upto 24 hours and recorded on form.

Table 1. Age, sex, ASA status and duration of surgery

		Group A	Group B
Age(years)	18-40	12(40%)	14(46.67 %)
	41-60	18(60%)	16(53.33%)
Sex	Male	6(20%)	7(23.33%)
	Female	24(80%)	23(76.67%)
ASA status	I	11(36.67%)	9(30%)
	II	19(63.33%)	21(70%)
Duration of surgery (minutes)	= 30	10(33.33%)	12(40%)
	= 30	20(66.67%)	18(60%)

Table 2. Mean postoperative pain score on VAS scale

Postoperative pain score on VAS scale	Group A (mean ± SD)	Group B (mean ± SD)	p- value
4 HOURS	6.54 ± 1.98	3.54 ± 1.87	0.0001
8 HOURS	5.51 ± 1.16	2.89 ± 1.65	0.0001
12 HOURS	4.89 ± 1.11	2.13 ± 1.25	0.0001
24 HOURS	4.47 ± 1.07	1.63 ± 0.85	0.0001

RESULTS:

Data was analyzed in SPSS 25. Demographic profile including age, sex, ASA status and duration of surgery is shown in table 1.

Postoperative pain as measured on visual analog scale is shown as mean ± SD in table 2. There was statistically significant difference in postoperative pain score in both groups at different intervals that shows that Dexmedetomidine when added as adjuvant to Bupivacain in TAP block is superior for pain management as compared to Bupivacain alone

Stratification was done with respect to age , gender ,ASA status and duration of surgery as shown in table 3 and 4. Bupivacain along with Dexmedetomidine was found to be statistically superior to Bupivacain alone in terms of pain relief. This shows that adjuvant effect of Dexmedetomidine is not affected by age gender, ASA status or duration of surgery

DISCUSSION:

According to PROSPECT recommendations for pain relief after laproscopic cholecystectomy, perioperative use of NSAIDS and COX 2 inhibitors remains the first line of treatment until and unless there is some well defined contraindication to their use. Second line of treatment includes opiods, however their use was limited due to their side effects. Gapapentinoids are other modalities for pain relief especially in patients who are allergic to NSAIDS, however their use is limited by dizziness, sedation and vomiting as their potential side effects. Keeping in view these limitations, port side infiltration of local anesthetics or regional blocks started gaining priority as compare to traditional intravenous analgesics.[5]

TAP block was first introduced by Rafi [15] as an effective alternative to intravenous analgesics as local pain control

Table 3: stratification with respect to age and gender

		Group A	Group B	p value
		Postoperative pain score on VAS scale (mean ±SD)	Postoperative pain score on VAS scale (mean ±SD)	
Age	18-40	4.58 ± 1.08	1.86 ± 0.86	0.0001
	41-60	4.39 ± 1.09	1.44 ± 0.81	0.0001
Gender	Male	4.67 ± 0.82	1.86 ± 0.38	0.0001
	Female	3.42 ± 1.14	1.57 ± 0.95	0.0001

Table 4: stratification with respect to ASA status and duration of surgery

		Group A	Group B	p value
		Postoperative pain score on VAS scale (mean ±SD)	Postoperative pain score on VAS scale (mean ±SD)	
Age	I	4.45 ± 1.13	1.44 ± 0.88	0.0001
	II	4.47 ± 1.07	1.71 ± 0.85	0.0001
Gender	= 30 minutes	4.60 ± 1.08	1.75 ± 0.75	0.0001
	= 30 minutes	4.40 ± 1.10	1.56 ± 0.92	0.0001

for patients undergoing surgical procedures. At that time TAP block was performed with landmark technique. Owen et al demonstrated that the same procedure can be done by open surgical approach. TAP block by laparoscopic technique was first introduced in 2011. Both techniques allow surgeons to apply TAP block under direct vision prior to the surgery.[16] A study by Dr. Usha Shukla has shown that VAS for pain score were statistically significantly to be low at different time interval in patients who were given 0.25% Bupivacaine and 1 µg/kg Dexmedetomidine then those who were given Bupivacaine 0.25% alone. Mean ± standard deviation of pain score on VAS at 2 hours was 2.06 ± 0.90 versus 5.02 ± 1.00, at 6 hours was 2.02 ± 0.20 versus 4.12 ± 0.90, at 12 hours was 1.61 ± 0.50 versus 5.00 ± 0.80, at 24 hours was 1.06 ± 0.81 versus 3.00 ± 0.86 in study group and control group respectively. Overall VAS in 24 hours was also significantly lower in study group (1.80 ± 0.36) then control group (4.5 ± 0.92).[11] Moreover time for rescue analgesia was high and average analgesic consumption was significantly less in Dexmedetomidine group as compared to placebo and Tramadol group. Results of this study were similar to our trial as far as pain score is considered however in our trial we hadn't measured time for rescue analgesia and postoperative analgesic consumption.

The effect of Bupivacaine and Dexmedetomidine added to Bupivacaine used in TAP block by ultrasound guidance on postoperative pain was evaluated by Aksu et al. He selected patients with age 18-65 years, ASA status 1-2, undergoing lower abdominal surgeries (open appendicectomy and inguinal hernia repair). He divided patients in three groups having 21 patients in each group.After induction of anesthesia, he performed TAP block under ultrasound guidance. Group B was given injection Bupivacain in normal saline, group C was given normal saline only and group BD was given injection Bupivacain with Dexmedetomidine. Patients were followed in postoperative period for pain score on VAS scale, postopewrative analgesic requirement in terms of morphine consumption, postoperative nausea and vomiting and patient satisfaction score. Results demonstrated that the addition of Dexmedetomidine with Bupivacain was superior to placebo group and Bupivacain alone in terms of postoperative pain (p value < 0.05), analgesic requirement (p value < 0.001), as well as patient satisfaction (p value < 0.001) . However No difference was found on nausea and vomiting score (p value 0.129) , neither in the requirement of antiemetics.[17] The result of this study were similar to our trial.

In addition to human studies, animal studies also support adjuvant effect of Dexmedetomidine in terms of analgesia. Brummett et al. [18] have presented that high dose Dexmedetomidine added to Bupivacain improved local anesthetic blockade in rats without exhibiting any neurotoxicity. He performed bilateral sciatic nerve block in rats using Bupivacain alone, Bupivacain mixed with Dexmedetomidine and normal saline. After block, sensory and motor functions were assessed at thirty minutes interval. After 24 hours and 14 days of applying block sciatic nerve was analyzed for nerve damage aswell as perineural inflammation. He found that when Dexmedetomidine 0.005% is added as adjunct to Bupivacain, it enhances the duration of both sensory and motor block. However when used alone it doesn't cause any sensory or motor deficit. No neurological damage to axon or myelin sheath was identified after 24 hours and upto 14 days after procedure. Signs of perineural inflammation were less marked in Dexmedetomidine group as compared to Bupivacain group. This trial depicting safe use of high dose of Dexmedetomidine in rats regarding enchancement of antinociception effect of bupivacain, proved to be a milestone for encouraging studies in human beings. On the other hand, Ozalp et al.[19] compared Dexmedetomidine-Ropivacaine combination to Ropivacaine alone in patient controlled interscalene analgesia. He selected 40 patients undergoing upper limb surgeries. Before administering general anesthesia ,through posterior approach of interscalene block of brachial plexus, a catheter was introduced. Catheter placement was confirmed by positive contraction of bicep, tricep and deltoid muscle at less than 0.5milliampere of intensity. Group A was given 0.2 % Ropivacain alone while group 2 was given 0.2% Ropivacain with 1 ug/ml Dexmedetomidine. After procedure pain was managed by PCA infusion that deliver 5 ml of drug bolus at 30 minutes interval. Pain score was measured at rest and at movement and compared in both groups. They stated similar pain scores in both groups without any beneficial effect of Dexemedetomidine. This is in contrary to our trial where addition of Dexmedetomidine as adjunct prolongs analgesic effect of local anesthetic. However in our study local anesthetic agent used was Bupivacain and our trial was done in TAP block, so adjuvant effect of Dexmedetomidine in terms of analgesia may not be as significant in interscalene block as compare to TAP block.

A systematic review for randomized controlled trials by Fusco P et al, that assessed the efficacy of ultrasound guided TAP block following cesarean delivery and concluded that there was a lot of controversy regarding utility of ultrasound guided TAP block in cesarean section. This controversy may be operator dependant and due to expertise of person performing block. However evidence suggests that when correctly executed as part of a multimodal analgesic regimen, TAP block may reduce postoperative opioid consumption and opioid-related side effects, improving postoperative pain control and patient satisfaction.[20]

Similarly, Abdulatif M et al. performed a randomized double blinded study in patients undergoing arthroscopy of knee under femoral block. He observed effects of different doses of Dexmedetomidine when administered perinuerally in femoral nerve block. Procedure was done under general anesthesia. Using ultrasound guidance femoral nerve block

was done. Control group was given 25 ml of Bupivacain plain with normal saline. There were three treatment groups receiving 25,50 and 75 ug of Dexmedetomidine. He reported that addition of 25 mcg of Dexmedetomidine did not make any difference in the pharmacodynamics of Femoral Nerve Block noted with Bupivacaine alone ($p>0.05$). Addition of 50 and 75 mcg of Dexmedetomidine were associated with a decrease in time to onset of sensory as well as motor block, postoperative analgesia consumption and increase in duration of sensory and motor block and time to first rescue analgesia ($p< 0.05$). 75 mcg of Dexmedetomidine was associated with increased incidence of preoperative and intraoperative hypotension episodes ($p=0.002$). [21] These results may support dose dependent analgesic effect of Dexmedetomidine when used as an adjuvant. However this dose dependant response was not addressed in our trial.

Nag DS conducted a prospective randomized controlled trial in patients undergoing cesarean sections. He selected 100 patients and divide them in two groups. All patients underwent cesarean section under spinal anesthesia. At the end of surgery patients in group R were given injection Ropivacian diluted in normal saline and patients in group RD were given injection Ropivacain with Dexmedetomidine in TAP block. Vital monitoring was compared intraoperatively and no statistically significant difference was observed. VAS was compared at rest and on coughing among two groups. There was no statistically significant difference at shifting and at 4 and 8 hours postoperatively, however at 12 and 24 hours postoperatively, there was a significant difference in pain score among both groups showing that analgesic effect of Dexmedetomidine group is superior to Ropivacain alone. Demand for rescue analgesic was also low in Dexmedetomidine group. These results are partially contrary to our results as in our trial Dexmedetomidine proved to be superior in early postoperative hours also. However requirement for rescue analgesic was not measured in our trial.[22]

Korkutata et al conducted a prospective randomized controlled trial in patients undergoing laproscopic cholecystectomy to compare adjuvant effect of Tramadol versus Dexmedetomidine in TAP block. He enrolled 67 patients aged 20-60 years with ASA 1-2 status. After standard anesthesia induction and intubation, group T was given 0.25% Bupivacain with Tramadol 1.5mg/kg while group D was given Bupivacain 0.25% with Dexmedetomidine 0.5ug/kg in TAP block. At end of procedure patients were extubated postoperative pain was measured on VAS scale at varying intervals. Postoperative analgesia consumption was also compared among two groups. This trial showed that Dexmedetomidine and Tramadol were equally effective in terms of postoperative pain and postoperative analgesia consumption as well as side effects, however when hemodynamic stability was compared among both groups, Dexmedetomidine was found to be superior to Tramadol. [23]

Sinha J compared Dexmedetomidine with Dexamethasone as adjuvant to Levobupivacain in TAP block in patients undergoing total abdominal hysterectomies. Procedure was done in spinal anesthesia and after completion of surgical procedure, group 1 was given injection Levobupivacain 0.25% with 4 mg Dexamethasone in TAP block and group 2 was given Levobupivacain 0.25% with Dexmedetomidine 1 ug/kg in TAP block. Postoperatively patients were followed for pain intensity on VAS, rescue analgesia and patient satisfaction. Results of this study showed that VAS was same in both groups in first hour postoperatively, however at 6,9 and 12 hours VAS was significantly low in Dexmedetomidine group as compared to Dexamethasone group. Moreover rescue analgesia consumption was less in Dexmedetomidine group than Dexamethasone group. Results of this study are similar to our trial except that in our study Dexmedetomidine has significantly high analgesic effect in first hour as well. However this difference may be due to fact that we have compared Dexmedetomidine with placebo while in this study Dexmedetomidine was compared with another adjuvant Dexamethasone. [24]

CONCLUSION:

Dexmedetomidine in dose of 0.5 ug/kg when added as adjunct to Bupivacain in TAP block is superior to Bupivacain alone for postoperative pain score.

LIMITATIONS:

Main limitation in our study was sample size. Since results of previous studies are controversial, we need to have data on large population. Moreover dose of drug used may be different in other setups. Clinical expertise of person doing the procedure is another factor that can affect results.

Authors Contribution:
Meamoona Shabbir: Concept & Design of Study, Drafting, Revisiting Critically, Data Analysis, Final Approval of version
Ayesha: Concept & Design of Study, Drafting, Revisiting Critically, Data Analysis, Final Approval of version
Atif Nazir: Concept & Design of Study, Revisiting Critically, Final Approval of version
Mahnoor Nasir: Concept & Design of Study, Drafting, Final Approval of version
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REFERENCES:

1. Matam R, Chawla V, Trivedi S, Bhardwaj A, Singh S. Ultrasound-Guided Transversus Abdominis Plane Block Versus Intraperitoneal Instillation of Bupivacaine after Laparoscopic Cholecystectomy–A Randomized Control Trial. J Med Sci Health. 2023;9(2):169-176. Doi : 10.46347/jmsh.v9i2.22.394

2. Malik MJ, Malik NJ. Surgical Strategies for Gallbladder Disease in Cirrhotic Patients: A Comparison of Open versus Laparoscopic Cholecystectomy. Sjrmu. 2024;28(1):103-5.
3. Soni G, Singh D, Sood A, Rathore YS, Ranjan P, Singh A, Choudhary N, Chumber S. Pain Relief in Laparoscopic Cholecystectomy: Pre-emptive Versus Post-operative Local Anaesthetic Infiltration—A Randomized Control Trial. Indian Journal of Surgery . 2024:1-7. doi.org/10.1007/s12262-024-04127-5
4. Cho HY, Hwang IE, Lee M, Kwon W, Kim WH, Lee HJ. Comparison of modified thoracoabdominal nerve block through perichondral approach and subcostal transversus abdominis plane block for pain management in laparoscopic cholecystectomy: a randomized-controlled trial. Korean J Pain. 2023 ;36(3):382-391. doi: 10.3344/kjp.23114.
5. Bourgeois C, Oyaert L, Van de Velde M, Pogatzki-Zahn E, Freys SM, Sauter AR, Joshi GP, Dewinter G. Pain management after laparoscopic cholecystectomy: A systematic review and procedure-specific postoperative pain management (PROSPECT) recommendations. Eur J Anaesthesiol. 2024 ;41(11):841-55. doi: 10.1097/EJA.0000000000002047
6. El-misady MM, El-rahman AS, Shabayek IAE. Comparison between ultrasound guided transversus abdominis plane (tap) block and local anesthetic infiltration in patients undergoing laparoscopic cholecystectomy. Al-Azhar medical journal. 2023 ; 52(4):1107-18. doi:10.21608/amj.2023.326881
7. Rodriguez JZ, Edgley C, Lee S, Leigh N, Wolfe R, Sanford D, et al. Preoperative transversus abdominis plane block decreases intraoperative opiate consumption during minimally invasive cholecystectomy. Surg Endosc. 2023 ;37(3):2209-2214. doi: 10.1007/s00464-022-09445-x
8. Dost B, Cassai AD, Balzani E, Geraldini F, Tulgar S, Ahiskalioglu A, et al. Analgesic benefits of pre-operative versus postoperative transversus abdominis plane block for laparoscopic cholecystectomy: a frequentist network meta-analysis of randomized controlled trials. BMC Anesthesiol. 2023 ;23(1):408. doi: 10.1186/s12871-023-02369-6
9. Zikri ZHB, Volis M, Mazur A, Orlova T, Alon H, Bar Yehuda S, et al. The Effect of Various Combinations of Peripheral Nerve Blocks on Postoperative Pain in Laparoscopic Cholecystectomy: A Comparative Prospective Study. Int J Clin Pract. 2023 ;2023:8864012. doi: 10.1155/2023/8864012.
10. Korkutata Z, Tekeli AE, Kurt N. Intraoperative and Postoperative Effects of Dexmedetomidine and Tramadol Added as an Adjuvant to Bupivacaine in Transversus Abdominis Plane Block. J Clin Med. 2023 ;12(22):7001. doi: 10.3390/jcm12227001.
11. Shukla U, Prabhakar T, Malhotra K, Srivastava D. Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy: A comparative evaluation. Indian J Anaesth. 2015; 59(4): 234-9. Doi[;v c v: 10.4103/0019-5049.155001
12. Morgan GE, Mikhail MS. Morgan & Mikhail's clinical anesthesiology. McGraw-Hill Education. 2022; 18:477
13. Iaquinandi F, Mongelli F, Christoforidis D, Cianfarani A, Pini R, Saporito A, et al. Laparoscopic vs. ultrasound-guided transversus abdominis plane (TAP) block in colorectal surgery: a systematic review and meta-analysis of randomized trials. Surg Endosc. 2024;38(3):1119-30. doi: 10.1007/s00464-023-10658-x.
14. Varagani S, Safwan M, Makutam V, Moparthi S, Vaishnavi S, Kondru S, et al. A comparative study on assessment of safety and efficacy of Diclofenac, Naproxen and Etoricoxib in reducing pain in osteoarthritis patients-An observational study. Int J Curr Res Med Sci. 2024;10(8):31-8. doi:10.22192/ijcrms.2024.10.08.003
15. Khanum R, Anwar A, Faridi M, Gauhar TM, Ahmed HW, Ahmed R, et al. Is TAP block better than bupivacaine spray for relieving post-cholecystectomy pain?. J Rehman Med Inst. 2024 ;10(2):25-30. Doi: org/10.52442/jrmi.v10i2.839
16. Mowafi MM, Elsenity MA, Elbeialy MAK. Surgical transversus abdominis plane block versus surgical rectus sheath block for postoperative pain control in morbid obese patients undergoing major gynaecological surgery: a prospective, randomized, blinded study. Ain-Shams J Anesthesiol . 2022;14(1):1-9. https://doi.org/10.1186/s42077-022-00223-4
17. Aksu R, Patmano G, Biçer C, Emek E, Çoruh AE. Efficiency of bupivacaine and association with dexmedetomidine in transversus abdominis plane block ultrasound guided in postoperative pain of abdominal surgery. Bras J Anestesiol 2018;68(1): 49-56. doi: 10.1016/j.bjan.2017.04.021
18. Brummett CM, Norat MA, Palmisano JM, et al. Perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. Anesthesiology. 2008;109(3):502-51. doi: 10.1097/ALN.0b013e318182c26b.
19. Ozalp G, Tuncel G, Savli S, Celik A, Doger C, Kaya M. The analgesic efficacy of dexmedetomidine added to ropivacaine patient controlled interscalene analgesia via the posterior approach. J Anaesth. 2006;21: 409-12. DOI:10.1097/00003643-200606001-00790
20. Roofthooft E, Joshi GP, Rawal N, Van de Velde M. PROSPECT guideline for elective caesarean section: updated systematic review and procedure-specific postoperative pain management recommendations. Anaesthesia. 2021 ;76(5):665-680. doi: 10.1111/anae.15339.
21. Chen Z, Liu Z, Feng C, Jin Y, Zhao X. Dexmedetomidine as an Adjuvant in Peripheral Nerve Block. Drug Des Devel Ther. 2023;17:1463-1484. doi: 10.2147/DDDT.S405294.
22. Nag DS, Gehlot P, Sharma P, Kumar H, Kumar Singh U. Comparative Study of Ropivacaine and Ropivacaine With Dexmedetomidine in Transversus Abdominis Plane (TAP) Block for Post-operative Analgesia in Patients Undergoing Cesarean Sections. Cureus. 2024 ;16(7):e65588. doi: 10.7759/cureus.65588.
23. Korkutata Z, Tekeli AE, Kurt N. Intraoperative and postoperative effects of dexmedetomidine and tramadol added as an adjuvant to bupivacaine in transversus abdominis plane block. J Clin Med. 2023 ;12(22):7001. doi: 10.3390/ jcm12227001
24. Sinha J, Pokhriyal AS, Asthana V, Nautiyal R. Dexmedetomidine vs Dexamethasone as an Adjuvant to Levobupivacaine in Ultrasound-Guided Transversus Abdominis Plane Block for Postoperative Analgesia in Patients Undergoing Total Abdominal Hysterectomies. Anesth Pain Med. 2023;13(6):e142059. doi: 10.5812/aapm-142059.

Original Article **Open Access**

Pattern of Congenital Heart Diseases in Patients Presenting in a Tertiary Care Hospital of Karachi

Hajra Begum, Nadeem Sadiq, Saqlain Anwar, Ahmad Hassan, Zohab Ahmed, Hassan Waqar

ABSTRACT

Objective: To identify the frequency and pattern of congenital heart defects (CHD) in referred cases at a tertiary care hospital in Karachi, Pakistan.

Methodology: To carry out this research, we reviewed the medical records of referred patients from various regions of Sindh province from September 2023 to August 2024. The data was collected from the Pediatric Cardiology Department of a tertiary care hospital via a computerized data system and was analyzed to calculate the frequency and pattern of CHD.

Results: A total of 1,423 echocardiograms were reviewed; however, only 1,400 patients met the inclusion criteria and were included in the final analysis. Among these 1400 cases, 791(56.5%) were consistent with normal echo, and 609 (43.5%) were found to have a single or a combination of two or three CHDs. Among 609 CHD cases, 346 (56.8%) were male and 263 (43.1%) were female. Among these 609 cases, a total of 824 heart defects were diagnosed, 655 (79.4%) were acyanotic CHD, 119 (14.4%) were cyanotic CHD, and 50 (6.0%) others. In acyanotic heart defects, septal defects including VSD and ASD were most prevalent. However, among cyanotic heart defects, TOF was the most common abnormality identified.

Conclusion: CHD is very prevalent in Karachi and is among the most common causes of mortality and morbidity. Early detection and screening of heart defects through fetal and neonatal echocardiography allows timely interventions to improve this overall burden of mortality and morbidity.

Keywords: Atrial septal defect, Congenital heart defect, Tetralogy of Fallot, Ventricular septal defect,

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INTRODUCTION:

Congenital heart disease (CHD) consists of the most common birth defects in children worldwide with significant regional variability.[1] CHD has received considerable critical attention because of its potential to cause mortality in certain individuals and has become a growing public health concern worldwide.[2] As the word (congenital) suggests, these defects exist at birth and may persist throughout an individual's life, however often these defects resolve spontaneously, and the patient can lead their normal life without complications.[2-3] There are several types of congenital heart defects including malformations or abnormal development of some structures of the heart, the presence of abnormal openings within heart chambers, and even rhythm disturbances in some cases.[3] These defects are usually diagnosed in an individual's early life, but this early detection and screening depends upon the availability of adequate diagnostic equipment.[4] The importance of implementing systematic screening programs cannot be overstated, as they play a vital role in identifying CHD in asymptomatic patients.[5]

The birth defects often resolve spontaneously barely affecting an individual's health; however, if they persist they can potentially progress and increase the severity of the disease leading to complications and certain medical conditions including pulmonary hypertension, disrupting normal rhythms of the heart causing severe arrhythmia, certain infections to the heart structures and even congestive heart failure in severe cases.[6] The incidence of CHD is regionally dependent, but recent studies have concluded that this incidence is around 9.5/1000 live births globally[1] on average ranging from 4/1,000 to 50/1,000 live births.[7] and in Pakistan, 60000

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children are born with CHD annually with a prevalence of 3.4 per 1000 live births in the year 2023,[8] This statistic underscores that a significant segment of the Pakistani population is living with these birth defects, highlighting the necessity for improved healthcare strategies.[9]

The common types of congenital heart diseases (CHD) globally include Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), and Atrioventricular Septal Defect (AVSD). Other frequently observed conditions are Patent Ductus Arteriosus (PDA), Tetralogy of Fallot (TOF), Coarctation of the Aorta, Aortic Stenosis, and Pulmonary Stenosis. More complex forms of CHD include Tricuspid Atresia, Pulmonary Atresia, Transposition of the Great Arteries, and Single Ventricle anomalies. These conditions collectively represent a spectrum of structural heart abnormalities with varying clinical implications.[1,4]

It is now well established from a variety of studies, that, septal defects account for 40% of CHD in Pakistan, including ASD, VSD, and atrioventricular septal defects.[8] Early diagnosis of these defects plays a crucial role in controlling disease severity and timely interventions, in this way the outcome has been noticeably improved, enhancing the quality of life for individuals with these defects.[1] Moreover, targeted public health initiatives can facilitate access to specialized care and improve the overall management of CHD .[10]

The detection of congenital heart diseases (CHD) commonly involves a range of diagnostic tests. These include echocardiography, which provides detailed images of the heart's structure and function, and electrocardiography (ECG), used to evaluate the heart's electrical activity. Additional diagnostic tools include chest X-rays for assessing heart size and lung involvement, cardiac MRI and CT scans for advanced imaging and pulse oximetry to measure blood oxygen levels, which can indicate underlying cardiac issues. These tests play a crucial role in accurately diagnosing CHD and guiding appropriate management.[1]

In Pakistan, newborn screening for critical CHD involves a simple bedside test called pulse oximetry. Existing meta-analyses have found specificity for critical CHD of 99.9%, a sensitivity of about 76%, and a false positive rate of 0.14%.[1] The ultimate diagnosis of CHD comes via cardiac imaging, usually an echocardiogram.[1]

There is a lack of enough diagnostic facilities in certain regions of Pakistan[2] however, the past decade has seen increasingly rapid advances in the field of health and has established imperative means of early detection and screening of heart defects through fetal and neonatal echocardiography.[8] These diagnostic modalities are now under practice in most of the tertiary care pediatric hospitals nationwide.

METHODOLOGY:

This is a retrospective descriptive study in which 2D echocardiograms of pediatric patients referred to the cardiology department of PNS Shifa Hospital were analyzed. This study aimed to assess the trends of various congenital heart diseases and determine the frequency of cardiac abnormalities and distribution of different heart diseases based on gender and cause of referral for echocardiography.

We analyzed the echocardiograms of 1423 patients who were referred to PNS Shifa Hospital due to an abnormal clinical finding between September 2023 and August 2024. Only those patients who were selected were referred to our hospital due to an abnormal clinical finding that had not yet been diagnosed with congenital heart disease.

Investigators collected and analyzed 2D echocardiogram reports from hospitals' electronic health records. The data was categorized into several groups based on outcome (normal or abnormal), gender, type of disease, and reason for referral. The data was verified and cross-checked to prevent errors regarding patient age, address, and findings on the echocardiogram. The same pediatric cardiologist performed all echocardiograms of referred cases.

Descriptive statistical methods were used to analyze the data. The frequencies and percentages were calculated for each category including the distribution of normal and abnormal echocardiograms, types of diseases, gender distribution, and causes of referral for echocardiography.

RESULTS:

In our comprehensive evaluation involving a total of 1400 patients, we observed a significant prevalence of congenital heart disease (CHD). Among these patients, 791 individuals, representing 56.5%, were found to exhibit normal echocardiographic results. In contrast, 609 patients, constituting 43.5% of the evaluated cohort, were diagnosed with various forms of congenital heart disease, underscoring the importance of early detection and intervention in this population.

Gender Distribution: A closer examination of the 609 patients diagnosed with CHD revealed notable differences in gender distribution Table 1. The breakdown is as follows: Male patients: 346 cases, accounting for 56.8% of the diagnosed population, Female patients: 263 cases, representing 43.1%.

These figures indicate a distinct higher prevalence of congenital heart disease among male patients compared to their female counterparts. This observation aligns with existing literature suggesting that males are more frequently affected by CHD, potentially due to genetic or environmental factors. [11]

Distribution of Congenital Heart Diseases: 609 patients who presented with abnormal echocardiographic findings were diagnosed with a total of 824 cases of congenital heart disease. It is common for individuals to have multiple concurrent conditions, as reflected in our findings.

Among the 609 patients with confirmed CHD, a total of 824 distinct cardiac lesions were diagnosed, indicating that

multiple concurrent abnormalities were common. Acyanotic heart defects accounted for 79.4% of all anomalies, significantly outnumbering cyanotic conditions. Ventricular Septal Defect (VSD) was the most frequently observed lesion, representing 29.1% of all cases, followed by Atrial Septal Defect (ASD) and patent Ductus Arteriosus (PDA).

Cyanotic heart diseases made up 14.4% of all diagnoses. Tetralogy of Fallot (TOF) was the most common cyanotic lesion, accounting for 35.2% of cyanotic cases, followed by transposition of the great arteries (TGA), double outlet right ventricle (DORV), and pulmonary atresia. The higher frequency of TOF mirrors findings from previous Pakistani studies and suggests improved early detection strategies in tertiary referral centers. [3,14]

An additional 6% of diagnosed cases fell outside classical CHD classifications. These included dilated cardiomyopathy (DCM), bicuspid aortic valve (BAV), and left ventricular dysfunction. While not congenital in origin, these conditions were captured due to their significant structural or functional findings on echocardiography. DCM was the most common among these and, although classified as acquired or inherited rather than congenital, is an important differential diagnosis in symptomatic pediatric patients. [12]

Regarding referral patterns, heart murmurs were the most common reason for echocardiographic evaluation, accounting for 31.7% of referrals. Other prevalent indications included repeated upper respiratory tract infections (22.5%) and failure to thrive (9.7%). Prenatal detection accounted for 7.35% of referrals, illustrating the increasing utility of fetal echocardiography. A substantial proportion of referrals (21%) lacked documented causes, which may indicate inconsistent clinical documentation or generalized suspicion. These trends are supported by earlier literature recognizing murmur and respiratory symptoms as leading indicators of CHD. [13]

Overall, this study reaffirms known epidemiological patterns of CHD in South Asian pediatric populations, particularly the predominance of acyanotic lesions, the male preponderance, and the central role of physical exam findings in guiding diagnostic echocardiography. By comparing the frequency of defects such as VSD, ASD, PDA, and TOF with historical cohorts, this dataset contributes to the regional literature and underscores the importance of early referral and accessible cardiac imaging.[3,14,15,16]

DISCUSSION:

There are only limited studies carried out in Karachi regarding the understanding of the pattern and frequency of CHD, considering the persistent increase in the burden of these anomalies. Few studies were published but lacked the gender variation of these defects or the causes of referral were not discussed or mentioned in many articles. By conducting this study, we offer an understanding of the increase in prevalence and importance of clinical evaluation and examinations in patients presenting to resource-limited settings.[14-15] If properly evaluated these patients should be referred to the tertiary care settings which provide adequate diagnosis, *figure 1* thus ensuring the timely interventions and control of disease burden. In our study, even though many referred cases were not found to have cardiac anomalies (56.5%), (43.5%) cases were diagnosed with CHD. This shows the importance of a proper referral system which ensures better outcomes and adequate management of these diseases.

The present study provides valuable insights into the prevalence of various congenital heart diseases (CHD) compared to previous studies as indicated in Table 5.

The Ventricular Septal Defect (VSD) prevalence in our

Table 1: Echocardiographic findings of referred cases (n=1400), gender-wise distribution of congenital heart disease (CHD) patients (n=609), and classification of cardiac diseases (n=824)

2D ECHO OF REFERRED CASES	
Total	1400
Normal	791(56.5%)
Abnormal	609 (43.5%)
GENDER WISE DIVISION OF CHD PATIENTS	
Total	609
Male	346 (56.8%)
Female	263 (43.1%)
TYPES OF CARDIAC DISEASES	
Total	824
Acyanotic	655 (79.4%)
Cyanotic	119 (14.4%)
Other cardiac conditions (non-CHD)	50 (6.0%)

Table 2: Frequency of acyanotic heart diseases among the total cases

ACYANOTIC	655
Ventricular septal defect (VSD)	191 (29.1%)
Atrial septal defect (ASD)	157 (23.9%)
Patent ductus arteriosus (PDA)	142 (21.6%)
Pulmonary stenosis	56 (8.5%)
Coarctation of aorta (COA)	18 (2.7%)
Aortic regurgitation	15 (2.2%)
Partial anomalous pulmonary venous return (PAPVR)	15 (2.2%)
Mitral regurgitation	14 (2.1%)
AV septal defect (AVSD)	10 (1.5%)
Aortic stenosis	9 (1.3%)
Right ventricular outflow tract obstruction (RVOTO)	8 (1.2%)
Aortopulmonary window	7 (1.0%)
Anomalous origin of the right pulmonary artery (AORPA)	7 (1.0%)
Mitral stenosis	5 (0.7%)
Left ventricular outflow tract obstruction (LVOTO)	1 (0.5%)

study was found to be 29.1%, which is lower than the 32.1% reported in the study (Sadiq 2002)[16] and 40.6% in the study (Aman 2011),[18] but higher than the 21.5% in the study (Pate N 2016 Jan-Feb).[3] This variation may highlight differences in referral practices or diagnostic criteria across the studies.

Table 3 Frequency of cyanotic heart diseases and other cardiac conditions among the total cases

CYANOTIC	119
Tetralogy of Fallot (TOF)	42 (35.2%)
Transposition of great arteries (TGA)	21 (17.6%)
Double outlet right ventricle (DORV)	16 (13.4%)
Pulmonary atresia	15 (12.6%)
Tricuspid atresia	15 (12.6%)
Truncus arteriosus	4 (3.3%)
Single ventricle	3 (2.5%)
Bilateral superior vena cava (bilateral SVC)	1 (0.8%)
Total anomalous pulmonary venous return (TAPVR)	1 (0.8%)
Taussig-Bing anomaly	1 (0.8%)
OTHER CARDIAC CONDITIONS	50
(NON-CHD)	
Dilated cardiomyopathy (DCM)	30 (60%)
Bicuspid aortic valve (BAV)	12 (24%)
Dextrocardia	3 (6%)
Mild left ventricular dysfunction	3 (6%)
Hypertrophic cardiomyopathy (HCM)	1 (2.0%)

Table 4 Causes of referral

CAUSES OF REFFERAL	**Total (1400)**
Heart Murmur	445 (31.7%)
Repeated upper respiratory infections	315 (22.5%)
Failure to thrive	137 (9.7%)
Prenatal diagnosis	103 (7.35%)
Echo screening	95 (6.7%)
CXR abnormality	7 (0.5%)
Tachycardia/ Tachypnea	4 (0.2%)
Unknown	294 (21%)

For Atrial Septal Defect (ASD), our study showed a significantly higher occurrence of 23.9% compared to the 9.3% reported in the study (Pate N 2016 Jan-Feb).[3] This suggests an increasing recognition of ASD in our patient population, potentially reflecting improved awareness and referral systems in Karachi.

The prevalence of Patent Ductus Arteriosus (PDA) in this study was 21.6%, markedly higher than the 12.8% seen in the study (Aman 2011)[18] and 9.79% in the study (Ahmad 2002).[17] This finding might indicate an emerging trend or enhancements in diagnostic capabilities. In the case of Pulmonary Stenosis, the prevalence was 8.5%, which aligns closely with the study (Ahmad 2002)[17] reporting 7%, indicating consistency across these datasets.

Notably, Tetralogy of Fallot (TOF) was observed at a prevalence of 35.2% in our study, significantly higher than other studies. This finding underlines the necessity for heightened awareness and early diagnosis of cyanotic lesions in the clinical setting. Overall, our study confirms and expands upon the established trends in congenital heart disease (CHD), emphasizing the ongoing importance of conditions like VSD and TOF in pediatric cardiology practice

The study aimed to analyze the CHD trends among the referred cases to the pediatric cardiology department from different regions mainly Karachi, Pakistan. This included the gender distribution Figure 1, frequency of the diseases, and pattern of various types of congenital heart defects among the patients referred from other health institutes with

Figure 1: Gender wise distribution of common congenital heart defects

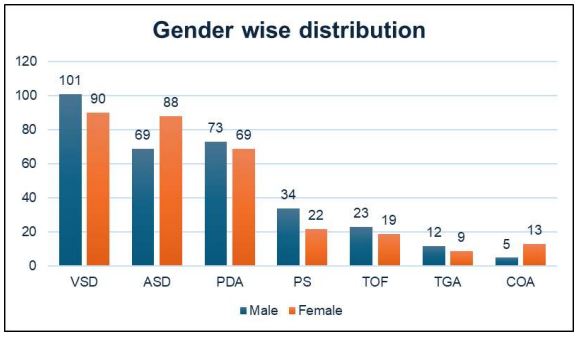

Table 5: Comparison of the frequency of common congenital heart diseases (VSD, ASD, PDA, PS, TOF) across different studies

Lesion / Study	**Sadiq (2002)[14] (n=6620)**	**Ahmad (2002)[15] (n=398)**	**Aman (2011)[16] (n=3072**	**Pate N (2016 Jan-Feb)[3] (n=1003)**	**Present study (n=609)**
VSD	1343 (32.1%)	180 (42.2%)	1248 (40.6%)	216 (21.5%)	191 (29.1%)
ASD	552 (13.2%)	56 (14.08%)	493 (16%)	93 (9.3%)	157 (23.9%)
PDA	536 (12.8%)	39 (9.79%)	394 (12.8%)	86 (8.6%)	142 (21.6%)
PS	336 (8.03%)	28 (7%)	236 (7.7%)	31 (3.1%)	56 (8.5%)
TOF	372 (16.1%)	38 (9.54%)	473 (15.4%)	245 (24.4%)	42 (35.2%)
No of patients	6620	398	3072	1003	609

suspicion of heart anomalies.

Due to limited diagnostic resources and equipment in basic health units across Pakistan, patients who show clinical signs suggestive of congenital heart defects (CHD) are typically referred to the nearest tertiary care facility for further assessment and management. As in our case there were around 1423 patients referred to PNS Shifa Hospital due to an abnormal clinic finding between September 2023 to August 2024 and 1400 patients were included in our study. The causes of these referrals are listed in the table. The trends observed in this study reveal a consistent pattern in the prevalence and types of congenital heart disease (CHD) encountered. It signifies that acyanotic heart diseases are more common, supported by previous literature which showed that out of 1003 studies 609 were acyanotic lesions and the most common acyanotic lesions were VSD[3] which is the case in our study as well. Among cyanotic lesions, we found the most common lesion was Tetralogy of Fallot as supported by previous literature.[19] Diseases that are not categorized as cyanotic or acyanotic heart defects are listed under the "others" category. Among these diseases Dilated Cardiomyopathy was found to be most prevalent in our study. However, existing studies have reported septal hypertrophy as the most prevalent.[3] This difference in findings is suggestive of some varying prevalence of heart anomalies across different ethnic groups.[20]

The data also indicates that heart murmur and upper respiratory tract infections are the most common causes of referral, which aligns with previous literature reporting heart murmur to be the most frequent symptom in patients with a cyanotic heart disease.[18] Our findings align well with existing literature, confirming the reliability of our data, and reinforcing the significance of our study in the broader landscape of congenital heart disease research. By supporting established trends, our study not only verifies these patterns but also emphasizes the ongoing importance of conditions like VSD and TOF in current clinical practice.[21] This alignment with previous research adds valuable context to our observations and enhances our understanding of the prevalence and distribution of CHD in our patient population.[22]

In conclusion, the necessity for increased awareness and better screening practices in our healthcare system is paramount.[23] Addressing the healthcare disparities that exist within Pakistan will facilitate early diagnosis and management of congenital heart diseases, ultimately reducing morbidity and mortality rates associated with these conditions.[24] Moreover, continuous training and development of healthcare professionals can improve the identification of CHD, particularly in primary care settings.[25] Finally, future studies should aim to explore the long-term outcomes of patients with CHD to provide comprehensive insights into the effectiveness of current treatment modalities.[26]

LIMITATIONS:

Our study has a few limitations as it was carried out in a single tertiary care facility and included only the patients who were being referred from resource-limiting settings. The results that were calculated might have suggested different frequencies and patterns of CHD if other centers of Pakistan were included and if the study were carried out on larger scale.

CONCLUSION:

CHD are among the most prevalent congenital diseases in Karachi and are among the most common causes of mortality and morbidity. We found that amongst 1400 cases that we reviewed VSD and TOF were the most common in acyanotic and cyanotic heart diseases respectively whilst the cause of referral was heart murmurs mostly. Early detection and screening of heart defects through fetal and neonatal echocardiography allows timely interventions to improve the overall burden of mortality and morbidity.

Authors Contribution:
Hajra Begum: Conceptualization of study design, writing
Nadeem Sadiq: Research supervision
Saqlain Anwar: Data analysis and interpretation
Ahmad Hassan: Literature search
Zohab Ahmed: Data collection and analysis
Hassan Waqar: Proof reading

REFERENCES:

1. Hasan AA, Abu Lehyah NAA, Al Tarawneh MK, Abbad MY, Fraijat AG, Al-Jammal RA, Moamar DM, Shersheer QA, Guthrie SO, Starnes JR. Incidence and types of congenital heart disease at a referral hospital in Jordan: retrospective study from a tertiary center. Front Pediatr. 2023 Sep 15;11:1261130 DOI: 10.3389/fped.2023.1261130
2. Ali F, Wazir HD, Akbar A, Khan AM, Rehman Y, Hussain I, Gul H, Ullah I, Khan K, Afridi AK. Frequency of Congenital Cardiac Disease in Various Divisions of Khyber Pakhtunkhwa (KPK) Based on a Six-Month Analysis of Inpatients at a Tertiary Care Hospital's Pediatric Cardiology Unit. Cureus. 2023 Feb 20;15(2):e35209 DOI: 10.3389/fped.2023.1261130
3. Pate N, Jawed S, Nigar N, Junaid F, Wadood AA, Abdullah F. Frequency and pattern of congenital heart defects in a tertiary care cardiac hospital of Karachi. Pak J Med Sci. 2016 Jan-Feb;32(1):79-84 DOI: 10.7759/cureus.35209
4. Sehar, T., Sheikh, A. M., & Kanwal, A. (2019). TO IDENTIFY PATTERN OF CONGENITAL HEART DISEASES IN A NEWLY DEVELOPED TERTIARY CARE UNIT. Pakistan Armed Forces Medical Journal, 69(4), 831-36 https://pafmj.org/PAFMJ/article/view/3209
5. Knowles R, Griebsch I, Dezateux C, Brown J, Bull C, Wren C. Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis. Health Technol Assess. 2005 Nov;9(44):1-152, iii-iv DOI: 10.3310/hta9440
6. Ministeri M, Alonso-Gonzalez R, Swan L, Dimopoulos K. Common long-term complications of adult congenital heart disease: avoid falling in a H.E.A.P. Expert Rev Cardiovasc Ther. 2016;14(4):445-62 DOI: 10.1586/14779072.2016.1133294

7. Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol. 2002 Jun 19;39(12):1890-900 DOI: 10.1016/s0735-1097(02)01886-7

8. Rao PS. Advances in the Diagnosis and Management of Congenital Heart Disease in Children. Children (Basel). 2023 Apr 21;10(4):753 DOI: 10.3390/children10040753

9. Jenkins KJ, Botto LD, Correa A, et al. Public Health Approach to Improve Outcomes for Congenital Heart Disease Across the Life Span. J Am Heart Assoc. 2019;8(8):e009450 doi: 10.1161/JAHA.118.009450

10. Rossano JW. Congenital heart disease: a global public health concern. Lancet Child Adolesc Health. 2020;4(3):168-169 DOI: 10.1016/S2352-4642(19)30429-8

11. Pugnaloni F, Felici A, Corno AF, Marino B, Versacci P, Putotto C. Gender differences in congenital heart defects: a narrative review. Transl Pediatr. 2023;12(9):1753-1764 doi: 10.21037/tp-23-260

12. Shah GS, Singh MK, Pandey TR, Kalakheti BK, Bhandari GP. Incidence of congenital heart disease in tertiary care hospital. Kathmandu Univ Med J (KUMJ). 2008;6(1):33-36 https://pubmed.ncbi.nlm.nih.gov/18604112/

13. Ford B, Lara S, Park J. Heart Murmurs in Children: Evaluation and Management. Am Fam Physician. 2022;105(3):250-261 https://www.aafp.org/pubs/afp/issues/2022/0300/p250.html

14. Sadiq M,RB,KA,LF,BI,&SSA. Pattern of pediatric heart diseases in Pakistan. JCPSP Journal of the College of Physicians and Surgeons Pakistan. 2002;: 149-153 https://inis.iaea.org/search/search.aspx?orig_q=RN:34015814

15. Ahmad R&AZA&BF. A prevalence study of congenital heart disease in NWFP, Pakistan. Pakistan Journal of Medical Sciences. 2002;: 95-98 https://www.researchgate.net/publication/ 289896415_A_prevalence_ study_of_congenital_heart_disease_in_NWFP_Pakistan

16. Aman W,SA,&HM. Frequency Of Congenital Heart Diseases In Patients Under The Age Of Twelve Years At Lady Reading Hospital Peshawar. Journal of Postgraduate Medical Institute. 2011;: 20. https://jpmi.org.pk/index.php/jpmi/article/view/136

17. Song L, Wang Y, Wang H, et al. Clinical profile of congenital heart diseases detected in a tertiary hospital in China: a retrospective analysis. Front Cardiovasc Med. 2023;10: 1131383. Published 2023 Sep 8 doi: 10.3389/fcvm. 2023. 1131383

18. Siddiqui, M. F. ., Farooq, S. ., Khan, A. K. ., & Kausar, H. . (2021). Congenital Heart Disease: Causes and Risk Factors: Congenital Heart Disease: Causes and Risk Factors. Pakistan BioMedical Journal, 4(1) DOI: https://doi.org/10.52229/pbmj.v4i1.58

19. Rahim, Faris & Younas, M. & Gandapur, A.J. & Talat, A.. (2003). Pattern of congenital heart Diseases in children at tertiary care center in Peshawar. Pakistan Journal of Medical Sciences. 19. 19-22 https://www.researchgate.net/publication/289273911 _Pattern_of_congenital_heart_Diseases_in_children_at_tertiary_care_center_in_Peshawar

20. Knowles RL, Ridout D, Crowe S, et al. Ethnic and socioeconomic variation in incidence of congenital heart defects. Arch Dis Child. 2017;102(6):496-502 DOI: 10.1136/archdischild-2016-311143

21. V Sabarigirivasan, R S Sivera, A C Crucean, A C Cook, The ventricular septal defect in tetralogy of Fallot: A multi-centre morphological and statistical shape analysis study, European Heart Journal, Volume 45, Issue Supplement_1, October 2024, ehae666.2110 https://doi.org/10.1093/eurheartj/ehae666.2110

22. Pasha, W., Ramchand, R., Khokhar, R. A., Sathio, S. N., Kanwal, M., & Aurangzeb, A. (2023). Congenital heart diseases pattern among children presenting to tertiary care hospital: A cross sectional study. International Journal of Health Sciences, 7(S1), 2389–2396 https://doi.org/10.53730/ijhs.v7nS1.14516

23. Krishna MR, Kumar RK. Diagnosis and Management of Critical Congenital Heart Diseases in the Newborn. Indian J Pediatr. 2020;87(5):365-371 DOI: 10.1007/s12098-019-03163-4

24. Chowdhury D, Elliott PA, Asaki SY, et al. Addressing Disparities in Pediatric Congenital Heart Disease: A Call for Equitable Health Care. J Am Heart Assoc. 2024;13(13) :e032415 DOI: 10.1161/JAHA.123.032415

25. Smith P. Primary care in children with congenital heart disease. J Pediatr Nurs. 2001;16(5):308-319 DOI: 10.1053/jpdn.2001.26572

26. Razzaghi H, Oster M, Reefhuis J. Long-term outcomes in children with congenital heart disease: National Health Interview Survey. J Pediatr. 2015;166(1):119-124 doi: 10.1016/j.jpeds.2014.09.006

Original Article **Open Access**

Risk Factors and Frequency of Vitamin B12 Deficiency among Patients Visiting Primary Care Clinics in Karachi, Pakistan

Fakhrunnisa Waheed, Mohammad Minhaj, Nida Ghouri, Faridah Amir Ali, Muhammad Junaid Patel

ABSTRACT

Objective: To examine the associations of sociodemographic factors, comorbidities, diet, medications, vitamin D levels, hematological indices, and symptoms with vitamin B12 status among primary care patients in Karachi, Pakistan.

Methods: This cross-sectional study was conducted in 2023 at the Family and Internal Medicine clinics of Indus Hospital and Health Network. Adults recently tested for vitamin B12 as advised by physicians were enrolled (n=252). Data on demographics, comorbidity, medications, diet, and symptoms were collected through structured interviews, alongside BMI and laboratory results. Associations were analyzed using descriptive statistics, Chi-square, and correlation coefficient, with $p<0.05$ considered significant.

Results: Of 252 participants (71.4% female, median age 46 years), fatigue (79.5%), muscle weakness (73.2%), and numbness/tingling (69%) were the most frequent symptoms in those with B12 deficiency or insufficiency. Decreased appetite ($p=0.003$) and weight loss ($p=0.010$) were significantly associated with low B12 levels. Dietary patterns showed strong associations: reduced milk intake (72% deficient) and infrequent red meat consumption (49.6% deficient) were linked to deficiency. Vitamin D correlated positively with B12 levels ($r=0.215$, $p=0.006$), while mean corpuscular volume correlated negatively ($r=-0.151$, $p=0.019$). No significant associations were found with BMI ($p=0.175$), comorbidities ($p>0.05$), or metformin/PPI use ($p>0.05$).

Conclusion: Low vitamin B12 levels were associated with specific dietary insufficiencies, constitutional and neurological symptoms, and hematological indices. These findings highlight the need for heightened clinical awareness and integration of dietary counseling within primary care. These findings highlight the need for targeted screening and interventions to prevent deficiency in underprivileged populations.

Keywords: Cobalamin deficiency, B12 deficiency, macrocytic anemia, megaloblastic anemia, nutritional anemia, vitamin B12 deficiency, Pakistan

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INTRODUCTION:

Vitamin B12 (Cobalamin) is an essential micronutrient crucial for various physiological processes, hence its deficiency leads to a wide array of clinical manifestations, including hematological, dermatological and gastrointestinal abnormalities, neurological impairment and cognitive decline. The prevalence of vitamin B12 deficiency is common and is more frequent in low- and middle-income countries with a poor or inadequate diet of animal foods.[1,2] Risk factors for its deficiency have been identified world over, such as old age, vegetarian diet, inflammatory bowel disease, hypothyroidism, history of gastrointestinal resection and prolonged use of medications like proton pump inhibitors (PPI) and metformin.[3,4]

In impoverished countries, insufficient dietary intake is a significant cause of vitamin B12 deficiency.[5,6] For example, certain groups with reduced meat intake due to cultural or societal factors have up to 86.5% vitamin B12 deficiency.[7] Yet, due to variable and vague signs and symptoms, and a high cost of screening, it is often unnoticed by clinicians.[7-9]

Routine screening is not cost-effective, hence the prevalence of vitamin B12 deficiency among healthy individuals in Pakistan remains unknown. A large study conducted among pregnant women found more than half of them to be vitamin B12 deficient, with an association with gestational diabetes mellitus (GDM).[10] Another study showed that 41.9% of adolescents in a vulnerable group had vitamin B12 deficiency.[9] A study conducted in Karachi on diabetics revealed vitamin B12 deficiency in 46.3% of patients, out of which 18.4% were on metformin. This was supported by another study that showed a 31% prevalence among diabetics.[11,12] However, another study on another population in Pakistan did not find correlation between vitamin B12 insufficiency and diabetes.[13] Other studies found B12 deficiency to be associated with old age,[14] depression,[15] and dementia, with significant improvement in symptoms following adequate vitamin B12 replacement.[16] Despite the deficiency is common in the Pakistani population, no consistent correlation has been found among the risk factors examined. Also, local studies have reported specific risk factors among various vulnerable populations, multiple risk factors have not been assessed in a single population. This study therefore aims to determine the socio-demographic factors, co-morbid illnesses, medications, symptoms, weight, dietary factors, various blood parameters and vitamin D levels with vitamin B12 insufficiency and deficiency among an underprivileged population presenting to primary care clinics at Indus Hospital and Health Network (IHHN) in Karachi, Pakistan. The findings of this study could contribute towards creating a screening model to detect early B12 deficiency and therefore lead to targeted interventions to help reduce the burden of B12 deficiency and hence associated morbidity in our population.

METHODOLOGY:

This is a cross-sectional study conducted for a year (2023), in Family Medicine and Internal Medicine primary care clinics, at Indus Hospital and Health Network (IHHN), Korangi campus Karachi. IHHN is a free tertiary care health network, catering to the underprivileged population throughout the city. Adult patients who had serum vitamin B12 levels checked within the past one week as advised by the physician, were approached for consent to participate. Patients with malabsorption syndrome, alcoholism, liver disease, malignancies, inflammatory bowel disease, history of gastric/intestinal resection, or those who were unable to give consent (mentally incapacitated), pregnant females, and bed-bound patients were excluded.

The sample size for this study was calculated to be 252 through WHO sample size calculator, using the prevalence of vitamin B12 deficiency in adults 8.78%,[17] margin of error 3.5% and confidence level 95%.

A structured questionnaire was administered to collect data. The data was collected by postgraduate medical trainees of Family Medicine who were trained by the principal investigator. This was completed as a one-on-one interview, in an appropriate private setting. The questionnaire had 7 sections: sociodemographic information, self-reported co-morbid illnesses, medication history, eating habits, body mass index (BMI) and available lab parameters. The BMI (kg/m^2) was calculated following the WHO standard guidelines, categorized as underweight (<18.5), normal weight (18.5-24.9) and overweight (=25.0).

Risk factors were compared among three groups based on vitamin B12 levels as follows: Normal level: = 400 pg/ml, vitamin B12 insufficiency (200-399 pg/ml) and deficiency (< 200 pg/ml).[3,18]

Statistical Analysis: Collected data were analyzed on SPSS version 26, a p-value of less than 0.05 was considered significant. Means (SD) or median (IQR) is reported for quantitative variables such as age, lab parameters and anthropometric measure measurements on the basis of normality. Normality was checked through Shapiro wilk test. Frequency and percentage were reported for categorical variables such as gender, co-morbid illnesses, sociodemographic variables, symptoms, dietary factors and vitamin B12 deficiency . The Mann-Whitney U test was used to analyze differences in continuous variables between independent groups. For categorical data, Chi-square test, with the Fisher-exact test was applied in instances of small sample sizes. After univariate analysis, Pearson correlation was applied to determine a linear relationship between B12 and other quantitative variables such as blood parameters and vitamin D.

Ethical Considerations: For conducting this research, we adhered to the highest ethical standards to ensure the integrity and well-being of all participants. We obtained verbal informed consent from each participant, with a clear explanation of the study's purpose, procedures, and potential risks. This study was approved by Institutional Review Board (IRB) of Indus Hospital and Health Network (IRB Number: IHNN_IRB_2022_06_005).

RESULTS:

The study included 252 participants with 71.4% females and 28.6% males. The median age of the participants was 46 years (IQR: 35-56). Majority of females were housewives (51%) and a quarter of males were retired. A quarter of the participants were illiterate while almost 50% had not completed 10^{th} grade. There was no association of age groups (p=0.170), gender (p=0.310), educational status (p=0.63), and working status (p=0.100) with vitamin B12 deficiency or insufficiency.

Around one-third of participants were had a normal BMI, one third were overweight, while 19.4% were obese and 13.5 % were under weight. There was no association of BMI with vitamin B12 levels (p=0.175). (Figure 1)

Among all participants, almost half (48%) were deficient in vitamin B12, 43.7% had insufficiency, while only 8.3% had a normal level. More than half (58.7%) had co-morbid illnesses. Among these, 59.3% had hypertension, 43.4% had diabetes, 19.3% had hypothyroidism, and 7.6% had depression/anxiety. There was no significant difference among distribution of co-morbid illnesses among participants with normal, insufficient or deficient vitamin B12 levels (Table 1) however, hypertension was the more common among vitamin B12 insufficient as compared to deficient patients but p value was not statistically significant (p 0.617). Cardiovascular diseases were most common (44.4%) in the study population followed by hypertension (34.1) and diabetes (25%).

Most common symptoms among patients with vitamin B12 insufficiency and deficiency included fatigue (79.5%), weakness in muscles (73.2%), tingling/numbness (69%), irritability (64.4%), and balance issues in walking (57.7%). Decreased appetite (p 0.003) and weight loss (p 0.010) were more common among participants with B12 insufficiency or deficiency than those with normal B12 levels.

There was no significant association found between vitamin B12 levels and the use of medications, smoking status, or other addictive behaviors, as indicated in Table-2. A trend was observed among participants taking multivitamins, with a higher proportion having normal vitamin B12 levels

Table 1: Association of demographic characteristics with vitamin B12 levels among patients

	B12 Normal N=21	B12 Insufficient N=110	B12 Deficient N=121	Total N=252	P-value
Age in year					
Median (IQR)	60(31-70)	47(35-57)	44(35-55)	46(35-56)	0.179†
Min-Max	17-80	15-80	15-81	15-81	
Members in household					
Median (IQR)	6(5-10)	6(5-8)	5(4-7)	6(5-6)	0.108¶
Min-max	2-20	2-17	1-29	1-29	
Numbers of children					
Median (IQR)	5(2-6)	3(1-5)	3(1-4)	4(1-6)	0.069¶
Min-max	0-10	0-10	0-10	0-13	
Gender					
Male	7(33.3)	26(23.6)	39(32.2)	72(28.6)	0.310†
Female	14(66.7)	84(76.4)	82(67.8)	180(71.4)	
Total	21(100)	110(100)	121(100)	252(100)	
Working Status					
Employed	3(14.3)	2(1.8)	6(5)	11(4.4)	0.109†
Housewife	11(52.4)	62(56.4)	56(46.3)	129(51.2)	
Retired	3(14.3)	30(27.3)	33(27.3)	66(26.2)	
Unemployed	4(19)	16(14.5)	26(21.5)	46(18.3)	
Total	21(100)	110(100)	121(100)	252(100)	
Education					
Above Matric	7(33.3)	28(25.5)	25(20.7)	60(23.8)	0.639†
Matric	7(33.3)	28(25.5)	37(30.6)	72(28.6)	
Under Matric	2(9.5)	29(26.4)	30(24.8)	61(24.2)	
Uneducated	5(23.8)	25(22.7)	29(24)	59(23.4)	
Total	21(100)	110(100)	121(100)	252(100)	
BMI status					
Underweight	3(14.3)	13(11.8)	18(14.9)	34(13.5)	0.175†
Normal	10(47.6)	30(27.3)	45(37.2)	65(33.7)	
Overweight	6(28.6)	46(41.8)	32(26.4)	83(33.3)	
Obese	2(9.5)	21(19.1)	26(21.5)	49(19.4)	
Total	21(100)	110(100)	121(100)	252(100)	

*P-value<0.05, ¶ Mann Whitney U test, ǂChi-square test, † Fisher-exact test
*Vitamin B12 Normal level: > 400 pg/ml, insufficiency (200-399 pg/ml) and deficiency (< 200 pg/ml)

Table 2: Association of comorbidities with vitamin B12 levels among patients

		B12 Normal N=21	B12 Insufficient N=110	B12 Deficient N=121	Total N=252	P-value
Cardiovascular Disease	No	10(47.6)	59(53.6)	71(58.7)	140(55.6)	0.555ǂ
	Yes	11(52.4)	51(46.4)	50(41.3)	112(44.4)	
Diabetes	No	13(61.9)	79(71.8)	97(80.2)	189(75)	0.12ǂ
	Yes	8(38.1)	31(28.2)	24(19.8)	63(25)	
Hypertension	No	15(71.4)	69(62.7)	82(67.8)	166(65.9)	0.617ǂ
	Yes	6(28.6)	41(37.3)	39(32.2)	86(34.1)	
Hypothyroidism	No	19(90.5)	100(90.9)	105(86.8)	224(88.9)	0.59ǂ
	Yes	2(9.5)	10(9.1)	16(13.2)	28(11.1)	
Stroke History	No	21(100)	108(98.2)	119(98.3)	248(98.4)	1†
	Yes	0(0)	2(1.8)	2(1.7)	4(1.6)	
Depression/Anxiety	No	20(95.2)	103(93.6)	118(97.5)	241(95.6)	0.267†
	Yes	1(4.8)	7(6.4)	3(2.5)	11(4.4)	
Coronary Artery Disease	No	19(90.5)	109(99.1)	116(95.9)	244(96.8)	0.066†
	Yes	2(9.5)	1(0.9)	5(4.1)	8(3.2)	
Others	No	14(66.7)	102(92.7)	109(90.1)	225(89.3)	0.002*ǂ
	Yes	7(33.3)	8(7.3)	12(9.9)	27(10.7)	

compared to those with B12 insufficiency and deficiency (47.6%, 29.1%, and 25.6% respectively, P=0.086) (Table-2). Results also indicated a significant association between dietary habits and vitamin B12 levels, with a higher proportion of normal B12 patients among those consuming multivitamins, red meat and egg (2-3 times per week). Majority of vitamin B12 deficient patients were those who do not drink milk (Table -3).

The correlation between age and various blood parameters, with B12 levels was computed. Age showed a weak positive correlation with B12 levels (r = 0.091), indicating a slight tendency for B12 levels to increase with age, though statistically not significant (p = 0.148). Conversely, vitamin D exhibited a moderate positive correlation with B12 levels (r = 0.215) (p = 0.006) (Figure 2). Hemoglobin showed a weak positive correlation with B12 levels (r = 0.100) but statistically insignificant (p = 0.121). Mean corpuscular volume (MCV) levels had a statistically significant negative correlation with B12 levels (r = -0.151) (p = 0.019). However, mean corpuscular hemoglobin concentration (MCHC) exhibited no correlation with B12 levels (r = 0.007) (p = 0.917). Overall, while some blood parameters showed significant associations with B12 levels, others exhibited weak or negligible correlations, suggesting varied relationships between B12 levels and various blood parameters.

DISCUSSION:

This study reports an alarmingly high frequency of vitamin B12 deficiency and insufficiency among patients whose B12 levels were requested by the physicians. B12 levels were below normal among 91.6 % of the patients; while 48% had documented deficiency of the micronutrient. Low B12 levels have also been reported in various other studies conducted in specific groups in Pakistan.[9,11,12] The exceptionally high frequency of B12 deficiency in our study is likely, because only patients who were requested by physicians to have their B12 levels checked due to high suspicion of deficiency, were included.

Vitamin B12 plays an important role in various bodily functions; therefore, its deficiency is marked by several symptoms. Lack of energy, weakness in muscles, irritability, numbness/tingling and trouble walking were the most reported patient complaints. These symptoms match the findings reported by Wolfenbüttel and colleagues,[8] who also found improvement in these symptoms post cobalamin therapy for 6 months. Weight loss (56%) was also a significant among the insufficient and deficient group, and it is one of the known gastrointestinal manifestations of low B12 levels.[5] Hence, it is worth reiterating the importance of recognizing these symptoms earlier in at-risk groups.

Our study reports an interesting positive relationship between vitamin D and vitamin B12 levels. As majority of the participants were females, preexisting low vitamin D levels due to less consumption of dairy products and decreased sun exposure in females in our population could provide an explanation for this result.[6,19] This relates to the findings of Karabayir et.al which also conclude that vitamin D deficiency could be common in vitamin B12 deficient patients.[20] More comprehensive studies are needed to reveal the relationship between vit B12 and vit D deficiency.

Vitamin B12 deficiency is a known cause of macrocytic anemia,[3] and our study supported this association. MCV

Table 3: Association of symptoms with vitamin B12 levels among patients

		B12 Normal N=21	B12 Insufficient N=110	B12 Deficient N=121	Total N=252	P-value
Muscle Weakness	Yes	12(60)	80(73.4)	83(68.6)	175(70)	0.397†
	No	7(35)	25(22.9)	36(29.8)	68(27.2)	
	Sometimes	1(5)	4(3.7)	2(1.7)	7(2.8)	
Dyspepsia	Yes	14(70)	53(48.2)	42(34.7)	109(43.4)	0.018*ǂ
	No	4(20)	46(41.8)	68(56.2)	118(47)	
	Sometimes	2(10)	11(10)	11(9.1)	24(9.6)	
Numb or tingling feeling in hands	Yes	14(70)	46(41.8)	52(43)	112(44.6)	0.102ǂ
	No	4(20)	57(51.8)	63(52.1)	124(49.4)	
	Sometimes	2(10)	7(6.4)	6(5)	15(6)	
Trouble walking	Yes	15(75)	51(46.4)	72(59.5)	138(55)	0.003*†
	No	5(25)	51(46.4)	49(40.5)	105(41.8)	
	Sometimes	0(0)	8(7.3)	0(0)	8(3.2)	
Nausea	Yes	7(35)	24(21.8)	27(22.3)	58(23.1)	0.425†
	No	11(55)	75(68.2)	87(71.9)	173(68.9)	
	Sometimes	2(10)	11(10)	7(5.8)	20(8)	
Decreased appetite	Yes	14(70)	32(29.4)	48(39.7)	94(37.6)	0.003*†
	No	5(25)	75(68.8)	70(57.9)	150(60)	
	Sometimes	1(5)	2(1.8)	3(2.5)	6(2.4)	
Weight loss	Yes	7(35)	40(36.7)	64(53.8)	111(44.8)	0.022*†
	No	13(65)	69(63.3)	53(44.5)	135(54.4)	
	Sometimes	0(0)	0(0)	2(1.7)	2(0.8)	
Irritability	Yes	15(75)	65(59.6)	74(61.7)	154(61.8)	0.317ǂ
	No	4(20)	36(33)	43(35.8)	83(33.3)	
	Sometimes	1(5)	8(7.3)	3(2.5)	12(4.8)	
Fatigue	Yes	19(95)	85(78)	86(71.7)	190(76.3)	0.14†
	No	1(5)	23(21.1)	33(27.5)	57(22.9)	
	Sometimes	0(0)	1(0.9)	1(0.8)	2(0.8)	
Diarrhea	Yes	10(50)	20(18.3)	18(15)	48(19.3)	0.01*†
	No	9(45)	76(69.7)	93(77.5)	178(71.5)	
	Sometimes	1(5)	13(11.9)	9(7.5)	23(9.2)	
Smooth and tender tongue	Yes	6(28.6)	8(7.3)	9(7.6)	23(9.2)	0.06†
	No	15(71.4)	99(90.8)	108(90.8)	222(89.2)	
	Sometimes	0(0)	2(1.8)	2(1.7)	4(1.6)	
Fast heart rate	Yes	8(38.1)	46(42.2)	56(46.7)	110(44)	0.182ǂ
	No	13(61.9)	46(42.2)	52(43.3)	111(44.4)	
	Sometimes	0(0)	17(15.6)	12(10)	29(11.6)	
Reduced Smell	Yes	3(14.3)	10(9.1)	9(7.5)	22(8.8)	0.346†
	No	17(81)	97(88.2)	110(91.7)	224(89.2)	
	Sometimes	1(4.8)	3(2.7)	1(0.8)	5(2)	
Forgetfulness	Yes	12(57.1)	36(33)	31(25.8)	79(31.6)	0.004*ǂ
	No	7(33.3)	58(53.2)	83(69.2)	148(59.2)	
	Sometimes	2(9.5)	15(13.8)	6(5)	23(9.2)	

*P-value<0.05, ¶ Mann Whitney U test, ǂ Chi-square test, † Fisher-exact test

Table 4: Association of medications and smoking with vitamin B12 levels among patients

	B12 Normal N=21	B12 Insufficiency N=110	B12 Deficiency N=121	Total N=252	P-value
Use of Proton Pump Inhibitors					
Yes	3(15)	12(11.1)	6(5.2)	21(8.6)	0.168†
No	17(85)	96(88.9)	109(94.8)	222(91.4)	
Total	20(100)	108(100)	115(100)	243(100)	
Use of Metformin					
Yes	5(62.5)	19(61.3)	14(58.3)	38(60.3)	1.000†
No	3(37.5)	12(38.7)	10(41.7)	25(39.7)	
Total	8(100)	31(100)	24(100)	63(100)	
Currently on Pregabalin/ Duloxetine					
Yes	-	5(4.7)	1(0.9)	6(2.5)	0.493†
No	19(100)	102(95.3)	113(99.1)	234(97.5)	
Total	19(100)	107(100)	114(100)	240(100)	
Smoke Cigarettes (at least once a day for a month in the last 1 year)					
Yes	1(4.8)	2(1.9)	4(3.3)	7(2.8)	0.279†
No	20(95.2)	106(98.1)	116(96.7)	242(97.2)	
Total	21(100)	108(100)	120(100)	249(100)	
Use of Tobacco on regular basis					
Yes	-	13(11.8)	14(11.6)	27(10.7)	0.525†
No	21(100)	97(88.2)	107(88.4)	225(89.3)	
Total	21(100)	110(100)	121(100)	252(100)	
Use Beetle nut					
Yes	3(14.3)	17(15.5)	20(16.5)	40(15.9)	0.109†
No	17(81)	91(82.7)	89(73.6)	197(78.2)	
Sometimes	1(4.8)	2(1.8)	12(9.9)	15(6)	
Total	21(100)	110(100)	121(100)	252(100)	

increased as B12 levels decreased, indicating a negative correlation between the two parameters.

Adequate vitamin B12 can be obtained through diets rich in this micronutrient, such as red meat and milk. Therefore, certain groups who avoid these sources due to cultural, religious, or financial reasons are more at risk of developing B12 deficiency. We found that 72% of those who do not drink milk, and 49.6% of those who consumed red meat less than once per week or consumed no red meat at all had documented vitamin B12 deficiency. Our findings are in line with the report of Bacha and colleagues,[6] who reported reduced diversity in food sources and reduced milk consumption in the Pakistani population.

There was no correlation of BMI or co-morbid illnesses with vitamin B12 levels, however the frequency of patients with known cardiovascular diseases, hypertension and diabetes among our study population was 44%, 34% and 25% respectively. These numbers are concerning especially in a population with meager resources and heath care access, and warrants a need for nationwide awareness and interventions to screen and prevent non-communicable diseases.

Further there was no correlation of B12 deficiency with medication usage (metformin and proton pump inhibitors) (PPI) in our results. This is surprising as vitamin B12 deficiency is a well-known side effect of these medications. A possible explanation could be that the duration and dosage of metformin or PPI use were not systematically recorded in our study, and deficiency risk increases with long-term or high-dose exposure. Moreover, B12 deficiency is multifactorial and may be influenced by dietary patterns, malabsorption, age, or co-morbid conditions, which may have masked any direct association with these medications in our sample. Additionally, the relatively small number of participants with normal vitamin B12 levels could have further diluted the association of variables.

CONCLUSION:

This study underscores the clinical importance of recognizing vitamin B12 deficiency in underprivileged primary care populations. Dietary insufficiency and nonspecific symptoms remain key challenges, while laboratory correlations highlight the complexity of its detection. Although limited by selection bias and lack of generalizability, the findings emphasize the need for greater clinical awareness, integration of dietary

Table 5: Association between the use of multivitamins and dietary intake with vitamin B12 levels among patients

	B12 Normal N=21	B12 Insufficiency N=110	B12 Deficiency N=121	Total N=252	P-value
Use of Multivitamins (for last 3 months)					
Yes	10(47.6)	32(29.1)	31(25.6)	73(29)	0.086†
No	11(52.4)	78(70.9)	90(74.4)	179(71)	
Total	21(100)	110(100)	121(100)	252(100)	
Use of Red Meat					
Not at all	8(38.1)	23(20.9)	21(17.4)	52(20.6)	0.072†
Less than once a week	3(14.3)	36(32.7)	39(32.2)	78(31)	
At least once a week	2(9.5)	24(21.8)	35(28.9)	61(24.2)	
2-3 times per week	8(38.1)	23(20.9)	25(20.7)	56(22.2)	
Almost daily	-	4(3.6)	1(0.8)	5(2)	
Total	21(100)	110(100)	121(100)	252(100)	
Use of Egg					
Not at all	6(28.6)	40(36.4)	38(31.4)	84(33.3)	0.338†
Less than once a week	3(14.3)	27(24.5)	26(21.5)	56(22.2)	
At least once a week	2(9.5)	18(16.4)	26(21.5)	46(18.3)	
2-3 times per week	8(38.1)	16(14.5)	20(16.5)	44(17.5)	
Almost daily	2(9.5)	9(8.2)	11(9.1)	22(8.7)	
Total	21(100)	110(100)	121(100)	252(100)	
Use of Milk on a daily basis					
Not at all	12(57.1)	63(57.8)	87(72.5)	162(64.8)	0.227†
Less than once a week	2(9.5)	9(8.3)	8(6.7)	19(7.6)	
At least once a week	2(9.5)	13(11.9)	8(6.7)	23(9.2)	
2-3 times per week	-	10(9.2)	7(5.8)	17(6.8)	
Almost daily	5(23.8)	14(12.8)	10(8.3)	29(11.6)	
Total	21(100)	109(100)	120(100)	250(100)	

Table 6: Correlation of Vitamin B12 with Vitamin D

	R-Value	p-value
Vitamin D	0.215	0.006

counseling, and development of cost-effective screening strategies in primary care to enable earlier diagnosis and management

LIMITATION:

Our study was limited to patients presenting to the primary care clinics of a single charitable hospital, which restricted recruitment primarily to individuals from low or lower middle income groups, thereby reducing the generalizability of the findings. In addition, the inadequate number of participants with normal vitamin B12 levels (control group) prevented us from conducting a case-control study, which would have been a more suitable design. Lastly, due to limited funds for testing B12 levels according to study protocol, we were only able to include patients who had already been advised by their physicians to undergo B12 level assessment, hence the actual prevalence could not be calculated and the frequency of abnormal B12 levels is exaggerated.

DECLARATION:

The datasets generated and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request

Authors Contribution:
Fakhrunnisa Waheed: Conceptualization, study design, and supervision.
Mohammad Minhaj: Data collection and analysis.
Nida Ghouri: Literature review and methodology.
Faridah Amir Ali: Manuscript writing and editing.
Muhammad Junaid Patel: Data interpretation and final manuscript review

REFERENCES:

1. Melaku EE, Urgie BM, Tilahun AT, Assefa HK, Abebe AA, Tefera AS. Prevalence of vitamin B 12 deficiency and associated factors among primary school children: North East Ethiopia: multicenter cross-sectional study. J Health Popul Nutr. 2024;43(1):82;https://doi.org/10.1186/s41043-024-00568-6.

2. Mucha P, Kus F, Cysewski D, Smolenski RT, Tomczyk M. Vitamin B12 metabolism: a network of multi-protein mediated processes. Int J Mol Sci. 2024;25(15):8021;https://doi.org/10.3390/ijms25158021.
3. Langan RC, Goodbred AJ. Vitamin B12 Deficiency: Recognition and Management. Am Fam Physician. 2017;96(6):384-9.
4. Jabbar A, Yawar A, Waseem S, Islam N, Ul Haque N, Zuberi L, et al. Vitamin B12 deficiency common in primary hypothyroidism. J Pak Med Assoc. 2008;58(5):258-61.
5. Obeagu EI, Babar Q, Obeagu GUJIJCRMS. Megaloblastic anaemia-a review. Int J Curr Res Med Sci, 2021•researchgate net. 2021;7(5):17-24.
6. Yousaf S, Bacha U, Zafar M, Raza A, Arbaz Khan M, Bano S, et al. Evaluation of Dietary Intake and Food Insecurity: A Case Study on Selected Households from Lahore,Pakistan. J Nutr Food Secur. 2021;10.18502/jnfs.v6i4.7617.
7. Pawlak R, Lester SE, Babatunde T. The prevalence of cobalamin deficiency among vegetarians assessed by serum vitamin B12: a review of literature. Eur J Clin Nutr. 2014;68(5):541-8;10.1038/ejcn.2014.46.
8. Wolffenbuttel BHR, Wouters H, Heiner-Fokkema MR, van der Klauw MM. The Many Faces of Cobalamin (Vitamin B(12)) Deficiency. Mayo Clin Proc Innov Qual Outcomes. 2019;3(2):200-14;10.1016/j.mayocpiqo.2019.03.002.
9. Saeedullah A, Khan MS, Andrews SC, Iqbal K, Ul-Haq Z, Qadir SA, et al. Nutritional Status of Adolescent Afghan Refugees Living in Peshawar, Pakistan. Nutrients. 2021;13(9):3072;10.3390/nu13093072.
10. Kanwal A, Bashir A. Vitamin B12 in Pregnancy and its Relationship with Maternal BMI and Gestational Diabetes Mellitus - A study from Pakistan. Pak J Med Sci. 2022;38(4Part-II):807-10;10.12669/pjms.38.4.5120.
11. Miyan Z, Waris N, Mibd. Association of vitamin B(12) deficiency in people with type 2 diabetes on metformin and without metformin: a multicenter study, Karachi, Pakistan. BMJ Open Diabetes Res Care. 2020;8(1):e001151;10.1136/bmjdrc-2019-001151.
12. Iftikhar R, Kamran SM, Qadir A, Iqbal Z, bin Usman H. Prevalence of vitamin B12 deficiency in patients of type 2 diabetes mellitus on metformin: a case control study from Pakistan. Pan Afr Med J. 2013;16:67;10.11604/pamj.2013.16.67.2800.
13. IQBAL J, ZIA MA, USMAN M. Frequency of Vitamin B12 Deficiency in Type 2 Diabetics. pjmhs. 2019.
14. Tasleem MW, Rajpoot SR, Irfan M, Irfan M, Imran M, Asad M, et al. Risk Assessment of Vitamin B12 Deficiency in Male Population of Bahawalpur District. Ind J of Inn and App Sci. 2022;2(1):18-22;10.47540/ijias.v2i1.396.
15. Syed EU, Wasay M, Awan S. Vitamin B12 supplementation in treating major depressive disorder: a randomized controlled trial. Open Neurol J. 2013;7:44-8;10.2174/1874205X 013070 10044.
16. Sashindran VK, Aggarwal V, Khera A. Prevalence of Vitamin B12 deficiency in elderly population (>60 years) presenting with dementia to outpatient department. Med J Armed Forces India. 2022;78(1):94-8;10.1016/j.mjafi.2020.11.003.
17. Patel SV, Makwana AB, Gandhi AU, Tarani G, Patel J, Bhavsar V. Factors associated with vitamin B12 deficiency in adults attending tertiary care Hospital in Vadodara: a case control study. Egypt J Intern Med. 2022;34(1);10.1186/s43162-022-00104-0.
18. Ankar A, Kumar A. Vitamin B12 deficiency. StatPearls [Internet]: StatPearls Publishing; 2022.
19. Shamsi U, Azam I, Shamsi A, Shamsi D, Callen D. Frequency and determinants of vitamin D deficiency among premenopausal and postmenopausal women in Karachi Pakistan. BMC women's health. 2021;21(1):194;https://doi.org/10.1186/s12905-021-01339-9.
20. Karabayir N, Teber BG, Dursun HK, Pehlivan LS. Is there an association between vitamin B12 level and vitamin D status in children? J Pediatr Hematol Oncol. 2022;44(3):e677-e81; DOI: 10.1097/MPH.0000000000002329

Original Article **Open Access**

Maternal and Fetal Outcomes Following Caesarean Section in Second Stage of Labour

Sadaf Moin, Ayesha Akram, Shazia Iffet, Farwah Arif, Maryam Nisar, Nayab Gull

ABSTRACT

Objectives: The primary objectives of this study were to establish the frequency of caesarean sections conducted during the second stage of labour, identify the reasons leading to this intervention, and evaluate the maternal and fetal outcomes associated with second-stage caesarean deliveries.

Study Design and Setting: Cross sectional study in Combined Military Hospital Abbottabad.

Methodology: After approval from ethical committee, this study was conducted from 1st January 2024 to 30th June 2024. Via non-probability consecutive sampling, pregnant women between ages 20-45 years, with a singleton pregnancy, and gestation age greater than 37 weeks were included. The study evaluated indications for caesarean section, preoperative instrumentation, intraoperative complications (uterine incision extension, haemorrhage, atonic post-partum haemorrhage), and postoperative complications (wound infection, febrile illness, and neonatal morbidity and mortality).

Results: There were a total of 1195 deliveries over the research period. 642 (54%) babies born via cesarean section. Amongst these, 25 (3.8%) cesarean sections were performed in the second stage. The most common indication for second-stage CS in the present study was non-progress of labour (36%). Among women undergoing second-stage CS, the most common maternal complication was atonic PPH (32%), followed by blood transfusion (28%). In our study, there was no case of maternal and neonatal deaths. For neonates, the most common causes of NICU admission were RDS (36%) and HIE (32%)

Conclusion: Several intra-operative maternal problems and neonatal morbidity are linked to cesarean sections that are performed during the second stage of labour.

Key words: Caesarean Section, Fetal Health,"Labor Stage, Second", Pregnancy Outcome, Fetomaternal Outcome, Maternal Health, Obstetric procedures.

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INTRODUCTION

The global rate of caesarean section has risen significantly over the past decades. The rise is largely attributed to advances in surgical safety, anaesthesia, improved postoperative care, and a reduction in instrumental vaginal deliveries [1]. Despite these improvements, CS continues to carry greater risks of maternal complications compared to vaginal birth, particularly when performed in the later stages of labour[2]. The timing of a CS is critical: when performed during the second stage of labour, both maternal and neonatal risks increase due to technical and clinical challenges unique to this period [3].

A second-stage caesarean section is defined as a CS performed after the cervix has become fully dilated, usually following a failed vaginal delivery attempt or the emergence of complications that rule out a safe vaginal birth[4,5]. The incidence of second-stage CS has grown, with recent data showing an increase from 0.9% to 2.2% in some populations, highlighting a concerning trend in contemporary obstetric practice [1].

Many factors contribute to this rise, including a lack of experience among junior staff in making decisions during advanced labour and limited proficiency in assisted vaginal delivery [6]. According to the Royal College of Obstetricians and Gynaecologists (RCOG), 6% of primary CS are performed at full dilatation, and in half of these, no prior attempt was made at instrumental vaginal delivery. The presence of experienced obstetricians is therefore crucial, as the absence of skilled personnel can result in unnecessary surgeries and increased maternal and neonatal morbidity [7].

Performing a CS at full cervical dilatation presents several technical challenges [4]. Delivering a deeply engaged fetal head may require specialized techniques such as the Patwardhan or push methods, both of which add to operative complexity and risk [7]. Second-stage CS are associated with higher maternal morbidity, including uterine angle extensions, postpartum haemorrhage (PPH), and longer operative times. Additional complications such as bladder injuries and postoperative fevers are also more frequently observed [8].

Neonates delivered by second-stage CS also face increased risks, including a higher likelihood of admission to neonatal intensive care units (NICU), fetal acidemia, and extended NICU stays. Low Apgar scores and abnormal fetal heart rate patterns are more common in this group [9]. This underscores the importance of prompt and expert decision-making to minimise risks for both mothers and neonates.

Non-progression of labour is the most common indication for second-stage CS, with fetal distress and obstructed labour also frequently cited. These indications are consistently associated with adverse maternal and neonatal outcomes, reinforcing the need for diligent perioperative management.

Technical difficulties during second-stage CS, such as unintentional uterine incision extensions and increased risk of infection and bleeding, are well documented. Specialized delivery techniques are often necessary, but they bring their own set of risks, including increased operative time and postoperative complications [7].

The impact on neonatal outcomes is notable, with respiratory distress syndrome (RDS) and hypoxic-ischemic encephalopathy (HIE) being the leading causes of NICU admission among babies delivered by second-stage CS. These conditions carry significant short- and long-term health implications.

Finally, the rising incidence of second-stage CS poses challenges for healthcare systems, including increased hospital stays, resource use, and costs [10]. Women undergoing these procedures are more likely to experience slower recoveries, a higher incidence of wound infections, and delays in returning to daily activities [11]. Thus, access to skilled obstetric and neonatal care is critical, as timely interventions and expert management play a key role in reducing the risks associated with second-stage CS.

METHODOLOGY:

This cross-sectional was conducted at a tertiary care hospital Abbottabad from *1st January 2024 to 30th June 2024.* Ethical approval was obtained from the institutional review board via the letter Number *(File No.CMH-Atd-ETH-157-Gyne-24)* and the informed consent was collected form all participants. Sample size was calculated through *non-probability consecutive sampling technique*. *Inclusion criterion* encompassed pregnant women between ages 20-45 years with a singleton pregnancy, and gestation age greater than 37 weeks. *Exclusion criterion* encompassed pregnancies with a documented medical condition present before conception, pregnancies characterized by significant foetal malformations and restricted fetal growth, preterm and multiple pregnancy cases. After the informed consent from the eligible participants, demographics and clinical details were recorded using a predesigned Performa. The study evaluated indications for caesarean section, preoperative instrumentation, intraoperative complications such as uterine incision extension, haemorrhage, and atonic post-partum haemorrhage (PPH), as well as postoperative complications including wound infection, febrile illness, and neonatal morbidity and mortality. SPSS version 21 was utilized to analyse the data. Continuous variables were presented as mean and standard deviation, while categorical data was represented as frequency and percentage.

RESULTS

During the research period, there were a total of 1,195 deliveries. Of these, 642 (54%) were caesarean sections, and 25 (3.8% of caesarean cases) were performed during the second stage of labour.

The primary indications for opting for caesarean section in these second-stage cases are presented in Figure 1. Maternal complications observed during the study are summarised in Table 1. Importantly, there were no maternal deaths recorded.

Among notable complications, one patient developed a broad ligament haematoma requiring a peripartum hysterectomy. Another patient experienced uterine rupture during the second stage of labour, necessitating an emergency caesarean section; this patient subsequently developed a pulmonary embolism post-operatively, which was managed conservatively, resulting in favourable outcomes for both mother and infant.

Fetal outcomes following second-stage lower segment caesarean section (LSCS) are detailed in Table 2, with no neonatal deaths or stillbirths reported. Demographic and clinical variables for all study participants are presented in Table 3. All data analyses were performed using SPSS version 21.

DISCUSSION

In recent years, both global and national rates of caesarean sections (CS) have increased, particularly at full cervical

dilatation, raising concerns about maternal and neonatal health. This trend is driven by factors such as medicolegal pressures, maternal and fetal morbidities linked to sociodemographic factors, and more frequent instrumental interventions. In Pakistan, CS rates rose from 3.2% in 1990 to 19.6% in 2018, reflecting shifts in clinical practice and a higher incidence of high-risk pregnancies at tertiary hospitals. Our hospital reported a CS rate of 54%, exceeding national averages, and 3.8% at full dilatation, higher than rates documented in Sudan. These increases are linked to the complexity of cases referred from catchment areas. Recent studies indicate that the growing use of advanced diagnostic technologies has contributed to earlier detection of potential complications, influencing decisions towards elective caesarean sections. Additionally, emerging evidence suggests that patient preference and evolving cultural attitudes about childbirth play an increasing role in the rise of CS rates. Researchers are also exploring the long-term impacts on maternal health and subsequent pregnancies, which may prompt the development of revised guidelines to optimise outcomes for mothers and infants.Caesarean sections performed during the second stage of labour are technically more challenging due to changes in pelvic anatomy, such as widened and stretched muscles and ligaments, as the baby descends. This makes extraction more difficult, increasing the risk of maternal and neonatal complications like severe bleeding,

Figure: 1 Indications of second Stage LSCS

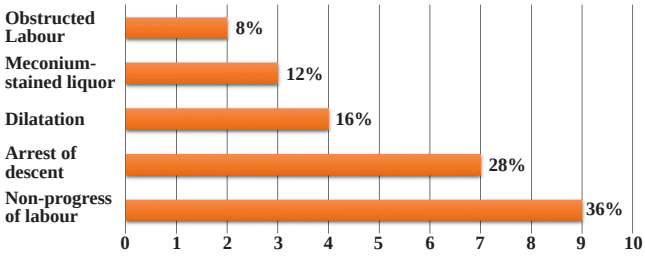

Table 1: Maternal complications

Maternal Complications	N (%)
Atonic PPH	8 (32%)
Uterine Incision Extension	2 (8%)
Postoperative Fever	3 (12%)
Wound Infection Requiring Re-suturing	3 (12%)
Maternal Death	0
Bowel Or Bladder Injury	1 (4%)
Blood Transfusion Required	7 (28%)
Blood Stained Urine	1 (4%)

Table 2: Perinatal complications

Perinatal complications	N (%)
Meconium stained liquor	3 (12%)
Apgar score <7 at 5 min	5 (20%)
Neonatal deaths	0
Stillbirth	0
Respiratory distress (RDS)	9 (36%)
Hypoxic-ischaemic encephalopathy (HIE)	8 (32%)

Table 3: Sociodemographic Profile

Variables	N (%)
AGE	
Age (years)	28.45±4.4
20-30 years	15 (60%)
31-40 years	8 (32%)
Above 40 years	2 (8%)
PARITY	
Primiparous	17 (68%)
Multiparous	8 (32%)
LABOUR	
Induced	17 (68%)
Spontaneous	8 (32%)
Labour duration	7.43±2.3

pelvic tissue trauma, and injuries to the baby. The higher CS rate at our hospital is likely because it serves as a referral centre for a large, remote area with limited medical facilities, and may also reflect more cases of arrested labour or failed labour induction.

Maternal complications that have been associated with second-stage CS, are well-documented, and include a higher incidence of postpartum haemorrhage (PPH), bladder injury, uterine rupture, infection, and prolonged hospital stay.[4,5,6] In our study we have found that, atonic PPH was the most common maternal complication, which was observed in 32% of cases. This rate was lower in comparison to a rate of 47.5% which was shown by Mamoona et al [16] and comparable to rate of 25% cases suffering from atonic PPH as published by Anusha et al in their study (materanal /fetal outcome)[10] The difference in rate here can be attributed to the fact that institutional policies are strict in our setup mandating regular follow ups and better staff to patient ratio.[16] In our study blood transfusion which was done in 28% of patients after the CS, which is significantly more than the value of 8.2% posted in the study by Omer Mander in Sudan, in 15.38% of patients in study by Bijal in India, and less than a value of 73.8% shown by Seval Yilmaz in Turkey.[17,18,19] In our setting we postulate this increased rate of blood products transfusions to the fact, that most of our patients who required CS, are referred cases with history of poor handling in the periphery which is concurrence to a short communication published by Noore Saba.[20] In our study we observed that postoperative fever and wound infection were manifested in 12% of cases respectively, figures that were slightly less than a value of 24.1% occurrence rate shown by Nasreen in her study.[21] Again we

postulate this betterment to the fact that our setup has strict protocols and mechanisms that ensure implementation of these protocols as well.

Nexus, performing a CS during the second stage has its association with maternal morbidity owing to the manoeuvrability required for extraction of a deeply engaged foetal head.[9] Owing to this extensive handling of the pelvic area during the CS we observed that uterine incision extension was observed in 8% of cases which is less as compared to a risk of 58.5% and 54.2% as published by Gilad Karawani and Renana et al.[22,23] This significant difference may be due to the reason that both these studies were conducted over a span of 5 years and had a bigger proportion of the patients were involved in the studies. Other possibilities, may due to the employment of the extensive obstetrical team that handles such cases in our setup and the bulk of the patients are regular booked due to institutional policies. Nonetheless, the risk of complications remains substantial, and careful preoperative assessment and planning are essential highlighting the urgency and complexity of decision-making in the second stage of labor, where timely intervention is critical to prevent adverse outcomes for both mother and baby.

The impact of second-stage CS on neonatal outcomes is equally significant. Studies consistently report a higher rate of neonatal intensive care unit (NICU) admissions, birth asphyxia, and respiratory distress among infants delivered by second-stage CS compared to those delivered by first-stage CS.[7] We report diagnosed neonatal admissions with percentages of, 36% admissions with respiratory distress syndrome, 32% with hypoxic ischemic encephalopathy, 20% with APGAR score of <7 and 12% with meconium-stained labour. These results are in comparison to the data published by Ahazeej who has reported a neonatal admission rate of 30% with birth asphyxia, 40% with meconium aspiration and 8.3%/10% for TTN and Grunting.[4] Similarly, the study conducted by Anusha demonstrated that neonatal admissions consisted of birth asphyxia with 16.66%, respiratory distress with 41.66% and meconium aspiration with 25 % of cases.[10] Neonatal outcomes are affected by the timing and circumstances of CS. The risk of birth asphyxia, respiratory distress, and NICU admission is significantly higher in second-stage CS cases, reflecting the challenges related with delivering a deeply engaged fetal head and the potential for intraoperative hypoxia.[7,9] In our study, the absence of stillbirths and neonatal deaths is a noteworthy finding and may, in large part, be credited to the presence of timely and effective neonatal resuscitation protocols, as well as the immediate availability of neonatal intensive care services. These factors likely played a critical role in stabilizing compromised neonates who were delivered during the particularly high-risk period of the second stage of labour. The presence of trained neonatologists, rapid assessment at birth, and access to advanced supportive care such as mechanical ventilation, intravenous therapy, and continuous monitoring likely contributed to the favourable short-term outcomes observed in our cohort. While our institution's preparedness and efficient neonatal care may have mitigated the most severe consequences, the possibility of significant neonatal morbidity persists. In this context following were some limitations that have been identified in the study.

Limitations of the study.

1. Single center design: since the study has been performed in only one institute and with a peculiar clientele the results cannot be generalized in other settings particularly catering for the resources available at our center.

2. Cross-sectional study design: in order to get an elaborate data about the maternal and foetal outcomes, extensive studies with long term follow ups are necessitated.

3. Small sample size: during the study period available only 25 patients had a caesarean delivery in the second stage which does not permit a robust statistical analysis.

In conclusion, CS performed in the second stage of labor is associated with increased maternal and neonatal morbidity, including higher rates of postpartum hemorrhage, infection, and NICU admission.[7] The technical difficulty of the procedure and the altered pelvic anatomy at this stage contribute to these risks, underscoring the need for skilled obstetric care and timely intervention.[9] The findings from our study and its comparison with available data, highlight the importance of careful decision-making, preoperative planning, and postoperative care in optimizing outcomes for both mother and baby.

CONCLUSION

Second-stage caesarean sections comprised 3.8% of all procedures, mainly due to non-progress of labour, and were linked to maternal and fetal complications. The findings stress the need for expert obstetric judgment, careful use of instrumental delivery, and diligent perioperative care to improve outcomes in this high-risk group.

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REFERENCES

1. Rahim A, Lock G, Cotzias C. Incidence of second stage (fully dilated) caesarean sections and how best to represent it: a multicentre analysis. Int J Gynaecol Obstet. 2022;156(1): 119–123. https://doi.org/10.1002/ijgo.13672.
2. Archibong MS, Adenikinju WS, Olayemi OJ, Amuda M. Caesarean section in second stage of labour: a commentary on principles and techniques. Int J Reprod Contracept Obstet Gynecol. 2021;10(10):4038–4040. https://doi.org/10.18203/2320-1770.ijrcog20213888.

3. Bhatia S, Revankar VM. Study of maternal and perinatal outcome of caesarean delivery in late first stage and second stage of labour. Int J Reprod Contracept Obstet Gynecol. 2021;10(4):1503–1508. https://doi.org/10.18203/2320-1770.ijrcog20211128.
4. Gurashi A, Osman A, Suliman H, Eltigani A, Siralkatim I, et al. Second Stage of Labor Cesarean Section Maternal and Fetal Outcomes. Clin J Obstet Gynecol. 2024;7:25–33. 10.29328/journal.cjog.100115.
5. Dahiya P, Agarwal S, Najam R. Retrospective analysis of second stage of cesarean section and pregnancy outcomes: an observational study. J South Asian Feder Obstet Gynaecol. 2022;14(1):54–58. https://doi.org/10.5005/jp-journals-10006-1991
6. Vashi CA, Vijay N, Bhalerao A, Shetty A, Vashi C. Obstetrics outcomes in women undergoing second-stage cesarean section: a cross sectional study. Cureus. 2023;15(6):e39911. https://doi.org/10.7759/cureus.39911 ouci.dntb.gov.ua+13 pubmed.ncbi.nlm.nih.gov+13ijmedph.org+13
7. Cegolon L, Mastrangelo G, Maso G, Dal Pozzo G, Ronfani L, Cegolon A, et al. Understanding factors leading to primary cesarean section and vaginal birth after cesarean delivery in the Friuli Venezia Giulia Region (North Eastern Italy), 2005–2015. Sci Rep. 2020;10(1):380.DOI: 10.1038/s41598-019-57037-y
8. Second stage of labor cesarean section showed more complications of postpartum hemorrhage, sepsis, and extended tears, as well as more fetal complications. Clin J Obstet Gynecol. 2024;7:025–033.DOI: 10.29328/journal .cjog. 1001159.
9. Cornthwaite K, Bahl R, Lenguerrand E, Winter C, Kingdom J, Draycott Impacted foetal head at caesarean section: a national survey of practice and training. J Obstet Gynaecol. 2021;41(3):360–6. https://doi.org/10.1080/ 01443615. 2020.1780422.
10. Anusha S. Our experience of maternal and foetal outcomes in 2nd stage caesarean deliveries tertiary care centre study. Blood Transfus. 2020;29:58.DOI: https://doi.org/10.33545/gynae.2020.v4.i3a.566
11. Vousden N, Cargill Z, Briley A, Tydeman G, Shennan AH. Caesarean section at full dilatation: incidence, impact and current management. Obstet Gynaecol. 2014;16(3):199–205. https://doi.org/10.1111/tog.12112.
12. Sabir SF, Baig FS, Safdar Z, Zeb S, Tariq F, Shehzadi K. Rising Cesarean Section Rate, Need to Revisit Cesarean Section Indications. Pakistan J Med Heal Sci. 2022;16(4) :687–90.
13. Mahfooz A, Reza TE, Uzam Q et al. A review of Cesarean section Rates and associated Factors in Pakistan Using Anderson Health Behaviour Model. J Gynecol Womens Health.2023;25(5):001-006.
14. Sarwar S, Bibi N, Ashraf N. Increasing Trends of Cesarean Section in Pakistan. P J M H S.2021; 15:626-628.
15. Rami BD, Kaul S, Sailor A, Jindani S. A study of caesarean section at full cervical dilatation. Int J Reprod Contracept Obstet Gynecol. 2020;9(4):1672–6.
16. Riaz M, Mehdi M, Kulsoom S, Khairunnisa, Mushtaq I, Alam K. Risk Fcators , Causes, and Management of Primary Post Partum Hemorrhage at POF Hospital Wah Cantt. J Soc Obstet Gynaecol Pak.2023;13(2):177-180.
17. Mandar O, Hassan B, Abdelbagi O, Eltayeb R, Alhabardi N, Adam I. Prevalance and Associated Factors for Post Caesarean Delivery Blood Transfusion in Eastern Sudan: A Cross-Sectional Study. Journal of Blood Med.2022;13:219-227.
18. Rami BD et al. A study of Caesarean Section at Full Cervical Dilatation. Int J Reprod Contracept Obstet Gynecol.2020; 9:1672-1675.
19. Ergani SY et al. Postoperative Care in the Caesarean Intensive Care Unit: experience from a Tertiary Maternity Hospital. J Turk Ger Gynecol Assoc.2023; 24:42-47.
20. Saba N, Khokhar O K, Waheed U. Rational use of Blood in Obstetrics and Gynaecology in Pakistan: Perspective from a Developing Country. J Soc Obstet Gynaecol Pak.2024; 14:373-376.
21. Fatima N, Ellahi A, Shawita. Surgical Site Infection and Factors Responsible for It After Emergency Caesarean section. Journal of Surg Pak.2020; 25:27-30.
22. Karawani G et al. Risk factors for Uterine Incision Extension During Caesarean delivery.2020. DOI:10.1080/14767058 .2020.1783230.
23. Renan WS et al. Unintended Uterine Extension at the time of Caesarean Delivery-risk factors and associated adverse maternal and neonatal outcomes. The Journal of Maternal-Fetal & Neonatal Medicine.2023;36:1

Original Article **Open Access**

Outcomes of Endoscopic Variceal Band Ligation for Esophageal Varices in Children

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ABSTRACT

Objective: To determine outcomes of endoscopic variceal band ligation (EVBL) for esophageal varices (EV) in children presenting to a tertiary childcare hospital of Pakistan.

Study Design and Setting: A prospective observational cohort study was conducted at the Department of Pediatric Gastroenterology, The Children's Hospital and Institute of Child Health, Faisalabad (June 2023–March 2025).

Methodology: Children aged 2–16 years with endoscopically confirmed EV scheduled for EVBL were analyzed. Baseline demographics, EV grade, and etiology were recorded. Follow-up endoscopies were performed at 4-week intervals. Outcomes included number of sessions, grade reduction, obliteration, and rebleeding. Data were analyzed using SPSS v26 with p=0.05 considered significant.

Results: In a total of 97 children, the median age was 11 years (interquartile range: 8-13 years), while 51.5% children were female. Endoscopic grading showed Grade III, and IV varices in 67% cases. The mean follow-up was 8.8±2.6 months. Variceal grade reduction was achieved in 93.8%, and complete obliteration in 87.6%. One or two EVBL sessions were sufficient in 82.4%; 17.5% required =3. Rebleeding occurred in 8.2%, with no mortality. Higher-grade varices significantly required more sessions (p=0.0332), though other outcomes showed no significant grade-wise association.

Conclusion: EVBL is a safe, well-tolerated, and effective modality for the management of EV in children.

Keywords: Children, esophageal varices, endoscopic variceal band ligation, hematemesis, melena

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INTRODUCTION

Upper gastrointestinal (GI) bleeding is a critical clinical entity that requires prompt evaluation and management, particularly when associated with portal hypertension and esophageal varices (EV). In adults, the incidence ranges between 50 to 150 per 100,000 annually, making it a commonly encountered emergency.[1] In contrast, upper GI bleeding is relatively uncommon in children, with global estimates suggesting an annual incidence of only 1 to 2 cases per 10,000 pediatric patients.[2,3] This rarity, coupled with differences in anatomy, physiology, and etiology between adults and children, makes pediatric upper GI bleeding a unique diagnostic and therapeutic challenge.[4]

In the pediatric population, hematemesis, melena, and signs of hemodynamic instability are classic presenting symptoms. The differential diagnosis is broad, ranging from mucosal lesions such as gastritis or esophagitis, to coagulation disorders, prolapse gastropathy, and esophageal varices.[4] Esophageal varices, in particular, are dilated submucosal veins that develop as a result of sustained portal hypertension, most commonly secondary to chronic liver disease (CLD) or extrahepatic portal vein obstruction. A recent local study from Pakistan estimated the prevalence of chronic liver disease in children to be 1.6%,[2] highlighting the potential disease burden in resource-limited settings where late presentation is not uncommon.

The management of variceal bleeding in children requires a structured approach, beginning with hemodynamic stabilization, pharmacologic therapy, and supportive measures including blood transfusion if necessary.[5] Laboratory investigations, including complete blood count, liver and renal function tests, and coagulation profile, play an integral role in the initial workup and risk stratification.[5] However, upper GI endoscopy remains the cornerstone of diagnosis and treatment. Ideally performed within 12 to 24 hours of presentation depending on clinical stability, endoscopy allows for both localization of bleeding and definitive intervention.[6] Endoscopic variceal band ligation (EVBL) has emerged as the first-line endoscopic therapy for esophageal varices due to its high efficacy, lower complication rates, and repeatability, particularly in pediatric patients where sclerotherapy carries higher risks of ulceration and stricture formation. Nonetheless, most guidelines, including the recent 2021 update from the British Society of Pediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN), have acknowledged a lack of robust, high-quality pediatric data to guide practice.[6]

The available literature shows wide variability in EVBL outcomes among children. For instance, one study reported a 100% obliteration rate with 1–4 sessions of EVBL but noted a high rebleeding rate of 60%.[7] Another study observed rebleeding in 64.1% of cases during the follow-up period.[8] In contrast, a more favorable study found no rebleeding after the first session, with grade reduction of varices in 56.4% of patients and complete obliteration in 28.2%.[9] These disparities may be attributed to differences in patient populations, operator experience, underlying disease etiology, and duration of follow-up.

In the adult population, EVBL has been extensively validated as a safe and effective intervention.[10] However, in children, the evolving nature of guidelines, differences in disease spectrum, and variable responses necessitate more targeted pediatric research. Understanding the number of sessions required, the timeline for obliteration, and risk of complications such as rebleeding is vital for developing standardized protocols that can guide both acute management and long-term surveillance. This study was therefore designed to evaluate the frequency and pattern of outcomes following EVBL in children with esophageal varices, with a particular emphasis on real-world data from a tertiary pediatric center in a low- to middle-income country setting. Disease etiologies in children such as extrahepatic portal vein obstruction, congenital hepatic fibrosis, and metabolic liver diseases differ significantly from those seen in adults, potentially influencing treatment response and outcomes. By systematically analyzing a prospectively followed cohort, this study aims to fill this gap by providing detailed evidence on procedural success, complications, rebleeding rates, and the number of sessions required for variceal obliteration. The findings are expected to inform the development of locally relevant protocols, guide resource allocation, and aid pediatric gastroenterologists and hepatologists in decision-making regarding endoscopic surveillance and intervention. Ultimately, the study aspires to enhance the safety, effectiveness, and consistency of care for children with esophageal varices in similar clinical settings.

METHODOLOGY

A prospective observational cohort study was conducted at the Department of Pediatric Gastroenterology, The Children's Hospital and Institute of Child Health, Faisalabad, from June 2023 to March 2025. Ethical approval was obtained from the institutional review board prior to the commencement of the study (Ref. No. 59-60, dated: 15-05-2023). Informed written consents were obtained from parents or legal guardians of all eligible participants. The inclusion criteria were children of either gender, aged 2-16 years, diagnosed with EV and scheduled to undergo EVBL. Diagnosis of esophageal varices was confirmed on upper GI endoscopy performed by a consultant pediatric gastroenterologist.[11] Children were excluded if they had a previous history of EVBL or endoscopic sclerotherapy, presence of gastric varices, an international normalized ratio (INR) greater than 1.8, or platelet count below 50,000/mm^3. A sample size of 97 was calculated using the OpenEPI online sample size calculator, with a 95% confidence level, 8% margin of error, and anticipated rate of variceal obliteration of 79.8%.[12] Sampling was performed using a non-probability consecutive technique.

Baseline demographic and clinical data including age, gender, residence, presenting symptoms, and etiology of varices were recorded. All patients underwent EVBL under sedation according to institutional protocol. The grade of EV (I–IV) was assessed endoscopically at the time of the first session, using the Paquet classification system. Follow-up endoscopy was scheduled at four-week intervals to assess for grade reduction and obliteration. EVBL was repeated as required based on endoscopic findings. The number of sessions, time to obliteration, and any adverse events were recorded. Rebleeding was defined as recurrence of hematemesis or melena after initial EVBL, and was further categorized into early (within two weeks of the procedure) and late (beyond two weeks).[13] All patients were scheduled for follow-up endoscopy at four-week intervals until variceal obliteration was achieved. Compliance with follow-up was actively monitored through reminder phone calls and counseling of parents/guardians at discharge. Children who missed their scheduled follow-up were contacted and motivated to attend subsequent visits to minimize loss to follow-up. A special form was designed to record all relevant study data throughout the study period.

Data analysis was conducted using IBM-SPSS, version 26.0. Quantitative variables such as age, and follow-up duration were reported as mean±standard deviation (SD) or median

and interquartile range (IQR), while categorical variables such as gender, variceal grade, and EVBL outcomes were expressed as frequencies and percentages. The Chi-square test was applied for comparison of categorical data, with a p-value = 0.05 considered statistically significant.

RESULTS

A total of 97 children underwent EVBL for EV. Of these, 47 (48.5%) were male and 50 (51.5%) were female. The median age was 11 years (IQR: 8-13 years), while 54 (55.7%) children were aged between 2-10 years. Sixty-one (62.9%) children were from rural areas. Table-1 is showing baseline demographic and clinical characteristics of children with esophageal varices. Portal vein thrombosis was the leading underlying cause of esophageal varices, identified in 42 (43.3%) cases. Chronic liver disease accounted for 14 (14.4%) cases, with Wilson disease (n = 2, 2.1%), Caroli disease (n = 1, 1.0%), post-Kasai chronic liver disease (n = 4, 4.1%), and congenital hepatic fibrosis (n = 5, 5.2%) comprising the spectrum of chronic liver diseases (Figure-1). Endoscopy revealed the distribution of EV grades was as grade-I, II, III, and IV in 4 (4.1%), 28 (28.9%), 36 (37.1%), and 29 (29.9%) children, respectively (figure-2).

The mean duration of follow-up was 4.8±2.6 months. A reduction in variceal grade was noted in 91 (93.8%) children. Regarding the number of EVBL sessions required, 40 (41.2%) children achieved the desired outcome (grade reduction or obliteration) with a single session, 40 (41.2%) required two sessions, and 17 (17.5%) needed three or more sessions. Complete obliteration of varices was achieved in 85 (87.6%) children, whereas 12 (12.4%) required further sessions or alternative management. Vomiting was reported in 7 (7.2%), and mild retreosternal pain in 5 (5.2%) children. These complications were self-limited and managed conservatively. Rebleeding was observed in 8 (8.2%) children during the follow-up period. Of these, 5 (5.2%) experienced early rebleeding within two weeks of the procedure, while 3 (3.1%) had late rebleeding. All episodes of rebleeding were successfully managed with endoscopic intervention, and no child required surgical management. No mortality was reported during the study period. Significant association (p=0.0332) was found between initial grade of EV and number of EVBL sessions required, with higher-grade varices (III–IV) more likely to need =2 sessions. Other outcomes such as obliteration, rebleeding, and complications did not show statistically significant associations with variceal grade, though numerically worse outcomes were noted with Grade III-IV (table-2).

Among males, 27 (57.4%) required more than two sessions compared to 30 (60.6%) females (p=0.798). Grade reduction was achieved in 44 (93.6%) males, and 47 (94.0%) females (p=0.937), while complete obliteration occurred in 41 (87.2%) and 44 (88.0%) patients (p=0.909). Complications were observed in 6 (12.8%) males and 6 (12.0%) females (p=0.909). In the 2–10 years age group, 33 (61.1%) required more than two sessions compared to 24 (55.8%) in the 11–16 years group (p=0.599). Among children living in rural areas, 38 (62.3%) required more than two sessions compared to 19 (52.8%) in urban areas (p=0.358). Table-3 is showing details about the association of outcomes with respect to demographic variables.

Table 1: Demographic and clinical characteristics of children with esophageal varices (n=97)

Parameter	Categories	Frequency (%)
Gender	Male	47 (48.5%)
	Female	50 (51.5%)
Age Distribution	2-10 years	54 (55.7%)
	11-16 years	43 (44.3%)
Residence	Rural	61 (62.9%)
	Urban	36 (37.1%)
Frequency of clinical presentation	Hematemesis	52 (53.6%)
	Melena	28 (28.9%)
	Hematemesis and malena	17 (17.5%)

Figure-1: Frequency of causes of esophageal varices (N=97)

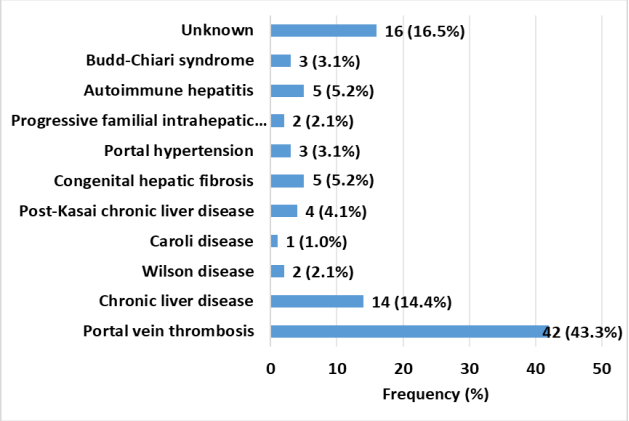
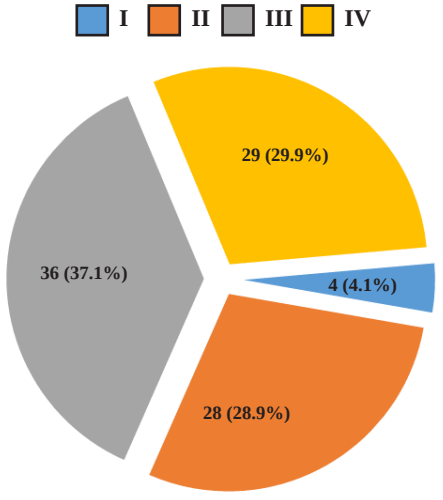


Figure-2: Grades of Esophageal varices (n=97)



DISCUSSION

This study reported higher rates of variceal grade reduction, observed in 93.8% of the children, and the achievement of complete obliteration in 87.6% of cases. Voroniak et al.,[9] reported grade reduction in 56.4% of pediatric patients after just one EVL session, with obliteration achieved in 28.2% of cases. The findings from Celinska-Cedro et al.,[14] also align with this study's results, where variceal obliteration was achieved in 90.3% of children after an average of two EVL sessions. These findings reaffirm the current study's outcomes and underscore the safety and efficacy of EVBL in achieving sustained variceal obliteration in the pediatric population. The association between the initial grade of varices and the number of EVBL sessions required was found to be statistically significant (p=0.0332). Higher-grade varices (grades III and IV) were more likely to require two or more sessions.[10,15] Studies like Farhana et al.,[16] Mahmud et al.,[7] also demonstrated that children with hepatic causes required multiple EVBL sessions, whereas 50% of those with pre-hepatic portal hypertension achieved obliteration in a single session. Re-bleeding was observed in 8.2% of children in the present study, with early re-bleeding occurring in 5.2% and late re-bleeding in 3.1%. These findings are in agreement with those of Kang et al.,[17] who documented four re-bleeding episodes over a 3-year follow-up period among 37 children. The low re-bleeding rate in both studies reflects the durability of EVBL as a secondary prophylactic intervention in pediatric patients with portal hypertension. Contrary to these findings, Mahmud et al.,[7] reported a much higher re-bleeding rate, especially among children with hepatic causes of portal hypertension, where re-bleeding occurred in all hepatic cases. The lower re-bleeding rate in the current study may reflect a higher proportion of extra-hepatic etiologies (e.g., portal vein thrombosis), which constituted 43.3% of the study population.

Complications observed in this study were minimal and self-limited, with vomiting (7.2%) and mild retreosternal pain (5.2%) being the most common. No mortality or procedure-related severe adverse events were reported. These findings are consistent with the studies by Kim et al.,[8] and Li et al.,[18] which documented complication rates ranging from 4.8% to 10.3% in children undergoing EVBL. The contemporary data confirm the safety profile of EVBL in pediatric populations, with no cases of perforation or embolization reported.[8,18]

An important clinical implication of this study is the identification of a significant correlation between initial variceal grade and treatment intensity, suggesting that children

Table-2: Association of outcomes of Endoscopic Variceal Band Ligation with respect to Esophageal varices grades

Outcomes		Frequency (%)	Esophageal varices grade				P-value
			I (n=4)	II (n=28)	III (n=36)	IV (n=29)	
Number of EVBL sessions required	1	40 (41.2%)	2 (50.0%)	17 (60.7%)	14 (38.9%)	7 (24.1%)	0.0332
	2	40 (41.2%)	1 (25.0%)	9 (32.1%)	18 (50.0%)	12 (41.4%)	
	>3	17 (17.5%)	1 (25.0%)	2 (7.1%)	4 (11.1%)	10 (34.5%)	
Grade reduction in EVB	Yes	91 (93.8%)	4 (100%)	27 (96.4%)	34 (94.4%)	26 (89.7%)	0.6862
	No	6 (6.2%)	-	1 (3.6%)	2 (5.6%)	3 (10.3%)	
Complete obliteration achieved	Yes	85 (87.6%)	4 (100%)	25 (89.3%)	31 (86.1%)	25 (86.2%)	0.8580
	No	12 (12.4%)	-	3 (10.7%)	5 (13.9%)	4 (13.8%)	
Post-EVBL complications	Re-bleeding	8 (8.2%)	-	1 (3.6%)	3 (8.3%)	4 (13.8%)	0.5036
	Vomiting	7 (7.2%)	-	1 (3.6%)	3 (8.3%)	3 (10.3%)	0.7154
	Transient retreosternal pain	5 (5.2%)	-	1 (3.6%)	2 (8.3%)	2 (6.9%)	0.9175

Table-3: Association of outcomes of with respect demographic variables (N=97)

Variables		>2 sessions required	Grade reduction	Complete Obliteration	Complications
Gender	**Male**	27 (57.4%)	44 (93.6%)	41 (87.2%)	6 (12.8%)
	Female	30 (60.6%)	47 (94.0%)	44 (88.0%)	6 (12.0%)
Age groups (years)	**P-value**	0.798	0.937	0.909	0.909
	2-10	33 (61.1%)	51 (94.4%)	47 (87.0%)	8 (14.8%)
	11-16	24 (55.8%)	40 (93.0%)	38 (88.4%)	4 (9.3%)
	P-value	0.599	0.773	0.843	0.413
Residence	**Rural**	38 (62.3%)	57 (93.4%)	53 (86.9%)	8 (13.1%)
	Urban	19 (52.8%)	34 (94.4%)	32 (88.9%)	4 (11.1%)
	P-value	0.358	0.843	0.772	0.772

with higher-grade varices require closer monitoring and possibly more aggressive follow-up to achieve obliteration.[19] This highlights the need for individualized treatment plans based on baseline variceal grading. The high obliteration rate and low rebleeding rate observed support the role of EVBL as a safe and effective strategy in the secondary prophylaxis of EV in children.[20,21]

Limitations: Certain limitations must be acknowledged as well. Although the sample size was adequate for primary outcome assessment, it may be underpowered for detecting subtle differences in complication rates or stratified analyses based on etiology. The absence of a control group, such as children undergoing sclerotherapy or receiving non-endoscopic management, limits comparative interpretation.[22] The study focused on short- to mid-term outcomes; long-term durability of obliteration, variceal recurrence, and survival could not be assessed. The absence of control or comparator group was another limitation of this study.

CONCLUSION

EVBL is a safe, well-tolerated, and effective modality for the management of EV in children. EVBL achieved high rates of variceal grade reduction and obliteration with low rebleeding and complication rates. EVBL was clearly most efficient in Grade I–II, with outcomes progressively less favorable in Grades III–IV. The significant association between higher-grade varices and the need for multiple sessions has clinical implications for individualized patient care and resource allocation. Further large-scale, multicenter, randomized studies are warranted to explore the long-term efficacy and optimal follow-up strategies in EV.

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REFERENCES

1. Perisetti A, Kopel J, Shredi A, Raghavapuram S, Tharian B, Nugent K. Prophylactic pre-esophagogastroduodenoscopy tracheal intubation in patients with upper gastrointestinal bleeding. Proc (Bayl Univ Med Cent). 2019;32(1):22-25. doi: 10.1080/08998280.2018.1530007
2. Abou-Taleb A, Ahmed ARH, El-Hennawy A. Pediatric Chronic Liver Diseases: A clinicopathological study from a tertiary care center. Int J Pediatr. 2019;7(4):9305-9315. doi: 10.22038/ijp.2019.37294.3246
3. Nasher O, Devadason D, Stewart RJ. Upper Gastrointestinal Bleeding in Children: A Tertiary United Kingdom Children's Hospital Experience. Children (Basel). 2017;4(11):95:1-6.
4. Jafari SA, Kiani MA, Kianifar HR, Mansooripour M, Heidari E, Khalesi M. Etiology of gastrointestinal bleeding in children referred to pediatric wards of Mashhad hospitals, Iran. Electron Physician. 2018;10(2):6341-5.
5. Bai Y, Li ZS. Standardize the diagnosis and treatment of acute non-variceal upper gastrointestinal bleeding based on the update guidelines. Zhonghua Nei Ke Za Zhi. 2019;58(3):161-3.
6. Jung K, Moon W. Role of endoscopy in acute gastrointestinal bleeding in real clinical practice: An evidence-based review. World J Gastrointest Endosc. 2019;11(2):68-83.
7. Mahmud S, Ahmed SS, Gulshan J, Tasneem F, Baidya M. Outcome of band ligation in esophageal varices of Bangladeshi children: A tertiary centre experience. Bangladesh J Child Health. 2017;41(1):28-33.
8. Kim SJ, Oh SH, Jo JM, Kim KM. Experiences with endoscopic interventions for variceal bleeding in children with portal hypertension: a single center study. Pediatr Gastroenterol Hepatol Nutr. 2013;16(4):248-53.
9. Voroniak DI, Godik OS, Fedoniuk LY, Shapoval OÌ, Piliponova VV. Role of stage endoscopic variceal band ligation in treatment of children with portal hypertension. Wiad Lek. 2020;73(10):2133-7.
10. Farooqi JI, Shah HA, Khan AA, Salamat A, Alam A, Khattak AK, et al. Clinical Practice Guidelines on the Management of Variceal Bleeding. J Coll Physicians Surg Pak. 2016 Jan;26(1):63-5. Available from: https://pubmed.ncbi.nlm.nih.gov/26787034/
11. Alvi H, Zuberi BF, Rasheed T, Ibrahim MA. Evaluation of endoscopic variceal band ligation sessions in obliteration of esophageal varices. Pakistan Journal of Medical Sciences 2020;36(2):37.
12. Abbasi A, Bhutto AR, Bhatti KI, Mahmood K, Lal K. Outcome of band ligation in esophageal varices. J Pak Med Assoc. 2013;63(8):983-987.
13. Butt N, Haleem F, Khan MA, Abbasi A. Efficacy and safety of N-butyl 2 cyanoacrylate injection for treatment of gastric varices: a five-year experience from a tertiary care hospital in Karachi, Pakistan. Pak J Med Sci. 2022;38(5):1360.
14. Celińska-Cedro D, Teisseyre M, Woynarowski M, Socha P, Socha J, Ryzko J. Endoscopic ligation of esophageal varices for prophylaxis of first bleeding in children and adolescents with portal hypertension: preliminary results of a prospective study. J Pediatr Surg. 2003;38(7):1008-11. doi: 10.1016/s0022-3468(03)00181-7
15. Guo H, Zhang M, Zhang N, Yin X, Cheng Y, Gu L, et al. Number of endoscopic sessions to eradicate varices identifies high risk of rebleeding in cirrhotic patients. BMC Gastroenterol. 2022;22(1):213. doi: 10.1186/s12876-022-02283-0
16. Farhana T, Mahmud S, Tasneem F, haque E, Rashid R, Baidya M, et al. Management of childhood esophageal varices: learnings from an advanced medical centre. Gastroenterol Hepatol. 2025;16(2):61-65. Available from: https://medcraveonline.com/GHOA/GHOA-16-00609.pdf

17. Kang KS, Yang HR, Ko JS, Seo JK. Long-term outcomes of endoscopic variceal ligation to prevent rebleeding in children with esophageal varices. J Korean Med Sci. 2013;28(11):1657-60. doi: 10.3346/jkms.2013.28.11.1657

18. Li MM, Sun F, Huai MX, Qu CY, Shen F, Zhang Y, et al. Endoscopic variceal ligation combined with sclerotherapy for management of gastroesophageal variceal bleeding in pediatric patients: a single-center retrospective study. Front Pediatr. 2024;12:1325419. doi: 10.3389/fped.2024.1325419

19. Pallio S, Melita G, Shahini E, Vitello A, Sinagra E, Lattanzi B, et a. Diagnosis and Management of Esophagogastric Varices. Diagnostics (Basel). 2023;13(6):1031. doi: 10.3390/diagnostics13061031

20. Alatas FS, Monica E, Ongko L, Kadim M. Endoscopic Primary Prophylaxis to Prevent Bleeding in Children with Esophageal Varices: A Systematic Review and Meta-Analysis. Pediatr Gastroenterol Hepatol Nutr. 2023;26(5):231-238. doi: 10.5223/pghn.2023.26.5.231

21. Shrestha B, Sudhamshu KC, Chaudhary S, Basnet BK, Mandal AK, Poudyal NS. Outcome of Endoscopic Variceal Band Ligation. J Nepal Med Assoc 2017;56(206):198-202. Available from: https://pdfs.semanticscho lar.org/adb3/b3120dfe3162baf87b59285e074d42520f40.pdf

22. Gana JC, Cifuentes LI, Gattini D, Torres-Robles R. Band ligation versus sclerotherapy for primary prophylaxis of oesophageal variceal bleeding in children with chronic liver disease or portal vein thrombosis. Cochrane Database Syst Rev. 2020;11(11):CD011803. doi: 10.1002/14651858.CD011803.pub2

Original Article **Open Access**

Association of Acupressure at Sanyinjiao Point 6 with C-Reactive Protein, Interleukin 6, Prostaglandin F2α, and Vasopressin in Medical College Students with Primary Dysmenorrhea.

Samira Amjad, Qamar Aziz, Ruqaya Nangrejo

ABSTRACT

Objective: To observe the changes in biochemical markers after applying acupressure in Primary Dysmenorrhea (PD) at Sanyinjiao Point 6 (SP6) and ascertain whether pain relief is biochemically mediated.

Study design and setting: A quasi-experimental design was adopted. The study was carried out from September 2022 to April 2023, in Karachi, Pakistan, at a private medical college.

Methodology: After ethical approval (BMU-EC/04-2022), 50 participants were selected using a modified menstrual symptom questionnaire, who were healthy, experienced regular PD, and abstained from analgesics. Written informed consent was taken, then in the first month of the study, blood samples (pre-intervention) were taken on day one of the menstrual cycle (MC). In the following three MCs, acupressure was self-applied at acupoint SP6, taught by a qualified acupressurist. During dysmenorrhea, it was applied on both legs, three times/day, for two to five minutes. In the third month of acupressure, second (post-intervention) blood samples were taken. Plasma levels of C-reactive protein (CRP), Interleukin-6 (IL-6), Prostaglandin F2α (PGF2α), and Vasopressin (VP) were measured and compared with pre-intervention samples using Statistical Package for Social Sciences 23 (SPSS 23).

Results: Median with interquartile ranges (IQR) of PGF2α, IL-6, VP, and CRP were obtained and compared, reporting a statistically significant increase in the post-intervention plasma CRP level (p=0.03), whereas plasma levels of PGF2α, IL-6, and VP showed no significant change (p=0.60, p=0.84, p=0.19, respectively).

Conclusions: Except CRP, the biochemical markers showed no significant change; hence, acupressure mediates its pain relief through additional mechanisms.

Keywords: Acupressure, C-Reactive Protein, Interleukin 6, Dysmenorrhea, Prostaglandins F, Vasopressins

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INTRODUCTION

Dysmenorrhea is pain during menstrual cycles (MC), and it is the most common gynecological problem found among women.[1] Without pelvic pathology, it is called primary dysmenorrhea (PD), and secondary if pathology is present.[2] PD starts with ovulatory cycles, often one year after menarche, but in some cases it may start after 2 years.[1] For some women, this pain is minimal and bearable, but for some it is so severe that it interferes with normal daily life.

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Dysmenorrhea is not reported as much as it actually prevails, nor is it adequately treated.[1] The prevalence in different countries; in Pakistan at 91.5%,[1] in Kuwait at 85.6%,[4] in Lebanon at 80.9%,[5] Spain at 47.8%,[4] and Poland at 94%.[1] Due to dysmenorrhea, in one year 58% of students missed at least one academic day, 13.9% missed one exam, 26% needed a clinical visit, and 4.1% were hospitalized.[4] In a Spanish study, 51.3% of dysmenorrhea sufferers claimed a lack of concentration, of which 47.8% had PD.[6]

Considering the risk factors, a study found that medical students had a greater chance of having PD than non-medical students, we can speculate that this may be due to increased stress levels in medical students but further research is required.[5] Heavy flow and family history also showed a greater risk for PD, as did attempts at weight loss presumably due to nutrional deficiencies but in this case too, more research is needed for scientific evidence.[5]

Though poorly understood, PD is considered to be due to prostaglandins (PG) produced in the uterus, suggested as early as 1965 by Pickles and associates.[8] Progesterone stabilizes lysosomes in ovulatory cycles, which decreases before menstruation, releasing phospholipase A2 from the

lysosomes. Phospholipase A2 will gives rise to the Arachidonic acid which is broken into PGs and leukotrienes.[2] The main PGs are PGF2α and PGE2. PGF2α is a strong stimulator of smooth muscle contraction,[7] causing myometrial contractions which produce ischemia leading to pain. This myometrial contraction also leads to increased nerve sensitivity. PGs also lower the pain threshold. This highlights why ovulatory cycles are associated with dysmenorrhea.[1,9]

Though there is inadequate literature to establish a single etiology, multiple factors have been found, including increased PGF2α and increased Vasopressin (VP).[2] VP is a posterior pituitary gland hormone, the level of which varies in the MC, and it may also play a role in myometrial contractility and ischemia.[2] Plasma PGF2α metabolites were found in significantly greater levels in the group with dysmenorrhea, in contrast to the non-dysmenorrheic group,[2,8] and women with greater symptoms have higher levels.[9] Plasma levels of VP and IL-6 were also reported to be higher in the dysmenorrheic group when compared with the women without dysmenorrhea.[10] VP receptor blockers have shown pain relief, but the results have not been consistent.[1,9] Higher C-Reactive Protein (CRP) levels are found during menstruation compared to other parts of the monthly cycle but the increased levels are not related to the hormonal changes in MCs,[7] and dysmenorrheic women had significantly higher levels than non-dysmenorrheic women.[11]

A study showed that 23.6% of dysmenorrheic university students avoided using any pharmacological methods to relieve their pain, of which 22.9% abstained from analgesics due to a fear of side effects such as vomiting, diarrhea, constipation, headache and drowsiness that were reported in their study.[5] In Traditional Chinese Medicine (TCM), acupressure is a technique involving pressure application on the body with a finger, thumb, or device at specific points (known as acupoints).[12] Systematic reviews studying the effects of acupressure have found support for its significant effectiveness.[12] Studies have shown that acupressure relieves pain by the production of endogenous analgesics by stimulating the autonomic nervous system.[13]

Few studies have delved into the precise events that mediate these outcomes. Specifically, there is a need for comprehensive research on how acupressure modulates neurohormonal pathways it activates, beyond general opioid peptide and endorphin release. So, the present research aimed to study the effects of acupressure on plasma levels of CRP, IL-6, PGF2α, and VP. To find changes in plasma levels, if any, in CRP, IL-6, PGF2α, and VP after applying acupressure therapy in the PD participants.

METHODOLOGY

A quasi-experimental design was used. A single group was studied, measuring the pre and post-acupressure levels of the biochemical markers mentioned above. The research was approved by the ethical committee of Baqai Medical University (ERC number BMU-EC/04-2022), and the "Code of Ethics of the World Medical Association" (Declaration of Helsinki) was taken into consideration while conducting the research. Data was collected from fifty participants of a private medical college in Karachi in a duration of eight months between September 2022 and April 2023. Participation was purely voluntary. The participants were explained in detail the requirements of the study, after which a written informed consent was taken. A modified menstrual questionnaire was distributed to select participants. It inquired about age, height, weight, marital status, menarche age, number of bleeding days, and regularity. Closed-ended questions were used to exclude diabetes, hypertension, pelvic disease or surgery, any neuropathies, and stress or depression. For menstrual pain characteristics and analgesic/alternative method use, a Likert scale was used with the options; never, occasionally, sometimes, often, and always.

Openepi was used to calculate the sample size by a professional statistician. A sample size of twenty before and twenty after intervention was obtained with a Confidence Interval (two-sided) of 95% and Power of 80%. To strengthen the study, we recruited an additional thirty students, increasing the sample size to fifty participants.

For blood testing, ELISA kits were used; Human Prostaglandin F2α ELISA kit, Cat. No. E0973Hu (BT laboratory, Birmingham, UK), Human Interleukin 6 ELISA Kit, Cat. No. E0090Hu (Li StarFish srl, Italy), Human antidiuretic hormone Kit, Cat. No. E1048Hu (Li StarFish srl, Italy) and Human C-Reactive Protein ELISA Kit, Cat. No. E1798Hu (BT laboratory, Birmingham, UK).

Convenient sampling was used. Students at a private medical institute who suffered from dysmenorrhea every single month and did not use a painkiller were recruited. See Figure 1 for the diagrammatic representation. 250 questionnaires were distributed, of which 240 were filled out and returned. 224 students suffered from PD, out of which 112 had PD every month. Of these 112 students, 66 used analgesics while 46 did not use any analgesics. 46 students fulfilled our criteria, and four analgesic users volunteered to abstain from using them for the required duration of the study, thus bringing the total sample size to 50 students.

Inclusion criteria were students who were healthy with ages between 16 and 25, having regular, normal, menstrual cycles, experiencing PD every month, and avoiding analgesics. All categories of Body Mass Index according to the World Health Organization were included.

Exclusion Criteria[5] was any pelvic disease, any history of pelvic surgery, diabetes mellitus, hypertension, a recent stressful incident, depression or mental illness, any other co-morbid conditions, any neuropathies or injury in the lower leg.

The students were taught about the self-application of

acupressure at SP6 by a certified acupressurist. SP6 acupoint is located four fingers above the medial malleolus between the tibia bone and the muscle.[14] This acupoint is shown in Figure 2. After the first blood sample (pre-intervention), the participants applied acupressure with their finger or thumb during the three subsequent MCs during PD on both legs, one by one, for two to five minutes each. The participants reported no adverse effects of acupressure.

Blood samples were collected in the first month of the study on the first day of the MC without intervention, which comprised the pre-acupressure samples. Then during the third month of acupressure application, the post-intervention blood samples were taken on the first day of MC approximately one hour after acupressure. Samples were stored at -20^{0} C till further analysis.

Data Analysis was done using SPSS version 23.0. Means with standard deviations of the baseline characteristics were calculated. The median (Interquartile Range – IQR) of the biochemical marker levels were compared before and after intervention. The Wilcoxon Sign Rank test was used instead of the paired sample t-tests as the data was not normally distributed due to some outliers.

RESULTS

Table 1 reports the baseline characteristics of studied samples, in the present study there were 50 participants, Mean Age (years) was 20.92 (SD=±1.56), mean Weight (kg) was 54.6 (SD=±10.8), mean Height (m) was 1.615 (SD=±0.063), mean BMI (kg/m2) was 20.91 (SD=±3.6), mean Age of Menarche was 13.28 (SD=±1.58), mean Number of bleeding days was 5.30 (SD=±1.38).

Table 2 reports the pre and post-acupressure plasma levels in the PD group. The Wilcoxon Signed Rank test was used in place of paired sample t-tests because the data were not normally distributed due to some outliers. The pre-acupressure PGF2α Median was 383.4(IQR=98.9), IL-6 Median was 75.49(IQR=35.87), VP Median was 50.07(IQR=24.48), and CRP Median was 0.66(IQR=0.4019) and post-acupressure PGF2α Median was 374.3(IQR=360.2), IL-6 Median was 72.18(IQR=23.71), VP Median was 50.32(IQR=26.09), and CRP Median was 0.8(IQR=0.4858). The Wilcoxon signed-rank test showed a significant increase in CRP after treatment ($p = 0.03$), while no significant changes were found in PGF2α, IL-6, and VP markers ($p > 0.05$).

DISCUSSION

Acupressure is a type of massage, and massage has been shown to lower the production of IL-6 along with other products. Thus, acupressure may decrease the inflammatory responses, both local and systemic.[15] There is evidence that acupoint stimulation produces a variety of effects, including changes in neurohormone secretion.[16] Studies regarding the effects of acupressure on plasma levels of biochemical markers in PD were not found. On the basis of the available

Figure 1. Diagrammatic description of the recruitment and induction of study subjects

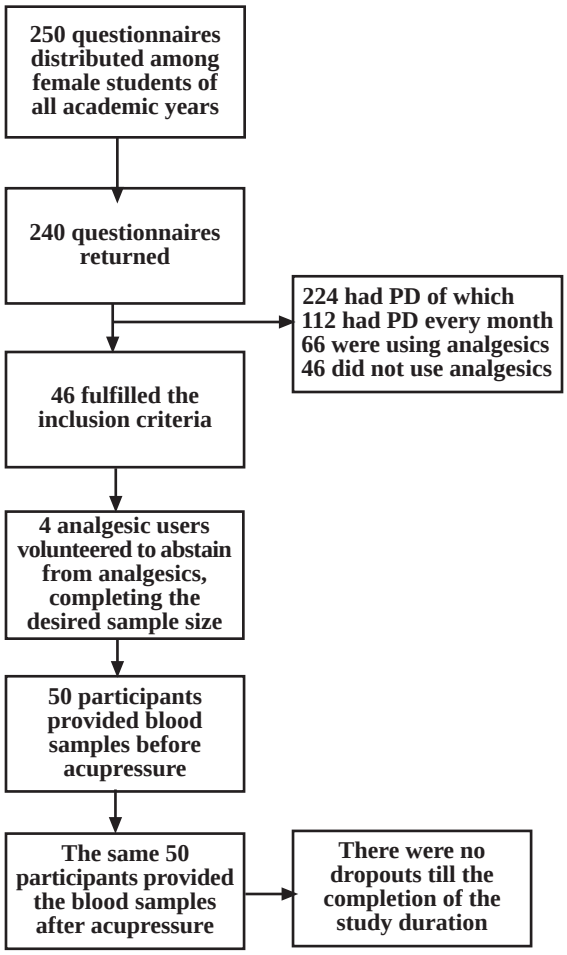

Figure 2. Location of the acupoint Sanyinjiao Point 6 (SP6). (Photograph taken of a study participant with consent).

Table 1: Baseline Characteristics of Studied Samples (n=50)

PARAMETERS	*Mean±SD (N=50)*
Age (years)	20.92±1.56
Height (m)	1.615±0.063
Weight (kg)	54.6±10.8
BMI (kg/m^2)	20.91±3.60
Duration of bleeding (days)	5.30±1.38
Age of Menarche (Years)	13.28±1.52

Table 2: Comparison of pre and post-acupressure levels of PGF2a, IL-6, VP, and CRP

Parameters	*Median (IQR) Pre-acu*	*Median (IQR) Post-acu*	*P-value*
PGF2a pg/ml	383.4 (464.3-365.4)	374.3 (698.8-338.6)	0.60
IL-6 pg/ml	75.49 (103.9-68.03)	72.18 (88.52-64.81)	0.84
VP pg/ml	50.07 (68.43-43.95)	50.32 (70.59-44.5)	0.19
CRP mg/L	0.66 (0.8976-0.4957)	0.80 (1.061-0.5752)	0.03*

*P<0.05 was considered statistically significant using the Wilcoxon Signed Ranks test

IQR: Interquartile Range, Pre-acu: Pre-acupressure, Post-acu: Post-acupressure, PGF2á: Prostaglandin F2á, IL-6: Interleukin 6,VP: Vasopressin, CRP: C-Reactive Protein

literature and with the best of our knowledge, we can say that this is the first study to determine the influence of acupressure at SP6 on plasma levels of PGF2α, VP, CRP, and IL-6 in women with PD.

In this study, despite significant pain relief,[17] only CRP showed a statistically significant greater value in the post-acupressure plasma levels (p=0.03). Interestingly, CRP is known to be an inflammatory marker and is higher during menstruation as pointed out earlier, but its increased level after acupressure despite pain relief appears contradictory. On the other hand, IL-6, also a known inflammatory marker, showed no increase. This may mean that the CRP rise was not necessarily inflammatory-mediated, or it rose via a non-IL-6 pathway. There may be confounding factors other than those excluded (coexisting morbidity, infection, injury, and known chronic stress) during the selection of the participants. The other confounding factors may be physical exertion, temporary stress, sleep disturbance, subclinical undiagnosed infection or diet-based factors. Laboratory or handling errors may also partially contribute. The fact that there was significant pain relief suggests that the pain relief is not due to decreased inflammation (as endometrial sloughing persists), it is more likely neuromodulated, but further research is needed with larger sample sizes. Other studies observing the effects of acupressure on CRP were not found, albeit a Polish study studied the effects of manual therapy on PD[7]. In contrast to the present study, they found no difference in CRP plasma levels after manual therapy in PD despite pain relief. Their sample size was 20 with similar baseline characteristics.

In the current study, PGF2α plasma levels showed a slight decrease in the post-acupressure levels but were not statistically significant (p=0.60) despite significant pain relief. This may lead to the speculation that the pain reduction was not PGF2α mediated, even though PGs, especially PGF2α sensitize nerve endings to pain.[18] No studies were found where PGF2α was measured pre and post-acupressure in PD. One study in Poland[7] compared PGF2α plasma levels in PD before and after "manual therapy" and reported no significant difference despite significant pain relief similar to our findings. Available data suggests that the pain relief by manual therapy is due to the vagal nerve stimulation. Through the stimulation of the parasympathetic nervous system, there is vasodilation in the pelvis which relieves the ischemia.[7]

Conversely, an Indonesian study reported PGF2α changes in PD after Slow Stroke Back Massage (SSBM), Warm compress, and Cold compress, but NOT acupressure.[19] Significantly decreased levels of PGF2α levels were found in the intervention group (p=0.01) when compared with the control group. (n=13 per group). SSBM is a massage over the whole back, while acupressure is a type of massage only at specific points. Likewise, temperature changes occur with warm and cold compresses that may affect the synthesis and metabolism of PGF2α.

Also in opposition to our findings, Kannan and co-workers found a reduction in metabolites of PGF2α and pain after aerobic exercise in PD and concluded that the pain relief may be chemically mediated.[20] The age range of the participants was similar to the current study but their sample size was 10 for the exercising group and 10 for the control group.

Tyas and his coworkers compared PGF2α levels in a younger reproductive age group (11-17 years) before and after abdominal stretching, dysmenorrhea exercises, and yoga.[21] They reported a significant reduction after dysmenorrhea exercises and yoga, but significant pain reduction was reported only after the dysmenorrhea exercises. Thus implying that pain relief is not solely dependent on chemical mediation supporting our finding. Another research regarding acupuncture with auricular acupressure effects on menstrual headaches, NOT PD, found significant reductions (p<0.01) in plasma PGF2α levels.[22]

The present study found no significant difference between the VP levels before and after intervention (p=0.19). Other studies measuring VP before and after acupressure for PD were not found, based on the current knowledge we have. One study showed that acupuncture with auricular

acupressure reduced the VP levels, but this research studied the effects on menstrual headache, NOT PD.[22]

In the current study, post-acupressure IL-6 levels revealed a mild reduction but not significant (p=0.84). Other studies where IL-6 levels after acupressure were evaluated in PD were not found. Rahimi and coworkers compared pain and blood levels of IL-6 before and after 2 months of high-intensity interval and moderate continuous training on PD. The sample size of the study was 30 and had a similar age range to our study. They found no significant difference in the IL-6 levels.[23] In contrast, a study regarding acupressure effects on low back pain, not PD, found a rise in IL-6 levels after auricular acupressure when compared with a control group.[24] Their sample size was 19, of which 10 used auricular acupressure and 9 used a sham acupressure and the age of participants was over 40 years as they studied low back pain and not PD. A study by Yeh in 2023 supports the role of inflammatory markers in analgesia by acupressure.[25] They correlated auricular point acupressure, pain intensity (chronic low back pain) and inflammatory markers that included IL-2, NOT IL-6. A significant decrease was found in the pre and post-acupressure levels of IL-2 as opposed to our results.

There is scanty literature available on the current topic, so there is a crucial need to evaluate the mechanism of analgesia mediated by various hormones, cytokines, and other inflammatory markers in PD to enhance the level of comfort among a diverse population of women. Non-significant results are not the limitations of the study, because it pointed out an important cost-effective, reliable, authentic, and independent method for pain suppression mediated by specific biomarkers. However, an innovative mechanism can be more clearly identified by the implication of a more generalized study design.

Strength of the study: The strength of the study is, from our perspective, that it is probably the first study of this specific type in Pakistan and the South Asian region.

Limitations: The limitation of this study is that the participants included all medical students, so we can not generalize the findings to the total population.

CONCLUSÝON

The study findings suggest that the amelioration of pain by acupressure at SP6 in PD is not purely mediated via biochemical markers, and other pathways are also involved. Continued research is required to comprehend the complexity of the association of biomarkers with analgesia via acupressure. Future recommendations are to conduct studies to map the precise cellular pathways through which PGF2α vasopressin, IL-6, and CRP contribute to uterine contractility and pain. This could involve studying signalling cascades in myometrial and endometrial cells. Investigate how signalling might interact at a molecular level, such as receptor co-activation or shared downstream targets in uterine tissue.

Authors Contribution:
Samira Amjad: Conceptualized the study, planned the design, methodology, and data curation, wrote the manuscript and statistical analysis, and is responsible for the integrity of the research.
Qamer Aziz: study design, and assisted in the result interpretation, critically reviewing, and approval of the final version of the draft.
Ruqaya Nangrejo: study design, data analysis, and drafting the article

REFERENCES

1. Ferries-Rowe E, Corey E, Archer JS. Primary dysmenorrhea: diagnosis and therapy. Obstet Gynecol 2020 Nov 1;136(5):1047-58. DOI: 10.1097/AOG.0000000000004096
2. Barcikowska Z, Rajkowska-Labon E, Grzybowska ME, Hansdorfer-Korzon R, Zorena K. Inflammatory markers in dysmenorrhea and therapeutic options. Int. J. Environ. Res. Public Health. 2020 Feb;17(4):1191. doi:10.3390/ ijerph17041191
3. Ullah A, Fayyaz K, Javed U, Usman M, Malik R, Arif N, et al. Prevalence of dysmenorrhea and determinants of pain intensity among university-age women. Pain Med. 2021 Dec 1;22(12):2851-62. doi: 10.1093/pm/pnab273
4. Al-Matouq S, Al-Mutairi H, Al-Mutairi O, Abdulaziz F, Al-Basri D, Al-Enzi M, et. al. Dysmenorrhea among high-school students and its associated factors in Kuwait. BMC pediatr. 2019 Dec;19:1-2. doi.org/10.1186/s12887-019-1442-6
5. Karout S, Soubra L, Rahme D, Karout L, Khojah HM, Itani R. Prevalence, risk factors, and management practices of primary dysmenorrhea among young females. BMC womens health. 2021 Dec;21:1-4. doi.org/10.1186/s12905-021-01532-w
6. Abreu-Sánchez A, Ruiz-Castillo J, Onieva-Zafra MD, Parra-Fernández ML, Fernández-Martínez E. Interference and impact of dysmenorrhea on the life of Spanish nursing students. Int J Environ Res Public Health. 2020 Sep;17(18):6473. doi:10.3390/ijerph17186473
7. Barcikowska Z, Grzybowska ME, W¹¿ P, Jaskulak M, Kurpas M, Sotomski M, et. al. Effect of manual therapy compared to ibuprofen on primary dysmenorrhea in young women—concentration assessment of C-reactive protein, vascular endothelial growth factor, prostaglandins and sex hormones. J. Clin. Med. 2022 May 10;11(10):2686 doi.org/10.3390/jcm11102686
8. Lundström V, Green K. Endogenous levels of prostaglandin F2α and its main metabolites in plasma and endometrium of normal and dysmenorrheic women. Am J Obstet Gynecol. 1978 Mar 15;130(6):640-6.
9. Gutman G, Nunez AT, Fisher M. Dysmenorrhea in adolescents. Curr. Probl. Pediatr. Adolesc. Health Care. 2022 May 1;52(5):101186. doi.org/10.1016/j.cppeds.2022.101186
10. Ma H, Hong M, Duan J, Liu P, Fan X, Shang E, et al. Altered cytokine gene expression in peripheral blood monocytes across the menstrual cycle in primary dysmenorrhea: a case-control study. PloS one. 2013 Feb 4;8(2):e55200. doi:10.1371/journal.pone.0055200
11. Mucuk S, Yýlmaz M, Onur A. Relationship between dysmenorrhea, dietary inflammatory index, and C-reactive protein level. Prog. Nutr. 2022;23:e2021156. DOI 10.23751/pn.v23i4.11382

12. Murphy SL, Harris RE, Keshavarzi NR, Zick SM. Self-administered acupressure for chronic low back pain: a randomized controlled pilot trial. Pain Med. 2019 Dec 1;20(12):2588-97. doi: 10.1093/pm/pnz138

13. Li T, Li X, Huang F, Tian Q, Fan ZY, Wu S. Clinical efficacy and safety of acupressure on low back pain: A systematic review and meta-analysis. Evid Based Complement Alternat Med. 2021;2021(1):8862399. doi.org/10.1155/2021/8862399

14. Othman S, Aly S, Mady M. Effect of acupressure on dysmenorrhea among adolescents. j. med. sci. res. 2019 Jan 1;2(1):24-. DOI:10.4103/JMISR.JMISR_2_19

15. Chang LH, Hsu CH, Jong GP, Ho S, Tsay SL, Lin KC. Auricular acupressure for managing postoperative pain and knee motion in patients with total knee replacement: a randomized sham control study. Evid Based Complement Alternat Med. 2012;2012(1):528452. doi:10.1155/2012/528452

16. Hsieh LL, Kuo CH, Yen MF, Chen TH. A randomized controlled clinical trial for low back pain treated by acupressure and physical therapy. Prev. Med. 2004 Jul 1;39(1):168-76. doi:10.1016/j.ypmed.2004.01.036

17. Amjad S, Aziz Q, Nangrejo R, Samina M. Effect of Acupressure at Sanyinjiao Point 6 on pain in primary dysmenorrhea among medical students at a private institute in Karachi. Pak J Med Sci. 2025 Apr;41(4):1121. doi: 10.12669/pjms.41.4.10818

18. Dias SF, Pereira LC, Oliveira AP, Santos RF, Nunes LC. Scientific and technological prospection on transdermal formulations and complementary therapies for the treatment of primary dysmenorrhea. Expert Opin. Ther. Pat. 2019 Feb 1;29(2):115-26. DOI:10.1080/13543776.2019.1562547

19. Mukhoirotin K, Fatmawati DA. The Influence of Slow Stroke Back Massage, Cold-compress and Warm-compress to the Level of Prostaglandin F2α (PGF2α) in Primary Dysmenorrhea. Indian J. Forensic Med. Toxicol. 2020 Apr;14(2):2301.

20. Kannan P, Cheung KK, Lau BW. Does aerobic exercise induced-analgesia occur through hormone and inflammatory cytokine-mediated mechanisms in primary dysmenorrhea?. Med. Hypotheses. 2019 Feb 1;123:50-4.

21. Tyas ES, Hartono S, Wahyuni ES, Muhammad HN, Prasetya FI, Sasmito P. The Effect of Abdominal Stretching, Yoga, and Dysmenorrhea Exercises on Prostaglandin Levels and Pain. Int Jou of PHE. 2023 Dec 31;3(1):442-9. DOI: 10.55299/ijphe.v3i1.734

22. Sun L, Liang Y, Li X, et al. [Efficacy of acupuncture combined with auricular point sticking on the content of serum prostaglandin F2α, and plasma arginine vasopressin in patients with menstrual headache]. Zhongguo Zhen Jiu. 2015 Feb;35(2):137-140. PMID: 25854019.

23. Rahimi N, Bambaiechi E, Reisi J. Comparison the effect of eight weeks high intensity interval and moderate continuous trainings on pain reduction and blood levels of IL-6 and TNF-á in woman with primary dysmenorrhea. J Res Med Sci . 2017;41:258-68.

24. Yeh CH, Chien LC, Albers KM, Ren D, Huang LC, Cheng B, et al. Function of auricular point acupressure in inducing changes in inflammatory cytokines during chronic low-back pain: a pilot study. Med. Acupunct. 2014 Feb 1;26(1):31-9. DOI: 10.1089/acu.2013.1015

25. Yeh CH, Lukkahatai N, Huang X, Wu H, Wang H, Zhang J, et. al. Biological correlates of the effects of auricular point acupressure on pain. Pain Manag Nurs. 2023 Feb 1;24(1):19-26. doi.org/10.1016/j.pmn.2022.11.004

Original Article **Open Access**

Comparison of Mean Postoperative Pain Score in Patients Undergoing Thyroidectomy with and Without Superficial Cervical Block

Kainat, Adil Ashraf, Ahsan Ali Ghauri

ABSTRACT:

Objectives: To compare the average postoperative pain scores in patients undergoing thyroidectomy with the use of a superficial cervical block.

Study design and setting: This randomized controlled study was conducted in the Department of Anesthesiology at Lahore General Hospital, Lahore, over six months, from May 3, 2021, to November 2, 2021.

Methodology: After the hospital's ethical committee approval, a study was conducted involving 60 patients (both genders) belonging to ASA class I-II aged (18-60) years, scheduled for elective thyroidectomy under general anesthesia; randomly assigned to two groups by lottery method. Patients in Group-I received additional superficial cervical plexus block while those in Group-II were taken as controls. Outcome variable was mean Visual Analogue Scale (VAS) score for post-operative pain, which was assessed after 2 hours of surgery in the recovery room in both groups. Written informed consent was taken from each patient.

Results: The mean age of patients ranged between 36.6 ± 12.6 years, with the majority (58.3%) aged 26-50 years. Most were female (80%), with a male to female ratio of 1:4. Patients receiving superficial cervical plexus block had significantly lower post-operative pain (mean VAS 2.17±0.84) compared to controls (3.60±1.04), with similar significant differences across age, gender, body mass index, ASA status, and surgery duration.

Conclusions: Superficial cervical plexus block significantly reduces post-operative pain in thyroidectomy patients under general anaesthesia, potentially decreasing opioid use and promoting faster recovery, making it a preferred part of anaesthetic technique for future practice.

Key Words: Bupivacaine, Post-Operative Pain, Superficial Cervical Plexus Block, Thyroidectomy

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INTRODUCTION:

Thyroid disease is highly prevalent in the general population and represents the most common type of endocrine disorder though its exact epidemiology remains elusive but some factors like age, gender, obesity, high education/status and geographical distribution are stated in literature as carrying amplified risk.[1] The thyroid, a small endocrine gland, produces hormones that regulate various metabolic functions in the body. Thyroid conditions can be classified as either benign or malignant or as a hormonal disorder (Hashimoto's thyroiditis and Graves' disease). Goiter is defined as diffuse growth of thyroid gland, more endemic in iodine- deficient areas. Total thyroidectomy, a surgical procedure in which the thyroid gland is removed, is commonly performed to treat a range of thyroid diseases.[2]

Thyroid surgery has advanced significantly with the development of modern equipment and increased surgical expertise. Despite reductions in skin incision size and operating time, voice changes(hoarseness), dysphagia and neck pain along with systemic side effects of pain continue to be common, particularly during the early postoperative period.[3,4] The major contributory risk factors being excessive blood loss during surgery, prolonged hypotension, high endotracheal tube size and duration of surgery are to be controlled for optimal post-operative outcome.[4]

Systemic adverse effects of pain following thyroid surgery can lead to significant complications if not properly managed. Cardiovascular responses, including increased heart rate and blood pressure, may result in arrhythmias or myocardial ischemia.[5] Voice change, difficulty in swallowing, throat

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and neck pain are the most common post-operative complaints after thyroid surgery.[3,4] Respiratory issues like shallow breathing and reduced lung capacity can raise the risk of atelectasis and pneumonia.[6] Gastrointestinal problems, such as nausea, constipation, and delayed gastric emptying, may occur.[7] Pain triggers stress hormones like cortisol, causing hyperglycemia and immune suppression, which increases infection risk.[8] Additionally, it delays recovery by impairing wound healing, prolonging hospital stays, including financial burden and causing psychological stress, anxiety, and chronic pain.[9] Specifically, in thyroid surgery, pain may strain the wound and cause swallowing difficulties or voice changes due to nerve irritation.[10] Effective pain management is crucial for reducing these complications.

Managing postoperative pain is thus very crucial, with the primary goal being to enhance patient comfort and reduce hospital stay following surgery.[11]

However, there is currently no standardised protocol for the management of postoperative pain, particularly after thyroidectomy. Medications used for controlling post-operative surgical pain after thyroidectomy include opioid analgesics (respiratory depression, nausea), non-steroidal anti-inflammatory drugs (risk of post-operative bleeding), various types of blocks.[12]In 2019, Karakis et al. conducted a study comparing the mean postoperative pain scores in patients undergoing thyroidectomy with and without a superficial cervical block. They found the scores to be 2.2 ± 0.44 for the group receiving the block and 3.62 ± 1.18 for the group without it, with a statistically significant difference ($p < 0.01$).[12]

To the best of the candidate's knowledge, there is currently no locally published data on this topic. The mean postoperative pain score, as measured by the Visual Analog Scale (VAS), is significantly lower in patients who receive a superficial cervical block compared to those who do not, as demonstrated by the aforementioned study.[12]As postoperative pain is one of the major complaints of the patient and is usually managed by opioid analgesics which carry their own side effects and complications like prolong hospital stay, nosocomial infection and delayed recovery of the patient.[13,14] Hence, the rational of this this study in the local population undergoing thyroid surgery is that: the mean postoperative pain score will be determined between the two groups and can help us in opting for this technique in the local population, which will help in reducing the morbidity associated with early postoperative pain and aid in early recovery and discharge from the hospital, thereby reducing the burden on the economy.[11, 15, 16]

METHODOLOGY:

The study protocol was approved on May 03, 2021 against RTMC#ANS-2019-069-2148, by the hospital ethical committee. This study was a randomized controlled trial conducted in the Department of Anesthesiology at Lahore General Hospital, Lahore, over a six-month period from May 3, 2021, to November 2, 2021. A total of 60 patients, aged 18 to 60 years, of both genders undergoing thyroidectomy were selected through non-probability, consecutive sampling. The patients were divided into two groups of 30 each by lottery method. The sample size was calculated with an 80% power of the test and a 95% confidence interval, based on expected postoperative pain scores in patients treated with and without a superficial cervical block.

Patients included in the study had goiter(American Society of Anesthesiologists (ASA) grade-I and II) with thyroid-stimulating hormone (TSH) levels within the normal range (0.4-4 mIU/L) and did not exhibit symptoms such as tachycardia, palmar sweating, or significant weight loss.[12] Exclusion criteria comprised patients placed in (ASA) grade III or higher, those with bleeding disorders, cardiac failure, pulmonary or renal dysfunction, or raised leukocyte count.[4] Written informed consent was obtained from all participants to ensure their voluntary participation.

The selected patients were randomly assigned to either the superficial bupivacaine group (Group-I) or the non-bupivacaine group (Group-II) using the lottery method. All participants underwent general anesthesia, with Group-I receiving a superficial cervical block. This block was performed under aseptic conditions using a 22-gauge needle to administer 10 mL of 0.25% bupivacaine bilaterally at the midpoint of the lateral border of the sternocleidomastoid muscle. The injection was given using a three-point technique to effectively block the plexus branches.

Post-thyroidectomy, all patients received 1000 mg of paracetamol, and pain levels by visual analogue scale were assessed two hours after their arrival in the recovery room. Demographic details were meticulously recorded, and measures were taken to minimize bias by having all superficial cervical blocks performed by the same anesthesiology consultant and all surgeries carried out by the same surgical team, led by the consultant surgeon, so as to avoid bias in the study. Statistical analysis will be performed using SPSS version 25.0.

RESULTS:

The study involved 60 patients aged between 18 to 60 years, with a mean age of 36.6 years. The majority (58.3%) were aged 26-50 years, and 80% were female, resulting in a male to female ratio of 1:4. The mean body mass index (BMI) was 27.4 kg/m², with 35% of the participants classified as obese. The patients were evenly distributed across ASA Class I (45%) and Class II (55%). Surgery duration ranged from 60 to 100 minutes, with an average of 78.9 minutes (as shown in Table 1). Both study groups were well-matched regarding mean age (p=0.952), BMI (p=0.850), surgery duration (p=0.882), and distribution across age, gender, BMI, and ASA subgroups ($p > 0.5$) (depicted in Table 2).

Postoperative pain, assessed using the Visual Analog Scale (VAS), ranged from 1 to 5, with an average score of 2.88. Patients who received a superficial cervical plexus block reported significantly lower VAS scores (2.17 ± 0.84) compared to the control group (3.60 ± 1.04), with a statistically significant difference ($p < 0.001$) (shown in Table 3). This significant difference in pain scores was consistent across all subgroups, including age, gender, BMI, ASA status, and surgery duration (Table 4).

Table 1: Baseline Characteristics of Study Sample

Characteristics	Participants (n=60)
Age (years)	36.6±12.6
• <25 years	16 (26.7%)
• 26-50 years	35 (58.3%)
• >50 years	9 (15.0%)
Gender	
• Male	12 (20.0%)
• Female	48 (80.0%)
BMI (Kg/m^2)	27.4±4.0
• Non-Obese	39 (65.0%)
• Obese	21 (35.0%)
ASA Status	
• ASA-I	27 (45.0%)
• ASA-II	33 (55.0%)
Duration of Surgery (minutes)	78.9±12.9
• <80 minutes	31 (51.7%)
• >80 minutes	29 (48.3%)

Table 2: Baseline Characteristics of Study Groups (n=60)

Characteristics	SCP Block n=30	Controls n=30	P-value
Age (years)	36.7±12.6	36.5±12.9	0.952
• <25 years	8 (26.7%)	8 (26.7%)	0.933
• 26-50 years	17 (56.6%)	18 (60.0%)	
• >50 years	5 (16.7%)	4 (13.3%)	
Gender			
• Male	7 (23.3%)	5 (16.7%)	0.519
• Female	23 (76.7%)	25 (83.3%)	
BMI (Kg/m^2)	27.3±4.3	27.5±3.9	0.850
• Non-Obese	20 (66.7%)	19 (63.3%)	0.787
• Obese	10 (33.3%)	11 (36.7%)	
ASA Status			
• ASA-I	13 (43.3%)	14 (46.7%)	0.795
• ASA-II	17 (56.7%)	16 (53.3%)	
Duration of Surgery	78.7±12.8	79.2±13.2	0.882
• <80 minutes	15 (50.0%)	16 (53.3%)	0.796
• >80 minutes	15 (50.0%)	14 (46.7%)	

The Chi-square test and independent sample t-test indicated that the observed differences were statistically insignificant, SCP; Superficial Cervical Plexus

Table 3: Comparison of Mean VAS Scores for Postoperative Pain Between the Study Groups (n = 60)

	SCP Block n=30	Controls n=30	P-value
VAS Score (mean ±SD)	2.17±0.84	3.60±1.04	<0.001*

Independent sample t-test, * observed difference was statistically significant, SCP; Superficial Cervical Plexus

Table 4: Comparison of Mean VAS Score for Post-Operative Pain between the Study Groups across various Subgroups (n=60)

Subgroups	VAS Score (mean ±SD)		P-value
	SCP Block n=30	Controls n=30	
Age			
• <25 years	2.13±0.64	3.50±0.93	0.004*
• 26-50 years	2.18±0.95	3.61±1.15	<0.001*
• >50 years	2.20±0.84	3.75±0.96	0.036*
Gender			
• Male	2.14±0.38	3.60±0.89	0.003*
• Female	2.17±0.94	3.60±1.08	<0.001*
BMI			
• Non-Obese	2.10±0.64	3.58±1.02	<0.001*
• Obese	2.30±1.16	3.64±1.12	0.015*
ASA Status			
• ASA-I	2.15±0.69	3.57±0.85	<0.001*
• ASA-II	2.18±0.95	3.63±1.20	0.001*
Duration of Surgery			
• <80 minutes	2.00±0.66	3.44±0.89	<0.001*
• >80 minutes	2.33±0.98	3.79±1.19	0.001*

DISCUSSION:

Thyroid surgery, a common procedure for both benign and malignant conditions, typically causes mild to moderate pain requiring analgesics, particularly on the first day.[4] This pain, along with discomfort during swallowing and throat burning, is managed with opioids and NSAIDs. However, these medications can lead to postoperative nausea, vomiting, pneumonia, and respiratory depression, complicating recovery.

Regional techniques, such as superficial cervical plexus blocks, may reduce postoperative pain and the need for systemic analgesics. This technique targets the second to fourth cervical nerves to anaesthetize the neck's anterior triangle. Recent studies suggest that cervical plexus blocks can effectively decrease postoperative pain and opioid use, though local evidence is sparse. This study aimed to compare postoperative pain scores in patients receiving thyroidectomy with and without the superficial cervical block.

In the present study, the mean age of patients undergoing thyroidectomy was 36.6 ± 12.6 years. Recent studies have reported similar findings, including Ahmed et al. (2021), who reported a mean age of 37.2 ± 12.3 years in Islamabad

and Malik et al. (2022), who found an average age of 35.8 ± 11.7 years in Karachi.[17,18] In Lahore, Raza et al. (2023) reported a mean age of 36.5 ± 13.0 years.[19] Additionally, Patel et al. (2020) in India and Rahman et al. (2021) in Bangladesh found comparable mean ages of 36.4 ± 12.8 years and 37.1 ± 13.1 years, respectively.[20,21] In Saudi Arabia, Al-Qahtani et al. (2023) reported an average age of 35.6 ± 8.4 years, while Gebremedhin et al. (2022) found it to be 38.2 ± 14.0 years in Ethiopia.[22,23] Our study observed that 58.3% of patients were aged 26-50 years, 26.7% were under 25 years, and 15.0% were above 50 years. Similar distributions were reported by Saqlain et al. (2018) with 70.2% in the 26-50 years range and 7.0% over 50 years, and by Shrestha et al. (2021) who found 64.0% in the 26-50 years range and 10.0% over 50 years.[24,25] In Bangladesh, Rahman et al. (2021) observed similar frequencies.[21]

The study also noted a female predominance with a male to female ratio of 1: 4. Recent studies align with this finding, including Ahmed et al. (2020), who reported a similar ratio [17] and Al-Qahtani et al. (2023) with a ratio of 1:4.3.[22] In India, Patel et al. (2022) and Krishna et al. (2021) observed comparable ratios of 1:4 and 1:3.5, respectively.[20,26] In Bangladesh, Rahman et al. (2021) reported a higher female predominance with a ratio of 1: 6.5.[21]

The study found that patients receiving a superficial cervical plexus block had significantly lower post-operative pain scores (2.17±0.84) compared to controls (3.60 ± 1.04, $p < 0.001$). This finding is consistent with Karakis et al. (2021), who reported significantly lower pain scores in patients receiving the block (2.2±0.44 vs. 3.62±1.18, $p<0.01$).[12] The study highlights the benefits of using superficial cervical plexus blocks to reduce post-operative pain, potentially leading to quicker recovery and reduced opioid use. The study's strengths include a large sample size of 60 and a randomized design, with strict exclusion criteria and stratified results.

CONCLUSION:

In the present study, superficial cervical plexus block was found to be associated with significantly lesser post-operative pain in patients undergoing thyroidectomy under general anesthesia which is desirable as it may reduce the need for post-operative opioids and may in turn enable enhanced recovery and thus advocates the preferred use of this novel approach in future anesthetic practice.

LIMITATIONS OF THE STUDY:

However, limitations included not comparing analgesic requirements or recovery times, and not assessing side effects, which warrants further research.

Authors Contribution:
Kainat: Concept & Design of Study, Drafting, Revisiting Critically, Data collection & Analysis, Final Approval of Version.
Adil Ashraf: Drafting, Revisiting Critically, Data collection & Analysis.
Ahsan Ali Ghauri: Drafting, Revisiting Critically, Data collection & Analysi

REFERENCES

1. Zhang X, Wang X, Hu H, Qu H, Xu Y, Li Q. Prevalence and trends of thyroid disease among adults, 1999-2018. Endocr Pract. 2023 Nov;29(11):875-880. Epub 2023 Aug 22. PMID: 37619827. DOI: https://doi.org/10.1016/j.eprac.2023.08.006
2. Biello A, Kinberg EC, Wirtz ED. Thyroidectomy. 2022 Nov 14. In: StatPearls [Internet]. Treasure Island(FL): StatPearls Publishing; 2024 Jan–. PMID: 33085426.Bookshelf ID: NBK563279
3. Patel KN, Yip L, Lubitz CC, et al. The American Association of Endocrine Surgeons Guidelines for the Definitive Surgical Management of Thyroid Disease in Adults. Ann Surg. 2020;271(3): e21-e93. doi:10.1097/SLA.0000000000003580
4. Chawaka HJ, Teshome ZB. The Underreported Postoperative Suffering after Thyroid Surgery: Dysphagia, Dysphonia, and Neck Pain-A Cross-Sectional Study. Anesthesiol Res Pract. 2023 Aug 7;2023:1312980. DOI: https://doi.org/10.1155/2023/1312980
5. Rosenfeld DM, Schroeder KM, Pieper KL. Cardiovascular responses to surgical pain: Implications for postoperative management. J Clin Anesth. 2019;54:65-72. DOI: https://doi.org/10.1016/j.jclinane.2018.10.019
6. Lee J, Park JM, Choi JY. Respiratory complications in thyroid surgery: An overview. Surg Today. 2020;50(8):719-727. doi:10.1007/s00595-019-01936-3.
7. Myles PS, Williams DL, Hendrata M, Anderson H, Weeks AM. Patient satisfaction after anaesthesia and surgery: results of a prospective survey of 10,811 patients. Br J Anaesth. 2000 Jan;84(1):6-10. DOI: https://doi.org/10.1093 /oxford journals.bja.a013383
8. Desborough JP. The stress response to trauma and surgery. Br J Anaesth. 2000;85(1):109-117. DOI: https://doi.org/10.1093/bja/85.1.109
9. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. Am J Surg. 2002;183(6):630-641. DOI: https://doi.org/10.1016/s0002-9610(02)00866-8
10. Al-Qurayshi Z, Randolph GW, Srivastav S, Aslam R, Kandil E. Pain following thyroid surgery and its impact on patient-reported outcomes. J Clin Endocrinol Metab. 2017;102(1):167-175. DOI: https://doi.org/10.1016/j.surg.2013.04.068
11. Rawal N. Current issues in postoperative pain management. Eur J Anaesthesiol. 2016;33(3):160-171. DOI: https://doi.org/10.1097/eja.0000000000000366
12. Ozgun M, Hosten T, Solak M. Effect of Bilateral Superficial Cervical Plexus Block on Postoperative Analgesic Consumption in Patients Undergoing Thyroid Surgery. Cureus. 2022 Jan 13;14(1):e21212. DOI: https://doi.org/10.7759/cureus.21212

13. Gan TJ, Habib AS, Miller TE, White W, Apfelbaum JL. Incidence, patient satisfaction, and perceptions of post-surgical pain: Results from a US national survey. Curr Med Res Opin. 2014;30(1):149-160. DOI: https://doi.org/10.1185/ 03007995. 2013.860019

14. Apfelbaum JL, Chen C, Mezei G, et al. Postoperative pain management: A review of the evidence. Anesth Analg. 2003;97(5):1340-1349. doi:10.1213/01.ANE. 0000088870. 39477.66.

15. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. Am J Surg. 2002;183(6):630-641. DOI: https://doi.org/10.1016/s0002-9610(02)00866-8

16. A de Mel, Three-dimensional printing and the surgeon, British Journal of Surgery, Volume 103, Issue 7, June 2016, Pages 786–788. DOI: https://doi.org/10.1002/bjs.10188

17. Ahmed S, Iqbal S, Khan A. Age distribution of patients undergoing thyroid surgery in Islamabad: A retrospective analysis. Pak J Surg. 2021;37(3):183-187. doi:10.21699/ pjs.v37i3.1005.

18. Malik M, Fatima S, Rehman A, Hussain A. Epidemiological study of thyroid disorders in Karachi: A 2-year retrospective study. J Pak Med Assoc. 2022;72(1):45-50. doi:10.47391/ JPMA.1311.

19. Raza A, Saeed M, Ahmed N. Demographic profile of patients undergoing thyroid surgery in Lahore: A 5-year review. Ann Punjab Med Coll. 2023;17(1):15-20. doi:10.47982/apmc. v17i1.635.

20. Patel S, Shah D, Desai C. Clinical profile of patients undergoing thyroid surgeries in a tertiary care center in India. Indian J Surg. 2020;82(4):311-316. doi:10.1007/s12262-020-02403-1.

21. Rahman M, Hossain A, Ahmed S. A retrospective analysis of thyroid surgery outcomes in Bangladesh: A single-center experience. Bangladesh J Surg. 2021;29(1):25-30. doi: https://doi.org/10.3329/bjs.v29i1.54899

22. Al-Qahtani A, Alzahrani A, Alghamdi H, et al. Characteristics of thyroidectomy patients in Saudi Arabia: A multicenter study. Saudi Med J. 2023;44(2):165-170. doi: 10.15537/ smj.2023.44.2.20220423 .

23. Gebremedhin S, Belayneh A, Meleseb A, et al. Pattern of thyroid disease and its management in Ethiopia: A retrospective study. Ethiop J Health Sci. 2022;32(4):641-648. DOI: https:// doi.org/10.4314/ejhs.v32i4.4

24. Saqlain M, Shams S, Ghaffar S. Epidemiological study of thyroid diseases in a tertiary care hospital. Pak J Med Sci. 2018;34(6):1505-1509. doi:10.12669/pjms.346.16820.

25. Shrestha S, Kafle R, Chaudhary S. Demographic profile and outcomes of thyroid surgery: A retrospective study from a tertiary care hospital. Nepal Med Coll J. 2021;23(4):246-250. doi:10.3126/nmcj.v23i4.38555.

26. Krishna R, Gupta A, Sharma K. Demographic and clinical characteristics of thyroid disorders in Indian population. J Indian Med Assoc. 2021;119(12):54-60. doi:10.1056/ NEJMoa2029344.

Original Article **Open Access**

Visual Prostate Symptom Score versus International Prostate Symptom Score with Lower Urinary Tract Symptoms

Khalid Hussain, Maria Tariq, Muhammad Asif, Obaid Adil, Jawad Ahmed, Talal Habib

ABSTRACT

Objective: Benign prostatic enlargement is a common issue in ageing men, causing significant lower urinary tract symptoms (LUTS). This study compares the effectiveness of the International Prostate Symptom Score (IPSS) and the Visual Prostate Symptom Score (VPSS) in assessing LUTS severity among BPH patients in Pakistan, focusing on ease of use, symptom grading, and correlation with uroflowmetry results.

Study design and setting: Prospective observational study conducted at the OPD of Urology, Gujranwala Teaching Hospital and Gujranwala Medical College Teaching Hospital, from April 24 to September 24.

Methodology: A total of 220 patients over 40 years with LUTS completed IPSS and VPSS assessments, with time taken recorded. Uroflowmetry (Qmax), post-void residual volume (PVRV), and bladder wall thickness were measured before and after one month of á-blocker therapy. Data were analysed using paired t-test, Pearson's correlation, and chi-square test to evaluate association.

Results: VPSS took 3-4 minutes for those with primary education, compared to 8-10 minutes for IPSS. Symptom severity grading between IPSS and VPSS showed positive correlation ($r = 0.582$, $P < 0.001$). VPSS scores showed significant correlation with post-treatment improvements in Q max, bladder wall thickness and improvement in PMRV after treatment, confirming its reliability in symptom assessment and treatment monitoring.

Conclusion: VPSS is a reliable, quicker alternative to IPSS, especially for populations with lower literacy. It correlates well with symptom severity and treatment outcomes, making it suitable for broader clinical use in diverse settings.

Key words: Benign prostatic enlargement, Internal prostate scoring system, Visual prostate scoring symptom.

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INTRODUCTION:

Lower urinary tract symptoms (LUTS) are a common complaint in adult men with a major impact on quality of life (QoL) and have a substantial economic burden.[1] Benign Prostatic enlargement (BPE) is one of the causes of lower urinary tract symptoms and the leading healthcare problem in men over 50 years of age.[2] The prevalence of BPE increases with age due to hormonal changes, i.e conversion of testosterone into dihydrotestosterone, which stimulates prostate cell proliferation.[3] BPH is the histological diagnosis. BPE is the proliferation of smooth muscles and epithelial cells within the prostatic tissue.[4] A study estimated that 90% of men between 45 and 80 years of age will have lower urinary tract symptoms due to BPH.[2] Scoring of the LUTS is necessary to set the treatment options and to assess their effectiveness. So, for these various symptom scoring systems have been established in the world, including IPSS, the International Consultation on Incontinence Questionnaire for Male LUTS (ICIQ-MLUTS), Danish Prostate Symptom Score and VPSS.[5]

Most patients with BPE present with symptoms of difficulty in voiding. These complex symptoms are nonspecific and

are identified by a variety of terms collectively called lower urinary tract symptoms (LUTS).[6] Although LUTS secondary to BPE (LUTS/BPE) are often not life-threatening conditions, they significantly affect the quality of life (QoL).[7] The International Prostate Symptom Score (IPSS) is used to assess lower urinary tract symptoms (LUTS), which are most often due to benign prostatic enlargement (BPE), prostatic cancer or urethral stricture.[8-9] The first version of the International Prostate Symptom Score (IPSS) was developed in 1992 by the American Urological Association (AUA) and consisted of seven questions. Initially, it did not include the eighth question related to quality of life, so it was originally known as the AUA symptom Score (AUA) or AUA-7.

This scoring system was designed for the self-assessment of a patient about his urinary habits and urinary symptoms over the last 1 month. Moreover, it can be calculated multiple times to check the severity of symptoms and improvements without any bias of treating urologist or physician over the time period and can be compared over time.[10] The IPSS is an attempt to translate symptoms into numbers, which can be divided into different categories according to the symptom's severity into mild, moderate and severe symptoms. However, because of inter-individual differences in perceptions due to educational differences and interpretation of subjective symptoms, it is problematic to compare patients with one another in terms of symptom scores.

The real value of the IPSS is in longitudinal follow-up, where changes in the individual's symptom score can be used to assess response to treatment.[2] Patients with lower educational levels experience greater difficulty completing the IPSS by themselves.[7] Because of the complexity of questions of IPSS, it is very difficult to understand for especially for patients with lower educational levels and even for men with a relatively high level of education, patients often ask the doctors, nurses or paramedical staff for an explanation of the questions while completing the form. This invariably introduces the risk of influencing the patient's responses.[9] This subjective dependency for the elaboration of symptoms in men with LUTS demanded a need for developing a system care that can be used and reproduced to evaluate symptoms and hence can help to guide management strategies.[10] Shah et al. reported that 24-87% of 96 men with LUTS (depending on their level of education) required assistance to complete the IPSS questionnaire.[4] They thereby agreed that the IPSS is difficult to understand even for men with a high level of education. Adam E. Groeneveld, a urologist who has worked for many years in African countries, developed a simplified assessment of the force of the urinary stream. Using this concept, we developed a Visual Prostate Symptom Score (VPSS), which also assesses urinary frequency during the day and night, and the patient's overall quality of life.[7] VPSS differs from the IPSS by presenting the AUA questionnaire in a visual format, allowing older men, and in many cases those with low literacy levels, to assess their urinary problems more easily and reliably. Furthermore, the incorporation of a new concept of quality of life (QoL) into the VPSS facilitates a better understanding of symptoms and their impact on the patient's daily life. This study aimed to compare the effectiveness of IPSS and VPSS in assessing LUTS severity among BPE patients presenting in the outpatient department of Gujranwala Medical College teaching hospital, Gujranwala, focusing on ease of use, symptom grading, and correlation with objective uroflowmetry results and improvement in the Bladder wall thickness.

METHODOLOGY:

A prospective observational study was conducted involving 220 male patients aged 45 years and above, presenting with lower urinary tract symptoms (LUTS). The study was approved by the Institutional Review Board of Gujranwala Medical College, Gujranwala (Ref No: IRB.83/GMC), and carried out at the Outpatient Department of Urology, Gujranwala Teaching Hospital and Gujranwala Medical College Teaching Hospital, from April 2024 to September 2024.

The sample size of 220 was calculated for this prospective observation study using OpenEpi software, based on a previously reported prevalence of benign prostatic hyperplasia (BPH) in Pakistan at 17%, with a 95% confidence level [11]

All patients meeting the inclusion criteria were fully informed about the nature of the study, and written informed consent was obtained before enrollment. Inclusion criteria consisted of male patients aged over 45 years presenting with LUTS attributable to benign prostatic enlargement (BPE). A non-probability consecutive sampling technique was used to recruit patients. Exclusion criteria included patients with post-void residual volume (PVRV) less than 50 ml or greater than 500 ml, deranged renal function tests, suspected prostatitis, urethral stricture, prostate cancer, positive urine culture (to rule out chronic cystitis), and neurogenic bladder.

Following consent, a detailed medical history was obtained, and a thorough physical examination was performed. Digital rectal examination (DRE), as well as bulbocavernosus and cremasteric reflexes, were assessed to exclude neurogenic components. A structured proforma was used to record each patient's educational status, and participants were categorised into three groups based on literacy level. Ultrasonography was performed by a qualified radiologist in all cases to assess prostate size, bladder wall thickness, and post-void residual volume, and both investigations were repeated after one month of á-blocker to evaluate treatment response.

Data analysis was performed using SPSS software 26.0. Continuous variables such as prostate size, time taken to complete IPSS and VPSS, symptom scores, and uroflowmetry values (Qmax) were presented as mean ± standard deviation (SD). Categorical variables, including educational level, mode of questionnaire completion (self vs. assisted), and

severity grading, were reported as frequencies and percentages. To compare mean differences between multiple educational groups in terms of IPSS and VPSS completion time, one-way analysis of variance (ANOVA) was applied, followed by post-hoc Tukey's HSD test for pairwise comparisons. Paired sample t-tests were used to evaluate the change in Qmax before and after one month of treatment, as well as changes in symptom severity and post-void residual volumes.

Pearson's correlation coefficient (r) was used to assess the strength and direction of association between IPSS and VPSS domains (frequency, nocturia, weak stream), overall symptom scores, and quality of life scores. Additionally, the relationship between VPSS stream scores and Qmax was analysed using Pearson's correlation coefficient. Correlation values were interpreted based on standard criteria: values between 1-7 were considered mild, 8–19 moderate, and 10-35 were severe[12]. A chi-square test was employed to compare categorical variables, such as the mode of assessment across age groups and severity grading distribution between IPSS and VPSS. A p-value of <0.05 was considered statistically significant.

RESULTS:

Figure 1 illustrates the educational attainment of the 220 study participants. The largest subgroup (n = 102; 46.4%) had only primary schooling, followed by those who completed matriculation (n = 85; 38.6%), while the smallest group were university graduates (n = 33; 15.0%). As shown in Figure 1, nearly half of the cohort had only a basic education, which may influence their ability to self-complete symptom scores and underscores the importance of choosing patient-reported outcome measures that accommodate varying literacy levels.

As summarised in Table 1, the average time required to complete the IPSS questionnaire decreased markedly with higher educational attainment, from 10.10 ± 1.8 minutes among participants without formal schooling to 3.21 ± 0.8 minutes in graduates. A similar but even more pronounced trend was observed for the VPSS, with completion times falling from 4.05 ± 0.9 minutes in the primary-educated group to 1.20 ± 0.5 minutes among graduates. As shown in Table 2, mean prostate size increased with age, rising from 54.2 g in the 41–50 year group to a peak of 69.2 g in those aged 61–70, with an overall mean of 62.7 g. Completion modality differed markedly between the two instruments: only 19 of 220 men (8.6%) were able to self-complete the text-based IPSS, and self-completion rates dropped to zero in the = 81 cohort. By contrast, the pictogram-based VPSS yielded 90% self-completion (198/220) across all ages, with assistance required for just 22 patients—most commonly in the oldest group (8/30). This demonstrates the VPSS's superior usability, especially among older patients with larger prostates. Table 3 compares the classification of symptom severity between the IPSS and VPSS instruments. Both scales divide patients into mild, moderate, and severe categories—IPSS using ranges of 1–7 mild, 8–19 moderate, and 20–35 severe, and VPSS using 1–3 mild, 4–9 moderate, and 10–17 severe categories according to the criteria defined in the methodology, respectively. The overall Pearson correlation coefficient of r = +0.582 ($p < 0.001$) demonstrates a statistically significant, moderate positive relationship between the two grading systems, confirming that VPSS severity categories align reliably with those of the established IPSS. As shown in Table 4, uroflowmetry revealed a marked shift toward higher Qmax values after one month of á-blocker therapy. Before treatment, only 13 patients (6%) achieved a flow rate above 16 ml/sec; this number rose to 123 (56%) post-treatment. Those in the lowest category (1– 5 ml/sec) decreased from five to four patients, and the 6–10 ml/sec group fell dramatically from 85 to 22. Meanwhile, the 11–15 ml/sec cohort declined from 117 to 71. These results underscore a clinically significant improvement in urinary flow following VPSS-guided management.

Table 5 summarises the strength and significance of correlations between corresponding IPSS and VPSS symptom domains, and the relationship between the VPSS stream score and objective urinary flow (Qmax). Symptom frequency demonstrated a very strong positive correlation ($r = 0.845$, $p < 0.001$), as did overall quality-of-life scores ($r = 0.864$, $p < 0.001$). Nocturia showed a moderate correlation ($r = 0.425$, $p < 0.001$), whereas the weak-stream domain correlated more weakly and did not reach statistical significance ($r = 0.246$, $p = 0.069$). Notably, the VPSS stream score was inversely correlated with Qmax ($r = -0.365$, $p < 0.001$), confirming that higher bother from weak stream pictograms aligns with lower measured flow rates.

Figure 1: Distribution of Educational Levels among Study Participants (n=220)

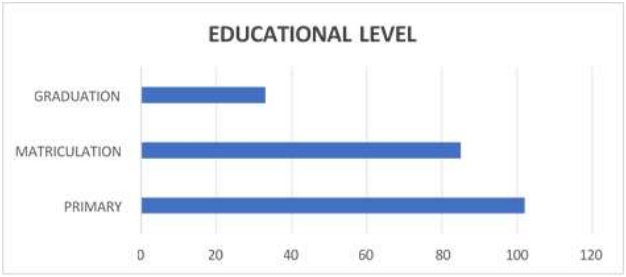

Table 1: Comparison of Average Completion Time for IPSS and VPSS across Different Educational Levels

Education Level	IPSS Completion (mean ± SD)	VPSS Completion (time mean ± SD)
Primary (no formal)	10.10 ± 1.8 min	4.05 ± 0.9 min
Matriculation	6.40 ± 1.2 min	2.28 ± 0.7 min
Graduate	3.21 ± 0.8 min	1.20 ± 0.5 min

P-value = 0.001

Table 2: Distribution of IPSS and VPSS Assessment Modes Across Age Groups and Mean Prostate Size

Age Group (years)	n	Mean Prostate Size (g)	IPSS Self-Completion	IPSS Assisted	VPSS Self-Completion	VPSS Assisted
41–50	25	54.2	10	15	22	3
51–60	57	58.7	7	50	54	3
61–70	62	69.2	2	60	60	2
71–80	46	60.3	2	44	40	6
= 81	30	64.2	0	30	22	8
Total	220	62.7	19	201	198	22

Table 3: Comparison of Severity Grading Between IPSS and VPSS Scores

Severity	IPSS Range	VPSS Range	Correlation (r)	p-Value
Mild	1–7	1–3	+0.582	< 0.001
Moderate	8–19	4–9		
Severe	20–35	10–17		

Table 4: Comparison of Qmax (ml/sec) Before and After á-Blocker Therapy (Uroflowmetry Results). Treatment as Assessed by VPSS

Qmax Category	Before Treatment (n)	After 1 Month (n)
1–5 ml/sec	5	4
6–10 ml/sec	85	22
11–15 ml/sec	117	71
> 16 ml/sec	13	123

Table 5: Correlation Between IPSS and VPSS Domains and Uroflowmetry Outcomes

Comparison	r-value	p-value
Frequency (IPSS vs. VPSS)	0.845	< 0.001
Nocturia (IPSS vs. VPSS)	0.425	< 0.001
Weak Stream (IPSS vs. VPSS)	0.246	0.069
Quality-of-Life (IPSS vs. VPSS)	0.864	< 0.001
Stream Score VPSS vs. Qmax	-0.365	< 0.001

DISCUSSION:

Benign prostatic hyperplasia (BPH) is a prevalent condition among ageing men, with significant effects on their health, quality of life, and healthcare systems globally.[13] This study highlights the importance of reliable tools for symptom assessment in patients with benign prostatic hyperplasia (BPH), while also exposing the challenges of applying them to diverse populations. The International Prostate Symptom Score (IPSS) has been a fundamental tool for the diagnosis and management of BPH-related symptoms for years; however, it is not without limitations. In response to these limitations, the Visual Prostate Symptom Score (VPSS) emerged as a more recent alternative that seeks to facilitate symptom assessment, especially among patients with low educational levels or difficulty understanding lengthy questionnaires.

IPSS, composed of seven questions, is widely recognised for allowing healthcare professionals to quantify the severity of lower urinary tract symptoms (LUTS). However, recent research has indicated that its effectiveness may be compromised in patients with low educational levels. Several studies have shown that many men with LUTS require assistance to complete the questionnaire, which can bias the results, as responses may be influenced by the person assisting them.[14-15] Another weakness of the IPSS lies in the subjectivity of its questions, as it is based on the individual patient's perception of their symptoms. This variability makes comparisons between different cases difficult and limits their usefulness in population studies. Furthermore, the IPSS focuses primarily on symptom severity, neglecting the psychosocial impact these symptoms can have on the patient's quality of life, something especially relevant in contexts where literacy is limited, as is the case in several regions of developing countries, including Pakistan [16]

VPSS was designed precisely to overcome these limitations. Through a visual format, it replaces the textual content of the IPSS with illustrations that allow patients to self-assess, even if they cannot read or write. This makes it a particularly useful tool in contexts with educational barriers, and in countries like Pakistan, it has shown notable potential for improving patient engagement and diagnostic accuracy.[17] One of the main strengths of the VPSS is that it includes a quality-of-life assessment in a more accessible format, allowing for the real impact that urinary symptoms have on the patient's daily life and emotional well-being. This comprehensive view aligns with current healthcare trends, which promote person-centred care.[18] Studies have shown that the VPSS correlates well with the IPSS in classifying symptom severity, supporting its validity as an alternative diagnostic tool.[19] Moreover, research has highlighted that patients complete the VPSS in less time than the IPSS, with this difference being more evident in people with basic or no formal education. This efficiency is especially valuable in clinical settings with high patient loads or with elderly patients who may become fatigued easily during prolonged Evaluations.[20-21] The findings of this research have important implications for the management of BPH. Considering the progressive ageing of the global population and the high prevalence of this condition, practical, understandable, and effective tools for its diagnosis and follow-up are essential. Instruments such as the VPSS can improve care in resource-limited settings by allowing for more equitable and inclusive assessment.[22-23]

The ability to accurately assess symptom severity allows for personalised treatment and more appropriate monitoring of clinical progress. Both the IPSS and VPSS allow for monitoring changes over time, which is key to tailoring therapeutic interventions. Furthermore,

some recent studies recommend complementing these tools with objective methods, such as uroflowmetry, to improve the diagnostic accuracy and clinical management of BPH.

In this context, future research must continue to refine instruments such as the VPSS to better adapt them to diverse populations. Further exploration is also needed into the psychosocial effects of BPH and how symptom assessment tools can more fully capture its impact on patients' lives.

CONCLUSION:

This prospective observational study demonstrated that the VPSS is a reliable and accessible alternative to the IPSS for evaluating LUST in men with BPH. Completion times for VPSS were significantly shorter across all educational levels compared to IPSS (ANOVA, $p < 0.001$), and VPSS severity grading showed a significant correlation with IPSS categories (chi-square, $p < 0.001$). Furthermore, VPSS scores correlated moderately with objective measures, including Qmax and PVRV (Pearson's $r = 0.582$, $p < 0.001$). These findings confirm that VPSS can be effectively used in populations with low literacy, where IPSS may be impractical. Health systems in regions such as Pakistan should consider adopting VPSS alongside IPSS to ensure inclusive and efficient assessment, while also strengthening patient education to improve accessibility of care.

LIMITATIONS

Limitations in this study were a single-centre design. This study was conducted at two teaching hospitals in a single city, which may limit the generalizability of the results to other regions and populations with different cultures and healthcare settings. Secondly, there was a short follow-up duration. Outcomes were assessed only after one month of alpha-blocker therapy, which may fully capture long-term symptom changes or treatment impacts. Thirdly, exclusion of comorbid conditions. Patients with prostate cancer, prostatitis, and neurogenic bladder were excluded, so the results may not apply to all men presenting with LUTS in real-world clinical practice.

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Khalid Hussain: Conception and final design
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Muhammad Asif: Revise critically
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Jawad Ahmed: Drafting of study
Talal Habib: Acquisition of data

REFERENCES:

1. Laranjo-Tinoco C, Ferreira F, Anacleto S, Cardoso A, Araújo AS, Oliveira C. A prospective comparison of the Visual Prostate Symptom Score versus the International Prostate Symptom Score in Portuguese men. Urological Science. 2024;35(1):51-6. Doi: 10.1097/us9.0000000000000003
2. Chatterjee S, Kumar A, Pal DK. Study of correlation between visual prostate symptom score and international prostate symptom score in men with lower urinary tract symptoms with reference to uroflowmetry parameters in the Indian population. Urologia Journal. 2023;90(2):377-80. Doi: 10.1177/03915603231157573
3. Rivera-Oliva DD. Visual prostate symptom score (VPSS). Is it an effective alternative for the assessment of lower urinary tract symptoms? Experience in a reference centre in southeastern Mexico. Revista Mexicanade Urología. 2022;81(6). Doi: 10.48193/rev istamexic anadeur ologa.v81i6.818
4. Shah RS, Mishra K, Sah S, Yadav D, Neupane B, Shakya I, Thapa N. Correlation between the Visual Prostate Symptom Score and International Prostate Symptom Score in Patients with Symptomatic Benign Prostatic Hyperplasia. Journal of Nobel Medical College. 2024;13(1):55-9. Doi: 10.3126 /jonmc.v13i1.68105
5. de Moraes Lopes MH, D'Ancona CA, Moretti TB, Higa R, Victal ML, Camisão AR, Braga DA, Reis LO. Validation of visual prostate symptom score (VPSS) in Brazilian sample population. Journal of Wound Ostomy & Continence Nursing. 2023;50(4):326-30. Doi: 10.1097/WON.0000000000000996
6. Liu Z, Guan Z, Lan H, Zhao Y, Ye Z, Lv D, Yu Q, Wang M, Peng K, Fu N, Mazzon G. Evaluating the lower urinary tract syndrome with a telemedicine application: an exploration of the electronic audiovisual prostate symptom score. Frontiers in Surgery. 2022;9:848923. Doi: 10.3389/fsurg.2022.848923
7. Schlatmann FW, van Balken MR, de Winter AF, de Jong IJ, Jansen CJ. How do patients understand questions about lower urinary tract symptoms? A qualitative study of problems in completing urological questionnaires. International Journal of Environmental Research and Public Health. 2022;19(15):9650. Doi: 10.3390/ijerph19159650
8. Glaser AP, Kristof TW, Judge C, Javitch G, Hirsch S, Talaty P, Helfand BT, Smith AR, Griffith JW. The 10-item LURN Symptom Index (LURN SI-10) detects additional symptoms and shows convergent validity with the IPSS in men presenting with lower urinary tract symptoms. Urology. 2023;171:184-9. Doi: 10.1016/j.urology.2022.10.019
9. Guzelsoy M, Erkan A, Ozturk M, Zengin S, Coban S, Turkoglu AR, Koc A. Comparison of three questionnaire forms used in the diagnosis of lower urinary tract symptoms: A prospective study. Prostate International. 2022;10(4):218-23. Doi: 10.1016/j.prnil.2022.06.001
10. Victor A, Okigbeye D. Benign Prostatic Enlargement, the International Prostate Symptoms Score and a Review of Other Symptom Scores. Open Journal of Urology. 2022;12(8):427-39. Doi: 10.4236/oju.2022.128042
11. Gewanter RM, Sandhu JS, Tin AL, Gross JP, Mazzarella K, Urban J, Elsebai N, Hopkins MF, Vickers AJ, Zelefsky MJ. Assessment of patients with prostate cancer and their understanding of the international prostate symptom score questionnaire. Advances in Radiation Oncology. 2023;8(4):101200. Doi: 10.1016/j.adro.2023.101200

12. Roy, Ashutosh; Singh, Amandeep1,; Sidhu, Darshan Singh; Jindal, R1; Malhotra, Mishi; Kaur, Haramritpal. New Visual Prostate Symptom Score versus International Prostate Symptom Score in Men with Lower Urinary Tract Symptoms: A Prospective Comparision in Indian Rural Population. Nigerian Journal of Surgery 22(2):p 111-117, Jul–Dec 2016. | DOI: 10.4103/1117-6806.189002

13. Tamalunas A, Schott M, Keller P, Atzler M, Ebner B, Buchner A, Stief CG, Magistro G. How does symptom severity impact clinical outcomes of men with lower urinary tract symptoms after holmium laser enucleation or transurethral resection of the prostate?. Central European Journal of Urology. 2022;75(4):387. Doi: 10.5173/ceju.2022.161

14. Yao MW, Green JS. How international is the International Prostate Symptom Score? A literature review of validated translations of the IPSS, the most widely used self-administered patient questionnaire for male lower urinary tract symptoms. LUTS: Lower Urinary Tract Symptoms. 2022;14(2):92-101. Doi: 10.1111/luts.12415

15. Hamza BK, Ahmed M, Bello A, Tolani MA, Awaisu M, Lawal AT, Oyelowo N, Abdulsalam KI, Lawal L, Sudi A, Maitama HY. Correlation of intravesical prostatic protrusion with severity of lower urinary symptoms among patients with benign prostatic hyperplasia. African Journal of Urology. 2021;27:1-7. Doi: 10.1186/s12301-020-00102-0

16. Young GJ, Metcalfe C, Lane JA, Lewis AL, Abrams P, Blair PS, Ito H, Chapple C, Drake MJ. Prostate surgery for men with lower urinary tract symptoms: do we need urodynamics to find the right candidates? Exploratory findings from the UPSTREAM trial. European Urology Focus. 2022;8(5):1331-9. Doi: 10.1016/j.euf.2021.11.010

17. Vartolomei L, Cotru? A, Tãtaru SO, Vartolomei MD, Man A, Ferro M, Stanciu C, Sin AI, Shariat SF. Lower urinary tract symptoms are associated with clinically relevant depression, anxiety, and stress symptoms. The Aging Male. 2022;25(1):62-6. Doi: 10.1080/13685538.2022.2040981

18. Awaisu M, Ahmed M, Lawal AT, Sudi A, Tolani MA, Oyelowo N, Muhammad MS, Bello A, Maitama HY. Correlation of prostate volume with severity of lower urinary tract symptoms as measured by international prostate symptoms score and maximum urine flow rate among patients with benign prostatic hyperplasia. African Journal of Urology. 2021;27:1-7. Doi: 10.1186/s12301-021-00122-4

19. Albarqouni L, Sanders S, Clark J, Tikkinen KA, Glasziou P. Self-management for men with lower urinary tract symptoms: a systematic review and meta-analysis. The Annals of Family Medicine. 2021;19(2):157-67. Doi: 10.1370/afm.2609

20. Creta M, Russo GI, Bhojani N, Drake MJ, Gratzke C, Peyronnet B, Roehrborn C, Tikkinen KA, Cornu JN, Fusco F. Bladder outlet obstruction relief and symptom improvement following medical and surgical therapies for lower urinary tract symptoms suggestive of benign prostatic hyperplasia: A systematic review. European urology. 2024. Doi: 10.1016/j.eururo.2024.04.031

21. Law YX, Castellani D, Dell'atti L, Aho T, Teoh JY, Gauhar V. Differences in surgical and functional outcomes in benign prostate hyperplasia patients with only lower urinary tract symptoms versus those in retention: A systematic review and meta-analysis. Neurourology and Urodynamics. 2021;40(6):1389-401. Doi: 10.1002/nau.24708

22. Malde S, Umbach R, Wheeler JR, Lytvyn L, Cornu JN, Gacci M, Gratzke C, Herrmann TR, Mamoulakis C, Rieken M, Speakman MJ. A systematic review of patients' values, preferences, and expectations for the diagnosis and treatment of male lower urinary tract symptoms. European urology. 2021;79(6):796-809. Doi: 10.1016/j.eururo.2020.12.019

23. Cornu JN, Zantek P, Burtt G, Martin C, Martin A, Springate C, Chughtai B. Minimally invasive treatments for benign prostatic obstruction: a systematic review and network meta-analysis. European urology. 2023;83(6):534-47. Doi: 10.1016/j.eururo.2023.02.028

Original Article **Open Access**

Anatomical and Morphological Study of the Sternal Foramen Using Computed Tomography Imaging

Saman Ali, Zumirah Atiq, Zunaira, Aniba Zahid, Maria Binte Tariq, Athar Maqbool

ABSTRACT

Objective: This study aims to determine the prevalence and anatomical variations of the sternal foramen (SF) in Pakistani population, and to emphasize its critical clinical significance in preventing complications-such as cardiac tamponade and pneumothorax-during anterior chest wall interventions.

Study Design and Setting: This retrospective, observational CT based morphometric study on human sternum was carried out in Pakistani population at M. Islam Teaching Hospital, Gujranwala from December 2023 to October 2024.

Methodology: The evaluation of images was done using coronal multiplanar reconstruction (MPR) over axial images. The diameters of the detected sternal foramina along with its distance from suprasternal notch and xiphisternum were measured. Male and female groups were compared for differences in various dimensions of the sternal foramina. For statistical analysis, SPSS version 27.0 was used.

Results: In the present study, 580 CT scans were observed. The incidence of sternal foramina in our study is 9.31% (54 out of 580) with 19 men and 35 women. The results showed that both transverse and vertical diameters are generally larger in males than females, with p-value statistically significant. A larger proportion of females (68.6%) have the sternal foramen in the body of the sternum compared to males (52.6%). Maximum number of sternal foramina were observed at the level of the 5th intercostal space 16.67% (n=9).

Conclusion: Awareness of sternal foramina, a congenital defect, is essential for medical professionals to diagnose and prevent complications during surgery, particularly when considering varying prevalence and characteristics across populations.

Keywords: Congenital defect, CT, Human sternum, Morphology, Sternal foramen, Suprasternal notch, Xiphisternum.

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INTRODUCTION

The sternum is a flat bone which is present along the anterior midline of the chest. Anatomically it consists of three parts; the manubrium superiorly, the body in the middle, and the xiphoid process inferiorly. [1,2] The manubrium articulates laterally with the clavicles on both sides at the sternoclavicular joints. It also articulates with the first costal cartilage and the upper half of the second costal cartilage. Inferiorly, the manubrium connects with the body of the sternum at the manubriosternal joint. The body of the sternum establishes lateral articulations with the lower half of the second costal cartilage, the third to sixth costal cartilages, and the upper half of the seventh costal cartilage. Inferiorly, it articulates with the xiphoid process at the xiphisternal joint. The xiphoid process itself contributes to the thoracic wall by forming a junction with the lower part of the seventh costal cartilage laterally. Embryologically, the sternum is derived from a pair of mesenchymal sternal bars that develop on either side of the midline in the ventral thoracic wall. These bars begin to fuse in a craniocaudal sequence, a process that commences around the 10th week of intrauterine life. The fusion and subsequent ossification of the sternum occur through endochondral ossification, where cartilaginous templates

are gradually replaced by bone. This developmental sequence ensures the formation of a single, continuous sternum, with multiple ossification centers appearing in a segmental fashion from the manubrium to the xiphoid process.[1]

Sternal foramina (SF) are congenital defects arising from incomplete fusion of these ossification centers. These can be observed in any of the three parts of the sternum, most commonly observed in the lower part of the sternal body.[2] Skeletal variations, particularly those involving the sternum, are relatively common anatomical occurrences that may often be misidentified or misunderstood as pathological abnormalities.[3] Often asymptomatic, SF are usually discovered incidentally on imaging or autopsy. However, they carry immense clinical significance, as SF may lead to iatrogenic injury. The knowledge of their presence is crucial during acupuncture, bone marrow biopsy, and sternal aspiration, as they lie near vital structures like the heart and pericardium.[2,4] These anomalies may appear singly or as multiple defects along the sternum, with prevalence rates ranging from as low as 0.2% to as high as 57.8%.[5]

The sternum, known for its durability and resistance to deformation over time, plays a crucial role in determining both age and gender in forensic medicine. SF if misidentified as bullet wounds, may complicate cause-of-death determinations in cases of suspected homicide or suicide.[6,7] High-resolution CT scans have also linked them to accessory lung fissures and sternal clefts, as well as sclerotic bands near the foramen.[7,8] The sternal foramen is a developmental anomaly that is considerably more prevalent than commonly assumed, yet it often goes unrecognized in clinical and radiological settings.[9] This underscores the importance of its detailed evaluation and documentation, particularly in anatomical and imaging studies. A comprehensive understanding of the topographical relationship between the sternal foramen and the underlying vital structures—such as the heart, pericardium, and great vessels—is critically important.[10]

This study aims to evaluate the prevalence and anatomical dimensions of the SF to enhance clinical safety and diagnostic accuracy. Understanding its occurrence will help to mitigate risks during invasive blind sternal procedures, prevent misdiagnosis in radiological assessments, and aid forensic differentiation from trauma. An important aspect of this evaluation is the measurement of the distance of the SF from the suprasternal notch, which is crucial for identifying a safe zone for blind sternal procedures. Although several global studies have quantified the prevalence of SF, there is limited morphometric data from South Asia, particularly Pakistan, where genetic and environmental factors may influence ossification patterns.

To the best of our knowledge, no previous study on this topic has been conducted in Pakistan, highlighting the gap between existing information and its practical implications.

METHODOLOGY

This retrospective, observational CT based morphometric study on human sternum was carried out on Pakistani population at M. Islam Teaching Hospital, Gujranwala from December 2023 to October 2024. The Institute's Research Committee approved this study (Approval no: CM/MIMDC/00019/2023) and waived the requirement for informed consent, as it was conducted retrospectively. The exclusion criteria included: (1) patients younger than 18 years, (2) patients older than 65 years, (3) history of trauma, (4) prior sternal surgery, (5) presence of sternal fractures, (6) metastatic tumors or bony lesions, and (7) presence of a bifid xiphoid process.[2,4] The patients had undergone CT thorax for various reasons. Initially, the data collected from 800 patients was assessed out of which 580 met the inclusion criteria of which 408 were females and 172 were males. Thoracic CT scans of all patients with sternal foramen were evaluated by applying 3D bone configuration to evaluate foramina in the sternum.

The CT examinations were performed using a multidetector 128 slices Philips incisive CT (version 5.0.1.771, China). The parameters used were 120 kV, 100 mA, 1-mm slice thickness, and automatic exposure control in all patients. Chest CTs were taken during a breath-hold in deep inspiration. CT scans were obtained as images containing the entire sternum including xiphoid process. In the software of CT scan machine the evaluation of images was done using coronal multiplanar reconstruction (MPR) over axial images. 3D reforming volume rendering technique (VRT) and maximum intensity projection (MIP) were used to display the morphology of entire sternum. Final readings were taken after applying these techniques in bone window.

The diameters of the detected SF were measured transversely and vertically in the coronal section of the thoracic CT bone window. The planes and points of reference used for measuring various readings are shown in figures 1 and 2. The morphometric measurements were taken in millimeters (mm), and following linear readings were obtained;

1. From the deepest part of suprasternal notch to the superior part of SF (A)

2. From the tip of the xiphoid process to the inferior part of SF (B)

3. Transverse diameter (width) of the SF (C)

4. Vertical diameter (length) of the SF (D)

We also noted the level of costal cartilage or intercostal space at which SF was present. Two researchers along with one radiologist and one radiographer took the readings and evaluated the images with a consensus on the presence and morphometry of SF

For statistical analysis, IBM SPSS version 27.0 was used. Independent-samples t-test was used to compare male and female measurements; $p < 0.05$ was considered significant.

RESULTS

The incidence of SF in our study is 9.31% (54 out of 580) with 11.04% in males (19 out of 172) and 8.57% in females (35 out of 408). The mean age of those with SF was 49.88 ± 12.54 years, with 51 ± 14.69 years in males and 49.68 ± 12.15 years in females. The group statistics and independent samples t-test compare the transverse and vertical diameters between males and females. Results showed that both the transverse and vertical diameters are generally larger in males than females, with significant statistical evidence to support these differences as shown in Table no. 1. The percentage and frequency of SF at each level is given in Table no. 2.

Figure no. 1: Distance of Sternal Foramen (SF) from suprasternal notch (A) and tip of xiphoid process (B

DISCUSSION

Sternal foramina (SF) an overlooked anomaly offers an insight into human skeletal variation, with potential implications that extend beyond the bones themselves. SF are usually asymptomatic defects and are not visible on X-rays due to less tissue resolution. Multiplanar reconstruction images of CT scans have shown great efficiency in studying the normal bone anatomy and associated malformations.

The percentage of SF in our study is 9.31% which is somewhat similar to another CT based study by Kuzucuoglu[9] where it was 8.44%. The reported incidence of SF in CT scan based studies of Ma,[4] Gossner,[10] Turkay[11] and Boruah[2]

Figure no. 2: Sternal foramen (SF) Transverse Diameter (C) and Vertical Diameter (D)

Table No. 1: Statistical Overview and Gender Comparison of Sternal Foramina (SF)

	Mean±SD	Male	Female	p-value
Transverse diameter	3.6±1.73mm	5.10±1.73mm	3.43±1.74mm	0.001*
Vertical diameter	5.0±2.8 mm	4.80±1.44mm	3.60±1.61mm	0.009*
Distance from the deepest point of suprasternal notch	99.92±37.10mm	100.57±48.39mm	99.58±30.09mm	0.926
Distance from the tip of the xiphoid	46.36±43.09mm	54.02±49.01mm	42.20±39.65mm	0.341

Table No. 2: Percentage and Frequency of Sternal foramina (SF) at each level

Location	Frequency (n)	Percentage
Manubrium	10	18.51%
Third costal cartilage level	1	1.85%
Third intercostal space	3	5.55%
Fourth costal cartilage level	3	5.55%
Fourth intercostal space	4	7.40%
Fifth costal cartilage level	7	12.96%
Fifth intercostal space	9	16.67%
Sixth costal cartilage level	7	12.96%
Xiphoid	10	18.51%

The Bar Chart shows the gender-based distribution of sternal foramen location

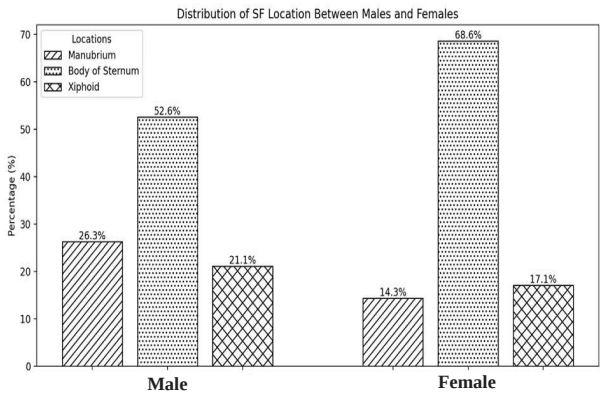

Table no. 3: Sternal foramina (SF) percentage and diameters in various populations

Authors (year)	Place / Country	Type of Study (specimen)	Sample size (sternum)	Percentage of Sterna presenting Sternal Foramen	Transverse Diameter ± SD (mm)	Vertical Diameter ± SD (mm)
Gossner 2013 [10]	Germany	Radiologic (CT)	352	4.5%	3.3	-
Babinski et al. 2015 [20]	Brazil	Radiologic (CT)	114	10.5%	-	-
Sandesh H Chaudhari 2016 [15]	India	Anatomic (dry specimens)	96	4.1%	7.0	5.5
Sukre Shivaji 2016 [7]	India	Anatomic (Dry Specimens)	71	4.22 %	-	-
Boruah et al. 2016 [2]	India	Radiologic (CT)	1180	11.6%	5.57 ± 2.27	6.65 ± 3.35
N. Gkantsinikoudis 2016 [1]	Greece	Anatomic (dry specimens)	35	14.2%	4.8	5.1
Turkay 2017 [11]	Turkey	Radiologic (MDCT)	500	5.2%	-	-
Vulovic 2019 [17]	Serbia	Radiologic (MDCT)	422	5.9%	3.9 ± 1.9	4.2 ± 1.7
Alok tripathi 2019 [19]	India	Anatomic (dry specimen)	100	10%	-	-
Kuzucuoglu 2020 [9]	Turkey	Radiologic (CT)	912	8.44%	5.13 ± 2.63	7.75 ± 4.72
Sunil duchania 2021 [18]	India	Anatomic (dry specimens)	350	6.57%	7.70	9.96
Vatzia 2021 [16]	Greece	Radiologic (MDCT)	950	4.9%	-	-
De-TingMa 2023[4]	China	Radiologic (CT)	2500	4.44%	6.0 ± 2.9	6.8 ± 3.9
Gautam 2023 [13]	India	Anatomic (Dry Specimens)	112	9.82%	5.75	7.16
Lema 2023 [3]	Ethopia	Anatomic (dry Specimens)	94	19.1%	7.08 ± 3.32	7.88 ± 4.28
Present study 2024	Pakistan	Radiologic (CT)	580	9.31%	3.6 ± 1.73	5.0 ± 2.8

was 4.4%, 4.5%, 5.2% and 11.6% respectively, which shows contrast to our study. The global comparison of SF incidence recorded by different researchers along with their transverse and vertical diameters from cadaveric dry specimens to CT scan-based studies is shown in Table no. 3.

Previous studies showed significant correlation between incidence of SF and gender, showing it to be more frequent in males,[2,4,12] and our study (11.4% in males, 8.7% in females) further augments this point.

The size of SF in our study was very different from other studies with mean transverse diameter being 3.6±1.73 mm which is quite less as compared to other studies. Boruah et al[2] measured the mean transverse diameter as 5.58±2.28 mm, Ma[4] reported it to be 6.0±2.29 mm, Gautam[13] reported it to be 5.75 mm and 5.13 ± 2.63 mm by Kuzucuoglu.[9]

Similar trend was observed with the mean vertical diameter in our study which was found to be 5.0±2.8 mm which is lesser than Gautum[13] (7.16 mm), Boruah[2] (6.65±3.35 mm), Ma[4] (6.8±3.9 mm) and Kuzucuoglu[9] (7.75±4.72 mm). These differences suggest that the ossification process in the sternum varies across populations. Our findings indicate less pronounced gaps when the ossification centers fail to fuse completely. This may be influenced by genetic and environmental factors specific to the Pakistani population, highlighting the importance of regional variations.

An interesting finding of our study was that both transverse and vertical diameters of the SF were greater in males as compared to female with p-values of 0.001 and 0.009 respectively (p-value<0.05). This statistically significant gender difference similar to Ma[4] study suggests that male patients may have different anatomical considerations during procedures involving the sternum, necessitating tailored approaches to ensure safety and effectiveness in surgical interventions.

The analysis of the distances between the SF and both the sternal notch and xiphoid tip demonstrates no notable differences between male and female measurements.

The distance of the SF from the suprasternal notch provides another method for sternal puncture site selection. This distance in our study ranged between 25 mm to 191 mm suggesting that the safe area for sternal biopsy will be anywhere within 25 mm from the suprasternal notch for the Pakistani population.

In our study, 62.96% (n=34) SF in the sternal body were reported. This result was quite similar to Gautam[13] where the percentage of SF in body was 72.73% and Kuzucuoglu[9] with 66.2% (n=45). Quite contrasting from Ma[4] where all the SF were observed in the body of the sternum from 4th to 6th costal cartilage only, with maximum SF present at 5th costochondral junction 45.95% (n=51). Boruah[2] also reported the maximum prevalence of SF at 5th costochondral junction being 78.8% (n=108) which was also seconded by Lema[3]and Sukre Shivaji B[7]. However, no foramen was reported in manubrium and xiphoid in all three of these studies which is contrasting to ours as we observed 18.51% SF both in manubrium and xiphoid separately. Also, in our

study maximum number of SF were observed at the level of the 5th intercostal space 16.67% (n=9). Another study by Bolatli[6] also reported 11.7% SF in the xiphoid as compared to only 5.1% in the sternal body. Boruah[2] suggested that sternal procedures should be avoided from 4th to 6th costal cartilages considering it to be a danger zone. This suggestion is valid but taking into consideration the greater percentage of foramina in manubrium and xiphoid in Pakistani population, preliminary CT should be advised before performing any sternal procedures. SF can easily be mistaken as an osteolytic lesion but smooth edges and contour of the foramen in CT differentiates it from osteolytic lesions which has irregular edges.[14]

LIMITATIONS:

The limitations of the study include its single-center design, which may limit the broader applicability of the findings to other populations. The use of advanced imaging techniques is also recommended for future studies to enable more detailed and spatially accurate evaluation of the sternal foramen. Furthermore, the study focused exclusively on adults aged 18 to 65 years, thereby excluding potential anatomical variations present in pediatric and elderly populations. Incorporating data from a wider age range in future research could offer a more comprehensive understanding of sternal anatomical variations.

CONCLUSION:

Sternal foramen (SF) emerges as a surprisingly frequent anatomical variant within the Pakistani population. Its often-overlooked presence carries serious clinical implications, particularly during invasive procedures where unrecognized SF can lead to devastating outcomes such as cardiac tamponade or pneumothorax. By shedding light on its prevalence and morphology, this study reinforces the need for heightened anatomical vigilance in surgical, radiological, and emergency settings. Future large-scale, multicenter investigations are warranted to map regional differences.

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Zumirah Atiq: Drafting, data collection, data analysis
Zunaira: Drafting, data collection
Aniba Zahid: Drafting, revising critically
Maria Binte Tariq: Drafting
Athar Maqbool: final approval of version

REFERENCES

1. Gkantsinikoudis N, Chaniotakis C, Gkasdaris G, Georgiou N, Kapetanakis S. Morphological approach of the sternal foramen: an anatomic study and a short review of the literature. Folia morphologica. 2017;76(3):484-90. Doi: 10.5603/FM.a2017.0006
2. Boruah DK, Prakash A, Yadav RR, Dhingani DD, Achar S, Augustine A, Mahanta K. The safe zone for blinded sternal interventions based on CT evaluation of midline congenital sternal foramina. Skeletal Radiol. 2016; 45: 1619–1628. Doi: 10.1007/s00256-016-2473-9.
3. Lema AS. Anatomical variations of the sternum: sternal foramen and variant xiphoid morphology in dried adult human sternum in Ethiopia. F1000Research 2023; 12: 934. Doi.org/10.12688/f1000research.133151.1
4. Ma DT, Wang JX, Wang ZH, Cui X. Sternal foramina: An imaging study. Clin Anat. 2024; 37(7): 692-700. Doi.org/10.1002/ca.24105
5. Pasieka P, Pasieka PM, Komosa A, Barnowska A, Pêkala J, Malinowski K, Tomaszewski K. Prevalence and morphometry of sternal and xiphoid foramen: a meta-analysis on 16,666 subjects. Surg Radiol Anat. 2023; 45(5): 623-635. Doi.org/10.1007/s00276-023-03116-9
6. Bolatlý G, Dogan NU, Koplay M, Fazlýoðullarý Z, Karabulut AK. Evaluation of sternal morphology according to age and sex in multidetector computerized tomography. Anat. 2020;14(1):29-38. Doi:10.2399/ana.20.016
7. Sukre Shivaji B, Chavan SR, Shinde Mahesh S, Laeeque M, Dope Santoshkumar A. Sternal Foramina: A Study in Marathwada Population. IJA. 2016; 5(3): 245-250. Doi: http://dx.doi.org/10.21088/ija.2320.0022.5316.8
8. Paraskevas GK, Tzika M, Natsis K. Double sternal foramina in a dried sternum: a rare normal variant and its radiologic assessment. Surg Radiol Anat. 2016; 38: 991-993. Doi: 10.1007/s00276-016-1663-4
9. Kuzucuoglu M, Albayrak I. Topographic evaluation of sternal foramen patients with thoracic computed tomography. SRA. 2020; 42: 405-409. doi.org/10.1007/s00276-019-02416-3
10. Gossner J. Relationship of sternal foramina to vital structures of the chest: a computed tomographic study. Anat. Res. Int. 2013; 1: 780193. Doi.org/10.1155/2013/780193
11. Turkay R, Inci E, Ors S, Nalbant MO, Gurses IA. Frequency of sternal variations in living individuals. Surg Radiol Anat. 2017; 39: 1273-1278. Doi 10.1007/s00276-017-1854-7
12. Gans, B.D., Neunuebel, A.D., Umbarger, L.J., Trumble, B.C., Cummings, D.K., Wann, L.S., Lehenbauer, K.R., Mahadev, A., Rodriguez, D.E., Michalik, D.E. and Rowan, C.J., 2021. High prevalence of sternal foramina in indigenous Bolivians compared to Midwest Americans and indigenous North Americans (sternal foramina in indigenous Bolivians). Anat. Sci. Int. 2021; 96: 517-523. Doi.org/10.1007/s12565-021-00618-7
13. Gautam RS, Rajput H, Doshi B, Parmar J. Morphometric and morphological study of most common sternal entity: sternal foramen. Int J Med Pharm Research 2023; 4(2): 62-65.

14. Anand A, Dougall P. Sternal foramina in patient with hepatocellular carcinoma: A diagnostic dilemma on bone scan. IJNM. 2019; 34(1):35-37.Doi:10.4103/ijnm.IJNM _126_18

15. Chaudhari SH, Kumar N, Thakre G, Kawanpure H, Gathe B. A study on medico-legal and clinical aspects of congenital sternal foramina. Indian J Forensic Community Med. 2016; 3(3): 194-197. Doi: 10.5958/2394-6776.2016.00043.6

16. Vatzia K, Fanariotis M, Makridis KG, Vlychou M, Fezoulidis IV, Vassiou K. Frequency of sternal variations and anomalies in living individuals evaluated by MDCT. Eur J Radiol. 2021; 142: 109828. Doi.org/10.1016/j.ejrad.2021.109828

17. Vuloviæ M, Živanoviæ-Maèužiæ I, Jeremiæ D, Đonoviæ N, Radunoviæ A, Jovanoviæ M, Miloševiæ B, Aleksiæ Z, Stankoviæ I, Vojinoviæ R. Multidetector computed tomography (MDCT) estimation of prevalence and anatomic characteristics of the sternal body foramen in the population of central Serbia. Vojnosanit Pregl 2019; 76(2): 186–191. Doi.org/10.2298/ VSP170321084V

18. Duchania S, Rani M, Singh RK. Sternal foramen-Incidence and medico-legal importance. IJFMTS. 2021; 6(4): 137–140. Doi.org/10.18231/j.ijfmts.2021.029

19. Tripathi A, Kumar A, Raizaday S, Khare S, Jain S. A Comprehensive Study of Sternal Foramen in Dry Sternum. J. Anat. Science. 2019; 27(1): 30-33.

20. Babinski MA, de Lemos L, Babinski MS, Gonçalves MV, De Paula RC, Fernandes RM. Frequency of sternal foramen evaluated by MDCT: a minor variation of great relevance. Surg Rad Anat. 2015; 37: 287-291. Doi.org/10.1007/s00276-014-1339-x

Original Article **Open Access**

Thyroid Profile Abnormalities in Pediatric Population and their Correlation with Age: A Cross-Sectional Study at a Tertiary Care Hospital of South Punjab

Mehvish Sana, Zille Rubab, Ayesha Fayyaz, Waqas Imran

Abstract

Objective: To determine prevalence and pattern of thyroid profile abnormalities (hypothyroidism, hyperthyroidism, subclinical hypothyroidism, and subclinical hyperthyroidism) in pediatric population and to correlate these abnormalities with age in children presenting to a tertiary care hospital of South Punjab.

Study design and setting: This cross-sectional study was conducted for two months from 5-Dec-2024 to 5-Feb-2025 in Pathology department of Children Hospital and Institute of Child Health (CH & ICH) Multan.

Methodology: All the patients of 1-14 years whose thyroid profile was requested for any clinical indication were included in the study using consecutive sampling technique. Participants were divided into 3 age groups of 1-5 years, 6-10 years and 11-14 years. Data was entered and analyzed using SPSS 22. P-value of <0.05 was considered statistically significant.

Results: Among 200 children included in the study 60(30%) were found to have thyroid disorders. Subclinical hypothyroidism was seen in 36(60%) children and was most common thyroid disorder. Thyroid disorders were slightly more common in females. Difference of Mean T3, T4 and TSH in various thyroid disorders was statistically significant with p value of 0.000. Majority of the children (44%) were in 1-5 years age group. No correlation was found between age of the patients and thyroid disorders (r=0.004, sig. 2 tailed=0.966).

Conclusion: Subclinical hypothyroidism is the most common thyroid disorder among children and thyroid profile abnormalities are not related to age.

Keywords: Autoimmune thyroiditis, Hyperthyroidism, Hypothyroidism, Thyroid function tests

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INTRODUCTION:

Normal thyroid function is vital for proper neurocognitive growth, as well as for development and maturation during childhood and adolescence. Thyroid function tests are commonly available and are routinely requested in pediatric healthcare setup.[1] The impact of thyroid hormones on tissue growth is regulated by age and is tissue or organ specific, therefore medical consequences of any thyroid function abnormality differ depending on the child's age. In infancy and childhood, thyroid dysfunction leads to metabolic disruptions and affects growth and development. Therefore in pediatric setting, thorough assessment and management of thyroid function are crucial, as thyroid disorders can significantly affect neurodevelopment, physical growth, and overall health in children. Thyroid disorders make up a substantial portion of pediatric endocrine conditions, second only to diabetes in children worldwide.[2] In Pakistan, where iodine deficiency is prevalent, high rates of thyroid diseases are observed, likely due to inadequate dietary iodine intake, or autoimmune diseases affecting thyroid function, leading to either hypothyroidism or hyperthyroidism.[3] However, due to underdiagnosis, lack of awareness, and inconsistent availability of diagnostic services, timely detection and effective management are frequently compromised.

Thyroid disorders represent a range of conditions, from hypothyroidism to hyperthyroidism, indicated by the levels of Thyroid Stimulating Hormone (TSH), Triiodothyronine (T3), and Thyroxine (T4). Hypothyroidism is more prevalent than hyperthyroidism, both globally and in countries like Pakistan. It occurs when the thyroid gland fails to produce sufficient amounts of thyroid hormones, leading to a slowing down of metabolic processes. This condition is more

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commonly seen in women and increases with age. In contrast, hyperthyroidism, which involves the overproduction of thyroid hormones, is relatively less common.[4] Thyroid dysfunction can be subclinical and asymptomatic, characterized by irregular thyroid hormone levels where T3 and T4 levels remain normal while TSH levels are abnormal. In contrast, clinically symptomatic thyroid dysfunction involves abnormal levels of both T3 and T4 along with TSH.[5] Autoimmune thyroid diseases (AITDs), such as Hashimoto thyroiditis and Grave's disease, are the most common thyroid conditions with two different extremes in children. These disorders may occur as isolated autoimmune conditions or alongside other autoimmune diseases like Type 1 diabetes, celiac disease, pernicious anemia, and others.[6,7] Autoimmune thyroiditis (AIT) is one of the main causes of acquired hypothyroidism in pediatric population, leading to inflammation, gradual glandular destruction, and reduced hormone production and many cases are detected incidentally before overt symptoms emerge.[8] Timely diagnosis and appropriate treatment are crucial to support normal growth, developmental progress, and academic performance in children.

In patients with severe hypothyroidism, key signs include growth failure and weight gain, though some children may show normal growth parameters for the population at first presentation. Enlargement of pituitary gland should be considered in every child with severe hypothyroidism.[8] In subclinical hypothyroidism, growth limitations or cognitive impairments are generally not noted, but subtle cardiac problems have been reported.[9] Most children with subclinical hyperthyroidism are usually asymptomatic, especially when the suppression of TSH is mild and short-lived. This is commonly seen in the early stages or recovery phase of thyroid dysfunction, or in cases where thyroid hormone is administered externally also called iatrogenic subclinical hyperthyroidism. Due to the subtle nature of symptoms, routine laboratory screening can be valuable particularly in children with known risk factors such as autoimmune conditions or a family history of thyroid disease. When subclinical hyperthyroidism is persistent or shows signs of progression, it requires close monitoring or intervention to prevent potential long-term complications affecting the heart, bone development, and neurological function.[10] Hyperthyroidism is rare but can have serious effects on a child's growth and development. Clinicians should be aware of subtle clinical manifestations of this condition. Early recognition and referral to a pediatric endocrinologist can help prevent complications associated with this condition.[11] In pediatric patients, thyroid function tests (TFTs) abnormalities can impart diagnostic challenges due to the wide range of clinical signs that may accompany them. Possible causes of abnormal TFTs include Grave's disease, Hashimoto thyroiditis, congenital hypothyroidism, resistance to thyroid hormone, iodine deficiency, sick euthyroid syndrome, medications and interference with thyroid function assays.[12]

This study aims to determine the prevalence and pattern of thyroid profile abnormalities in children and to correlate these abnormalities with age. In countries like Pakistan, where iodine deficiency remains a concern, there is a higher incidence of thyroid disorders, particularly in children. Thyroid disorders in children can significantly impact growth, neurodevelopment, and overall health. Among these, subclinical thyroid disorders are often overlooked due to the absence of obvious clinical symptoms. However, emerging evidence suggests that these subclinical disorders if left undiagnosed or untreated also contribute to subtle changes in growth patterns, cognitive function and cardiovascular risk over time. There is insufficient local data on the prevalence and pattern of thyroid dysfunctions in children. Identifying these patterns is crucial for early diagnosis, timely intervention, and long-term health monitoring. This study aims to address this gap by evaluating thyroid profile abnormalities, with a special focus on subclinical forms, and exploring their correlation with age in children attending a tertiary care hospital in South Punjab.

METHODOLOGY:

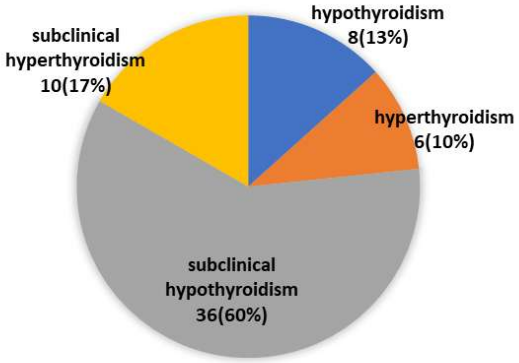
This cross-sectional study was conducted for two months from 5-Dec-2024 to 5-Feb-2025 in Pathology department of Children Hospital and Institute of Child Health (CH & ICH) Multan. Ethical approval was taken from Ethical Review Committee of institute before commencing the study (2364 DATED 5-12-24). All the Children of 1-14 years of both genders whose thyroid profile was requested for any clinical indication including but not limited to growth abnormalities, physical findings or constitutional symptoms indicating thyroid disorders, neurodevelopmental concerns, high risk individuals with family history of thyroid or autoimmune disorders were included in the study using consecutive sampling technique. Informed consent was taken from parents of the patients. Children with critical or chronic systemic illness, undergoing treatment for any thyroid disorder, receiving medications that could interfere with thyroid hormone levels, and individuals for whom informed consent was not obtained were excluded. Sample size of 130 was calculated using prevalence 13% margin of error 5% and confidence interval 95%.[13] However to overcome issue of missing data we enrolled 200 patients. Participants were divided into 3 age groups of 1-5 years, 6-10 years and 11-14 years. 2 ml blood for thyroid profile (TSH, free T4, free T3) was obtained in gel tube under aseptic conditions. Sample was allowed to clot, serum was separated after centrifugation and thyroid profile was performed on VITROS ECiQ immunodiagnostic system, chemiluminescence based homogeneous immunoassay analyzer. Demographic variables and thyroid profile results were recorded on a predesigned proforma. Reference ranges used for fT3, fT4 and TSH are 2.3-5.0pg/ml, 0.8-2.0ng/ml, 0.5-4.7uIU/ml. Thyroid profile

abnormalities (hypothyroidism or hyperthyroidism, subclinical hypothyroidism and subclinical hyperthyroidism) were defined as per the standard cut offs of fT3, fT4 and TSH. The data was entered and analyzed on SPSS version 22. Shapiro Wilk test was applied to check normality of data. Mean and SD was given for quantitative variables with normal distribution while Median and range was given for variables with skewed distribution. Independent *t*-test and analysis of variance (ANOVA) were used to test for statistically significant differences of T3, T4, TSH in males, females and different thyroid disorders respectively. Pearson correlation was used to see correlation between thyroid profile abnormalities and age. P-value of <0.05 was considered to be statistically significant.

RESULTS:

200 children were included in this study among which 94(47%) were male and 106(53%) were female. Participants were divided into 3 age groups. 88(44%) were included in 1-5 years age group, 80(40%) in 6-10 years age group and 32(16%) in 11-14 years age group. Mean age of the study participants was 6.3±3.7 years. Mean T3 and T4 were 3.7±1.03 pg/ml and 1.45±0.5 ng/dl respectively. Median TSH was 2.82(1.50-4.78) uIU/ml. 60(30%) patients were found to have thyroid disorders. Among all these thyroid disorders subclinical hypothyroidism was most prevalent as shown in figure 1. Thyroid disorders were found to be slightly more prevalent in females than in males as shown in figure 2 with a ratio of 1.4:1. Mean T3, T4 and TSH difference was statistically insignificant in males and females with p value of 0.59, 0.93 and 0.34 respectively. Difference of mean T3, T4 and TSH values were statistically significant (p=0.000) among euthyroid, hypothyroid, hyperthyroid, subclinical hypothyroid and subclinical hyperthyroid patients as shown in table 1. No correlation was found between thyroid disorders and age of the patients (r=0.004, sig. 2 tailed=0.966) (table 2).

Figure 1: Frequency of thyroid disorders(n=60)



DISCUSSION:

In our study, thyroid disorders were identified in 30% of patients. The most common thyroid disorder was subclinical hypothyroidism, accounting for 60% of cases, followed by subclinical hyperthyroidism (17%), overt hypothyroidism (13%), and hyperthyroidism (10%). The overall prevalence of thyroid disorders in the study group was as follows: subclinical hypothyroidism 36(18%), subclinical hyperthyroidism 10(5%), overt hypothyroidism 8(4%), and hyperthyroidism 6(3%). A study in India involving 498 children discovered thyroid abnormalities in 65 (13%) children, 6(93.8%) were diagnosed with hypothyroidism

Figure 2: Gender distribution of thyroid disorders. (n=60)

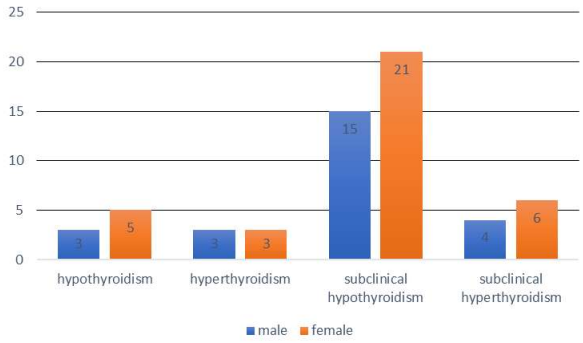


Table 1: Difference of mean T3, T4 and TSH values among different thyroid disorders

Thyroid profile	Thyroid disorders					*p* value
	Euthyroid	Hypothyroidism	Hyperthyroidism	Subclinical hypothyroidism	Subclinical hyperthyroidism	
T3	3.7±0.6	1.7±0.3	6.8±1.5	3.6±0.7	4.1±0.3	0.000
T4	1.4±0.3	0.24±0.16	0.24±0.16	1.5±0.3	1.5±0.4	0.000
TSH	2.6±1.1	2.4±0.8	2.4±0.8	8.8±5.2	0.3±0.19	0.000

Table 2: Correlation of age group and thyroid disorders

		Age group	Thyroid disorder
Age group	Pearson Correlation	1	.004
	Sig. (2-tailed)		.966
	N	200	200

and 4(6.2%) with hyperthyroidism, and a male-to-female ratio of 1:1.2 was noticed.[13] In Pakistan, the incidence of subclinical hyperthyroidism, subclinical hypothyroidism overt hyperthyroidism and overt hypothyroidism is reported to be 5.8%, 5.4%, 5.1% and 4.1% respectively.[14] Moreover, it is evident that both hyperthyroidism and hypothyroidism (subclinical or overt) are more widespread in females than in males.[14] Our research also showed that subclinical thyroid disorders are more frequent than overt thyroid disorders with female predominance. A smaller study in India reported 37% of children with thyroid dysfunction had hypothyroidism.[15] A Saudi Arabian study revealed that hypothyroidism is more frequent in pediatric population than hyperthyroidism, with 50.34% of cases being Hashimoto thyroiditis, and 64.2% of those affected were females.[16] A study conducted in Pakistan showed that thyroid disorders are five times more frequent in females than males.[17] Our findings align with these studies, indicating that hypothyroidism, particularly subclinical hypothyroidism, is more prevalent than hyperthyroidism, with thyroid disorders being more common in females. In our study, the male-to-female ratio was 1:1.4, which further supports prior studies.[13, 14, 16, 17]

Clinical evidence suggest that acquired thyroid disease with obvious clinical findings is rare. Most cases tend to have a subtle or asymptomatic onset, often going undetected until routine screening or evaluation for unrelated issues reveals abnormalities in thyroid function. As a result, many children with acquired thyroid dysfunction may not be diagnosed until the disease has progressed, emphasizing the importance of high clinical suspicion and timely screening especially in at-risk populations.[18]

Subclinical hypothyroidism (SCH) in children is generally considered a mild and often transient condition. Research shows that in approximately 68% to 88% of cases, SCH either remains stable or resolves spontaneously without advancing to overt hypothyroidism. Only a small proportion of patients experience progression to clinically significant hypothyroidism or develop autoimmune thyroid disorders, such as Hashimoto's thyroiditis. Despite its typically benign course, SCH often causes concern among parents and primary care providers, mainly due to the uncertainty of its long term outcomes. Even in asymptomatic cases, abnormal thyroid function test results can lead to anxiety and frequent referrals to pediatric endocrinologists for further assessment. This pattern highlights the importance of evidence based guidelines to help clinicians identify which children require active intervention versus those who can be safely observed over time. A better understanding of the natural course of SCH is key to avoid overtreatment while ensuring that children at risk of progression receive appropriate care.[19] Infants with subclinical hypothyroidism need careful follow-up, as elevated TSH level may be transitory in about half of the cases and resolve spontaneously or progress to overt hypothyroidism which may impair neurological development.[20] Iodine deficiency is one of the most common causes of subclinical hypothyroidism in children, though supporting evidence is lacking. Other causes include maternal thyroid dysfunction, autoimmune thyroid diseases (Hashimoto's thyroiditis), genetic syndromes (Down syndrome) and gene mutations in TSH receptor.[21]

Graves' disease (GD) accounts for 60-80% of hyperthyroidism cases in children, and some sources suggest it may be responsible for more than 95% hyperthyroid cases, making it nearly synonymous with hyperthyroidism particularly in school age children and adolescents..[22] Graves' disease is an autoimmune disorder characterized by the production of TSH receptor antibodies (TRAbs) stimulating the thyroid gland for overproduction thyroid hormones T3 and T4 and ultimately leading to clinical hyperthyroidism. Other causes of hyperthyroidism including Hashitoxicosis, toxic adenoma or multinodular goiter, thyroiditis and exogenous thyroid hormone ingestion are rare in children.

Thyroid disorders are influenced by different factors such as geographical dissemination, iodine utilization, nutritional habits and genetic susceptibility.[23] In geographical dissemination endemic goiter remains a health concern in parts of Asia, Africa, and Latin America, largely due to insufficient iodine intake. Although global initiatives have significantly lowered its prevalence but continued and targeted public health efforts are essential to reach the most vulnerable and isolated populations. Diet and nutrition stand out as modifiable factors that can improve thyroid function and reduce the frequency of thyroid conditions.[24] Unlike genetic or geographic factors, nutritional choices can be adjusted, offering both preventive and therapeutic benefits for various thyroid conditions. In developed economies, the prevalence of undetected thyroid disorder is declining due to widespread thyroid function assessments and lower treatment initiation thresholds.[21] Previously only overt thyroid disorders were treated but now proactive approach of treating subclinical thyroid disorders prevents progression to overt disease and reduces complications. While thyroid conditions are easily managed in advanced nations, low-income countries face a larger and often underestimated burden. Developing specialized healthcare centers for thyroid disorders which include comprehensive diagnostic services with tailored treatment options and postgraduate endocrinology education is crucial for meeting this need in developing nations.[25]

CONCLUSION:

This study concludes that subclinical thyroid disorders are more prevalent than overt thyroid dysfunction in the pediatric population, with subclinical hypothyroidism emerging as the most frequently observed abnormality. The findings underscore that thyroid profile abnormalities occur across all pediatric age groups without a significant correlation to age, suggesting that age alone should not be considered a

primary determinant in evaluating thyroid function in children.

LIMITATIONS:

This study was conducted in a tertiary care hospital therefore participants may not be representative of general pediatric population particularly those from underprivileged areas who may not have access to tertiary care hospital.

RECOMMENDATIONS:

It is recommended that children with symptoms suggestive of thyroid dysfunction and family history of thyroid or autoimmune disorder should undergo prompt thyroid evaluation. It is also recommended that TSH should be used for initial screening of thyroid disorders. Free T4 and free T3 should be advised when TSH is abnormal or if there is strong clinical indication. Availability of data: Authors confirm that data supporting the results of this study are available in the article.

Authors Contribution:
Mehvish Sana: Concept design, data collection, data analysis, manuscript writing
Zille Rubab: Proof reading and revision
Ayesha Fayyaz: Manuscript writing, proof reading
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REFERENCES:

1. Hanley P, Lord K, Bauer AJ. Thyroid disorders in children and adolescents: a review. JAMA pediatr. 2016; 170(10):1008-19 DOI: 10.1001/jamapediatrics.2016.0486
2. Oyenusi EE, Ajayi EO, Akeredolu FD, Oduwole AO. Pattern of thyroid disorders in children and adolescents seen at the Lagos University Teaching Hospital, Nigeria, over a 10-year period. Niger Med J. 2017; 58(3):101-6 DOI: 10.4103/nmj.NMJ_156_16
3. Lee H, Hodi FS, Giobbie-Hurder A, Ott PA, Buchbinder EI, Haq R, et al. Characterization of thyroid disorders in patients receiving immune checkpoint inhibition therapy. Cancer Immunol Res. 2017;5(12):1133-40 DOI: https://doi.org/10.1158/2326-6066.CIR-17-0208
4. Rivkees S, Bauer AJ. Thyroid disorders in children and adolescents. Sperling Pediatr Endocrinol: Elsevier. 2021: 395-424 DOI: https://doi.org/10.1016/B978-0-323-62520-3.00013-0
5. Shah N, Ursani TJ, Shah NA, Raza HMZ. Prevalence and manifestations of hypothyroidism among population of Hyderabad, Sindh, Pakistan. PAB. 2021; 10(3):668-75 DOI: https://dx.doi.org/10.19045/bspab.2021.100069
6. Calcaterra V, Nappi RE, Regalbuto C, De Silvestri A, Incardona A, Amariti R, et al. Gender differences at the onset of autoimmune thyroid diseases in children and adolescents. Front Endocrinol. 2020;11:229 DOI: https://doi.org/10.3389/fendo.2020.00229
7. Casto C, Pepe G, Li Pomi A, Corica D, Aversa T, Wasniewska M. Hashimoto's thyroiditis and Graves' disease in genetic syndromes in pediatric age. Genes. 2021;12(2):222 DOI: https://doi.org/10.3390/genes12020222
8. Kucharska AM, Witkowska-S?dek E, Labochka D, Rumiñska M. Clinical and biochemical characteristics of severe hypothyroidism due to autoimmune thyroiditis in children. Front Endocrinol. 2020; 11:364 DOI: https://www.frontiersin.org/articles/10.3389/fendo.2020.00364/full
9. Salerno M, Capalbo D, Cerbone M, De Luca F. Subclinical hypothyroidism in childhood—current knowledge and open issues. Nat Rev Endocrinol. 2016; 12(12):734-46
10. Metwalley KA, Farghaly HS. Subclinical hyperthyroidism in children. J Pediatr Endocrinol Metab. 2023; 36(4):342-5 DOI: https://doi.org/10.1515/jpem-2022-0534
11. Srinivasan S, Misra M. Hyperthyroidism in children. Pediatr Rev. 2015; 36(6):239-48
12. Kaðýzmanlý GA, Demir K. Interpretation, differential diagnosis, and clinical implications of abnormal thyroid function tests in children. Trends in Pediatr. 2023; 4(2):61-71 DOI: https://doi.org/10.59213/TP.2023.5321513.
13. Singh A, Purani C, Mandal A, Mehariya KM, Das RR. Prevalence of thyroid disorders in children at a tertiary care hospital in western India. J Clin Diagn Res. 2016; 10(2):SC01 DOI: https://doi.org/10.7860/JCDR/2016/16315.7189
14. Reza S, Shaukat A, Arain TM, Riaz QS, Mahmud M. Expression of osteopontin in patients with thyroid dysfunction. PLoS One. 2013; 8(2):56533 DOI: https://doi.org/10.1371/journal.pone.0056533
15. Shah NA, Modi PJ, Bhalodia JN, Desai NJ. Evaluation of thyroid diseases by hormonal analysis in pediatric age group. Natl J Med Res. 2013; 3(04):367-70
16. Al-Qahtani MH, ElYahia SA, AlQahtani AS, AlQahtani AJ, Alamer AA, AlQahtani SM, et al. Thyroid disorders spectrum in pediatric endocrine clinic; seven-year experience of a teaching hospital in Saudi Arabia. Children. 2023;10(2):390 DOI: https://doi.org/10.3390/children10020390
17. Mansoor R, Rizvi S, Huda S, Khan C. Spectrum of thyroid diseases, an experience in the tertiary care and teaching hospital. Pak Inst Med Sci. 2010; 6(2):101-6
18. Andersson M, Braegger CP. The role of iodine for thyroid function in lactating women and infants. Endocr Rev. 2022; 43(3):469-506 DOI: https://doi.org/10.1210/endrev/bnab029
19. Murillo-Vallés M, Martinez S, Aguilar-Riera C, Garcia-Martin MA, Bel-Comós J, Ybern MLG. Subclinical hypothyroidism in childhood, treatment or only follow-up? BMC pediatr. 2020;20:1-6
20. Kaplowitz PB. Neonatal thyroid disease. Current Adv Neonatal Care, an issue of pediatric clinics of North America. 2019 ;66:343-52 DOI: https.//doi.org/10.1016/j.pcl.2018.12.005
21. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol. 2018;14(5):301-16
22. Niedziela M. Hyperthyroidism in adolescents. Endocr Connect. 2021; 10(11):R279-R92
23. Iqbal MA, Naseem Z, Qureshy A, Shahid A, Roohi N. Prevalence and manifestations of thyroidal dysfunction in Central Punjab Pakistan (a case study). Sci Int. 2016; 28(4):3959-63
24. Shulhai A-M, Rotondo R, Petraroli M, Patianna V, Predieri B, Iughetti L, et al. The role of Nutrition on thyroid function. Nutr. 2024; 16(15):2496
25. Mallhi TH, Kanwal H, Mushtaq S, Akash MSH, Ahmad N, Khan YH, et al. Thyroid Disorder Management in Developing Countries. Handbook of medical and health sciences in developing countries: Education, practice, and research: Springer. 2023;1-23. DOI: 10.1007/978-3-030-74786-2_13-1

Original Article **Open Access**

Comparison of a Single 2mm Locking Miniplate with Two 2mm Non-Locking Miniplates in Symphysis or Para symphysis Fracture of Mandible

Anam Shahzad, Shahid Ali, Muhammad Mustafa, Adnan Haider, Fatima Imran, Kashif Adnan

ABSTRACT

Objective: To assess the treatment success between locking and non-locking miniplates when used for the constructive repair of mandibular symphysis and parasymphysis fractures of the mandible.

Study Design and Setting: This study is designed as a quasi-experimental conducted in the Oral and Maxillofacial Surgery Department of Punjab Dental Hospital and De Montmorency College of Dentistry, Lahore.

Methodology: This quasi-experimental was conducted in the Oral and Maxillofacial Surgery Department of Punjab Dental Hospital and De Montmorency College of Dentistry, Lahore. It enrolled 60 patients into each group consisting of locking and non-locking variants for a total of 120 participants. The data was evaluated through SPSS version 25 by applying the Chi-square test and one-way ANOVA test.

Results: Fracture stability was achieved in of patients in the locking miniplate group compared to in the non-locking group, with statistical significance (p=0.040). The need for additional IMFs was significantly lower in the locking group, with only required additional fixation, compared to the non-locking group (p=0.00095). Pain scores, measured using the VAS, were significantly lower in the locking miniplate group compared to the non-locking group with a p-value of 0.0001. Soft tissue healing was significantly better in the locking group, showing proper healing compared to the non-locking group (p=0.008).

Conclusion: The superior locking miniplate design achieves better fracture stability through increased mechanical stability as well as reducing postoperative discomfort and improving the healing of soft tissue structures, thus establishing their advantage over traditional non-locking miniplate methods.

Keywords: Fracture stability, locking miniplates, mandibular fractures, non-locking miniplates,

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INTRODUCTION

The mandible, a unique horseshoe-shaped bone, plays a critical role in cranial articulation, mastication, speech, respiration, and facial expression.[1] The maxillofacial injuries mainly stem from fractures because the bone's exposed position and particular structure create high susceptibility.[2,3] Interpersonal violence, together with road traffic accidents and falls and sports-related incidents, represent the typical situations that lead to mandibular fractures.[4] Mandibular symphysis, along with parasymphysis, stands out as the most vulnerable areas for fractures because of their position while under biomechanical stress.[5]

Traditional mandibular fracture treatment methods, including bandages and wire-based stabilization and splint fixation, caused patients to develop various complications, including facial asymmetry as well as functional impairment and malocclusion.[6, 7] Mandibular fracture treatment underwent a revolutionary change with the introduction of miniplates through the work of Champy and Michelet in the 1970s through open reduction and internal fixation (ORIF).[8] Champy's tension band osteosynthesis principle became the foundation for expansive clinical acceptance of two 2.0mm

non-locking miniplates positioned subapically and at the lower border to prevent torsional, compressive, and tensile forces from affecting the symphysis and parasymphysis regions.[9]

The stability of conventional miniplates requires bone compression for support but this technique generates complications including screw loosening together with cortical resorption and loss of fixation particularly in medically or nutritionally fragile patients.[10, 11] The locking plate system with screws emerged to resolve existing shortcomings.[12] The locking miniplates differ from non-locking plates by uniting screws to both plate structure and bone tissue through a fixed-angle construct which strengthens stability and reserves periosteal blood supply and minimizes screw movements.[13] The locking plate technology provides dual fixation to bone and plate, which decreases necrotic tissue development, enhances functional results, and eliminates the requirement of IMF treatment in most procedures.[14]

The latest studies propose an assessment of locking miniplates against non-locking miniplates for treating mandibular fractures.[15] A study by Elsayed et al. (2020) examined the mandibular parasymphysis fracture outcomes between 2mm locking and 2mm non-locking miniplates. The locking plate group exhibited superior bone healing compared to the non-locking plate group according to radiological assessments, even though clinical pain and swelling measurements remained identical and occlusal stability showed no substantial differences between the two groups.[16] Research by Pirwani et al. 2022 examined how different miniplates affected infection rates for patients who were 35 years old and older. The infection rates among 100 managed patients showed no noteworthy variations, which indicates that locking plates work equally well as non-locking miniplates for mandibular fracture treatment. The better bone healing capability of locking plates provides potential benefits for fracture rehabilitation by ensuring more stable fixation of fractures during healing.[17]

This research examines the effectiveness of a standalone 2.0mm locking miniplate when it replaces the traditional two 2.0mm non-locking miniplates for treating symphysis and parasymphysis fractures. Because of its time-saving characteristics, along with reduced instrumentation needs and superior stability, the locking system seems to offer patients an improved, efficient therapy. The study aims to examine postoperative pain, occlusal stability, and fractured segment stability with IMF requirements through the evaluation of single 2.0mm locking miniplates against two 2.0mm non-locking miniplates.

METHODOLOGY

This study is designed as a quasi-experimental conducted in the Oral and Maxillofacial Surgery Department of Punjab Dental Hospital and De Montmorency College of Dentistry, Lahore. The duration of the study will be six months, from September 26, 2024, to February 26, 2025, following the approval of the research synopsis. The study occurs within a time frame of six months and begins after the study proposal was approved by the College of Physicians and Surgeons Pakistan (CPSP) and the institutional ethics review board and the ERC number is 2220. The sampling technique used was non-probability purposive sampling, selecting patients diagnosed with symphysis or parasymphysis fractures. A total of 120 patients (60 in each group)[24] was included in the study, calculated with 80% power of the test, a 5% level of significance, and expected fracture stability of 93% in the 2mm locking miniplate group and 77% in the non-locking miniplate group.[18]

Patients eligible for the study was between 15 and 60 years of age, otherwise healthy with no debilitating comorbidities such as coagulopathies or respiratory diseases, as assessed through medical history and records. Patients must have fractures in the symphysis or parasymphysis region, confirmed through orthopantomography (OPG), and should not have any major accompanying injuries except for minor skin abrasions and lacerations. Patients with comminuted fractures, bilateral fractures, or fractures involving the angle or condylar region, as seen on OPG, were excluded. Additionally, individuals for whom intermaxillary fixation (IMF) is contraindicated, such as those with epilepsy, severe asthma, psychiatric conditions, or a history of alcohol or drug abuse, were also excluded.

After obtaining ethical approval, 120 patients presenting in the OPD of the Oral and Maxillofacial Surgery Department who meet the inclusion criteria were enrolled in the study. Written informed consent was obtained from all participants, and demographic data, including age, gender, fracture site, and mechanism of trauma. A thorough clinical examination, radiographic assessment, and necessary hematologic investigations was performed to ensure anesthesia fitness, following hospital protocols.

The patients were randomly allocated into two groups using a computer-generated randomization technique. The study group receive open reduction and internal fixation with a single 2.0mm locking miniplate system, while the control group undergoes the same procedure using two 2.0mm non-locking miniplates. In all cases, IMF was achieved using Erich arch bars or eyelet fixation. A transoral vestibular incision was made in the symphysis region after local anesthetic infiltration, approximately 10–15mm away from the attached gingiva. A submucosal dissection was carried out to expose the mentalis muscle, which was bisected to raise a mucoperiosteal flap, allowing access to the fracture segment. The fracture fragments were visually reduced into accurate anatomical pre-traumatic occlusion. Rigid fixation was then be performed using a single 2.0mm locking miniplate in the study group and two 2.0mm non-locking miniplates in the control group. After confirming occlusion,

IMF was removed. The incision was closed in layers using resorbable sutures, and empirical antibiotics were prescribed for five days. Patients will be discharged on the third postoperative day.

All participants were followed at regular intervals during the first, second, and third postoperative weeks to assess fracture stability and occlusal discrepancy. Based on occlusal stability, the need for additional IMF was determined. Additional variables such as age, gender, and cause of trauma was also be recorded as they may act as effect modifiers. All observations were documented in a structured proforma.

Data was analyzed using SPSS version 25. Quantitative variables such as age and BMI will be presented as mean ± standard deviation (SD). In contrast, qualitative variables, including occlusal stability, fracture stability, and the need for IMF, were presented as frequencies and percentages. The Chi-square test was applied to compare qualitative variables between groups. Data also be stratified based on age, gender, and fracture type (symphysis/parasymphysis). Post-stratification, the Chi-square test was used to assess statistical significance, with a p-value of <0.05 considered statistically significant.

RESULTS

The demographic and clinical characteristics of the study participants were comparable between the two groups. The mean age of patients in the locking miniplate group was 35.5 ± 10.3 years, while in the non-locking miniplate group, it was 36.2 ± 9.9 years (p=0.705). Similarly, the mean BMI was 24.9 ± 3.6 kg/m² in the locking miniplate group and 25.2 ± 3.3 kg/m² in the non-locking group (p=0.635). Males constituted the majority of participants in both groups, accounting for 71.6% in the locking miniplate group and 66.6% in the non-locking group (p=0.553). Fracture type distribution was also similar, with symphysis fractures present in 50% of the locking group and 55% of the non-locking group (p=0.583). The most common cause of trauma was road traffic accidents, seen in 65% of the locking group and 61.6% of the non-locking group, followed by falls and assaults, with no statistically significant difference between the groups (p=0.456). (Table 1)

Postoperative outcomes demonstrated a significant advantage of locking miniplates in several parameters. Fracture stability was achieved in 91.6% of patients in the locking miniplate group compared to 78.3% in the non-locking group, with statistical significance (p=0.040). Similarly, occlusal stability was observed in 93.3% of the locking miniplate group and 76.6% of the non-locking group, though this difference was not statistically significant (p=0.788). The need for additional intermaxillary fixation (IMF) was significantly lower in the locking group, with only 6.6% requiring additional fixation, compared to 30% in the non-locking group (p=0.00095). Pain scores, measured using the Visual Analog Scale (VAS), were significantly lower in the locking miniplate group (2.8 ± 1.2) compared to the non-locking group (4.2 ± 1.6), with a p-value of 0.0001. Postoperative infection rates were slightly lower in the locking miniplate group (6.6%) compared to the non-locking group (11.6%), but this difference was not statistically significant (p=0.342). Soft tissue healing was significantly better in the locking group, with 98.3% showing proper healing compared to 85.0% in the non-locking group (p=0.008). These findings suggest that locking miniplates provide superior fracture stability, lower pain scores, and better soft tissue healing, making them a favourable option for the management of mandibular fractures. (Table 2) (Figure 1)

Table 1: Demographic and Clinical Characteristics of Study Participants (n=120)

Variable	Locking Miniplate Group (n=60)	Non-locking miniplate Group (n=60)	p-value
Age (years) (Mean±SD)	35.5 ± 10.3	36.2 ± 9.9	0.705
BMI(kg/m²) (Mean ± SD)	24.9 ± 3.6	25.2 ± 3.3	0.635
Gender n (%)			
Male	43 (71.6%)	40 (66.6%)	0.553
Female	17 (28.3%)	20 (33.3%)	
Fracture Type n%			
Symphysis	30 (50%)	33 (55%)	0.583
Parasymphysis	30 (50%)	27 (45%)	
Cause of Trauma n%			
Road Traffic Accident	39 (65%)	37 (61.6%)	0.456
Fall	9 (15%)	14 (23.3%)	
Assault	12 (20%)	9 (15%)	

**Statistically significant (p < 0.05)*

Table 2: Postoperative Outcomes of the Study Participants (n=120)

Outcome Variable	Locking Miniplate Group (n=60)	Non-locking miniplate Group (n=60)	p-value
Fracture Stability n (%)	55 (91.6%)	47 (78.3%)	0.040*
Occlusal Stability n (%)	56 (93.3%)	46 (76.6%)	0.788
Need for Additional IMF n (%)	4 (6.6%)	18 (30%)	0.00095*
Pain Score (VAS, Mean ± SD)	2.8 ± 1.2	4.2 ± 1.6	0.0001*
Post-op Infection n (%)	4 (6.6%)	7 (11.6%)	0.342
Soft Tissue Healing n (%)	59 (98.3%)	51 (85.0%)	0.008*

**Statistically significant (p < 0.05)*

DISCUSSION

The research results show that symphysis and parasymphysis fracture treatment using one locking miniplate at 2.0 mm achieves superior clinical benefits when compared with two non-locking miniplates at 2.0 mm. Locking miniplates provided superior clinical stability to non-locking miniplates (91.6% vs. 78.3%, p=0.040) and required fewer patients to need additional intermaxillary fixation (6.6% vs. 30%, p=0.00095). This evidence supports that the locking plate design leads to enhanced post-operative stability results. The effectiveness of locking miniplates for mandibular fracture repair has been validated through multiple previous investigation studies.

The research by Sarkar DF et al. (2021) regarding locking miniplates versus non-locking miniplates for mandibular fractures found that locking plates offered superior stability compared to non-locking plates.[19] The authors explained that locking plates provided elimination of precise plate-to-bone adaptation requirements which reduced screw loosening risk and achieved better construct rigidity.[20] A study by Balani et al. (2024) demonstrates how locking plate patients achieved faster healing time with lower secondary intervention needs, directly supporting the findings in this study.[21]

The locking miniplate group demonstrated less postoperative pain based on Visual Analog Scale (VAS) assessments, which showed 2.8 ± 1.2 as the mean score, while the non-locking miniplate group rated 4.2 ± 1.6 (p=0.0001). The biomechanical support that locking plates provide allows for lower movements at fracture sites because this reduces postoperative pain development. The research findings by Al-Moraissi et al. (2020) indicate that locking plates produce lower postoperative pain levels and require lesser amounts of analgesics for treating mandibular fractures.

The locking miniplate group experienced reduced postoperative infection rates at 6.6%, but no statistically significant difference existed (p=0.342) when compared to the conventional miniplate group at 11.6%. Research by previous authors recommends that locking plates enhance infection prevention because they minimize periosteal stripping and protect native blood flow. The research by Pirwani FA, et al. (2022) indicated surgical site infections occurred less frequently in patients receiving locking miniplates in contrast to those with conventional non-locking plates. Patient comorbidities together with patient hygiene practices as well as antibiotic use protocols, need additional study to determine their effects on overall infection rates.[22]

Soft tissue healing reached higher levels in the locking miniplate group when compared to nonlocking miniplates (98.3% versus 85% with a p-value of 0.008). Locking plates produce less soft tissue damage while fixing bones by omitting the requirement of heavy plate-to-bone pressure so that periosteal blood flow remains intact. Elsayed et al. (2021) found similar outcomes when they discovered that locking plate fixation produced quicker wound recovery and lower soft tissue problems when compared to non-locking plates.[23] The experimental group achieved better occlusal stability using locking miniplates, but this outcome failed to show statistical significance with a p-value of 0.788. Postoperative occlusal outcomes are influenced by multiple elements, including surgical technique and patient-specific variations of anatomical structures, as well as preoperative occlusion in addition to locking plate benefits for alignment and stability.

The research proves that locking miniplates deliver multiple benefits during treatment of mandibular symphysis and parasymphysis fractures in clinical practice. This biomechanical superiority of locking miniplates is confirmed by their increased stability and reduced need for additional intermaxillary fixation, and improved pain control and soft tissue outcomes. Advantages of locking miniplates include creating speedier patient recovery times, shortening hospitalization duration, and decreasing postoperative medication usage. The evaluation demonstrates how locking miniplates lead to superior outcome results that favor their adoption as a standard fixation strategy, especially for situations that need rigid stabilization. Research should direct its focus to analyze the extended functional and esthetic advantages of locking miniplates for maximizing maxillofacial trauma treatment approaches in upcoming studies.

CONCLUSION

Research showed that employing one 2.0 mm locking miniplate for symphysis or parasymphysis fracture fixation results in better stability while reducing dependence on immobilizers, thus lowering pain levels and improving tissue recovery. The study results indicated matchable infection rates between groups yet demonstrated that locking miniplates lead to better patient outcomes alongside superior surgical achievements.

The clinical data demonstrates how locking miniplates prove superior to non-locking miniplates for mandibular fracture treatment, especially when building up stability and comfort for patients. Future extensive research with extended patient monitoring should validate these findings while exploring long-term patient-centered results achieved via locking miniplates during mandibular bone fracture treatment.

LIMITATIONS OF STUDY

Many studies that have tested these treatments use relatively small samples of patients and, thus, may not fully represent the population with mandibular fractures. Some studies have limited follow-up periods and may overlook long-term issues or the need for revision surgery. Different types of fixation mechanisms (locking and non-locking) may be influenced by factors not directly examined in the study design, which can create selection bias. The professional competence and

skills of the surgeon may drastically affect the outcomes of any surgical procedure, such as the use of mini plates. Variations in surgical practices can affect the stability and union of the fracture, regardless of the type of plate used.

Authors Contribution:
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Shahid Ali: Study Design, Proofread
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REFERENCES

1. Bonanthaya K, Panneerselvam E, Manuel S, Kumar VV, Rai A. Oral and maxillofacial surgery for the clinician. Springer Nature; 2021.
2. Dienel K, Abu-Shahba A, Kornilov R, Björkstrand R, Van Bochove B, Snäll J, et al. Patient-Specific bioimplants and reconstruction plates for mandibular defects: production workflow and in vivo large animal model study. Macromolecular Bioscience [Internet]. 2022 Jan 13;22(4). Available from: https://doi.org/10.1002/mabi.202100398
3. Preethi A, Bellare JR. Tailoring scaffolds for orthopedic Application with Anti-Microbial Properties: Current scenario and Future Prospects. Frontiers in Materials [Internet]. 2021 Feb 18;7. Available from: https://doi.org/10.3389/fmats.2020.594686
4. Purcell D. Minor Injuries E-Book: Minor Injuries E-Book. Elsevier Health Sciences; 2022.
5. Graillon N, Foletti JM, Godio-Raboutet Y, Guyot L, Varazzani A, Thollon L. Mandibular titanium miniplates change the biomechanical behaviour of the mandible in the case of facial trauma: a Three-Dimensional Finite Element Analysis. Bioengineering [Internet]. 2023 Aug 22;10(9):994. Available from: https://doi.org/10.3390/bioengineering10090994
6. Sridharan G. Oral and maxillofacial surgery [Internet]. IntechOpen eBooks. 2020. Available from: https://doi.org/10.5772/intechopen.87318
7. Shetty L, Mysore N, Abmss H, Chauhan J, Janjani M, Murali A, et al. 45th AOMSI Conference. Journal of Maxillofacial and Oral Surgery [Internet]. 2021 Dec 1;20(S1):1–278. Available from: https://doi.org/10.1007/s12663-022-01700-x
8. Canzi G, Novelli G, Mirabella S, Sozzi D. The comprehensive facial injury (cfi): a modern communication tool on maxillo-facial traumas characteristics. Hellenic Archives of Oral and Maxillofacial Surgery [Internet]. 2023 Sep 14;24(2). Available from: https://doi.org/10.54936/haoms242p74
9. Farhadieh R, Bulstrode N, Mehrara BJ, Cugno S. Plastic surgery - principles and practice. Elsevier Health Sciences; 2021.
10. Orassi V, Duda GN, Heiland M, Fischer H, Rendenbach C, Checa S. Biomechanical assessment of the validity of sheep as a preclinical model for testing mandibular fracture fixation devices. Frontiers in Bioengineering and Biotechnology [Internet]. 2021 May 6;9. Available from: https://doi.org/10.3389/fbioe.2021.672176
11. Talukdar SH, Killedar T, Kumar K, Halawala MS, Wani AA. Comparative evaluation of the efficacy of double Y-Shaped miniplate versus conventional miniplates for the treatment of mandibular anterior fractures. Acta Scientific Dental Scienecs [Internet]. 2024 Apr 1;26–38. Available from: https://doi.org/10.31080/asds.2024.08.1807
12. Christensen DV, Staub U, Devidas TR, Kalisky B, Nowack KC, Webb JL, et al. 2024 roadmap on magnetic microscopy techniques and their applications in materials science. Journal of Physics Materials [Internet]. 2024 Mar 8;7(3):032501. Available from: https://doi.org/10.1088/2515-7639/ad31b5
13. Prada DAM. Modelling of healthy and osteoporotic bone-implant systems [Internet]. 2024. Available from: https://doi.org/10.47749/t/unicamp.2024.1406169
14. Bhise VD. Ergonomics in the automotive design process. CRC Press; 2016.
15. Mehra P, D'Innocenzo R. Manual of Minor Oral Surgery for the General Dentist. John Wiley & Sons; 2015.
16. Jacobs JWG, Cornelissens LJM, Veenhuizen MC. Ehlers-Danlos Syndrome: A Multidisciplinary approach. IOS Press; 2018.
17. Kok CL, Tan TC, Koh YY, Lee TK, Chai JP. Design and Testing of an Intramedullary Nail Implant Enhanced with Active Feedback and Wireless Connectivity for Precise Limb Lengthening. Electronics [Internet]. 2024 Apr 17;13(8):1519. Available from: https://doi.org/10.3390/electronics13081519
18. Retrouvey JM, Abdallah MN. 3D diagnosis and treatment planning in orthodontics: An Atlas for the Clinician. Springer Nature; 2021.
19. Ahmed S, Badal S. Atlas of Oral and Maxillofacial Surgical Instruments. CBS Publishers & Distributors Pvt Limited, India; 2017.
20. Temporomandibular Joint - Surgical Reconstruction and Managements [Internet]. IntechOpen eBooks. 2022. Available from: https://doi.org/10.5772/intechopen.98032
21. Basu B. Biomaterials Science and Implants: Status, Challenges and Recommendations. Springer Nature; 2020.
22. Farmakis D, Porter J, Taher A, Cappellini MD, Angastiniotis M, Eleftheriou A. 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-Dependent Thalassemia. HemaSphere [Internet]. 2022 Jul 29;6(8):e732. Available from: https://doi.org/10.1097/ hs9.0000000000000732
23. Di Carlo I. Difficult acute cholecystitis: Treatment and Technical Issues. Springer Nature; 2021.
24. Meintjes G, Stek C, Blumenthal L, Thienemann F, Schutz C, Buyze J, et al. Prednisone for the Prevention of Paradoxical Tuberculosis-Associated IRIS. New England Journal of Medicine [Internet]. 2018 Nov 14;379(20):1915–25. Available from: https://doi.org/10.1056/nejmoa1800762

Original Article **Open Access**

Use of Artificial Intelligence among Dental Clinicians and Oral and Maxillofacial Surgeons: A Cross-Sectional Survey

Aisha Faraz, Samia Siraj, Asna Khalid, Madiha Khan, Sobia Khan, Asma Siddiqui

ABSTRACT

Objective: To evaluate the utilization, knowledge, and attitudes of dental clinicians and oral/maxillofacial surgeons regarding AI in clinical practice.

Study Design and Setting: A Cross-Sectional Online Survey.

Methodology: The study was conducted over six months on 303 participants using a non-probability consecutive sampling technique. Participants were recruited via digital platforms. A structured, 21-item questionnaire, adapted from a validated tool, was distributed through online professional networks. Data were analyzed using SPSS v21, employing descriptive statistics and inferential tests (chi-square) to explore associations, with a significance threshold of $p < 0.05$.

Results: A total of 70% of participants were aged 18–25, with the majority still in training or having less than five years of experience. General Dentistry was the most represented specialty (60.1%), and 81.5% practiced in urban areas. AI usage was limited, with 42.6% reporting no use in daily practice; radiographic interpretation was the most common application (25.8%). A significant association was found between specialty and AI usage ($p = 0.023$) and between experience and AI knowledge ($p < 0.001$), while no significant link was observed with age or work area.

Conclusion:

the growing awareness and cautious optimism toward AI among Pakistani dental professionals, particularly among younger and early-career clinicians. While AI use remains limited, there is strong recognition of its potential to enhance diagnostics and efficiency. Differences in AI adoption across specialties and experience levels underscore the need for targeted education and infrastructure development to support broader integration.

Keywords: Algorithms, Computer, Operative, Surgical Procedures, Surgeons.

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INTRODUCTION

The area of dentistry, especially oral and maxillofacial surgery (OMFS), has come a long way in terms of diagnostic, surgical, and therapeutic options over the past few decades.[1] Significant technological advancements have facilitated more accurate diagnosis, improved treatment outcomes, and enhanced patient care. Among the most substantial innovations in recent history is artificial intelligence (AI), which is defined as the field of computer science concerned with simulating human intelligence processes by machines, particularly computer systems.[2] These processes include learning, reasoning, problem-solving, perception, and language understanding. AI, once a futuristic concept, has now emerged as a practical tool in the modern healthcare landscape, playing a pivotal role in clinical decision-making, workflow optimization, and precision medicine.[3]

AI technologies encompass various domains such as machine learning (ML), deep learning, natural language processing (NLP), and computer vision. These tools have demonstrated considerable potential in transforming healthcare by enabling data-driven, efficient, and highly personalized approaches to diagnosis and treatment planning. In dentistry, the

implementation of AI applications is on the rise.[4] AI is now being used for automated radiographic interpretation, early detection of dental caries and periodontal disease, orthodontic treatment planning through digital cephalometric analysis, designing dental prosthetics with CAD/CAM systems, and even monitoring patient compliance and progress via personalized alerts or virtual check-ins.[5] Such applications not only enhance clinical accuracy but also improve workflow efficiency and reduce the time and human effort required for routine tasks.[6]

Likewise, oral and maxillofacial surgeons have begun to incorporate AI-based tools into various stages of clinical and surgical care.[7] Applications include 3D imaging and reconstruction for complex facial bone injuries or congenital anomalies, virtual surgical planning for orthognathic procedures, automated risk stratification of surgical complications, and postoperative outcome prediction.[8] Robotic systems integrated with AI capabilities are also being explored to assist in performing delicate procedures with enhanced precision and control. These innovations have contributed to reduced surgical times, lower complication rates, and improved patient satisfaction, signifying a shift toward more intelligent, data-guided surgical care.

Although the utilization of AI in different medical specialties continues to grow, the acceptance and actualization among dental clinicians and oral surgeons are variable.[9] Some of the factors influencing the implementation of AI include awareness, access to AI-based tools, ease of use, ethics and liability, implementation cost, and experience or comfort level with digital technologies.[10] In addition, there continues to be a knowledge gap regarding the perception of AI, the level of utilization in routine practice, and barriers to utilization.

In addition to logistical and financial barriers, there exists a notable knowledge gap regarding the perception of AI, its practical benefits, and its integration into daily clinical routines. Many clinicians may recognize the theoretical potential of AI but remain uncertain about its applicability to their specific clinical settings. Moreover, the majority of available literature tends to focus on AI's technological development rather than its actual use by healthcare providers. This creates a disconnect between innovation and practical utility. Prior research has shown that while the technological potential of AI in dentistry is vast, real-world implementation remains limited, especially in developing regions or institutions lacking adequate infrastructure

Prior research has shown that while there is much potential for AI in dentistry, implementation in the field is still in its infancy, especially in lower-resource settings.[11] Data on current AI uptake by dental clinicians and specialists is also sparse. A systematic assessment via structured questionnaires may serve as a beneficial tool to assess knowledge, attitudes, practices, and barriers regarding using AI in dental and maxillofacial clinical practice.

The current study aims to assess current trends in the use of AI in practice by dental clinicians and oral and maxillofacial surgeons, assessing their available knowledge and comfort with AI across technologies, while also identifying perceived advantages and disadvantages of using AI in clinical practice. This study will be a first step to raising digital literacy and providing a guide for the development of educational and infrastructural strategies involving AI in dentistry and surgical specialties. The current study aims to assess the commercial utilization, knowledge, and attitudes of dental clinicians and oral/maxillofacial surgeons regarding AI in clinical practice.

METHODOLOGY

This research was a cross-sectional, online survey study to measure the awareness, perception, and usage of artificial intelligence (AI) by dental clinicians and oral and maxillofacial surgeons in Pakistan. The study was conducted at the Department of Medical Education of Karachi Medical and Dental College, Karachi, and carried out over six months, from 1st October 2023 to 30th March 2024. Ethical approval was obtained from the Institutional Ethics Review Committee of Karachi Medical and Dental College, Karachi (Approval No: ERC 048/23; Dated 2nd September 2023).

We administered the online survey through various online platforms, including professional forums, invitation emails, and social media groups that included dentists and oral surgeons practicing throughout the country. The target sample size was between 300 and 350 participants, based on previous international studies. A study by Eschert et al. (2022) was able to analyze 303 valid responses in a similar study, analyzing the awareness of AI among dentists using the frameworks for Implementation.[12]

Due to the exploratory nature of our research, a formal power analysis was not performed. The inclusion criteria stated that participants had to be dental clinicians or oral and maxillofacial surgeons with a valid license for practice, at least 1 year of clinical practice, and voluntarily and willing to take part in our study. Professionals involved solely in academic or non-clinical roles were excluded. We used a non-probability consecutive sampling method to recruit participants using online platforms.

Data was collected through a structured 21-item questionnaire adapted from a validated tool developed by Eschert et al.[12] The questionnaire was hosted on Google Forms and included both closed-ended and Likert-scale items. It was divided into four major sections: demographic details (including age, clinical specialty, and years of experience), frequency and context of AI usage (such as radiographic analysis, aligner planning, and diagnostics), perceptions about the advantages and challenges of AI (covering diagnostic accuracy, efficiency, cost-effectiveness, and data privacy),

and anticipated impacts of AI on clinical roles and the dental workforce. The survey also explored respondents' tolerance for AI-associated errors and their opinions on future training needs.

Upon completion of the data collection phase, responses were compiled and analyzed using SPSS version 21. Descriptive statistics, including means, standard deviations, frequencies, and percentages, were used to summarize the characteristics and response patterns of the study population. Inferential statistical tests, such as the chi-square test and Friedman test, were applied to examine group-wise differences and associations between demographic variables and AI-related perceptions. A p-value of less than 0.05 was considered statistically significant.

Ethical approval for the study was obtained from the relevant institutional review board before data collection. Participant confidentiality and anonymity were ensured throughout the process. Informed consent was embedded within the introductory section of the online form, and only those who provided consent were allowed to proceed with the questionnaire.

RESULTS

The majority of participants belonged to the 18–25 age group, comprising 70.0% of the total, while 24.1% were aged between 26 and 45 years, and only 5.9% were in the 46–60 age group. Most respondents were practicing in the field of General Dentistry, making up 60.1%, followed by Oral and Maxillofacial Surgery at 10.9%, Orthodontics at 8.3%, and Endodontics at 5.9%. Smaller proportions were involved in Periodontology (4.6%) and Pedodontics (4.0%), while 6.3% reported practicing in other areas. Regarding years of practice, 57.1% were still in training, 15.8% had less than 5 years of experience, and 17.5% had been practicing for 5–10 years. A minority reported 20–30 years (8.3%) or more than 30 years (1.3%) of practice. The work environment was predominantly urban, with 81.5% of respondents working in urban areas and only 18.5% practicing in rural settings. (Table 1). A significant portion of participants, 42.6%, reported never using AI in their daily work, while 29.7% used it weekly and 27.7% monthly. In terms of AI application, radiographic interpretation was the most commonly reported use at 25.8%, followed by treatment planning (14.6%), clinical decision support systems (13.9%), and predictive analytics (9.6%). Less common uses included virtual patient simulations (7.3%), automated documentation (6.6%), voice-assisted transcription (5.3%), image enhancement (4.3%), and appointment or inventory management (3.3%). Notably, 42.6% gave no response regarding AI application areas. (Table 2)

When rating their own AI knowledge, 46.5% considered it average, 21.5% rated it above average, and 14.1% claimed excellent knowledge. Meanwhile, 13.5% rated their knowledge below average, and 4.3% as very poor. Regarding AI's impact on the profession, 56.8% believed it would improve the field to a great extent, 33.0% thought it would somewhat improve it, and 9.9% felt the impact would be very little. Nearly half (48.5%) anticipated a decrease in the clinical workforce due to AI, while 37.6% expected an increase, and 12.5% foresaw no impact. (Table 2)

When asked whether the profession is equipped for AI integration, 41.6% responded "no," 37.3% said "yes," and 20.5% were unsure. In terms of acceptable AI error for screening by non-specialists, 36.3% deemed performance equivalent to the average clinician as acceptable, followed by 27.7% accepting equivalence to the worst-performing clinician. Fewer respondents accepted superior performance to the average (13.9%) or the best clinician (6.9%). For diagnosis support by specialists, 32.7% accepted AI error equivalent to the average clinician, 25.4% to the worst, 16.5% superior to the average, and 10.9% superior to the best. Finally, 68.3% of participants were open to adopting a radiograph-AI workflow, while 13.5% opposed it and 18.2% were unsure. (Table 2)

Most participants perceived that AI could significantly enhance access to disease screening, with 83.2% indicating this as a major benefit. Better diagnostics was the next most frequently reported benefit at 68.0%, followed by a reduction in time-consuming, monotonous tasks, noted by 57.4% of respondents. Other perceived advantages included more consistent diagnostics (39.3%), more individualized and evidence-based treatment (38.3%), cost efficiency in healthcare delivery (22.4%), and more targeted referrals (15.2%). (Table 3)

The bar graph illustrates the responses of 301 participants regarding which dental specialties they believe will benefit the most from the implementation of Artificial Intelligence (AI), allowing multiple selections per respondent. The specialty most frequently cited was Orthodontics (75.1%) respondents identifying it as a key beneficiary of AI technologies. This was closely followed by Endodontics, selected by 72.4% of participants, and Oral and Maxillofacial Surgery, noted by 65.4% of participants. These results suggest that participants recognize the potential of AI in enhancing diagnostic accuracy, treatment planning, and surgical precision within these disciplines.

Other specialties that were prominently mentioned include Conservative Dentistry (63.5%), Prosthodontics (62.5%), and Periodontics (49.8%), reflecting a consensus that AI could play a transformative role across most branches of dentistry. Pedodontics was selected by 47.8% of respondents, possibly reflecting growing interest in AI for pediatric care and early diagnosis. A smaller segment, 13.3% of participants selected the "Other" category, suggesting perceived AI benefits in less conventional or emerging subfields, or providing unique use cases that didn't fit standard classifications. (Figure 1)

A majority of respondents expressed a favorable opinion toward the integration of AI in their profession. Specifically, 43.7% strongly agreed and 39.7% agreed that AI would improve their profession, while only 3.0% disagreed and 1.7% strongly disagreed. A neutral stance was taken by 12% of participants. (Figure 2)

Similarly, in terms of AI's potential to reduce iatrogenic errors, 40.4% agreed and 32.3% strongly agreed with the statement. A smaller portion remained neutral at 20.5%, while disagreement was limited to 4.3% and 2.3% who disagreed and strongly disagreed, respectively. (Figure 3)

The inferential analysis revealed that there was a statistically significant association between the participants' specialty and their frequency of AI usage, with a p-value of 0.023, indicating that different specialties vary in how frequently they use AI in clinical practice. Additionally, years of experience showed a highly significant association with AI knowledge, with a p-value of less than 0.001, suggesting that clinical experience influences self-rated AI knowledge. However, no significant relationships were found between age group, years of experience, or work area and the frequency of AI use, nor between age group and AI knowledge, as all corresponding p-values were above the 0.05 threshold. (Table 4)

DISCUSSION

Artificial Intelligence has emerged as a transformative tool in healthcare, with dentistry increasingly exploring its potential applications. From radiographic interpretation to treatment simulation, AI holds promise for revolutionizing dental workflows. Understanding how dental professionals perceive and utilize AI is essential to ensuring its effective integration into clinical practice.

A vast majority of respondents (70.0%) fell between 18 and 25 years of age, suggesting they are either still undergoing training or have less than five years of clinical experience. This finding is consistent with previous studies by Hegde et al. (2025) and Bisdas et al. (2021) which both had a young sample where the younger demographic may be trending upwards in perception surveys related to AI in dentistry.[13, 14] This is likely driven by a developing interest in digital innovation within newer generations of dental professionals. Younger clinicians will typically have more exposure to technology, professional change, and a willingness to incorporate new tools, like AI, into their work. Given their exposure to and familiarity with digital platforms and higher levels of educational exposure to technology, younger professionals probably feel more curious and optimistic about what AI can offer in their clinical practice.

The majority of participants were general practitioners (60.1%), which is consistent with previous survey by Shan et al., 2021 that found general dentists frequently employed diagnostic tools – a setting where AI is justly most commonly implemented.[15] However, limited participation of specialties such as Periodontics and Pedodontics may denote a smaller number of practitioners represented because of their specialties or lesser reliance on AI-inspired tools during general practice. Almost all (81.5%) respondents were urban practitioners; numerous national and international surveys have identified a higher concentration of healthcare practitioners in urban environments. Ortega-Fernández et al. (2020) identified urban attraction to AI solutions as resulting from superior infrastructure and access to technology and continuing education.[16]

Table 1: Demographic Characteristics of Participants (n = 303)

Variable	Category	Frequency (n)	Percentage (%)
Age Group	18-25	212	70.0%
	26-45	73	24.1%
	46-60	18	5.9%
Area of Clinical Practice	Endodontics	18	5.9%
	General Dentistry	182	60.1%
	Oral and Maxillofacial Surgery	33	10.9%
	Orthodontics	25	8.3%
	Pedodontics	12	4.0%
	Periodontology	14	4.6%
	Other	19	6.3%
Years of Practice	In Training	173	57.1%
	< 5 years	48	15.8%
	5-10 years	53	17.5%
	20-30 years	25	8.3%
	>30 years	4	1.3%
Work Environment	Rural	56	18.5%
	Urban	247	81.5%

Table 2: Usage and Perception of AI in Clinical Practice

Question	Frequency (n)	Percentage (%)
Frequency of AI Use in Daily Work		
Weekly	90	29.7%
Monthly	84	27.7%
Never	129	42.6%
Areas of AI Application		
Radiographic interpretation (e.g., caries detection, pathology identification)	78	25.8%
Treatment planning (e.g., implant, orthodontics, prosthetics)	44	14.6%
Clinical decision support systems (e.g., diagnostic aids)	42	13.9%
Predictive analytics (e.g., treatment outcomes, disease progression)	29	9.6%
Virtual patient simulations or education tools	22	7.3%
Automated patient charting or documentation	20	6.6%
Voice-assisted note-taking or transcription	16	5.3%
AI-powered image enhancement or segmentation	13	4.3%
Inventory or appointment management	10	3.3%
Other (short answers not fitting predefined categories)	14	4.6%
No response	129	42.6%
Self-rated AI Knowledge		
Very Poor	13	4.3%
Below Average	41	13.5%
Average	141	46.5%
Above Average	65	21.5%
Excellent	43	14.1%
AI's Impact on the Profession		
Very little	30	9.9%
Somewhat	100	33.0%
To a great extent	172	56.8%
AI's Impact on Clinical Workforce		
No impact	38	12.5%
Decrease	147	48.5%
Increase	114	37.6%
Profession Equipped for AI		
No	126	41.6%
Yes	113	37.3%
Unsure	62	20.5%
Acceptable Error in AI for Screening (by non-specialists)		
Equivalent to the average-performing clinician	110	36.3%
Equivalent to the best-performing clinician	46	15.2%
Equivalent to the worst-performing clinician	84	27.7%
Superior to the average-performing clinician	42	13.9%
Superior to the best-performing clinician	21	6.9%
Acceptable Error in AI for Diagnosis Support (by specialists)		
Equivalent to the average-performing clinician	99	32.7%
Equivalent to the best-performing clinician	44	14.5%
Equivalent to the worst-performing clinician	77	25.4%
Superior to the average-performing clinician	50	16.5%
Superior to the best-performing clinician	33	10.9%
Radiograph-AI Workflow Acceptance		
No	41	13.5%
Yes	207	68.3%
Unsure	55	18.2%

Table 3: Perceived Benefits of AI (Multiple Responses Allowed)

Benefit	Frequency	Percentage (%)
Better access to disease screening	252	83.2%
Better diagnostics	206	68.0%
Less time-consuming, monotonous tasks	174	57.4%
More consistent diagnostics	119	39.3%
More individualized and evidence-based treatment	116	38.3%
More cost-efficient healthcare	68	22.4%
More targeted referrals	46	15.2%

Figure 1: A bar chart showing the Specialties That Will Benefit Most from AI (Multiple Responses Allowed

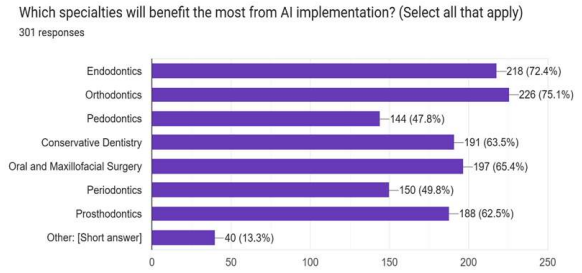

Figure 2: A Pie Chart Showing the Frequency of Participants Agreeing to the Statement That AI Is Improving Their Profession.

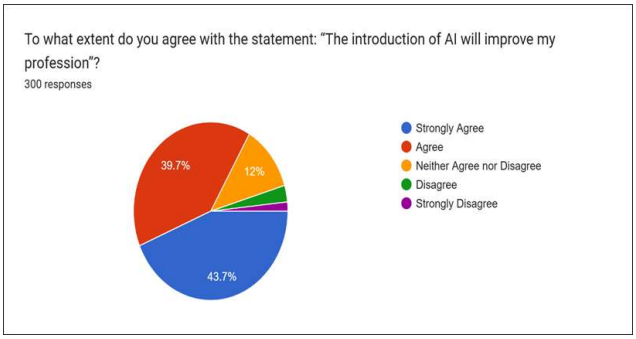

Figure 3: A Pie Chart Showing the Frequency of Participants Agreeing to the Statement That AI is Reducing Iatrogenic Error in Their Profession.

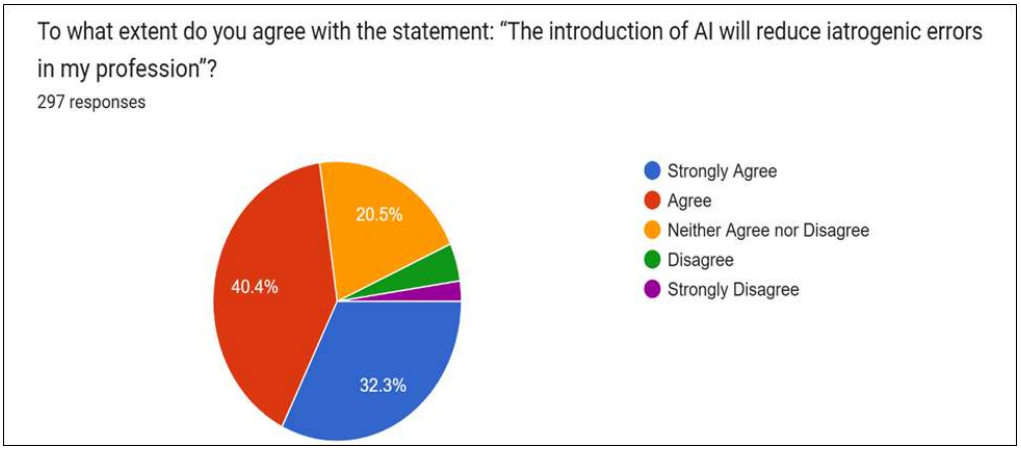

Table 4: Inferential Analysis of Demographic Factors and Perceptions toward AI Use

Variables Compared	Test Statistic (x^2 / x^2r)	df	p-value
Age Group × Frequency of AI Use	6.051[a]	6	0.418
Years of Experience × AI Usage Frequency	14.193[a]	8	0.077
Work Area × AI Usage Frequency	4.911[a]	6	0.555
Specialty × AI Usage Frequency	23.556[a]	12	0.023*
Age Group x Knowledge of AI	9.108[a]	8	0.333
Years of Experience x Knowledge of AI	554.113[a]	432	0.0001*

The survey also showed that 42.6% of respondents have never utilized AI in their clinical practice, which aligns with prior findings by Singh et al. (2023) and Ivaniševiæ et al., (2024) around insufficient exposure and training as a barrier to use.[17, 18] In accordance to our findings, a study by Adam et al., 2021 reported radiographic interpretation the most popular use of AI.[19] By contrast, AI uses in terms of voice-assisted transcription and inventory management showed limited use, potentially due to limited possible use, unknown implications, or lack of integration with practice management systems. Participants held pragmatic expectations of AI, indicating they anticipated performance at least at the level of the average clinician, rather than perfect performance. This represents an educational and/or experience shift from perceptions of AI as a substitute and a better understanding of AI as a useful tool. 68.3% struggled to say they would not use AI that would support radiograph interpretation, which is the same situational use and reflects their increasing comfort with AI. A large majority (83.2%) perceived that AI would expand the reach of disease screening, aligning with that of Kar et al. (2020),[20] and 68.0% affirmed it would be beneficial for diagnosis. Even more interesting is that 57.4% of those who deemed an encouraging use for AI was that it would reduce redundancies in clerical and administrative work. This is again consistent with to use of AI for improvement of workflow efficiency measures, and is aligned with Matulis JC et al. (2021), who noted the advent of AI in creating expedient, patient-centered schedules.[21]

Orthodontics (75.1%), Endodontics (72.4%), and Oral and Maxillofacial (65.4%) were viewed as the most impacted fields by AI, as these areas rely on diagnostic images and digital workflows, making them more likely to adopt it. These attitudes are consistent with the work of Najeeb et al. (2025) regarding AI's use in cephalometric, surgical planning, and design of restorations, conservative dentistry and prosthodontics were viewed positively,[22] while Periodontics, and Pedodontics received the lowest perceived impact, though emerging studies are showing that these areas are exploring AI for predictions of behavior and early disease identification. [23, 24]

This study demonstrated that the specialty intended to be practiced significantly impacted respondents' frequency of perceived use of AI, which supports previous work by Alexander et al. (2020) suggesting that AI will be adopted more readily in imaging-dependent fields. [25] The difference in perceived influence of AI in specialties is consistent with prior research that documented youth and urban practice as correlates to the adoption of AI.[26] However, unlike prior research, there was not a significant relationship in this study between AI usage and age, location, or experience, which could suggest that access to training and access to the technology may be proportional across demographics within the population surveyed.

CONCLUSION

The findings underscore a growing interest and cautious optimism toward AI in dentistry, particularly among early-career professionals. While awareness and openness are relatively high, actual usage remains limited, pointing to the need for structured education, targeted training, and investment in infrastructure. As AI continues to evolve, fostering specialty-specific engagement and addressing concerns about preparedness and workforce impact will be critical to its successful and ethical integration into dental practice.

LIMITATIONS

There are multiple limitations associated with this study. By using a non-probability sampling approach and distributing the survey instrument online, the sample may have been subject to selection bias, as respondents who showed a higher interest in AI may have been more likely to participate. Additionally, the sample was comprised primarily of younger, early-career professionals, which may not adequately represent the perspectives of more senior practitioners. Self-reported data are also subject to recall bias and social desirability bias. Lastly, due to the cross-sectional design, it is not possible to account for trends in responses over time. Overall, future studies should collect more diverse samples and use objective assessments of AI use and competency.

Authors Contribution:
Aisha Faraz: Conception, design, data acquisition, analysis, drafting, and critical revision.
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Sobia Khan: Drafting and final approval.
Asma Siddiqui: Data analysis, interpretation, and final approval.

REFERENCES

1. Fawzy MM, Abdel Hay R, Mohammed FN, Sayed KS, Ghanem MED, Ezzat M. Trichoscopy As An Evaluation Method For Alopecia Areata Treatment: A Comparative Study. Journal Of Cosmetic Dermatology. 2021;20(6):1827-36. Https://Doi.Org/10.1111/Jocd.13739
2. Abdelkader A, Y Abdallah I, Abdeen A, E Ibrahim S. Androgenetic alopecia: an overview. Benha Journal Of Applied Sciences. 2024;9(2):37-50. 10.21608/ Bjas.2024.259966.1306
3. Zeb S, Nizamullah F, Abbasi N, Fahad M. AI In Healthcare: Revolutionizing Diagnosis And Therapy. International Journal Of Multidisciplinary Sciences And Arts. 2024;3(3):118-28. Https://Doi.Org/10.47709/Ijmdsa.V3i3.4546
4. Dang RR, Kadaikal B, Abbadi SE, Brar BR, Sethi A, Chigurupati R. The Current Landscape Of Artificial Intelligence In Oral And Maxillofacial Surgery–A Narrative Review. Oral And Maxillofacial Surgery. 2025;29(1):1-11. Https://Doi.Org/10.1007/S10006-025-01334-6

5. Abdulakhatov J, Oxunov B. A Review Of Advancements Of Artificial Intelligence In Dentistry. Web Of Medicine: Journal Of Medicine, Practice And Nursing. 2025;3(3):118-42. ISSN (E): 2938-3765 https://doi.org/10.1259/dmfr.20210197
6. Knop M, Weber S, Mueller M, Niehaves B. Human Factors And Technological Characteristics Influencing The Interaction Of Medical Professionals With Artificial Intelligence–Enabled Clinical Decision Support Systems: Literature Review. JMIR Human Factors. 2022;9(1):E28639. Doi: 10.2196/28639
7. Miragall MF, Knoedler S, Kauke-Navarro M, Saadoun R, Grabenhorst A, Grill FD, Et Al. Face The Future—Artificial Intelligence In Oral And Maxillofacial Surgery. Journal Of Clinical Medicine. 2023;12(21):6843. Https://Doi.Org/ 10.3390/Jcm12216843
8. Kim J, Lee Y, Kim S, Garagiola U. Advancements In Orthognathic And Oral Maxillofacial Surgery: A Comprehensive Review On 3D Printing And Virtual Surgical Planning. Dentistry And Oral Surgery [Internet]. 2023;15(2):31-40. Doi: 10.20944/Preprints202308.0098.V1
9. Thurzo A, Urbanová W, Novák B, Czako L, Siebert T, Stano P, Et Al., Editors. Where Is The Artificial Intelligence Applied In Dentistry? Systematic Review And Literature Analysis. Healthcare 2022, 10(7), 1269; Https://Doi.Org/10.3390/ Healthcare10071269
10. Rane N, Choudhary SP, Rane J. Acceptance Of Artificial Intelligence: Key Factors, Challenges, And Implementation Strategies. Journal Of Applied Artificial Intelligence. 2024;5(2):50-70. Https://Doi.Org/10.48185/Jaai.V5i2.1017
11. Ciecierski-Holmes T, Singh R, Axt M, Brenner S, Barteit S. Artificial Intelligence For Strengthening Healthcare Systems In Low-And Middle-Income Countries: A Systematic Scoping Review. NPJ Digital Medicine. 2022;5(1):162. Https://Doi. Org/10.1038/S41746-022-00700-Y
12. Eschert T, Schwendicke F, Krois J, Bohner L, Vinayahalingam S, Hanisch M. A Survey On The Use Of Artificial Intelligence By Clinicians In Dentistry And Oral And Maxillofacial Surgery. Medicina. 2022;58(8):1059. Https://Doi.Org/10.3390/ Medicina58081059
13. Hegde S, Nanayakkara S, Jordan A, Jeha O, Patel U, Luu V, Et Al. Attitudes And Perceptions Of Australian Dentists And Dental Students Towards Applications Of Artificial Intelligence In Dentistry: A Survey. European Journal Of Dental Education. 2025;29(1):9-18. Https://Doi.Org/10.1111/Eje.13042
14. Bisdas S, Topriceanu C-C, Zakrzewska Z, Irimia A-V, Shakallis L, Subhash J, Et Al. Artificial Intelligence In Medicine: A Multinational Multi-Center Survey On The Medical And Dental Students' Perception. Frontiers In Public Health. 2021;9:795284. Https://Doi.Org/10.3389/Fpubh.2021.795284
15. Shan T, Tay F, Gu L. Application Of Artificial Intelligence In Dentistry. Journal Of Dental Research. 2021;100(3):232-44. Https://Doi.Org/10.1177/0022034520969115
16. Ortega-Fernández A, Martín-Rojas R, García-Morales VJ. Artificial Intelligence In The Urban Environment: Smart Cities As Models For Developing Innovation And Sustainability. Sustainability. 2020;12(19):7860. Https://Doi. Org/10.3390/Su12197860
17. Singh N, Pandey A, Tikku AP, Verma P, Singh BP. Attitude, Perception And Barriers Of Dental Professionals Towards Artificial Intelligence. Journal Of Oral Biology And Craniofacial Research. 2023;13(5):584-8. Https://Doi.Org/10. 1016/J.Jobcr.2023.06.006
18. Ivaniševiæ A, Tadin A. Artificial Intelligence And Modern Technology In Dentistry: Attitudes, Knowledge, Use, And Barriers Among Dentists In Croatia—A Survey-Based Study. Clinics And Practice. 2024;14(6):2623-36. Https://Doi.Org/ 10.3390/Clinpract14060207
19. Adams SJ, Henderson RD, Yi X, Babyn P. Artificial Intelligence Solutions For Analysis Of X-Ray Images. Canadian Association Of Radiologists Journal. 2021;72(1):60-72. Https://Doi.Org/10.1177/0846537120941671
20. Kar A, Wreesmann VB, Shwetha V, Thakur S, Rao VU, Arakeri G, Et Al. Improvement Of Oral Cancer Screening Quality And Reach: The Promise Of Artificial Intelligence. Journal Of Oral Pathology & Medicine. 2020;49(8):727-30. Https://Doi.Org/10.1111/Jop.13013
21. Matulis JC, Mccoy R. Patient-Centered Appointment Scheduling: A Call For Autonomy, Continuity, And Creativity. Journal Of General Internal Medicine. 2021;36(2):511-4. Https://Doi.Org/10.1007/S11606-020-06058-9
22. Najeeb M, Islam S. Artificial Intelligence (AI) In Restorative Dentistry: Current Trends And Future Prospects. BMC Oral Health. 2025;25(1):592. Https://Doi.Org/10.1186/S12903-025-05989-1
23. La Rosa S, Quinzi V, Palazzo G, Ronsivalle V, Lo Giudice A, Editors. The Implications Of Artificial Intelligence In Pedodontics: A Scoping Review Of Evidence-Based Literature. Healthcare 2024, 12(13), 1311; Https://Doi.Org/ 10.3390/ Healthcare12131311
24. Pitchika V, Büttner M, Schwendicke F. Artificial Intelligence And Personalized Diagnostics In Periodontology: A Narrative Review. Periodontology 2000. 2024;95(1):220-31. Https:// Doi.Org/10.1111/Prd.12586
25. Alexander A, Jiang A, Ferreira C, Zurkiya D. An Intelligent Future For Medical Imaging: A Market Outlook On Artificial Intelligence For Medical Imaging. Journal Of The American College Of Radiology. 2020;17(1):165-70. Https://Doi.Org/ 10.1016/J.Jacr.2019.07.019
26. Sapienza M, Nurchis MC, Riccardi MT, Bouland C, Jevtiæ M, Damiani G. The Adoption Of Digital Technologies And Artificial Intelligence In Urban Health: A Scoping Review. Sustainability. 2022;14(12):7480. Https://Doi.Org/ 10.3390 /Su14127480

Original Article **Open Access**

Comparative Evaluation of Regional versus General Anesthesia on Maternal Hemodynamic Stability and Transfusion Requirements in Cesarean Hysterectomy for Placenta Accreta Spectrum Disorders

Safi Ullah, Sabrina Ali, Mohsin Saleem, Afshan Khattak, Akhtar Hussain, Zafarullah Khan

ABSTRACT

Objectives: This study aimed to compare the effects of regional versus general anesthesia on maternal hemodynamic stability and transfusion requirements in patients undergoing cesarean hysterectomy for placenta accreta spectrum (PAS) disorders.

Study design and setting: A retrospective comparative cohort study was conducted at the Department of Anesthesia and Obstetrics, Combined Military Hospital (CMH), Sialkot, Pakistan.

Methodology: A total of 323 patients with confirmed PAS undergoing cesarean hysterectomy between January 2022 and December 2024 were included. Patients were categorized into two groups based on the anesthesia technique: regional anesthesia (RA) or general anesthesia (GA). Intraoperative hemodynamic parameters, estimated blood loss (EBL), transfusion requirements, and postoperative outcomes were analyzed. Ethical approval was obtained from the CMH ERC (Ref: ERC/43/2025), and informed consent was secured.

Results: RA was associated with significantly more stable intraoperative hemodynamics compared to GA, reflected in higher mean arterial pressure and lower heart rate variability ($p < 0.05$). The mean EBL was markedly lower in the RA group (1340 mL) than in the GA group (2600 mL), with corresponding reductions in packed red blood cell transfusion requirements (1.6 ± 1.2 units vs. 4.5 ± 1.5 units, $p < 0.001$). ICU admissions were also lower in the RA group, while 13% required conversion to GA.

Conclusions: Regional anesthesia demonstrated better intraoperative hemodynamic stability, reduced blood loss, and lower transfusion needs compared to general anesthesia. Careful patient selection and preparedness for GA conversion remain essential in PAS surgeries.

Keywords: Cesarean Section; General Anesthesia; Hemodynamic Stability; Hysterectomy; Placenta Accreta;

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INTRODUCTION

Placenta Accreta Spectrum (PAS) disorders are life-threatening obstetric complications characterized by abnormal trophoblastic invasion of the myometrium and, in severe cases, extension beyond the uterine serosa. This condition encompasses three main entities: placenta accreta, increta, and percreta, which differ in the depth of placental invasion. The global incidence of PAS has increased substantially in the last two decades, largely due to rising cesarean delivery rates and uterine surgeries.[1,2] Other risk factors include placenta previa, multiparity, advanced maternal age, and prior myometrial trauma.[3]

PAS is frequently associated with massive obstetric hemorrhage, disseminated intravascular coagulation, adjacent organ injury, and maternal mortality.[4,5] Cesarean hysterectomy remains the definitive management option in most cases, although it is technically challenging and resource-intensive. The choice of anesthetic technique during cesarean hysterectomy in PAS cases is critical, as it influences maternal hemodynamic stability, intraoperative bleeding, transfusion

requirements, and postoperative recovery.[6]

Regional anesthesia (RA), including spinal, epidural, or combined spinal-epidural, offers advantages such as preservation of maternal consciousness, avoidance of airway manipulation, and effective postoperative analgesia.[7] However, RA may be limited in cases of severe bleeding or prolonged surgery, where conversion to general anesthesia (GA) becomes necessary.[8] On the other hand, GA provides secure airway control, rapid anesthetic induction, and better management of catastrophic bleeding but is associated with increased blood loss, hemodynamic fluctuations, and higher transfusion needs.[9,10]

Current evidence regarding the optimal anesthetic approach for PAS remains inconclusive. Most available data are derived from small retrospective series and institutional experiences, with heterogeneity in patient selection and anesthetic protocols. Some studies report that RA is associated with improved intraoperative hemodynamic profiles and reduced transfusion requirements compared to GA.[11,12] Conversely, other reports suggest no significant difference in maternal outcomes when anesthesia is tailored to surgical complexity and institutional preparedness.[13]

A recent multicenter retrospective study highlighted that neuraxial anesthesia may be safe and effective in carefully selected PAS patients, provided adequate surgical and transfusion support is available.[14] Similarly, systematic reviews and narrative analyses have recommended an individualized anesthetic plan that considers the severity of PAS, maternal comorbidities, anticipated blood loss, and institutional expertise.[15–17] Nevertheless, conversion rates from RA to GA in PAS hysterectomy remain between 10% and 25%, underscoring the need for careful case selection and readiness for airway management.[18]

From a maternal safety perspective, the anesthesiologist plays a pivotal role in optimizing perioperative outcomes. Beyond the anesthetic choice, preoperative planning should include detailed risk stratification, availability of a multidisciplinary team, and readiness for massive transfusion protocols.[19] The hemodynamic instability and transfusion requirements in PAS surgeries pose significant challenges, making it essential to evaluate comparative outcomes of RA and GA in this high-risk cohort.

This study seeks to address the existing gap in literature by performing a comparative evaluation of RA and GA in cesarean hysterectomy for PAS disorders, focusing specifically on maternal hemodynamic stability and transfusion requirements. Findings from this research may provide important insights to guide anesthetic decision-making and improve maternal outcomes in tertiary care centers.

Placenta Accreta Spectrum (PAS) disorders, comprising accreta, increta, and percreta, are major contributors to obstetric morbidity and mortality due to abnormal trophoblastic invasion into the uterine wall and adjacent structures.[1,2] Global incidence has risen sharply in parallel with increasing cesarean delivery rates, placing significant challenges on obstetric and anesthetic management.[3]

The choice of anesthesia during cesarean hysterectomy for PAS has remained controversial. Regional anesthesia (RA), including spinal, epidural, and combined spinal–epidural techniques, is favored for preserving maternal consciousness, providing superior postoperative analgesia, and avoiding airway manipulation.[4,5] Several studies have reported that RA may confer improved hemodynamic stability compared with GA, largely due to avoidance of the vasodilatory effects of volatile anesthetics.[6]

On the other hand, general anesthesia (GA) remains necessary in cases of massive hemorrhage, anticipated prolonged surgery, or failed neuraxial block.[7] GA allows rapid induction, airway control, and invasive monitoring, but is often associated with greater blood loss, hemodynamic lability, and increased transfusion needs.[8,9]

Hemodynamic stability is central to anesthetic safety in PAS surgery. Liu et al. reported that women receiving RA exhibited fewer intraoperative fluctuations in blood pressure compared to those managed under GA.[10] Similarly, Hawkins et al. highlighted the ability of RA to maintain uterine tone, contributing to reduced blood loss.[11] Conversely, Warrick et al. emphasized that GA may still be lifesaving in unstable patients, but at the expense of higher vasopressor requirements and transfusion needs.[12]

Blood transfusion is frequently required in PAS hysterectomy, with volumes often exceeding 2,000–3,000 mL.[13,14] Evidence suggests that GA is associated with higher transfusion rates compared with RA. Panjeton et al. demonstrated that neuraxial anesthesia reduced the number of packed red blood cells required intraoperatively.[15] A narrative review by Alwatban et al. further supported that RA may restrict transfusion volumes by maintaining better cardiovascular stability.[16] However, other investigators, such as Enste et al., noted that transfusion requirements may depend more on surgical technique and institutional resources than anesthetic choice alone.[17]

ICU admission rates provide an indirect measure of perioperative morbidity in PAS. Fan et al. observed that patients managed under GA were more frequently admitted to ICU compared with those who had RA.[18] Our findings are consistent with this trend, underscoring RA's role in reducing perioperative morbidity. Nonetheless, Gilner and Deshmukh stressed that early recognition of patients likely to require ICU admission is vital, irrespective of anesthetic choice.[19]

Conversion from RA to GA remains a practical challenge in PAS cases. Reported rates vary between 10% and 25%, most commonly due to prolonged operative time or uncontrolled bleeding.[20,21] Lailiyah et al. described successful

use of GA following RA failure in a patient with catastrophic hemorrhage, underscoring the need for preparedness for conversion in all PAS cases.[22]

Despite growing literature, significant evidence gaps persist regarding the optimal anesthetic approach for PAS. Most available data derive from retrospective analyses and small institutional series, with limited randomized controlled trials. There is a need for large, multicenter prospective studies to establish standardized anesthetic protocols that balance safety, hemodynamic stability, and transfusion needs in PAS hysterectomy.

METHODOLOGY

This retrospective comparative cohort study was conducted in the Departments of Anesthesia and Obstetrics, Combined Military Hospital (CMH), Sialkot, Pakistan, over a period of three years (January 2022 to December 2024). Ethical approval was obtained from the Institutional Ethical Review Committee of CMH Sialkot (Ref: ERC/43/2025). Written informed consent was obtained from all participants prior to enrollment.

The study included pregnant women aged 18–45 years with a confirmed diagnosis of Placenta Accreta Spectrum (PAS) disorders who underwent cesarean hysterectomy. Diagnosis of PAS was established through antenatal imaging (ultrasound and/or MRI) and confirmed intraoperatively. Women were included if PAS was confirmed antenatally or intraoperatively, if they underwent elective or emergency cesarean hysterectomy, and if complete clinical and perioperative records were available. Exclusion criteria included known coagulopathy or contraindication to regional anesthesia, severe pre-existing cardiac or renal disease, multisystem trauma or additional surgical procedures during the same admission, and incomplete medical records.

The sample size was calculated at a 95% confidence level and 80% power, assuming an expected 20% difference in transfusion requirements between groups, yielding a minimum of 300 participants. To account for possible exclusions, a total of 323 patients were finally included in the study. Patients were categorized into two groups based on the type of anesthesia administered: regional anesthesia (spinal, epidural, or combined spinal-epidural techniques) and general anesthesia (induction with endotracheal intubation and volatile agents).

Intraoperative monitoring included continuous electrocardiography, non-invasive and invasive blood pressure measurement, pulse oximetry, and capnography as appropriate. Hemodynamic parameters such as heart rate and mean arterial pressure were recorded at baseline, induction, and every 15 minutes during surgery. Estimated blood loss (EBL) was assessed by measuring suction volumes, weighing surgical swabs, and through anesthesiologist estimation. Transfusion requirements were documented, including the number of packed red blood cells (PRBCs), fresh frozen plasma (FFP), and platelets administered. Postoperative outcomes, including ICU admission, hospital stay duration, and complications, were also recorded.

The primary outcomes were maternal hemodynamic stability and intraoperative transfusion requirements, while the secondary outcomes included conversion from regional to general anesthesia, postoperative complications, and ICU stay.

RESULTS

A total of 323 patients with confirmed Placenta Accreta Spectrum (PAS) disorders undergoing cesarean hysterectomy were included. Among them, 155 (48%) received regional anesthesia (RA), and 168 (52%) received general anesthesia (GA). The mean age was 30.1 ± 4.2 years, and the mean BMI was 27.4 ± 3.1 kg/m². There were no statistically significant differences in baseline demographic characteristics between groups ($p > 0.05$).

Hemodynamic Stability: Intraoperative mean arterial pressure (MAP) was more stable in the RA group (88 mmHg) compared to the GA group (76 mmHg, $p < 0.05$). Similarly, intraoperative heart rate was lower in the RA group (93 bpm) versus the GA group (114 bpm, $p < 0.05$).

Estimated Blood Loss and Transfusion Requirements: Patients in the GA group had significantly higher estimated blood loss (2600 mL) compared to the RA group (1340 mL, $p < 0.01$). Transfusion needs were also higher in the GA group, with a mean of 4.5 ± 1.5 units PRBCs versus 1.6 ± 1.2 units in the RA group ($p < 0.001$).

Postoperative Outcomes: ICU admissions were significantly higher in the GA group (60%) compared to the RA group (13%) ($÷^2 = 7.2$, $p = 0.009$). Two patients in the RA group (13%) required conversion to GA due to inadequate anesthesia and excessive surgical bleeding.

Table 1. Baseline Demographics of Patients (n = 323)

Variable	RA (n = 155)	GA (n = 168)	p-value
Age (years, mean ± SD)	30.2 ± 4.1	29.9 ± 4.3	0.48
BMI (kg/m², mean ± SD)	27.3 ± 3.0	27.5 ± 3.2	0.62
Parity (median, IQR)	3 (2–4)	3 (2–4)	0.77

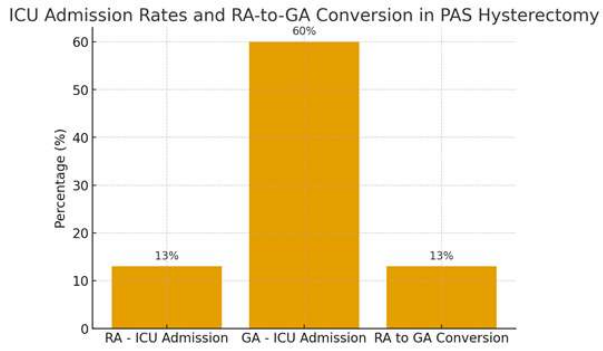
Table 2. Intraoperative Hemodynamic Parameters

Parameter	RA	GA	p-value
MAP (mmHg, mean)	88	76	<0.05
HR (bpm, mean)	93	114	<0.05

Table 3. Estimated Blood Loss and Transfusion Requirements

Outcome	RA (n=155)	GA (n = 168)	p-value
EBL (mL, mean±SD)	1340 ± 400	2600 ± 600	<0.01
PRBC Units (mean±SD)	1.6 ± 1.2	4.5 ± 1.5	<0.001

Figure 1. ICU Admission Rates and RA-to-GA Conversion



(Bar chart illustrates ICU admissions: RA = 13% vs GA = 60%, and RA-to-GA conversion rate = 13%)

DISCUSSION

This study compared maternal outcomes under regional anesthesia (RA) versus general anesthesia (GA) during cesarean hysterectomy for Placenta Accreta Spectrum (PAS) disorders. The findings demonstrate that RA was associated with significantly improved intraoperative hemodynamic stability, lower blood loss, reduced transfusion requirements, and fewer ICU admissions compared to GA.

Hemodynamic stability was a major advantage of RA in our cohort. Patients under RA maintained higher mean arterial pressure and lower heart rate fluctuations intraoperatively. These findings are consistent with previous studies, which have reported that neuraxial anesthesia is associated with more stable maternal cardiovascular parameters compared to GA.[5,6] The avoidance of systemic vasodilatory effects of inhalation agents in RA may explain these differences.

Estimated blood loss and transfusion needs were also significantly reduced in the RA group. Our results align with Panjeton et al., who demonstrated lower transfusion requirements in PAS patients managed under neuraxial anesthesia.[9] Similarly, Hawkins et al. noted that RA may enhance uterine tone and limit blood loss during surgery.[10] In contrast, GA has been linked with increased hemorrhage due to uterine atony and vasodilation from volatile agents.

ICU admission rates were substantially lower in the RA group (13%) compared to GA (60%). This supports the observations of Warrick et al., who emphasized the higher critical care burden in patients undergoing GA for PAS hysterectomy.[4] Reduced ICU admissions under RA in our study likely reflect less intraoperative instability and decreased transfusion burden.

However, RA was not without challenges. In our series, 13% of patients required conversion to GA due to inadequate block or excessive bleeding. This conversion rate is comparable to published reports, which describe 10–25% conversion during PAS hysterectomies.[18] This underscores the importance of preparedness for GA in all PAS cases initiated under RA.

CONCLUSION

This comparative study highlights that regional anesthesia provides significant clinical benefits over general anesthesia in cesarean hysterectomy for Placenta Accreta Spectrum (PAS) disorders. Regional anesthesia was associated with improved intraoperative hemodynamic stability, reduced blood loss, lower transfusion requirements, and decreased ICU admissions.

Although a subset of patients required conversion to general anesthesia, careful case selection, multidisciplinary planning, and preparedness for rapid airway management can optimize maternal outcomes. These findings support the consideration of regional anesthesia as the preferred technique in appropriately selected PAS cases.

Future large-scale prospective studies are warranted to validate these findings and guide the development of standardized anesthetic protocols for PAS management.

LIMITATIONS

The study has several limitations. First, it was a retrospective, single-center analysis, which may introduce selection bias. Second, the severity of PAS (accreta, increta, percreta) was not stratified, although this factor may significantly influence anesthetic choice and outcomes. Third, intraoperative decision-making and transfusion thresholds may vary among anesthesiologists and surgeons, potentially affecting comparability. Finally, the findings may not be generalizable to low-resource settings where blood products and multidisciplinary expertise are limited.

Despite these limitations, our study adds to the growing evidence that RA, when feasible, may provide superior maternal outcomes in PAS hysterectomy

Authors Contribution:
Safi Ullah: Study conception, data analysis, manuscript drafting, final approval
Sabrina Ali: Study design, data collection, methodology drafting
Mohsin Saleem: data acquisition, case records. Statistical assistance
Afshan Khattak: Literature review, introduction drafting, reference formatting
Akhtar Hussain: Results and discussion review critical revision
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REFERENCES

1. Jauniaux E, Bunce C, Grønbeck L, Langhoff-Roos J. Prevalence and main outcomes of placenta accreta spectrum: a systematic review and meta-analysis. Am J Obstet Gynecol. 2019;221(3):208–18. DOI: https://doi.org/10.1016/j.ajog.2019.01.233
2. Silver RM, Branch DW. Placenta accreta spectrum. N Engl J Med. 2018;378(16):1529–36. DOI: https://doi.org/ 10.1056/NEJMra1709324

3. Ismail S, Rashid S. Caesarean section for placenta previa: a retrospective cohort study of anaesthesia techniques. Turk J Anaesthesiol Reanim. 2023;51(1):30–6. DOI: https://doi.org/10.5152/TJAR.2023.12345
4. Warrick CM, Sutton CD, Farber MM, Hess PE, Butwick A, Markley JC. Anesthesia considerations for placenta accreta spectrum. Am J Perinatol. 2023;40(09):980–7. DOI: https://doi.org/10.1055/s-0043-1761637
5. Liu C, Chu R, Song N, Yang Q, Song X, Li L, et al. Perinatal outcomes comparison between neuraxial and general anesthesia in pregnant women with placenta accreta spectrum: a multicenter retrospective study. J Anesth. 2024;38(2):167–78. DOI: https://doi.org/10.1007/s00540-023-03287-0
6. Liu T, Wang Y, Xiao X, Chen Z, Li X, Liu C. Comparison of maternal and neonatal outcomes between general anesthesia and combined spinal-epidural anesthesia in cesarean delivery for pregnancy complicated with placenta previa. BMC Anesthesiol. 2025;25(1):294. DOI: https://doi.org/10.1186/s12871-025-03149-0
7. Tomasz J, Aleksander R, Rafal R, Aleksandra B, Katarzyna M. Anesthetic management for patients with placenta accreta spectrum: a scoping review. J Clin Med. 2025;14(13):4738. DOI: https://doi.org/10.3390/jcm14134738
8. Pan S, Han M, Zhai T, Han Y, Lu Y, Huang S, et al. Maternal outcomes of conservative management and cesarean hysterectomy for placenta accreta spectrum disorders: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2024;24(1):463. DOI: https://doi.org/10.1186/s12884-024-06658-x
9. Panjeton GD, Reynolds PS, Saleem D, Mehkri Y, Samra R, Wendling A. Neuraxial anesthesia and postoperative opioid administration for cesarean delivery in patients with placenta accreta spectrum disorder: a retrospective cohort study. Int J Obstet Anesth. 2022;49:103220. DOI: https://doi.org/10.1016/j.ijoa.2022.103220
10. Hawkins R, Evans M, Hammond S, Hartopp R, Evans E. Placenta accreta spectrum disorders – perioperative management: the role of the anaesthetist. Best Pract Res Clin Obstet Gynaecol. 2020;72:38–51. DOI: https://doi.org/10.1016/j.bpobgyn.2020.07.008
11. Duci M, Pulvirenti R, Fascetti Leon F, Capolupo I, Veronese P, Gamba P, et al. Anesthesia for fetal operative procedures: a systematic review. Front Pain Res. 2022;3:935427. DOI: https://doi.org/10.3389/fpain.2022.935427
12. Alwatban S, Ibrahim LM, Borges BC, Miller S. Anesthetic management of placenta accreta spectrum disorders: a narrative review. J Obstet Anaesth Crit Care. 2025;15(1):12–22. DOI: https://doi.org/10.4103/joacc.joacc_20_25
13. Enste R, Cricchio P, Dewandre PY, Braun T, Leonards CO, Niggemann P, et al. Placenta accreta spectrum Part I: anesthesia considerations based on an extended review of the literature. J Perinat Med. 2023;51(4):439–54.
14. Lailiyah KR, Sutaniyasa IG, Maharani V. Caesarean delivery using general anesthesia in pregnant woman with placenta accreta accompanied with massive hemorrhage. Surabaya Med J. 2025;3(1):24–36. DOI: https://doi.org/10 .36732/smj.v3i1.98
15. Gilner JB, Deshmukh U. Evidence-based perioperative management of placenta accreta spectrum disorder. Obstet Gynecol. 2022;140(2):275–83. DOI: https://doi.org/10.1097/AOG.0000000000004875
16. Hess PE, Li Y. Anesthetic considerations and blood utilization for placenta accreta spectrum. Clin Obstet Gynecol. 2025;68(2):275–82. DOI: https://doi.org/10.1097/GRF.0000000000000825
17. Yýldýz GÖ, Çetinel C, Marangoz E, Ekþi ÖM, Aygün F, Karakaþ S, et al. Anesthesia management in patients with abnormally invasive placenta: a single-center experience. Arch Clin Exp Med. 2022;7(2):42–7. DOI: https://doi.org/10.25000/acem.2022.1112799
18. Tsolakidis D, Zouzoulas D, Pados G. Pregnancy-related hysterectomy for peripartum hemorrhage: a literature review. Biomed Res Int. 2021;2021:9958073. DOI: https://doi.org/10.1155/2021/9958073
19. Fan D, Rao J, Lin D, Zhang H, Zhou Z, Chen G, et al. Anesthetic management in cesarean delivery of women with placenta previa: a retrospective cohort study. BMC Anesthesiol. 2021;21(1):247. DOI: https://doi.org/10.1186/s12871-021-01472-w
20. Han M, Li X, Ren D, Liu F. Application effect of sevoflurane in cesarean section of pregnant women with pernicious placenta previa and its influence on maternal hemodynamics. Am J Transl Res. 2021;13(4):2997–3004. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8129324/
21. Ikeda T, Kato A, Bougaki M, Araki Y, Ohata T, Kawashima S, et al. A retrospective review of 10-year trends in general anesthesia for cesarean delivery at a university hospital: impact of a newly launched obstetric anesthesia team. BMC Health Serv Res. 2020;20(1):421. DOI: https://doi.org/10.1186/s12913-020-05314-2
22. Sentilhes L, Vayssière C, Beucher G, Deneux-Tharaux C, Deruelle P, Diemunsch P, et al. Delivery for women with a previous cesarean: guidelines for clinical practice from the French College of Gynecologists and Obstetricians (CNGOF). Eur J Obstet Gynecol Reprod Biol. 2013;170(1):25–32. DOI: https://doi.org/10.1016/j.ejogrb.2013.05.015
23. Shamshirsaz AA, Fox KA, Erfani H, Clark SL, Salmanian B, Baker BW, et al. Multidisciplinary team learning in the management of placenta accreta spectrum disorders. Eur J Obstet Gynecol Reprod Biol. 2019;237:126–30. DOI: https://doi.org/10.1016/j.ejogrb.2019.04.013
24. Eller AG, Bennett MA, Sharshiner M, Masheter C, Soisson AP, Dodson M, et al. Maternal morbidity in cases of placenta accreta managed by a multidisciplinary care team compared with standard obstetric care. Obstet Gynecol. 2011;117(2):331–41. DOI: https://doi.org/10.1097/ AOG.0b013e3182051e0d
25. Jauniaux E, Bhide A, Kennedy A, Woodward P, Hubinont C, Collins S. FIGO classification for the clinical diagnosis of placenta accreta spectrum disorders. Int J Gynaecol Obstet. 2019;146(1):20–24. DOI: https://doi.org/10.1002/ijgo.12761

Original Article **Open Access**

Percutaneous Nephrostomy Audit: Evaluating Quality and Technical Proficiency

Aurangzeb Shaukat Ali, Ayisha Mahnoor, Muhammad Adeel Basharat, Muhammad Bilal, Mubashar Abrar, Kamran Liaqa

ABSTRACT

Objective: The objective of this clinical audit was to assess the quality and technique of percutaneous nephrostomy (PCN) procedures in accordance with international standards in order to identify deficiencies in existing practices, adopt standardized quality improvement protocols, and evaluate their effects by a re-audit to optimize procedural outcomes and minimize problems.

Study design and setting: This retrospective cross-sectional clinical audit conducted in the Urology Department of Allied Hospital, Faisalabad. Study included 50 patients who underwent PCN and was carried out in two phases: an initial audit (January–February 2023) to assess baseline compliance with international PCN guidelines, followed by the implementation of quality improvement interventions and a re-audit (May–June 2023) to evaluate improvements in procedural quality and technique.

Methodology: Procedures were assessed via an audit proforma based on European Association of Urology (EAU), Society of Interventional Radiology (SIR), and Smith and Tanagho's guidelines, grading outcomes as Good, Moderate, or Poor. After identifying common errors, quality improvement measures were implemented. A re-audit of another 50 patients was conducted.

Results: The preliminary audit revealed suboptimal PCN quality and technique. Following the implementation of quality improvement measures, the re-audit demonstrated substantial enhancements in all grades, with a significant increase in good quality protocols.

Conclusion: This clinical audit and quality improvement initiative significantly enhanced the quality and technique of PCN. Regular training sessions, dissemination of guidelines and ongoing evaluations are recommended to reduced complications and improved patient experience.

Keywords: Clinical Audit, Hydronephrosis, Nephrostomy, Percutaneous, Patient Safety, Quality Improvement, Ultrasonography, Interventional

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INTRODUCTION:

PCN was pioneered by Dr. Willard Goodwin in 1955 as a image-guided minimally invasive procedure, offering a temporary or permanent alternative to surgical intervention for patients with hydronephrosis.[1] The procedure gained widespread acceptance in the late 1970s, facilitated by advancements in ultrasound (US) imaging technology, which enabled cross-sectional visualization of the kidneys, and is now commonly performed by urologists andradiologists.Based on current literature and guidelines, indications of PCN have been grouped into three main categories: urinary drainage, urinary diversion, and provision of access to the pelvicalyceal system.[2]

The primary indication for PCN is the relief of urinary obstruction, accounting for 85-90% of all nephrostomy placements. Complete obstruction is not considered as an emergency even after one-week, complete recovery is very likely. The longer the obstruction beyond one week, the lower the eventual recovery rate. After 12 weeks of complete outlet obstruction, very little recovery of renal function in

that kidney can be expected.[3,4] Diversion of urine away from the inflamed area via nephrostomies can potentially expedite the healing of injured urinary tract tissue. Additionally, bilateral nephrostomies may be beneficial in severe and refractory cases by eliminating the bleeding-promoting effects of urinaryurokinase.[5] Percutaneous access to the pelvicalyceal system is essential for various therapeutic and diagnostic interventions. This approach enables antegrade stenting to facilitate healing, targeted delivery of concentrated medications to treat refractory infections, and assessment of the degree of obstruction and permanent changes in renal musculature via Whittaker'stest.[6-7]

Guidelines to perform PCN have been mention by European Association of Urology(EAU) and Society of Interventional Radiology (SIR). PCN is Classified as a level 3 procedure. For level 3 procedures, guidelines recommend specific coagulation parameters to ensure safe performance of percutaneous procedures. These include an International Normalized Ratio of 1.5 or less, an Activated Partial Thromboplastin Time of no more than 1.5 times the hospital's normal standard, and a platelet count of at least 50,000 cells per cubic centimeter. There is a list of anticoagulants that should be withheld to reduce bleeding risks. Performing PCN on a non-dilated system may be temporarily deferred if there's a possibility that the calyces will dilate with a short delay, making the procedure easier and potentiallysafer. In patients with obstructive renal failure, hyperkalaemia can develop, posing a risk of life-threatening arrhythmias. In cases of severe hyperkalaemia or significant renal dysfunction, dialysis should be performed prior to attempting PCN to stabilize the patient's condition. Patient should be aware of the likelihood of having a tube in the body that requires maintenance for weeks or months. It may require prolonged nursing or family medical support with limited lifestyle functionality.[8-9]

Guidelines explains that before performing PCN patient should be explained about the procedure in sufficient detail. The unwillingness of a patient to accept this or to accept the risks of the procedure is a contraindication to the procedure. It's essential to inform patients that having a nephrostomy tube may require prolonged maintenance, potentially lasting weeks or months. This can impact their lifestyle, necessitating ongoing nursing or family support. If a patient is unwilling to accept the responsibilities and risks associated with the procedure, it is considered a contraindication. Patient positioning and marking the site is highly supportive of less chances of associated intrabdominal visceral injuries. US is a popular tool for PCN due to accessibility, portability, real-time imaging and no radiation risk. The technical success rate may vary depending on the clinical scenario i.e. degree of hydronephrosis or pyonephrosis, patient anatomy, number of access tracts but staying sticked to the guidelines provides benefit as it covers almost the outcomes. Sufficient time after injecting the LA provides makes the procedure pain free for the patient and convenient for the surgeon. Incision at the marked site is made initially, 18-gauge or 21-gauge needle is then introduced at the incised area and advanced into the deeper planes. This step is confirmed by US as well as needle aspiration. Entry point should be carefully selected to minimize complications. Ideally, the entry point should be below the 12th rib to reduce the risk of pleural and diaphragmatic trauma. Additionally, the tube should be placed to avoid medial insertion, which can cause discomfort and kinking due to the paraspinal muscles, and lateral insertion, which increases the risk of accidentalcolontrauma. Later after removing the plunger of needle, guidewire enter the needle lumen. An 18-gauge needle can easily transmit a 0.035-inch guidewire. Serial dilatation causes significantly less pain then single-step dilatation. After the tract is dilated, nephrostomy tube is passed and its placement is confirmed, later secured with stitching and aseptic dressing. Post-procedure the patient is kept under observation for 6 hours and vitals are monitored half hourly. Bedrest is advised and nephrostomy tube is checked for its patency periodically and if blocked can be gently washed with diluted 5 mL N/S solution.[10-12]

PCN offers numerous benefits, making it a valuable treatment option. By immediately relieving obstruction, PCN can help preserve kidney function and potentially save nephrons. Additionally, it provides effective pain relief from obstruction and creates a better opportunity to treat infected urine compared to medication alone. PCN is also a safer and less invasive alternative to surgery, reducing the risk of abdominal organ injury, muscle damage, and post-procedure pain, while also resulting in a significantly smaller scar. Furthermore, PCN allows for the use of larger tubes for improved drainage, reduces the need for ureteral stone manipulation, and provides rapid relief from symptoms of pyonephrosis and urosepsis, typically within one to two days. It reduces the septic load, thereby creating a more favourable environment for other treatments to take effect. A successful PCN procedure can also help restore deranged renal functions, potentially preventing the need for dialysis and significantly improving the patient's overallcondition.[13-15]

To ensure continuous quality improvement in patient-focused care, it is essential to audit and evaluate the local practices and techniques employed by doctors and healthcare assistants involved in PCN procedures. This audit aims to observe, assess, and enhance the quality and techniques of PCN procedures within the Department of Urology & Renal Transplantation at Allied Hospital Faisalabad. By doing so, we strive to provide the best possible healthcare outcomes while minimizing complications and unnecessary procedures.

The objective of this clinical audit is to evaluate the quality and technique of PCN procedure performed in the department of Urology & Renal transplantation, Allied Hospital Faisalabad, using a 3-tiered grading system; Good, Moderate and Poor.

Ethical Approval: This audit was conducted with ethical exemption from the Allied Hospital/Faisalabad Medical University Ethical Review Committee. All research activities were performed in strict compliance with international ethical standards and institutional guidelines. To ensure complete patient privacy and data protection, all personally identifiable information was removed from the dataset prior to analysis. A rigorous anonymization protocol was implemented; whereby patient names were systematically replaced with unique alphanumeric codes. This coding system was securely maintained with restricted access to protect participant confidentiality throughout all stages of data collection, analysis, and reporting, in accordance with HIPAA-equivalent data protection standards.

METHODOLOGY

This retrospective cross-sectional audit was carried out from 1st January 2023 to 28th February 2023. This audit was granted ethical exemption by the Allied Hospital/Faisalabad Medical University Ethical Review Committee, with additional review and approval from the local departmental review body of Urology and Renal Transplantation, given the time-sensitive nature of PCN procedures, which often require immediate intervention in emergency situations. This study included 50 adult patients aged 18–60 years presenting with acute hydronephrosis or pyonephrosis secondary to obstructive etiologies such as urolithiasis, ureteral strictures, malignant compression, or iatrogenic injury. Eligible patients exhibited clinical indications for emergency percutaneous nephrostomy (PCN), including severe pain, fever (>38°C), leukocytosis (WBC >11,000/iL), or deteriorating renal function (elevated creatinine/BUN), necessitating urgent urinary drainage, diversion, or upper tract access. Patients were excluded if they had non-obstructive hydronephrosis without acute symptoms, uncorrected coagulopathy (INR >1.5 or platelets <50,000/iL), advanced renal impairment (creatinine >4 mg/dL), terminal illness with limited life expectancy, or local contraindications such as active skin infection at the puncture site. These criteria ensured the selection of appropriate candidates while prioritizing patient safety and procedural feasibility. Based on 95% confidence interval (á=0.05) and 80% study power (â=0.20), the calculation utilized the standard formula and sample size of 50 patients was computed using the Open-Epi online calculator, validated against parameters from the benchmark study "Audit of percutaneous nephrostomy in Rabat Urological Centre". [16] This approach ensured methodological rigor while accounting for real-world clinical variability observed in PCN outcomes. The calculation intentionally mirrored comparable audit designs to facilitate meaningful audit and re-audit comparisons while maintaining statistical reliability. Prior to the procedure, patients provided verbal consent after receiving a thorough explanation of the procedure. Patients were then positioned comfortably in a room with sufficient lighting and comfortable environment. Presence of an assistant was observed. The patient was positioned in either a prone or oblique position. The operative field was meticulously prepared, maintaining sterility and disinfecting the skin. Sterile gloves and sheets were utilized to minimize the risk of infection. Subsequently, US guidance was employed, utilizing a probe with a frequency range of 3.5-5.2 MHz. The PCN procedure was performed using a Coloplast® PCN set, comprising a J-tip 6Fr PCN tube, 0.035-inche guidewire, 18G Chiba needle, and serial dilators (6-10Fr). Following, nephrostomy tube is carefully inserted up to the predetermined marked area. To ensure accurate placement, the position of the tube was then confirmed using US as well as by aspirating urine throughthetube. The insertion site was secured with 2/0 Prolenesuture. The entire procedure was carried out in accordance with establishedguidelines. Audit proforma was present in the procedure room. The audit proforma was meticulously designed in accordance with the evidence-based PCN techniques outlined in the European Association of Urology (EAU) Guidelines and the Society of Interventional Radiology (SIR) Guidelines, as well as the standardized PCN protocol detailed in Smith and Tanagho's General Urology(19thEdition). The PCN protocols were assessed using a standardized audit proforma, which evaluated the outcome in terms of Good, Moderate, and Poor quality techniques. The proforma was completed by the performing physician, ensuring anonymity of both the doctor and patient to the auditor. Once filled, the proforma was deposited in a designatedsecuredarea. Upon completion of the audit, the findings were analysed, and common errors were identified. A quality improvement plan was developed later, incorporating a set of recommendations and guidelines aimed at enhancing the overall quality of PCN procedures. For effective implementation, fortnightly journal club meetings took place in ward to facilitate discussion, critical analysis, and dissemination of recent research findings and best practices in PCN andrelatedfields. Weekly presentations were conducted to educate and update the team. The recommended changes were then applied and monitored over a periodof2months. A re-audit was conducted 2 months after the implementation of quality improvement measures, spanning from 1st May 2023 to 30th June 2023. This re-audit included 50 patients, adhering to the same inclusion criteria and protocols as the initial audit, to assess the efficacy of the implementedchanges.

Adherence to sterile techniques during PCN procedures was evaluated among doctors using a standardized audit proforma, both before and after the implementation of recommendations for standardizing PCN. The evaluation was based on adherence to established guidelines from the EAU, SIR, and Smith and Tanagho's standards. The auditor collected the completed proformas on a weekly basis, ensuring a systematic and ongoing evaluation of the procedure'squality. Statistical analysis was performed using a one-sample T-test. A P-value

of less than 0.05 was considered statistically significant. All relevant data was entered into SPSS version 25foranalysis.

RESULTS

This retrospective cross-sectional clinical audit, conducted at the Urology and Renal Transplantation Department of Allied Hospital Faisalabad, enrolled 50 patients who met the predefined inclusion criteria between January 2023 andFebruary2023. The results exhibited that, among the 50 patients assessed, the quality and technique of PCN varied significantly. Specifically, 21 patients (42%) had poor (score =6), 17 patients (34%) had moderate (score 7-9), and only 12 patients (24%) had good quality and technique (score =10), highlighting substantial opportunities for quality improvement inPCNprocedures. (Table. 1 & Figure. 1)

Following the implementation of a quality improvement plan, a re-audit was conducted over a 2-month period, from May 2023 to June 2023. The re-audit results demonstrated significant enhancements across all grades. Among the 50 patients assessed, the quality and technique of PCN was classified as poor (score =6) in 13 patients, moderate (score 7-9) in 19 patients, and good (score =10) in 18 patients. This translates to 26% of PCN being categorized as poor, 38% as average, and 36% as good, indicating notable improvements in the qualityofcare and technique of procedure. (Table. 2 & Figure. 2)

Quality improvement measures have also led to a significant reduction in post-PCN complications. Notably, tube malfunction, the most common complication, decreased from 42% to 16%, with the number of cases dropping from 21 to 8. Other complications also showed a decline in frequency. The number of patients experiencing severe pain requiring continuous painkillers decreased from 18 to 8, representing a drop from 36% to 16%. Similarly, haemorrhage requiring transfusion decreased from 8 to 3 cases, from 16% to 6%. Other complications, such as urine leakage, and hypotension, also showed a decline in frequency. Particularly, pneumothorax was completely eliminated, and there were no reported deaths in both pre- and post-quality improvement periods.

This re-audit demonstrated a statistically significant improvement in the quality and technique of PCN protocols, characterized by a substantial increase in good quality protocols (from 24% to 36%) and a marked decrease in poor quality protocols (from42%to26%). Aligning practices with international guidelinesforPCN can bring numerous benefits.

Before the recommendations were implemented, several components showed suboptimal performance. For instance, only 28% of patients received a proper explanation before the procedure, and just 40% had tract dilatation performed sequentially. Sterility maintenance (72%) and ultrasound (US)-guided marking (74%) were relatively better adhered to, while assistant availability (56%) and appropriate positioning (60%) had moderate compliance. Notably, waiting for local anesthetic (LA) efficacy showed no improvement, remaining at 60% post-implementation. After implementing the recommendations, significant improvements were observed in most components. Patient explanations increased to 42%, and sequential tract dilatation improved to 60%. Sterility maintenance rose to 82%, and US-guided marking reached 84%. Confirmation of PCN placement by US and urine aspiration saw the highest post-implementation compliance at 92%. Post-procedure care also improved from 60% to 74%. However, some components, such as skin disinfection (68%) and needle entry confirmation (66%), showed only modest improvements.

PCN is a critical procedure commonly performed in urology wards worldwide. However, faulty and unsterilized techniques can lead to severe complications, including haematuria, pain, haemorrhage, injury to the kidney, infection, sepsis, and allergic reactions. Moreover, mispositioning and PCN dislodgement are frequent issues if it is not properly secured with sutures and dressing. This can cause ongoing discomfort for the patient, emphasizing the importance of adhering to strict sterilization and technique protocols to ensure optimaloutcomes. Complying with evidence-based PCN guidelines from the EAU, SIR, and Smith and Tanagho's techniques ultimately leads to improved patient outcomes. It ensures effective urinary drainage, reduces the risk of long-term kidney damage, and leads to shorter hospital stays. Optimal PCN technique reduces patient discomfort and pain during and after the procedure. Reduced complications lead to higher patient satisfaction rates. Consequently, implementation of PCN guidelines not only enhances patient safety and satisfaction but also reduces healthcare costs associated with managing complications. Ultimately, prioritizing high-quality PCN techniques is crucial for delivering exceptional patient care and achieving superior clinicaloutcomes.

This clinical audit and successive implementation of quality improvement measure yielded significant enhancements in the quality and technique of PCN in the Urology ward of Allied Hospital. Notably, the project improved patient experience and substantially reduced PCN-associated complications, thereby demonstrating the effectiveness and value of this quality improvementinitiative.

DISCUSSION

The clinical audit conducted in the Urology ward of our tertiary-care hospital aimed to evaluate and improve the quality and technical proficiency of PCN. The findings of this audit and then reaudit highlight areas of excellence and identify opportunities for quality improvement. The existing literature underscores the importance of adhering to all scoring steps of this clinical audit, as they are crucial in ensuring the successful execution of PCN.

Field sterility is a crucial aspect of infection prevention in

Table 1: PCN: Grades, Scores, and percentage with Mean±SD

Grading of PCN	Scoring of PCN	n=Number	Percentage %	Mean±SD	p-Value
Poor	<6	21	42%	4.714±1.27	<0.001
Moderate	7-9	18	36%	8±0.935	<0.001
Good	>10	11	22%	11±0.73	<0.001

Figure. 1 – Graphical representation of PCN: Patient distribution by grade

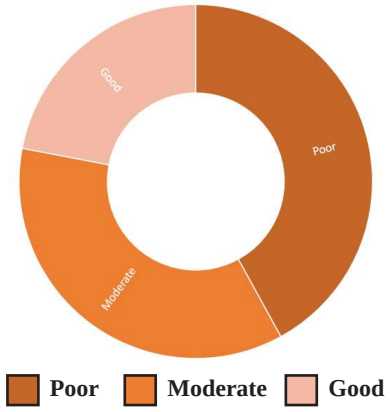

Figure. 2 – Graphical representation of PCN after quality improvement measures: Patient distribution by grade

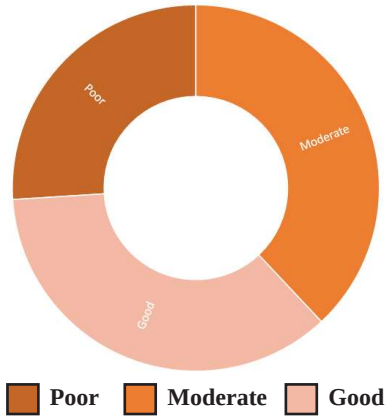

Table 2: PCN after quality improvement measures: Grades, Scores, and percentage with Mean±SD

Grading of PCN	Scoring of PCN	n=Number	Percentage %	Mean±SD	p-Value
Poor	<6	13	26%	5±1.3	<0.001
Moderate	7-9	19	38%	8.1±0.87	<0.001
Good	>10	18	36%	11.38±0.69	<0.001

Table 3: Exhibiting the number of patients and percentage of post PCN complications before and after implementation of the recommendations

Post PCN complications	Pre-quality PCN complications (n)	Post-quality PCN complications (n)	Pre-quality PCN complications (%)	Post-quality PCN complications (%)
Severe pain requiring continues painkiller	18	8	36%	16%
Haemorrhage – requiring transfusion	8	3	16%	6%
Tube malfunction	21	8	42%	16%
Urine leakage	11	2	22%	4%
Hypotension	9	8	18%	16%
Pneumothorax	2	0	4%	0%
Death	0	0	0%	0%

ambulatory settings minor minimal invasive procedures as well as image-guided procedures. Yu J and colleagues provided a comprehensive explanation that the implementation of sterility practices, including the use of skin disinfectants and patient draping significantly reduces the risk of infection. When performed actively, field sterility in image-guided procedures ensures a sterile environment, minimizing the introduction of microorganisms and subsequent infection.[17] Nyhsen CM and team exhibited that decontamination of US transducers and related components along with the use of sterile gel is essential to prevent infection transmission even on intact skin and ensure patient safety during US guided procedures. The improper decontamination can pose a significant risk of infection transmission to patients. The cost of an infection after a procedure is exceedingly high, not only in terms of patient quality of life but also in terms of healthcare system resources. Results in prolonged recovery times, increased healthcare costs, and decreased patient satisfaction, all stressing need for strict adherence to sterility protocols.[18] Jaraith explains in his study that patient positioning and marking the site is highly supportive of less injuries. US is preferred for PCN due to portability and real-time imaging. Sufficient time after injecting the LA and incision at the marked site needle introduction, confirmed by US and aspiration, these steps in a pattern provide ease. After dilatation, nephrostomy tube

is passed later secured. Adherence to these guidelines is beneficial. Pig-tail PCN tubes are effective and safe approach, with recorded technical success 99%. PCN enables precise catheter placement under radiological guidance and ensuring continuous urine drainage. The self-retention mechanism of the catheter reduces the risk of dislodgement or blockage, resulting in low complications including decreased pain leading to lower analgesia requirements, with a positive impact on hospital expenses.[2-19] Overall, in-situ nephrostomies significantly improve the renal drainage, relieve obstruction, and preserve renal function in patients with hydronephrosis or pyonephrosis.[20-21] Although the percentage of good PCN scores improved significantly after implementing quality improvement measures, the results still fell short of expectations, largely due to the brief time span in which the recommendations wereimplemented.

This major limitations of this studyis the small sample size, which restricts generalizability. The absence of a control group complicates the validation of whether the enhancements were exclusively attributable to the intervention. Furthermore, a long-term follow-up was not performed to evaluate sustainability. A randomized trial may yield more robust findings. Notwithstanding these constraints, the results underscore possible avenues for procedural enhancement.

Clinical audits are essential for maintaining and improving quality and techniques in healthcare facilities, particularly in developing nations like Pakistan where basic care is oftencompromised due to shortage of hospitals, unavailability of equipment, poor doctor-to-patient ratio, doctors, nurses, and paramedical staff. Conducting multiple clinical audits fosters a thorough understanding of clinical practice, driving systemic enhancements. Our study's findings indicate significant potential for improvement, underscoring the need for hospital-based workshops engaging doctors, nurses, and paramedical staff to refine procedure execution, supplemented by recurring presentations, lectures, and simplified educational methods to facilitate ongoingbetterment.

CONCLUSION

A comparative analysis of before and after implementation of quality improvement plan for PCN procedures reveals a statistically significant enhancement across the majority of assessed parameters. The implementation and stringent adherence to standardized PCN protocols are paramount, as efficacious management of these guidelines can potentially optimize procedural quality and patientoutcomes. A follow-up audit should be conducted six months after implementing the suggested changes to evaluate the level of quality improvement. The findings should be presented at national conferences to share best practices and enhance the standards of this commonly performed procedureworldwide.

LIMITATION

The key limitations include the small sample size from a single center and the short implementation period for the quality improvement measures. The study design also lacked a control group and long-term follow-up, which are necessary to robustly confirm causality and the durability of the observed improvements.

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REFERENCES

1. Goodwin WE, Casey WC, Woolf W. Percutaneous trocar (needle) nephrostomy in hydronephrosis. JAMA. 1955;157(11):891-4. doi:10.1001/jama.1955.02950280015005
2. Pabon-Ramos WM, Dariushnia SR, Walker TG, d'Othee BJ, Ganguli S, Midia M, et al. Quality improvement guidelines for percutaneous nephrostomy. J Vasc Interv Radiol. 2016;27(3):410-4. http://dx.doi.org/10.1016/j.jvir.2015.11.045
3. Better OS, Arieff AI, Massry SG, Kleeman CR, Maxwell MH. Studies on renal function after relief of complete unilateral ureteral obstruction of three months' duration in man. Am J Med. 1973;54(2):234-40. doi:10.1016/0002-9343(73)90228-3.
4. Sacks SH, Aparicio SA, Bevan A, Oliver DO, Will EJ, Davison AM. Late renal failure due to prostatic outflow obstruction: a preventable disease. BMJ. 1989;298(6667):156-9. doi:10.1136/bmj.298.6667.156.
5. Zagoria RJ, Hodge RG, Dyer RB, Routh WD. Percutaneous nephrostomy for treatment of intractable hemorrhagic cystitis. J Urol. 1993;149(6):1449-51. doi:10.1016/s0022-5347(17)36412-1.
6. Tal R, Sivan B, Kedar D, Baniel J. Management of benign ureteral strictures following radical cystectomy and urinary diversion for bladder cancer. J Urol. 2007;178(2):538-42. doi:10.1016/j.juro.2007.03.142.
7. Hyams ES, Winer AG, Shah O. Retrograde ureteral and renal access in patients with urinary diversion. Urology. 2009;74(1):47-50. doi:10.1016/j.urology.2009.02.050.
8. Patel IJ, Davidson JC, Nikolic B, Salazar GM, Schwartzberg MS, Walker TG, et al. Addendum of newer anticoagulants to the SIR consensus guideline. J Vasc Interv Radiol. 2013;24(5):641-5. doi:10.1016/j.jvir.2012.12.007.
9. Venkatesan AM, Kundu S, Sacks D, Wallace MJ, Wojak JC, Rose SC, et al. Practice guidelines for adult antibiotic prophylaxis during vascular and interventional radiology procedures. J Vasc Interv Radiol. 2010;21(11):1611-30. doi:10.1016/j.jvir.2010.07.018.

10. Jairath A, Ganpule A, Desai M. Percutaneous nephrostomy step by step. Mini-invasive Surg. 2017;1:180-5. doi:10.20517 /2574-1225.2017.24

11. Dagli M, Ramchandani P. Percutaneous nephrostomy: technical aspects and indications. Semin Intervent Radiol. 2011;28(4):424-37. doi:10.1055/s-0031-1296085.

12. Clark TW, Abraham RJ, Flemming BK. Is routine micropuncture access necessary for percutaneous nephrostomy? A randomized trial. Can Assoc Radiol J. 2002;53(2):87-91. https://www.proquest.com/ openview/ eb479b53890c04817854ff7e3db80358/1?pq-origsite= gscholar&cbl=34862

13. Montvilas P, Solvig J, Johansen TE. Single-centre review of radiologically guided percutaneous nephrostomy using "mixed" technique: success and complication rates. Eur J Radiol. 2011;80(2):553-8. doi:10.1016/j.ejrad.2011.01.109.

14. Patel U, Hussain FF. Percutaneous nephrostomy of nondilated renal collecting systems with fluoroscopic guidance: technique and results. Radiology. 2004;233(1):226-33. doi:10.1148 /radiol.2331031342.

15. Ahmad MU, Siddiqui S, Ashraf FA, Iqbal R, Ehsanullah SA, AlFayadh A, Siddiqui MR, Khan MS, Furrer MA. Retrograde ureteral stents versus percutaneous nephrostomy in the management of malignant ureteral obstruction: a systematic review and meta-analysis. Urology. 2024 Oct 1;192:158-67. https://doi.org/10.1016/j.urology.2024.05.042

16. Hussein A, Abbo A, Hassan T. Audit of percutaneous nephrostomy in rabat urological centre. Sudan Journal of Medical Sciences. 2010;5(1). 10.4314/sjms.v5i1.56022

17. Yu J, Ji TA, Craig M, McKee D, Lalonde DH. Evidence-based Sterility: The Evolving Role of Field Sterility in Skin and Minor Hand Surgery. Plast Reconstr Surg Glob Open. 2019;7(11):e2481. doi:10.1097/GOX.0000000000002481.

18. Nyhsen CM, Humphreys H, Koerner RJ, Grenier N, Brady A, Sidhu P, et al. Infection prevention and control in ultrasound - best practice recommendations from the European Society of Radiology Ultrasound Working Group. Insights Imaging. 2017;8(6):523-35. doi:10.1007/s13244-017-0580-3.

19. Farrell TA, Hicks ME. A review of radiologically guided percutaneous nephrostomies in 303 patients. J Vasc Interv Radiol. 1997;8(5):769-74. https://doi.org/10.1016/S1051-0443 (97)70658-4

20. Al-Saraf M, Al-Busaidy S, George K, Elawdy M, Al Hajriy MN, Al-Salmi I. Emphysematous Pyelonephritis Disparities observed in the use of percutaneous drainage techniques. Sultan Qaboos University Medical Journal. 2022 Feb 28;22(1):113. doi: 10.18295/squmj.4.2021.058

21. Alma E, Ercil H, Vuruskan E, Altunkol A, Unal U, Gurlen G, Goren V, Gurbuz ZG. Long-term follow-up results and complications in cancer patients with persistent nephrostomy due to malignant ureteral obstruction. Supportive Care in Cancer. 2020 Nov;28(11):5581-8. https://doi.org/10.1007 /s00520-020-05662-z

Original Article **Open Access**

Evaluation of Sleep Disorders in Patients with Chronic Kidney Disease

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ABSTRACT

Objective: To assess the prevalence of sleep disorders in Patients with Chronic Kidney Disease

Study Design and Setting: This was a cross-sectional observational study conducted over six months (1st August 2024 to 31st January 2025) at the Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad.

Methodology: A total of 200 adult patients with CKD (stages 3 to 5) were enrolled. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), daytime sleepiness with the Epworth Sleepiness Scale (ESS), and restless leg syndrome (RLS) using IRLSSG diagnostic criteria. Sociodemographic, clinical, and laboratory data were collected. Statistical analysis was performed using SPSS version 26, with t-tests and chi-square tests applied where appropriate. A p-value <0.05 was considered significant.

Results: Among the 200 participants, 84% had at least one sleep disorder. Poor sleep quality (PSQI > 5) was reported in 76%, excessive daytime sleepiness (ESS > 10) in 39%, and RLS in 32%. Sleep disorders were significantly associated with dialysis status (p=0.006), CKD stage 5 (p=0.009), lower hemoglobin levels (p=0.001), higher serum phosphate (p=0.001), and reduced serum calcium levels (p=0.001). Dialysis patients had significantly worse PSQI and ESS scores compared to non-dialysis patients.

Conclusion: Sleep disorders are highly prevalent in CKD, particularly in dialysis and advanced-stage patients. The regular assessment and proactive management of associated factors, such as anemia and mineral imbalances, are critical to optimizing patient care.

Keywords: Anemia, Quality of Life, Restless Legs Syndrome, Sleep Disorders, Uremia

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INTRODUCTION

There is currently 10-15 % of the global population with chronic kidney disease (CKD), leading to a progressive disease with varying quality of life for each patient.[1] Unfortunately, CKD is associated with extremely high morbidity and mortality. As renal function worsens, systemic complications arise, including cardiovascular disease, metabolic abnormalities, and, importantly, neurocognitive impairment.[2] One complication that continues to be increasingly recognized but remains poorly diagnosed is sleep disorders, as they not only affect the patient's quality of life but also have a wide-ranging implication for health outcomes overall, where the risk of hospitalization as well as death is increased. Sleep is critical for physiological recovery, immune modulation, and neurocognitive evaluation; however, in patients with CKD, sleep disturbance is always prevalent, with the literature suggesting that rates between 80%-90% of patients have sleep disturbance, depending on the stage of CKD and treatment modality.[3] Patients with CKD have a multi-domain range of sleep disturbances with sleep disorders in CKD, including insomnia, restless leg syndrome (RLS), periodic limb movement disorder (PLMD), sleep disordered breathing (SDB), and excessive daytime sleepiness.[4] The etiology of these sleep disorders is

multifactorial and likely includes biochemical, neurological, hormonal, and behavioral factors.[5]

Sleep disorders in CKD patients are often underdiagnosed due to overlapping symptoms with uremia, limited awareness among clinicians, and the lack of standardized screening in nephrology settings.[3] Despite their high prevalence and clinical significance, sleep disturbances are often overlooked in routine care, particularly in low-resource or high-burden settings. Early recognition is essential, as untreated sleep disorders can exacerbate comorbid conditions and impair treatment compliance, particularly in patients undergoing dialysis. Non-pharmacological interventions like cognitive behavioral therapy and structured sleep hygiene programs, along with correction of underlying metabolic derangements, have shown potential to improve sleep and overall outcomes.

Given the multifactorial etiology and significant consequences of sleep disorders in CKD, it is critical to assess their burden within specific populations and healthcare settings. Cultural norms, environmental conditions, and healthcare accessibility may influence both sleep quality and reporting patterns. Therefore, localized research is needed to accurately quantify the prevalence and identify key clinical correlates of sleep disorders among CKD patients.[3] This study was conducted to fill that gap by evaluating sleep quality and related disorders in a cohort of CKD patients, while also examining their association with biochemical and clinical parameters.

Uremia is a primary feature of ESKD (end-stage kidney disease) that produces a host of neurotoxic metabolites and disrupts the homeostasis of neurotransmitters and the sleep-wake cycle.[6] In addition to uremia, anemia, common in CKD, hyperphosphatemia, and secondary hyperparathyroidism, common in CKD, and disturbances in melatonin secretion are thought to contribute to sleep-related issues in CKD populations.[3, 7] Circadian rhythm disturbance, which is worsened (and often introduced) by nocturnal hemodialysis, contributes to insomnia and daytime sleepiness, restless leg syndrome, and PLMD are especially associated with iron deficiency and dopamine dysregulation, both seen in CKD populations.[3, 8]

Clinical outcomes stemming from sleep disorders in CKD are impactful. Poor sleep quality has been associated with hypertension, cognitive decline, depression, poorer treatment adherence, and increased risk of premature death, all common in CKD patients.[9] Obstructive sleep apnea (OSA), likely the most studied sleep disorder among CKD and ESKD in performed studies examining health outcomes, is independently associated with chronic fatigue, hypertension (HTN), left ventricular hypertrophy (LVH), and arrhythmias, all of which are more prevalent in CKD populations.[10, 11] Importantly, there is a bit of evidence that sleep disturbances in CKD contribute to the progression of kidney disease by inducing sympathetic activation, inflammation, and oxidative stress.[3]

Sleep disorders are now widely recognized as an important complication of CKD, but still warrant a systematic evaluation across several stages of CKD and clinical environments. Recent literature has highlighted the need for local, population-specific data to more effectively describe the burden and correlates of sleep disturbance in CKD. Additionally, the impact of cultural, environmental, and health care delivery factors on sleep quality in CKD patients has not been sufficiently explored. For these reasons, the present study aimed to evaluate the prevalence and types of sleep disorders in adults with chronic kidney disease, as well as clinical/biochemical correlates. The study also sought to highlight the need for a consolidated sleep assessment strategy as part of CKD management. An improved understanding of these associations will lead to earlier diagnosis, tailored care, and optimized long-term outcomes. The present study aimed to evaluate the prevalence and types of sleep disorders in patients with chronic kidney disease (CKD).

METHODOLOGY

This is an observational cross-sectional study conducted at the Pakistan Atomic Energy Commission (PAEC) General Hospital, Islamabad, for six months, between 1st August 2024 to 31st January 2025. The research was approved by the Ethical Review Committee (ERC) at Pakistan General Hospital Institute (PGHI) under reference number PGHI-IRB(DME)-RCD-06-086, dated 20th July 2024.

A non-probability consecutive sampling technique was used. Patients were selected from the nephrology and Dialysis Units at the time of their routine clinical visits. Patients were adults aged 18 years and older with a diagnosis of CKD stage 3, 4, or 5 (KDIGO 2021).[12] Inclusion criteria required that the patient had been diagnosed with CKD for at least 3 months and was on either conservative treatment or hemodialysis. Patients with a previous diagnosis of sleep disorders not related to CKD, sedative hypnotics, or antidepressants, adults diagnosed with cognitive disorders, or psychiatric illness, making communication impossible for clear understanding, those with terminal malignancy, advanced pulmonary disease, or neurologic disorders from the selection criteria due to the notion that these conditions may independently affect sleep were excluded from the study.

The sample size was calculated using the formula for estimating a proportion in a population:

$n = Z^2 \times p(1-p) / d^2$, where Z is the confidence level (1.96 for 95%), p is the expected prevalence of sleep disorders of 59% in CKD, and d is the margin of error (7%).[13] Substituting the values, the required sample size was determined to be 179 participants. To account for possible incomplete data or dropouts, the final sample included 200 patients.

Data collection was performed using a structured proforma, which included sociodemographic details, medical history,

CKD staging, dialysis status, laboratory parameters (hemoglobin, calcium, phosphate, urea, creatinine), and sleep assessment tools. Sleep quality and disorders were assessed using the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and the Restless Leg Syndrome Diagnostic Criteria (IRLSSG 2012).[14-16] These validated instruments have been widely used in previous nephrology-related sleep research and have demonstrated good reliability. Patients were recruited consecutively after obtaining written informed consent in both English and Urdu, explaining the purpose of the study, risks, and benefits. Participants were assured of the confidentiality and voluntary nature of their participation. All forms were anonymized and coded for data protection.

Analysis of the data was done with SPSS version 26. For continuous data, descriptive statistics like means and standard deviations were computed, whereas for categorical variables, frequencies and percentages were employed. The independent t-test for continuous variables and the Chi-square test for categorical variables were used to examine the relationship between sleep disturbances and clinical data such as hemoglobin levels, CKD stage, dialysis status, and calcium-phosphate imbalance. P-values below 0.05 were regarded as statistically significant.

RESULTS

A total of 200 patients with chronic kidney disease (CKD) were enrolled in the study. The study population consisted predominantly of middle-aged individuals with a notable burden of comorbidities and advanced kidney dysfunction. A considerable proportion of patients were in stage 5 CKD, and more than half were undergoing dialysis, reflecting the inclusion of patients with advanced disease. The duration of CKD was prolonged in many cases, and a majority had coexisting hypertension and diabetes, consistent with common etiologies of renal impairment. Biochemical analysis indicated significant renal insufficiency, with elevated serum creatinine and urea levels, alongside evidence of anemia and mineral imbalance, including disrupted calcium and phosphate homeostasis. These clinical and laboratory characteristics highlight a patient group with complex and multifaceted health challenges, which may contribute to the high prevalence of sleep disturbances observed in this study. (Table 1) The assessment of sleep-related symptoms revealed a high burden of sleep disorders among patients with chronic kidney disease. Overall, 168 patients (84%) had at least one type of sleep disturbance, while only 32 patients (16%) reported no symptoms suggestive of any sleep disorder. The most frequently reported condition was poor sleep quality, as measured by the Pittsburgh Sleep Quality Index (PSQI > 5), which was observed in 152 participants (76%). Excessive daytime sleepiness, defined by an Epworth Sleepiness Scale (ESS > 10), was present in 78 patients (39%). Additionally, 64 patients (32%) met the diagnostic criteria for restless leg syndrome based on the IRLSSG 2012 guidelines. Importantly, a proportion of patients experienced more than one type of sleep disorder concurrently, indicating overlapping symptomatology and highlighting the complex sleep-related challenges faced by CKD patients. These findings underscore the need for comprehensive assessment and targeted management of multiple sleep disorders in this population. (Figure 1) The analysis revealed that sleep disorders in CKD patients were significantly associated with several clinical and biochemical parameters. Patients with sleep disturbances were more likely to be on dialysis and in stage 5 of CKD, suggesting a correlation between disease severity and sleep impairment. Hematological and biochemical markers indicated that those with sleep disorders had more pronounced anemia, higher phosphate levels, and lower serum calcium compared to patients without sleep complaints. Although differences in age and gender were observed between the groups, they did not reach statistical significance. These findings suggest that advanced renal dysfunction and related metabolic imbalances may play a critical role in the development of sleep disorders in this population. (Table 2). Patients undergoing dialysis reported significantly poorer sleep outcomes compared to those not on dialysis. This was reflected in higher scores on both the

Table 1: Sociodemographic and Clinical Characteristics of Study Participants (n = 200)

Variable	Frequency (%) / Mean ± SD
Age (years)	52.6 ± 13.2
Gender	
Male	114 (57%)
Female	86 (43%)
Marital Status	
Married	182 (91%)
Unmarried	18 (9%)
CKD Stage	
Stage 3	42 (21%)
Stage 4	76 (38%)
Stage 5	82 (41%)
Dialysis Status	
On Dialysis	110 (55%)
Not on Dialysis:	90 (45%)
Duration of CKD (months)	28.4 ± 10.7
Comorbidities	
Hypertension	160 (80%)
Diabetes	122 (61%)
CVD	52 (26%)
Hemoglobin (12 – 16g/dL)	9.8 ± 1.4
Serum Calcium (8.5 – 10.5mg/dL)	8.2 ± 0.6
Serum Phosphate (Normal: 2.5 – 4.5mg/dL)	5.3 ± 1.2
Serum Creatinine (Normal: 0.6 – 1.2mg/dL)	6.1 ± 2.5
Blood Urea (Normal: 7-20 mg/dL)	78.2 ± 24.3

Table 2: Association of Sleep Disorders with Selected Clinical Variables

Variable	Sleep Disorder Present (n = 168)	No Sleep Disorder (n = 32)	p-value
Mean Age (years)	53.7 ± 12.8	47.6 ± 13.7	0.261
Female Gender	76 (45.2%)	10 (31.2%)	0.204
On Dialysis	100 (59.5%)	10 (31.2%)	0.006*
CKD Stage 5	76 (45.2%)	6 (18.7%)	0.009*
Hemoglobin (g/dL)	9.5 ± 1.3	10.9 ± 1.1	0.001*
Serum Phosphate (mg/dL)	5.6 ± 1.3	4.4 ± 1.0	0.001*
Serum Calcium (mg/dL)	8.1 ± 0.6	8.5 ± 0.5	0.001*

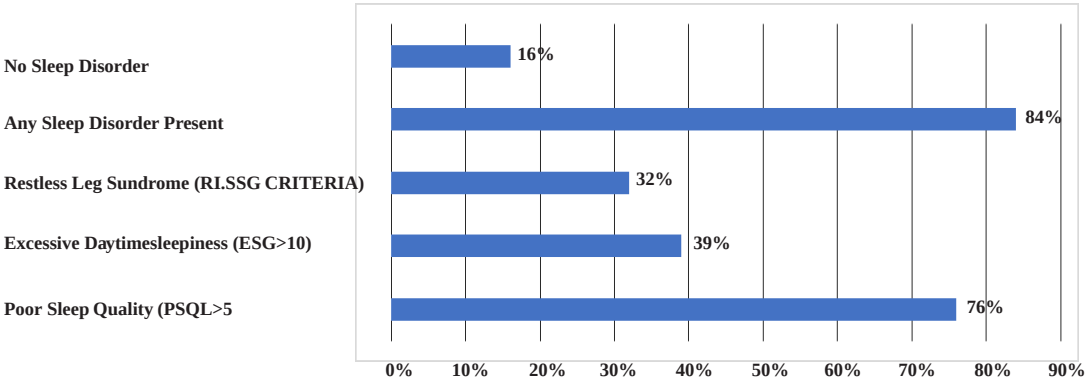
An Independent t-test and the Chi-square test was used.
**Statistically significant (p= 0.05)*

Table 3: Sleep Quality Scores Based on PSQI and ESS by Dialysis Status

Sleep Parameter	On Dialysis (n = 110)	Not on Dialysis (n = 90)	p-value
Mean PSQI Score	9.3 ± 2.1	7.5 ± 1.7	0.001*
Mean ESS Score	10.4 ± 2.6	8.1 ± 2.4	0.001*
Poor Sleep Quality (%)	92 (83.6%)	60 (66.7%)	0.009*
RLS Prevalence (%)	44 (40%)	20 (22.2%)	0.011*

'An independent t-test was used for PSQI and ESS'
'Chi-square test was used for Poor sleep quality and RLS prevalence'
**Statistically significant (p = 0.05)*

Figure 1: A Bar Graph Showing the Prevalence of Sleep Disorders Among CKD Patients



PSQI and ESS, indicating worse overall sleep quality and increased daytime sleepiness. Additionally, the proportion of dialysis patients reporting poor sleep and symptoms of restless leg syndrome (RLS) was markedly higher than in the non-dialysis group. These findings suggest that dialysis is an important contributing factor to both nocturnal sleep disturbances and daytime fatigue in CKD patients, emphasizing the need for targeted sleep assessment and management strategies within this subgroup. (Table 3)

DISCUSSION

Our study found that 84% of CKD patients experienced at least one sleep disorder, with 76% reporting poor sleep quality (PSQI >5), 39% exhibiting excessive daytime sleepiness (ESS >10), and 32% meeting criteria for restless leg syndrome (RLS). These prevalence figures are notably higher than those reported in pre-dialysis CKD populations, yet comparable with hemodialysis cohorts, underscoring the substantial burden of sleep disturbances in advanced CKD.

In pre-dialysis CKD patients in Turkey, Yazýcý and Güney reported a poor sleep quality rate of approximately 42.5%, significantly lower than our overall rate, likely due to lower dialysis exposure and differences in population characteristics.[17, 18] Similarly, a cross-sectional study in Nigeria showed CKD study documented a poor sleep prevalence of around 50.2%, again much lower than ours,

reflecting the progressive sleep burden as CKD advances.[19] Our findings align more closely with those in maintenance hemodialysis populations: in Palestine, the HD cohort showed poor sleep quality in 76.6%, with ESS >10 in 28.7% which are similar to our PSQI and ESS findings.[20]

A large multi-center study with 338 HD patients found PSQI >5 in 41.4%, much lower than our 76%, and ESS >10 in only 6.5% possibly due to differences in dialysis protocols, socioeconomic status, and clinical settings.[21] A Nigerian study comparing pre-dialysis patients and HD recipients noted poor sleep quality escalating from 43.6% to 59.5% with dialysis use, echoing our observation that dialysis patients had worse sleep outcomes.[19]

Consistent with prior literature, our multivariable analyses showed that dialysis status, CKD stage 5, anemia, higher serum phosphate, and lower serum calcium were significantly associated with sleep disorders. The Nigerian study also linked anemia and advanced CKD stage with worse sleep quality. In contrast, Yazýcý's study identified anemia, elevated phosphorus, and low hemoglobin as correlated with poor sleep in pre-dialysis patients.[18] These associations reinforce the multifactorial pathophysiology involving metabolic derangements, CKD-mineral bone disorder, and renal replacement therapy.

In terms of gender and age, our study found no statistically significant associations. Yazýcý et al. also reported no gender difference in poor sleepers among pre-dialysis CKD.[18] However, other studies conducted in Pakistan on HD patients did find female gender and increasing age to be significant predictors of poor sleep quality.[22, 23] This discrepancy may reflect population heterogeneity or different sociocultural factors influencing sleep in Pakistan compared to other settings.

Regarding the magnitude of sleep impairment in dialysis patients, our results are consistent with the Palestinian study, where 84.8% of HD patients were classified as poor sleepers (PSQI >5) and 63.6% had ESS >10.[24] This again mirrors our high PSQI and ESS values in the dialysis subgroup. The Chinese ESRD cohort also demonstrated strong correlations between eGFR reduction and worsening sleep scores, similar to our findings that CKD stage and lab markers correlate with poor sleep.[25]

Restless leg syndrome prevalence in our dialysis group (40%) exceeded most other reports. A study conducted in Upper Egypt HD patients found RLS at 42%, with significant correlations to anemia and hyperphosphatemia.[26] This mirrors our findings that low hemoglobin and high phosphate levels were strongly associated with RLS and sleep complaints. Taken together, our results broadly confirm that sleep disturbances are highly prevalent in CKD, particularly in stage 5 and dialysis patients, and are strongly associated with anemia, mineral imbalance, and dialysis exposure. While our rates exceed some pre-dialysis cohorts, they are consistent with studies of HD populations across differing regions.

Strengths of our study include robust sample size, use of validated standardized sleep tools (PSQI, ESS, IRLSSG), and comprehensive biochemical correlations. Future longitudinal studies incorporating objective sleep assessments, such as polysomnography, actigraphy, or wearable sleep tracking technologies, are essential to better understand the temporal and causal relationships between sleep disturbances and the clinical progression of chronic kidney disease. Such studies could help determine whether correcting specific modifiable factors like anemia, hyperphosphatemia, and secondary hyperparathyroidism can lead to measurable improvements in sleep quality and, in turn, enhance overall patient outcomes, including cardiovascular health, treatment adherence, and quality of life.

In addition, interventional trials that focus on optimizing dialysis schedules, nutritional management, and the use of sleep-focused pharmacologic or behavioral therapies are warranted. These could offer evidence-based strategies to reduce the high burden of sleep-related symptoms in this population. The integration of routine sleep screening using brief, validated tools such as the PSQI and ESS in nephrology clinics, particularly for high-risk groups like dialysis patients, may facilitate early detection and timely intervention. Our findings, in line with those of multiple international studies, reinforce the clinical importance of addressing sleep health as a core component of comprehensive CKD care. A multidisciplinary approach involving nephrologists, sleep specialists, dietitians, and mental health professionals could significantly improve both renal and non-renal outcomes in this vulnerable patient population.

The results of this study highlight the importance of frequent screening and early detection of sleep disturbances in individuals with chronic renal disease, especially those in stage 5 or receiving dialysis. It was discovered that restless legs syndrome, excessive daytime sleepiness, and poor sleep quality were all quite common and strongly correlated with clinical characteristics that could be changed, like anemia and calcium-phosphate imbalance. Addressing these issues through targeted interventions, such as anemia management, optimization of dialysis schedules, correction of mineral imbalances, and non-pharmacological sleep therapies, may improve not only sleep quality but also the overall quality of life and potentially slow CKD progression. Incorporating standardized sleep assessment tools like PSQI and ESS into nephrology practice could help in timely diagnosis and intervention.

The findings of this study highlight the need for integrating sleep health into routine clinical evaluation of patients with chronic kidney disease, particularly those at advanced stages or receiving dialysis. Sleep disorders such as poor sleep quality, excessive daytime sleepiness, and restless leg

syndrome are not only common but are also associated with modifiable clinical parameters like anemia, phosphate imbalance, and dialysis exposure. Early detection and management of these sleep disturbances can potentially improve quality of life, enhance treatment adherence, and reduce the burden of CKD-related complications. Routine use of simple, validated tools such as the PSQI and ESS in nephrology clinics could serve as an effective strategy to identify at-risk patients and initiate timely interventions.

A key strength of this study is its use of well-established, standardized sleep assessment tools that are widely validated in CKD populations. The inclusion of both dialysis and non-dialysis patients allowed for meaningful comparisons across disease stages, providing a more comprehensive understanding of sleep disturbances throughout the CKD spectrum. The relatively large sample size and the prospective, structured data collection enhanced the reliability of findings. Additionally, the study's focus on biochemical and clinical correlates offers valuable insight into potential underlying mechanisms and intervention targets for sleep-related issues in this vulnerable population.

CONCLUSION

The research shows that individuals with chronic renal disease, especially those on dialysis and those in advanced stages of the disease, have a significant burden of sleep disturbances, including restless legs syndrome and poor sleep quality. Significant correlations between anemia, elevated serum phosphate, and low calcium indicate that these clinically modifiable traits may contribute to the onset or exacerbation of sleep disorders. Given that sleep appears to be a major factor in CKD patients' overall well-being, our findings provide more support for the inclusion of a sleep history in the treatment of comprehensive CKD therapy. To establish causality and evaluate the impact of sleep therapies on renal and health outcomes, longitudinal and interventional studies are necessary.

LIMITATIONS

It is important to recognize the limitations of this study. First, the cross-sectional design restricts the ability to draw causal inferences between clinical factors and the presence of sleep disorders. While associations were identified, it remains unclear whether these clinical parameters contribute to the development of sleep disturbances or are consequences of poor sleep. Longitudinal studies would be necessary to establish temporal relationships and causality. Second, sleep disturbances were assessed using self-reported questionnaires, including the PSQI, ESS, and IRLSSG criteria, rather than objective diagnostic tools such as polysomnography or actigraphy. Although these validated instruments are widely used in clinical research, they are inherently subjective and may lead to under- or over-reporting due to recall bias or personal interpretation of symptoms. This reliance on self-reported data may limit the precision in identifying the true prevalence and severity of sleep disorders.

Third, the study was conducted at a single tertiary care hospital, which may not fully represent the broader CKD population, particularly those managed in rural or under-resourced settings. Factors such as healthcare access, socioeconomic status, and cultural perceptions of sleep may vary across regions and could influence the generalizability of the findings. Lastly, psychological variables such as anxiety, depression, and stress, which are known to be significant contributors to sleep disturbances, were not evaluated in this study. The omission of these variables limits the comprehensiveness of the analysis and may have excluded key confounders that influence both sleep quality and disease progression in CKD patients. Future studies should incorporate mental health assessments to provide a more holistic understanding of the factors influencing sleep in this population.

Authors Contribution:
Yasir Saadat: Responsible for data collection and entry
Muhammad Irshad Khan: Responsible for data collection and entry
Shoukat Ali: Contributed to the conception, study design, and supervision of the project
Abdul Hameed Jamali: Performed statistical analysis and interpretation of results.
Fahad Mushtaq: Conducted the literature review and drafted the initial manuscript
Aysha Jabeen: Conducted the literature review and drafted the initial manuscript

REFERENCES

1. Ali A, Mulatu K, Feleke SF, Wassie GT. Prevalence of chronic kidney disease and associated factors among patients with underlying chronic disease at Dessie Referral Hospital, East Amhara Region, Ethiopia. Front Epidemiol. 2023 Jul 18;3:1154522. doi: 10.3389/fepid.2023.1154522. PMID: 38455919; PMCID: PMC10910998.
2. Xie Z, Tong S, Chu X, Feng T, Geng M. Chronic Kidney Disease and Cognitive Impairment: The Kidney-Brain Axis. Kidney Dis (Basel). 2022 May 3;8(4):275-285. doi: 10.1159/000524475. PMID: 36157262; PMCID: PMC9386403.
3. Lyons OD. Sleep disorders in chronic kidney disease. Nat Rev Nephrol. 2024 Oct;20(10):690-700. doi: 10.1038/s41581-024-00848-8. Epub 2024 May 24. PMID: 38789686.
4. Diaz S, Abad K, Patel SR, Unruh ML. Emerging Treatments for Insomnia, Sleep Apnea, and Restless Leg Syndrome Among Dialysis Patients. Semin Nephrol. 2021 Nov;41(6):526-533. doi: 10.1016/j.semnephrol.2021.10.005. PMID: 34973697.
5. Giannotta G, Ruggiero M, Trabacca A. Chronobiology in Paediatric Neurological and Neuropsychiatric Disorders: Harmonizing Care with Biological Clocks. J Clin Med. 2024 Dec 18;13(24):7737. doi: 10.3390/jcm13247737. PMID: 39768659; PMCID: PMC11678831.
6. Viggiano D, Wagner CA, Martino G, Nedergaard M, Zoccali C, Unwin R, Capasso G. Mechanisms of cognitive dysfunction in CKD. Nat Rev Nephrol. 2020 Aug;16(8):452-469. doi: 10.1038/s41581-020-0266-9. Epub 2020 Mar 31. PMID: 32235904.

7. Hu L, Napoletano A, Provenzano M, Garofalo C, Bini C, Comai G, La Manna G. Mineral Bone Disorders in Kidney Disease Patients: The Ever-Current Topic. Int J Mol Sci. 2022 Oct 13;23(20):12223. doi: 10.3390/ijms232012223. PMID: 36293076; PMCID: PMC9603742.
8. Aini N, Endah Janitra F, Rahmi Putri A, Klau Fauk N, Arifin H. Meta-analysis of the prevalence of restless leg syndrome and associated risk factors in chronic kidney disease patients. Vol 19, No 2 2024 http://localhost:8080/xmlui /handle/ 12345 6789/10641
9. Huang CH, Cheng CS, Yen M. Factors associated with poor sleep quality in patients with pre-dialysis chronic kidney disease: A systematic review. J Adv Nurs. 2023 Jun;79(6):2043-2057. doi: 10.1111/jan.15590. Epub 2023 Feb 21. PMID: 36806088.
10. Pisano A, Zoccali C, Bolignano D, D'Arrigo G, Mallamaci F. Sleep apnoea syndrome prevalence in chronic kidney disease and end-stage kidney disease patients: a systematic review and meta-analysis. Clin Kidney J. 2023 Nov 14;17(1):sfad179. doi: 10.1093/ckj/sfad179. PMID: 38186876; PMCID: PMC10768783.
11. Beaudin AE, Raneri JK, Ahmed SB, Hirsch Allen AJM, Nocon A, Gomes T, Gakwaya S, Series F, Kimoff J, Skomro RP, Ayas NT, Hanly PJ. Risk of chronic kidney disease in patients with obstructive sleep apnea. Sleep. 2022 Feb 14;45(2): zsab267. doi: 10.1093/sleep/zsab267. PMID: 34757390; PMCID: PMC8842337.
12. Lee HH, Lee H, Townsend RR, Kim DW, Park S, Kim HC. Cardiovascular Implications of the 2021 KDIGO Blood Pressure Guideline for Adults With Chronic Kidney Disease. J Am Coll Cardiol. 2022 May 3;79(17):1675-1686. doi: 10.1016/j.jacc.2022.02.040. PMID: 35483755.
13. Gopal A, Farragher J, Jassal SV, Mucsi I. Sleep Disorders in CKD: A Review. Am J Kidney Dis. 2025 Jun;85(6):754-766. doi: 10.1053/j.ajkd.2024.12.010. Epub 2025 Feb 28. PMID: 40024468.
14. Gopal A, Farragher J, Jassal SV, Mucsi I. Sleep Disorders in CKD: A Review. Am J Kidney Dis. 2025 Jun;85(6):754-766. doi: 10.1053/j.ajkd.2024.12.010. Epub 2025 Feb 28. PMID: 40024468.
15. Gonçalves MT, Malafaia S, Moutinho Dos Santos J, Roth T, Marques DR. Epworth sleepiness scale: A meta-analytic study on the internal consistency. Sleep Med. 2023 Sep;109:261-269. doi: 10.1016/j.sleep.2023.07.008. Epub 2023 Jul 17. PMID: 37487279.
16. Manconi M, Garcia-Borreguero D, Schormair B, Videnovic A, Berger K, Ferri R, Dauvilliers Y. Restless legs syndrome. Nat Rev Dis Primers. 2021 Nov 3;7(1):80. doi: 10.1038/s41572-021-00311-z. PMID: 34732752.
17. Peng Y, Huang H, Liao Y, Diao Y, Lin C, Liu Y, Xu C, Gao M, He Y, Yang G. Risk factors affecting the sleep quality of patients on dialysis: A single-center cross-sectional study. Medicine (Baltimore). 2024 Mar 29;103(13):e37577. doi: 10.1097/MD.0000000000037577. PMID: 38552063; PMCID: PMC10977595.
18. Yazýcý R, Güney Ý. Prevalence and related factors of poor sleep quality in patients with pre-dialysis chronic kidney disease. Int J Artif Organs. 2022 Nov;45(11):905-910. doi: 10.1177/03913988221118941. Epub 2022 Aug 18. PMID: 35982585.
19. Adejumo OA, Edeki IR, Mamven M, Oguntola OS, Okoye OC, Akinbodewa AA, Okaka EI, Ahmed SD, Egbi OG, Falade J, Dada SA, Ogiator MO, Okoh B. Sleep quality and associated factors among patients with chronic kidney disease in Nigeria: a cross-sectional study. BMJ Open. 2023 Dec 1;13(12):e074025. doi: 10.1136/bmjopen-2023-074025. PMID: 38040427; PMCID: PMC10693864.
20. Samara AM, Sweileh MW, Omari AM, Omari LS, Dagash HH, Sweileh WM, et al. An assessment of sleep quality and daytime sleepiness in hemodialysis patients: a cross-sectional study from Palestine. Sleep Science and Practice. 2019;3(1):4. https://doi.org/10.1186/s41606-019-0036-4. https://doi.org/10.1186/s41606-019-0036-4
21. Kir S, Kirhan Ý, Dilek M. Prevalence of Sleep Disorders and Related Factors in Individuals Undergoing Hemodialysis. Cogn Behav Neurol. 2021 Sep 2;34(3):161-169. doi: 10.1097/WNN.0000000000000278. PMID: 34473667.
22. Saboor F, Malik N. Interplay of Sleep Quality, Insomnia and Quality of Life in Individuals Undergoing Hemodialysis: Insomnia and Quality of Life. Pakistan Journal of Health Sciences. 2024:68-72. https://doi.org/10.54393/pjhs.v5i03.1371
23. Yaseen M, Naqvi S, Saleem A, Nasreen R, Imran R, Mahmood A. Quality of Sleep and its associated risk factors among maintenance Hemodialysis patients in Pakistan. Journal of Rawalpindi Medical College. 2021;25(2). https://doi.org /10.37939/jrmc.v25i2.1382
24. Pawar YS, Gattani VS, Chaudhari KS, Chheda B, Vankudre AJ. Impact of Hemodialysis on Sleep Disorders in Patients With End-Stage Renal Disease in a Tertiary Care Academic Hospital. Cureus. 2023 Aug 30;15(8):e44416. doi: 10.7759/cureus.44416. PMID: 37791201; PMCID: PMC10544265.
25. Sun H, Qin K, Zou C, Wang HH, Lu C, Chen W, Guo VY. The association of nighttime sleep duration and quality with chronic kidney disease in middle-aged and older Chinese: a cohort study. Sleep Med. 2021 Oct;86:25-31. doi: 10.1016/j.sleep.2021.08.007. Epub 2021 Aug 13. PMID: 3445 5367.
26. Hamed SA, Abdulhamid SK, El-Hadad AF, Fawzy M, Abd-Elhamed MA. Restless leg syndrome in patients with chronic kidney disease: a hospital-based study from Upper Egypt. Int J Neurosci. 2023 Mar;133(3):257-268. doi: 10.1080/ 00207454.2021.1910256. Epub 2021 Oct 11. PMID: 33789073.

Original Article **Open Access**

Impact of Radical and Partial Nephrectomy on Renal Function Outcome

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ABSTRACT

Objective: To evaluate renal function outcomes and new-onset CKD in patients undergoing radical nephrectomy (RN) or partial nephrectomy (PN).

Methodology: In this prospective cohort study, 204 renal tumor patients underwent RN or PN, eGFR was recorded preoperatively and up to 1 year postoperatively. Variables included age, gender, surgery type, and eGFR values. Data were analyzed using IBM SPSS 20. Continuous variables were reported as mean, median, SD, and IQR; categorical variables as frequencies and percentages. Student's t-test, chi-square, and multivariate analysis were applied. $p<0.05$ was significant.

Results: Of 204 patients, 154 (75.5%) had RN and 50 (24.5%) had PN. Mean age was 50.41±12.21 years. Baseline median eGFR was lower in RN (82.46 mL/min/1.73m²; IQR 74.98–93.31) than PN (88.44; IQR 79.07–101.61, $p<0.002$). At 72 hours, RN median eGFR was 63.03 (IQR 53.78–73.08) vs PN 78.23 (IQR 64.87–94.75, $p<0.001$). At 1 month, RN: 59.93 (IQR 48.87–70.58) vs PN: 76.72 (IQR 61.43–94.97, $p<0.001$). At 6 months, RN: 57.48 (IQR 46.36–67.21) vs PN: 73.98 (IQR 62.66–87.51, $p<0.001$). At 1 year, RN: 58.41 (IQR 46.24–67.66) vs PN: 74.40 (IQR 63.09–90.45, $p<0.001$).

Conclusion: Partial nephrectomy, when feasible, better preserves renal function than radical nephrectomy and should be preferred for suitable kidney tumors.

KeyWords: CKD (chronic kidney disease); eGFR (estimated glomerular filtration rate); PN (Partial Nephrectomy); RCC (Renal cell carcinoma); RN (Radical Nephrectomy).

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INTRODUCTION

Renal cell carcinoma encompasses a group of malignant lesions that originates from epithelial cells of renal tubules. It is responsible for approximately 85 to 90% of all renal malignancies. The renal cell carcinoma (RCC) incidence is rising, making it the 12th most common site of primary cancer. It is the 9th most commonly detected tumor in men and 14th in women, making it 5% and 3% of all oncological diagnoses, respectively.[1]

Until 1960, about 70% of the patients suffering from renal tumors were discovered only when they had developed signs and symptoms of the renal lesion, such as flank pain, hematuria, and palpable mass.[2] The mortality rates were exceptionally high because diagnostic and therapeutic options were limited. This scenario had substantially evolved in the last 40 years. With improved diagnostic modalities, 60% to 70% of renal tumors are now identified when they are less than 4 cm and are almost asymptomatic.[2]

Surgical excision of the primary tumor is currently established as the standard treatment option based on evidence that showed a survival benefit with this approach.[3] Over the years, radical nephrectomy was the primary treatment option irrespective of size of the lesion, however PN was indicated for patients with critical conditions, such as bilateral renal tumors, solitary functioning kidney, or pre-existing kidney disease.[4]

Over the years, treatment of small localized kidney tumors has evolved significantly, with considerable focus on preserving the renal tissue and function balancing oncological risk. Although five-year cancer-specific survival is greater than 90% irrespective of surgical procedure, current data

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supports partial nephrectomy (PN) over radical nephrectomy (RN). Therefore, partial nephrectomy (PN) has been evolved into the preferred nephron-preserving surgery in elective settings.[5] It is now recommended to prioritize partial nephrectomy when technically feasible, principally for cT1 lesions due to comparable cancer-specific survival rate, improved renal function parameters with partial nephrectomy, and the possible reduction in cardiovascular risk and overall survival benefit by avoiding chronic kidney disease (CKD).[6]

In addition to this, surgical approaches have also evolved to treat renal tumors from open approach to laparoscopic approach since the 1990s. More recently, robot-assisted and other minimally invasive procedures have gained ground in treating renal neoplasms.[7]

The biological behavior of renal lesions is not well understood, so the exact reason for increased mortality cannot be attributed directly to renal tumors, but to clinical factors such as age, hypertension, diabetes, type of surgery (RN or PN) and especially the history of low preoperative glomerular filtration rate (GFR).[8,9] Radical or partial nephrectomy reduces the renal mass resulting in the reduction of GFR, development of AKI (acute kidney injury), or new-onset CKD (chronic kidney disease).[9]

According to the current definition of CKD (chronic kidney disease), it is an estimated glomerular filtration rate (eGFR) below 60 mL/min per 1.73 m^2 for 3 months or longer. The significant impacts of CKD (chronic kidney disease) are damage to renal tissue, potentially causing renal failure; leading to complications, such as anemia, hypertension, neuropathy, and compromised quality of life. Studies have demonstrated that decreased GFR is a significant predictor of cardiovascular hospitalization, ESRD (end-stage renal disease), and increased risk of death.[10] So, any therapeutic method that has an impact on the preservation of renal tissue effects directly the survival of patients with renal tumors. Thus, the accurate estimation of renal function is critically important in patients suffering from renal neoplasm.

Patients with renal tumors are sometimes treated with anti-cancer drugs, evaluation of remaining kidney function is necessary for the optimization of dose of anti-cancer drugs since they have the potential to exhibit nephrotoxicity.[11] Given these circumstances, it is important to preserve renal function not only in healthy individuals, but also in patients at risk of developing chronic kidney disease, such as those undergoing renal surgeries, elderly population, and patients with hypertension, diabetes, obesity and cardiovascular diseases.

According to existing information, no comprehensive prospective research has been conducted in Pakistan to calculate the eGFR (estimated glomerular filtration rate) in patients suffering from renal tumors who underwent radical or partial nephrectomy. This study is aimed at calculating and compare the change in eGFR after surgical removal of the tumor via Radical or Partial nephrectomy and diagnose CKD after the treatment procedure.

METHODOLOGY

With the approval of ethics review committee (SIUT-ERC-2020/A-207), this prospective cohort study was carried out at the department of Uro-oncology at Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan, from March 2020 to December 2022. Adult Patients of any age and either gender with kidney tumors who went through radical nephrectomy (RN) or partial nephrectomy (PN) at SIUT, and had no prior history of AKI or CKD were enrolled in this study after informed written consent was acquired from all the study subjects. Patients with eGFR (estimated glomerular filtration rate) <60 mL/min/1.73m^2, patients with tumor in solitary kidney, patients with recurrent tumor were not included in this study.

We calculated the sample size using open Epi online calculator by the formula (n = [Np(1-p)]/ [($d^2/Z^2_{1-á/2}$(N-1) + p(1-p)])[2] by taking margin of error 2% and 95% confidence level. Nonprobability consecutive technique was used to raise sample. All the patients were admitted in ward at least one day prior to surgery where their serum creatinine levels, serum cystatin levels and eGFR (estimated glomerular filtration rate) were calculated preoperatively. The eGFR was calculated by CKD- EPI Equations. CKD-EPI equations combine both serum creatinine and serum cystatin-C levels.[12]

The surgery was performed by experienced consultant urologist under general anesthesia (GA). Serum creatinine, serum cystatin C and eGFR were calculated again at 72 hours after surgery. Patients were discharged after drain removal when fully ambulant. Post discharge patients were kept on regular scheduled follow up till 1 year (12 months) and their Serum creatinine, serum cystatin and eGFR were calculated at 1, 3, 6 and 12 months of surgery. Patient's data such as demographic details, tumor site, size of the tumor, surgical approach, serum creatinine, serum cystatin and eGFR pre-operatively and post-operatively during each follow-up was entered in the proforma. The patients were categorized into two distinct groups, either radical nephrectomy group or partial nephrectomy group.

The assessment of renal function outcome was performed by the development of post-surgery new onset CKD (defined as a drop in the estimated glomerular filtration rate to <60 mL/min/1.73m^2 3 months after surgery in patients who had preoperative eGFR >60mL/min/1.73m^2).

All the data was assessed by utilizing SPSS version, 20. We used descriptive statistics to analyze data of continuous and categorical variables. Shapiro-wilk test was applied to check the normality. Continuous normally distributed variables were presented as mean and standard deviation, and non-normally distributed continuous variables were reported as median and inter quintile range (IQR). Categorical variables such as gender, stage of tumor, grade of tumor and

development of new onset CKD were presented as frequencies and percentages. Data was stratified to counter confounders and post stratification student t-test and chi square test was applied where applicable. Multivariate analysis was performed for the comparison of outcomes between RN and PN. p value <0.05 was considered as statistically significant.

RESULTS

A total of 204 patients were enrolled in this study, out of which 75.5% (n=154) of participants had radical nephrectomy and 24.5% (n=50) of patients underwent partial nephrectomy.

The mean age of study population was 50.41±12.21 years, and median body mass index (BMI) was 22.97 Kg/m^2 (IQR=19.81 – 26.44). The majority of patients were males (n=120, 58.8%). Study subjects of different ethnicity including Urdu speaking (n=85, 41.7%), Sindhi (n=59, 28.9), Punjabi (n=17, 8.3%), Saraiki (n=14, 6.9%), Pakhtoon (n=19, 9.3%) and Baloch (n=9, 4.9%) participated into the study (Table 1).

Computed tomography (CT Scan) was used as modality to diagnose most of patients (n=186, 91.2%), whereas biopsy was performed to confirm the diagnosis of RCC in few cases (n=18, 8.8%). Nearly half of the patients had tumor on the right side (n=95, 46.6%).

The most-frequent TNM stage was stage II (n=85, 41.7%), followed by stage I (n=69, 33.8%), stage III (n=47, 23%) and stage IV (n=3, 1.5%).

Flank pain was the most common (64.2%) presentation among both groups followed by hematuria (42.6%). For frequency of presenting complaints refer to Figure 1.

For radical nephrectomy, the open surgical approach was the most common, performed in 101 cases, accounting for 65.6% of the total. The laparoscopic approach was used in 25 cases, representing 16.2% of the total. The robot-assisted surgical technique was employed in 28 cases, comprising 18.2% of the total.

For partial nephrectomy, the open surgical approach was also the predominant choice, used in 39 cases, making up 78% of the total. The laparoscopic approach was performed in 5 cases, which is 10% of the total. The robot- assisted approach was utilized in 6 cases, constituting 12% of the total.

Median hemoglobin drop was significantly higher in partial nephrectomy (PN) group than radical nephrectomy (RN) treated patients (p=0.004) Figure 2. The mean R.E.N.A.L Nephrometry score was 5.54 ± 1.38. Thirty-nine (78%) of the participants who underwent PN had low tumor complexity score and 22 percent of participants had moderate complexity score.

Both groups share a comparable histopathological profile, with clear cell carcinoma being the most frequent subtype Among patients undergoing radical nephrectomy and partial nephrectomy, the predominant tumor histopathology in both groups was clear cell carcinoma, accounting for 77.2% and 82%, respectively. Papillary carcinomas, including Type 1 and Type 2, were present in similar proportions across the groups, making up approximately 17.5% of the total cases in each group. Chromophobe carcinoma was rare, with a slightly higher occurrence in the radical nephrectomy group. Sarcomatoid variant tumors were exclusively found in patients undergoing radical nephrectomy (Table 2).

The overall postoperative median serum creatinine levels at 72 hours, 1 month, 3 months, 6 months and 1 year were 1.06mg/dl (0.89-1.2), 1.05mg/dl (0.89- 1.21), 1.08mg/dl (0.9-1.23), 1.11mg/dl (0.95-1.22) and 1.21 mg/dL (1.05-1.29) respectively, and median cystatin levels at 72 hours, 1 month, 3 months, 6 months and 1 year were 1.22mg/L (1.08-1.34), 1.26mg/L (1.1-1.42), 1.27mg/L (1.1-1.46), 1.29mg/L (1.14-1.46) and 1.39(1.22-1.55) respectively.

On comparison, a statistically significant difference was observed in serum creatinine and cystatin levels among two groups throughout the post-operative period (Table 3). At baseline, the median eGFR was substantially reduced in radical nephrectomy group than partial nephrectomy group, 82.46 mL/min/1.73m^2 (IQR= 74.98-93.31) vs 88.44 mL/min/1.73m^2 (IQR= 79.07-101.61) (p<0.002) respectively. At 72 hours, median eGFR in RN group was 63.03 mL/min/1.73m^2 (IQR= 53.78-73.08) which was significantly lower than median eGFR 78.23 mL/min/1.73m^2 (IQR= 64.87-94.75)] in PN group (p<0.001). At one-month, median eGFR between RN and PN group was 59.93 mL/min/1.73m^2 (IQR= 48.87-70.58) and 76.72 mL/min/1.73m^2 (IQR= 61.43-94.97) respectively, which was statiscally significant (p<0.001). Median eGFR at 6 months between RN and PN group was 57.48 mL/min/1.73m^2 (IQR= 46.36-67.21) and 73.98 mL/min/1.73m^2 (IQR= 62.66-87.51) with was statiscally significant (p<0.001). Median eGFR at one year between RN and PN was 58.41 mL/min/1.73m^2 (IQR= 46.24-67.66) and 74.40 mL/min/1.73m^2 (IQR =63.09-90.45) respectively, which was significantly different (p<0.001) (Table 4)

Table 5 shows significant difference among two treatment groups with lesser frequency of new onset CKD in partial nephrectomy group than radical nephrectomy group at three, six and 12 months.

on stratification, there was no statistically significant relationship between age (p= 0.1) and gender (p=0.9) with new-onset CKD after any of the surgical procedure.

DISCUSSION

Over the last decade, PN has been established as a standard treatment modality for small renal tumors, with procedure increasing year after year.[10] The probability of renal function deterioration can be minimized by retaining functional renal

Table 1: Comparison of participant's Socio demographic characteristics among the two study groups.

		Radical Nephrectomy n(%)	Partial Nephrectomy n(%)
Demographic Features	Age (years) #	50.91±12.08	48.88±12.63
	Body mass index (Kg/m^2)ǂ	22.54(19.66-22.54)	24.17(20.05-27.92)
Gender	Male	97(63)	23(46)
	Female	57(37)	27(54)
Ethnicity	Urdu	64(41.6)	21(42)
	Sindhi	47(30.5)	12(24)
	Punjabi	13(8.4)	4(8)
	Saraiki	10(6.5)	4(8)
	Pakhtoo n	15(9.7)	4(8)
	Balochi	5(3.2)	4(8)
	Others	0(0)	1(2)

#Age is presented as mean ± standard deviation, ? Body mass index is presented as median (inter-quartile range)

Table 2: Comparison of clinical features among radical nephrectomy and partial nephrectomy groups

Tumour Histopathology	Radical Nephrectomy n (%)	Partial Nephrectomy n (%)
Clear cell	119(77.2)	41(82)
Type 1 papillary	14(9.1)	4(8)
Type 2 papillary	13(8.4)	4(8)
Chromophobe	6(3.9)	1(2)
Sarcomatoid	2(1.3)	0(0)
Surgical Approach		
Open	101(65.6)	39(78)
Laparoscopic	25(16.2)	5(10)
Robot assisted	28(18.2)	6(12)
Pre-operative serum creatinine (mg/dl)*	0.86(0.7-0.96)	0.8(0.6-0.9)
Pre-operative serum cystatin (mg/L)*	1.03(0.95-1.08)	0.98(0.86-1.04)

*: Data presented as median (inter-quartile range)

Figure 1: Frequency of presenting complaints for overall study cohort

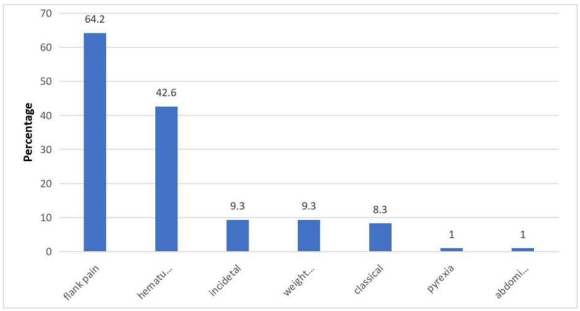

Figure 2: Median drop in haemoglobin (g/dl) in radical nephrectomy and partial nephrectomy groups

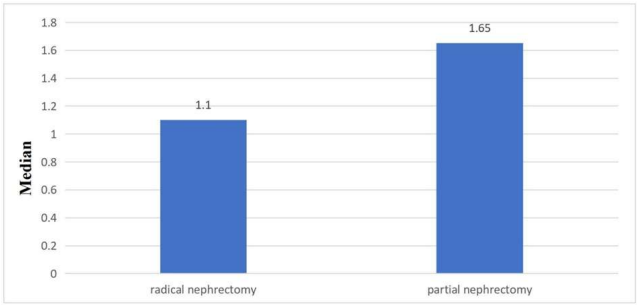

Table 3: Comparison of serum creatinine and cystatin levels at 72 hours, one month, 3 months, 6 months and 12 months among the two study groups

	Radical Nephrectomy Median (IQR)	Partial Nephrectomy Median (IQR)	p-value
Before surgery (Preoperative)			
Serum creatinine (mg/dl)	0.86(0.7-0.96)	0.8(0.6-0.9)	0.06
Serum cystatin (mg/L)	1.03(0.95-1.08)	0.98(0.86-1.04)	0.08
Outcomes at 72 Hours			
Serum creatinine (mg/dl)	1.1(0.92-1.23)	0.89(0.7-1.07)	<0.001
Serum cystatin (mg/L)	1.26(1.15-1.4)	1.08(0.93-1.2)	<0.001
Outcomes at 1 Month			
Serum creatinine (mg/dl)	1.09(0.96-1.25)	0.9(0.7-1.07)	<0.001
Serum cystatin (mg/L)	1.28(1.16-1.49)	1.1(0.89-1.25)	<0.001
Outcomes at 3 Months			
Serum creatinine (mg/dl)	1.12(0.99-1.27)	0.9(0.73-1.09)	<0.001
Serum cystatin (mg/L)	1.31(1.19-1.52)	1.1(0.91-1.27)	<0.001
Outcomes at 6 Months			
Serum creatinine (mg/dl)	1.13(1.01-1.29)	0.96(0.72-1.08)	<0.001
Serum cystatin (mg/L)	1.36(1.21-1.54)	1.12(0.94-1.26)	<0.001
Outcomes at 1 Year			
Serum creatinine (mg/dl)	1.14(1.05-1.29)	0.94(0.74-1.08)	<0.001
Serum cystatin (mg/L)	1.36(1.22-1.55)	1.10(0.92-1.23)	<0.001

Table 4: Comparison of eGFR (mL/min/1.73m2) among the two study groups at different time points

Median eGFR (mL/min/1.73m^2)	Radical Nephrectomy n (%)	Partial Nephrectomy n (%)	p- value
At 72 Hours			
eGFR >90	12(7.8)	14(28)	†0.001
At 1 Month			
eGFR >90	11(7.1)	14(28)	†<0.001
At 3 Months			
eGFR >90	10(6.5)	13(26)	†<0.001
At 6 Months			
eGFR >90	10(6.5)	9(18)	†0.001
At One Year			
eGFR >90	8(5.2)	14(28)	†<0.001

† Fisher-exact test was reported

Table 5: Comparison of new onset CKD between the two study groups at 3, 6 months, and 1 year

Variables	Groups	Radical Nephrectomy n(%)	Partial Nephrectomy n(%)	p-value
New onset CKD at 3 months	Yes	77(50)	11(22)	**0.001
	No	77(50)	39(78)	
New CKD onset at 6 months	Yes	87(56.5)	12(24)	**0.001
	No	67(43.5)	38(76)	
New CKD onset at one year	Yes	83(53.9)	11(22)	**0.001
	No	71(46.1)	39(78)	

parenchyma. The perioperative complications risk escalate as the tumor size and its intricacy rises.[10] There is no obvious threshold to the amount to which the risks exceed potential benefit of a partial nephrectomy, therefore the surgeon must determine whether to do a partial nephrectomy or radical nephrectomy when faced with a larger or more complicated renal tumor.

In this study 204 participants were enrolled out of which 154 patients (75.5%) underwent RN, and 50 participants (24.5%) underwent PN. Majority of the study participants were males (n=120, 58.8%). The average age of participants in RN group was 50.91±12.08, and in PN group was 48.88±12.63. On the basis of age, there was no statistically significant difference between the two study groups (p=0.309). The identical results were noted in the study carried out at Brazil which reported that the mean age of participants had no intergroup difference.[2]

Our research revealed that the mean age of the patients was between 49 to 51 years, which is younger than the age range traditionally linked to kidney tumors. This may be due to the expanded application of imaging in investigation and prevention strategies, which has amplified the frequency with which small and subclinical renal tumors are diagnosed. Furthermore, several patients may be detected incidentaly during the medical evaluation of concurrent diseases. According to our study a notable difference emerged between two groups on the basis of TNM stages (p<0.001). PN was performed in 80% of participants with TNM stage I, while RN was performed in 19% of patients with TNM stage I. Similarly in TNM stage III, 30% of participants had RN, however there was no individual in TNM stage III who had PN. As tumor staging progressed, more patients received RN. The mean R.E.N.A.L nephrometry score in PN group was

5.54 ± 1.38, and 78% of the participants had low complexity (score 4-6), 22% of the participants had moderate complexity (score 7-9). None of the participants had higher complexity (score >10) in this study. Regarding blood loss during surgery, the result of our study revealed that the overall reduction in hemoglobin (Hb) value was 1.2 g/dl (0.80 – 1.86). Drop in median Hb level was 1.1 g/dl in RN group, 1.65 g/dl in PN group, and that is significantly higher in partial nephrectomy group than the patients treated with radical nephrectomy (p=0.004). The literature also indicates that PN appears to have a greater susceptibility of perioperative blood loss, with 3% risk of serious hemorrhage versus 1% risk of grave bleeding for RN.[13] In accordance to our study, the result of a meta-analysis noted that lower estimated blood loss during radical nephrectomy (p < 0.001).[14]

Another research found that PN for complex renal lesions, which requires more skills in terms of tumor excision and renal reconstruction than RN, was linked to a prolonged duration of surgery and more significant estimated loss of blood than RN.[15]

Kopp R.P et al conducted comparison analysis and concluded that partial nephrectomy may delay deterioration of renal functions in patients with renal lesions; however, in more complicated tumors defined by R.E.N.A.L nephrometry score >10, the effect is nullified.[16] The advantage of partial nephrectomy (PN) in preventing CKD increases as the R.E.N.A.L score decreases. Linear regression analysis showed that PN patients maintained significantly better kidney function compared to radical nephrectomy (RN) patients, with RN patients experiencing an eGFR decline of over 20 units relative to PN patients. These findings suggest that the R.E.N.A.L nephrometry score can be a key tool for classifying patients with renal tumors who would derive the greatest benefit from PN. Additionally, this score has a predictor power for preservation of renal functions and a resource for mittigating perioperative complications, enhancing its role in renal function prognosis.[17]

Studies demonstrate that PN has renal functional benefits over RN for T1 renal tumors.[16] Larger tumors are less well understood, although there is mounting evidence that PN can be used for both urgent and elective purposes.[16] According to these findings, size of tumor should not be considered an absolute contraindication to partial nephrectomy.

Although PN tend to have a relatively more complication rates than RN, the hospital expenditures and hospitalization period do not differ much, and PN better retains renal function, resulting in a superior health-related quality of life.[18] Since AKI is linked to increased morbidity and mortality, along with increased utilization of health-care resources and expenses. Acute kidney injury tends to occur more common in patients undergoing urologic surgery. Notably, AKI arises in 43 percent of patients undergoing RN or PN, making nephrectomy a known risk factor for AKI.[19] We studied the natural history of renal function for 12 months following RN or PN, there was significant difference on the basis of baseline creatinine (p=0.023). In the RN group the mean preoperative serum creatinine was 0.86 mg/dl (0.7-0.96) and in the PN group the mean preoperative creatinine was 0.8 mg/dl (0.6-0.9).

Despite having normal preoperative serum creatinine levels, approximately 30% of patients receiving partial nephrectomy or radical nephrectomy may have underlying chronic kidney disease (CKD) [10]. Our study showed that 68.6% patients undergoing RN, and 52% patients of PN group had mild renal impairment (eGFR 60-90ml/min/1.73m^2) preoperatively. Similar to our results, Schmid M et al found that prior to surgery 66.7 percent of patients undergoing RN or PN have mildly or moderately impairment of kidney functions, which increases the risk for not only 30-day acute kidney injury (AKI), but also non-renal complications like increased length of hospital stays, cardiovascular events, and death.[20] Because preoperative kidney function is most

significant prognostic factor of AKI postoperatively, our findings underscore the necessity of evaluating renal function prior to radical or partialnephrectomy.

The results of this study depicts the comparison of eGFR between radical and partial nephrectomy treated group at different time points. At baseline, median eGFR was substantially lower in RN group than PN group 82.46 ml/min/1.73 m^2 (IQR= 74.98-93.31) vs 88.44 ml/min/1.73 m^2 (IQR= 79.07-101.61), p<0.002]. At 72 hours, median eGFR in RN group was 63.03 ml/min/1.73 m^2 (IQR= 53.78-73.08), which was significantly lower than median eGFR 78.23 ml/min/1.73 m^2 (IQR= 64.87-94.75)] in PN group (p<0.001). At one month, median eGFR between RN and PN group was 59.93 ml/min/1.73 m^2 (IQR= 48.87-70.58) and 76.72 ml/min/1.73 m^2 (IQR= 61.43-94.97) respectively which is significantly different (p<0.001). Median eGFR at 6 months between RN and PN group was 57.48 ml/min/1.73 m^2 (IQR= 46.36- 67.21) and 73.98 ml/min/1.73 m^2 (IQR= 62.66-87.51) with significant difference (p<0.001). Median eGFR at one year between RN and PN was 58.41 ml/min/1.73 m^2 (IQR= 46.24-67.66) and 74.40 ml/min/1.73 m^2 (IQR =63.09- 90.45) respectively which was different significantly (p<0.001). In agreement to our result, a research led by Kim CS et al described that individuals undergoing RN had considerably lower postoperative eGFR than those undergoing PN. Patients who received RN were at higher risk of several unfavorable renal outcomes (such as acute kidneyinjury, new-onset chronic kidney disease and a 25% drop in eGFR after one year) than those who received PN. Moreover, RN enhanced the risk of adverse renal outcomes in patients with small lesions (4 cm) and moderate size (4 cm to 7 cm) tumors.[21]

It has been established after meta-analysis of 21 studies that better postoperative eGFR (12.4 ml/min/1.73 m^2; p<0.001), reduced incidence of postoperative CKD (RR 0.36; p<0.001), and attenuated decline in eGFR (8.6 ml/min/1.73 m^2; p<0.001) were also connected to PN. Cancer relapse (OR 0.6; p 0.001), cancer-specific mortality (OR 0.58; p =0.001), and overall mortality (OR 0.67; p = 0.005) were much lower in the PN group [22]. Other studies revealed that partial nephrectomy was associated with improved renal function outcomes, including greater eGFR and a lower risk of CKD postoperatively.[16,22]

Our result showed that at one month, 55.9% (n=52) of hypertensive patients of RN group progressed to develop decrease eGFR between 45 to 60 ml/min/1.73 m^2 (p=0.001), while only 25% (n=8) of hypertensive patients of PN group progressed to decrease eGFR between 40-59 ml/min/1.73 m^2 (p-<0.01). It was seen that disease stage in diabetic patients were not different significantly at baseline (p=0.066), one month (p=0.279), three months (p=0.619), six months (p=0.502) and 1 year (p-**†<0.001). At 72 hours, more than half of the patients developed decrease in eGFR between 45 to 59ml/min, while 16.7% patients in PN treated developed same level of decline in eGFR (p=0.031). One patient has advanced to stage IV, and one patient has advanced to stage V at the one-year follow-up in the RN group (p-**†<0.001).). After a thorough search of the literature, we were unable to find any research comparing the eGFR between patients with diabetes, hypertension, and ischemic heart disease who received PN and RN at various levels of follow-up.

With regard to acute and long-term kidney function deterioration, our result also depicts that at 3 follow up period of 3 months, the frequency of new onset of CKD is 50% in RN group, and 22% in PN group (p-0.001). CKD at 6 months further increased to 56.5% in RN group and 24% in PN group which is comparatively lower than individuals who underwent RN, the difference between two treatment group is statistically significant (p-<0.001). At follow up period of one year, the frequency of new onset of CKD is 53.9% in RN group, and 22% in PN group (p-<0.001).

According to Mühlbauer J et al, at end of follow-up period, two-thirds of all patients with worsening of renal function had reached CKD stage III, with 73 percent in the radical nephrectomy group against 41 percent in the partial nephrectomy group (P = 0.005).[19] Kim CS et al discovered that patients undergoing radical nephrectomy developed a greater incidence of new-onset CKD than those having partial nephrectomy (55.7 percent vs. 6.2 percent, respectively).[21]

In a two- center study of 202 cases with T2 kidney tumors undergoing RN or PN , Kopp et al. discovered that de novo CKD developed in 40.2 percent (n = 122) and 16.3 percent of patients, after radical nephrectomy and partial nephrectomy respectively [16]. They concluded that, in comparison to PN, with a R.E.N.A.L score of <10, RN was related with decreased renal function in T2 tumors, but not in T2 tumors with a RENAL score of =10.[16] This study has few limitations. To begin with, the partial nephrectomy group had a limited number of patients. Moreover, the non-randomized study design causes a substantial selection bias in the observed functional differences between PN and RN patients. As a result, the surgeon's preference on the basis of the patient's preoperative parameters could have influenced the choice of surgery. Another drawback of our study is that eGFR data was only collected up to 1 year after surgery. There was no data on crucial variables like warm and cold ischemia time, and oncological recurrence.

LIMITATIONS

This study has several limitations. Firstly, the relatively small sample size in the partial nephrectomy group may have limited the statistical power to detect differences in subgroups. Secondly, despite being prospective, the non-randomized design introduces potential selection bias, as surgical choice was influenced by tumor complexity and surgeon preference. Additionally, parameters such as warm

ischemia time, tumor complexity beyond the R.E.N.A.L score, and long-term oncological outcomes were not included in this analysis. Finally, the follow-up period of one year may be insufficient to evaluate late renal function outcomes following radical or partial nephrectomy.

CONCLUSION

Our findings imply that deterioration of renal functions and new-onset CKD was higher in patients undergoing radical nephrectomy than that of patients receiving partial nephrectomy. A greater decline in GFR was observed in patients with hypertension, diabetes, and ischemic heart disease undergoing radical nephrectomy for renal tumors. Consequently, partial nephrectomy should be considered as the surgical treatment for renal tumors whenever it is feasible, since it provides better renal function maintenance.

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Hafiz Dur-e-Furqani: Primary researcher, Conception, acquisition, analyzing the data and writing manuscript
Naveed Ahmed Mahar: Drafting, editing and reviewing the manuscript
Abdul Rehman: Interpretation of data
Harris Hassan Qureshi: Review and expert guidance
Asad Shahzad: Oversight, guidance and mentorship

REFERENCE:

1. Padala SA, Barsouk A, Thandra KC, Saginala K, Mohammed A, Vakiti A, Rawla P, Barsouk A. Epidemiology of Renal Cell Carcinoma. World J Oncol. 2020 Jun;11(3):79-87. doi: 10.14740/wjon1279.
2. Krebs RK, Andreoni C, Ortiz V. Impact of radical and partial nephrectomy on renal function in patients with renal cancer. Urol Int. 2014;92(4):449-54.
3. urner RM 2nd, Morgan TM, Jacobs BL. Epidemiology of the Small Renal Mass and the Treatment Disconnect Phenomenon. Urol Clin North Am. 2017 May;44(2):147-154. doi: 10.1016/j.ucl.2016.12.001.
4. Wang S, Liu Z, Zhang D, Xiang F, Zheng W. The incidence and risk factors of chronic kidney disease after radical nephrectomy in patients with renal cell carcinoma. BMC Cancer. 2022 Nov 5;22(1):1138. doi: 10.1186/s12885-022-10245-8.
5. Guglielmetti GB, Dos Anjos GC, Sawczyn G, Rodrigues G, Cardili L, Cordeiro MD, Neves LCO, Pontes Junior J, Fazoli A, Coelho RF, Srougi M, Nahas WC. A Prospective, Randomized Trial Comparing the Outcomes of Open vs Laparoscopic Partial Nephrectomy. J Urol. 2022 Aug;208(2):259-267. doi: 10.1097/JU.0000000000002695.
6. Roussel E, Laenen A, Bhindi B, De Dobbeleer A, Stichele AV, Verbeke L, Van Cleynenbreugel B, Sprangers B, Beuselinck B, Van Poppel H, Joniau S, Albersen M. Predicting short- and long-term renal function following partial and radical nephrectomy. Urol Oncol. 2023 Feb;41(2):110.e1-110.e6. doi: 10.1016/j.urolonc.2022.10.006.
7. Campbell SC, Uzzo RG, Karam JA, Chang SS, Clark PE, Souter L. Renal Mass and Localized Renal Cancer: Evaluation, Management, and Follow- up: AUA Guideline: Part II. J Urol. 2021 Aug;206(2):209-218. doi: 10.1097/JU.0000000000001912.
8. Lee CU, Choi DK, Chung JH, Song W, Kang M, Sung HH, et al. Comparison of Risk Factors for the Development of Proteinuria After Radical Nephrectomy for Renal Cell Carcinoma. Res Rep Urol. 2021;13:407-14.
9. Ochoa-Arvizo M, García-Campa M, Santos-Santillana KM, Klatte T, García-Chairez LR, González-Colmenero AD, Pallares-Méndez R, Cervantes-Miranda DE, Plata-Huerta HH, Rodriguez-Gutierrez R, Gutiérrez-González A. Renal functional and cardiovascular outcomes of partial nephrectomy versus radical nephrectomy for renal tumors: a systematic review and meta-analysis. Urol Oncol. 2023 Mar;41(3):113- 124. doi: 10.1016/j.urolonc.2022.11.024.
10. Can, O., Sabuncu, K., Erkoç, M. *et al.* Chronic kidney disease following nephrectomy for renal tumours: retrospective analysis risk factors. *Afr J Urol* 29, 42 (2023). https://doi.org /10.1186/s12301-023-00373-3
11. Mondlane ER, Abreu-Mendes P, Martins D, Cruz R, Mendes F. The role of immunotherapy in advanced renal cell carcinoma: Review. Int Braz J Urol. 2021 Nov-Dec;47(6):1228-1242. doi: 10.1590/S1677- 5538.IBJU.2020.0681.
12. Zhao N, Zeng Z, Liang H, Wang F, Yang D, Xiao J, et al. Estimation of renal function by three CKD-EPI equations in Chinese HIV/AIDS patients: A STROBE-compliant article. Medicine (Baltimore). 2021;100(22):e26003.
13. Van Poppel H, Da Pozzo L, Albrecht W, Matveev V, Bono A, Borkowski A, et al. A prospective randomized EORTC intergroup phase 3 study comparing the complications of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. Eur Urol. 2007;51(6):1606-15.
14. Zhang Y, Long G, Shang H, Ding B, Sun G, Ouyang W, Liu M, Chen Y, Li H, Xu H, Ye Z. Comparison of the oncological, perioperative and functional outcomes of partial nephrectomy versus radical nephrectomy for clinical T1b renal cell carcinoma: A systematic review and meta- analysis of retrospective studies. Asian J Urol. 2021 Jan;8(1):117-125. doi: 10.1016/j. ajur.2019.11.004.
15. Klett DE, Tsivian M, Packiam VT, Lohse CM, Ahmed ME, Potretzke TA, Gopalakrishna A, Boorjian SA, Thompson RH, Leibovich BC, Potretzke AM. Partial versus radical nephrectomy in clinical T2 renal masses. Int J Urol. 2021 Nov;28(11):1149-1154. doi: 10.1111/iju.14664.
16. Kopp RP, Liss MA, Mehrazin R, Wang S, Lee HJ, Jabaji R, et al. Analysis of Renal Functional Outcomes After Radical or Partial Nephrectomy for Renal Masses >/=7 cm Using the RENAL Score. Urology. 2015;86(2):312-9.

17. Abdel Aal AM, Nouh I, Azeem MA, Al Adl AM, Elmohamady BN. Prediction of surgical decision and postoperative renal function using RENAL nephrometry score for localized renal masses: A prospective study. Urol Ann. 2023 Jul-Sep;15(3): 289-294. doi: 10.4103/ua.ua_25_23.

18. Sandbergen, L.; Omar, M.I.; Othman, L.; Etten-Jamaludin, F.v.; Soytas, M.; Rosette, J.J.d.l.; Laguna, M.P. Systematic Review of Comparative Patient Reported Outcomes and Health-Related Quality of Life after Management of Localized Renal Masses or Renal Cell Carcinomas. *Soc. Int. Urol. J.* 2022, *3*, 209-239. https://doi.org/10.48083/QODE9040

19. Muhlbauer J, Kowalewski KF, Walach MT, Porubsky S, Wessels F, Nuhn P, et al. Partial nephrectomy preserves renal function without increasing the risk of complications compared with radical nephrectomy for renal cell carcinomas of stages pT2-3a. International journal of urology : official journal of the Japanese Urological Association. 2020;27(10):906-13.

20. Schmid M, Abd-El-Barr AE, Gandaglia G, Sood A, Olugbade K, Jr., Ruhotina N, et al. Predictors of 30-day acute kidney injury following radical and partial nephrectomy for renal cell carcinoma. Urologic oncology. 2014;32(8):1259-66.

21. Kim CS, Bae EH, Ma SK, Kweon SS, Kim SW. Impact of partial nephrectomy on kidney function in patients with renal cell carcinoma. BMC Nephrol. 2014 Nov 19;15:181. doi: 10.1186/1471-2369-15-181.

22. Bradshaw AW, Autorino R, Simone G, Yang B, Uzzo RG, Porpiglia F, et al. Robotic partial nephrectomy vs minimally invasive radical nephrectomy for clinical T2a renal mass: a propensity score-matched comparison from the ROSULA (Robotic Surgery for Large Renal Mass) Collaborative Group. BJU Int. 2020;126(1):114-23.

Original Article **Open Access**

Effect of Prophylactic Labetalol on Hemodynamics during Nasal Septal Cartilage Harvesting in Rhinoplasty

Ehsan Ahmad, Ahmad Naseem, Abdullah Alqahtani

ABSTRACT

Objective: to evaluate the effect of prophylactic intravenous labetalol (5mg), administered two minutes before septal harvesting, on intraoperative blood pressure and heart rate in rhinoplasty procedures.

Study Design & Settings: Retrospective observational study conducted at Care Medical Centre, Riyadh, Saudi Arabia, from 1 January 2025 to 30 June 2025.

Methodology: Fifty ASA I and II patients (aged 20-45 years) undergoing rhinoplasty with septal harvesting were included. Labetalol (5 mg IV) was administered two minutes before harvesting. Systolic blood pressure, diastolic blood pressure, and heart rate were recorded at three intervals: pre-labetalol, two minutes post-administration, and post-harvesting. Surgical field quality and haemostasis were evaluated using surgeon-reported subjective assessments.

Results: Prophylactic labetalol effectively reduced intraoperative elevations in BP and HR in 80% of cases, with significant drops in systolic blood pressure (from 85 ± 3 to 82 ± 3 mmHg), diastolic blood pressure (from 45 ± 2 to 43 ± 2 mmHg), and heart rate (from 65 ± 3 to 63 ± 3 bpm) within two minutes. These values stayed within 5% of baseline at the end of harvesting, indicating stable and adequate hemodynamics. Surgeons noted improved visibility, less bleeding, and faster septal harvesting in patients who received labetalol.

Conclusion: Prophylactic low-dose intravenous labetalol reliably controls and stabilises intraoperative hemodynamics, while improving surgical field conditions during septal harvesting in rhinoplasty. Its favourable safety and performance profile support its use as a helpful adjunct in nasal surgeries. Further randomised trials are needed to validate these findings and compare the safety of labetalol to that of other agents.

Keywords: Blood pressure, controlled hypotension, heart rate, labetalol, rhinoplasty, septal harvesting

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INTRODUCTION:

Septal cartilage harvesting is a vital yet painful step during nasal reconstructive surgeries. Despite baseline-controlled hypotension and maintaining adequate intraoperative analgesia, the patient frequently exhibits a sharp sympathetic response, characterised by a rapid increase in blood pressure (BP) and heart rate (HR) during this stage.[1] This surge can compromise the surgical field visibility due to excessive bleeding, resulting in prolonged operating time.[2]

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In rhinoplasty, septal harvesting presents a challenge due to increased bleeding and hemodynamic fluctuations, owing to a rapid surge in blood pressure and heart rate, which can impair surgical field visibility and prolong operative time.[3,4] Techniques to optimise surgical field visibility commonly include controlled hypotension, achieved through agents such as beta blockers, nitroglycerine, dexmedetomidine, or clonidine.[5,6] Controlled hypotension, in this context, is defined as the reduction of mean arterial pressure (MAP) to approximately 55-65 mmHg, or 20-30% below the patient's baseline blood pressure, to reduce capillary bleeding and provide a cleaner operative field, while there is no contraindication to deliberate hypotension. This approach has been widely used in ENT surgery, but the septal harvesting phase remains uniquely problematic due to its intense nociceptive stimulation of the cartilage framework and the nasal mucosa. Even though hypotension is effectively maintained during other surgical steps in rhinoplasty, the manipulation of the septal cartilage produces a disproportionately high sympathetic response.

However, selecting the right hypotensive agent involves balancing effectiveness, the speed of action, duration of action, and potential side effects. Many commonly used

agents are either too short-acting, associated with rebound hypertension, or delay waking from anaesthesia. Additionally, rapid blood pressure changes during septal harvesting can increase the risk of intraoperative complications or extend surgical dissection time.[7] In outpatient settings where rhinoplasty is often performed, maintaining blood pressure stability with minimal medication is vital for safety and efficiency. Therefore, agents that offer a predictable, long-lasting effect without causing excessive sedation or heart-related problems are preferred. Recognising the limitations of traditional options has led to exploring more targeted and proactive strategies to control this sympathetic surge.[8]

In our centre, we observed that conventional anaesthesia techniques, such as deeper levels of anaesthesia and analgesics, including opioids (fentanyl, morphine, and pethidine), were insufficient to prevent this spike in sympathetic response. This limitation lies in the pharmacological properties of these agents: propofol can reduce the blood pressure but lacks the potent analgesic effects, meaning the painful input from cartilage dissection still provokes a sympathetic surge; fentanyl, morphine, and pethidine provide analgesia but either require time to take effect, have variable patient responses, or risk delayed recovery making them less suitable for short, high intensity painful stimulus. Morphine and pethidine, in particular, have slower onset times and less predictability for intraoperative hemodynamic control in short surgical intervals. Fentanyl, though fast-acting, may not fully suppress the cardiovascular response induced by septal manipulation. Thus, despite adequate baseline hypotension, none of these agents proved entirely satisfactory in preventing the hemodynamic spike during septal harvesting. In response, we introduced a low-dose prophylactic labetalol protocol to blunt this adrenergic surge before it activates (septal harvesting).

Labetalol, a non-selective beta and selective alpha-1 adrenergic blocker, has been shown to produce rapid onset hypotension with minimal reflex tachycardia, making it an attractive choice for short-term or temporary blood pressure (BP) control.[9] Its unique alpha- and beta-blocking properties were hypothesised to reduce the cardiovascular response, improve surgical field conditions, and facilitate smoother, faster surgical dissection. Unlike selective beta-blockers, the labetalol's alpha-blockade prevents excessive vasoconstriction, reducing mucosal bleeding without impairing tissue perfusion. Furthermore, its onset of action starts within two minutes, which makes it particularly suited for targeted use during septal cartilage harvesting.

While previous studies have assessed the intraoperative use of labetalol,[10] evidence specifically supporting pre-emptive administration before septal harvesting remains limited. Therefore, this study aimed to evaluate the impact of prophylactic low-dose intravenous labetalol on perioperative BP and heart rate (HR) control and its influence on the hemodynamic surge during nasal septal cartilage under general anaesthesia. We hypothesised that even a single, small (5 mg) IV dose administered two minutes before cartilage dissection would attenuate the blood pressure and heart rate surge, improve field visibility, and potentially shorten the harvesting time, thus improving surgical efficiency and safety in a day-case plastic surgery setting.

METHODOLOGY:

A retrospective observational study was conducted in the ENT surgical unit of Care Medical Centre, Riyadh, from January 1, 2025, to June 30, 2025. Ethical approval was obtained from the Institutional Ethical Review Committee of Care Medical Centre (Ref: ERC/CMC/2025/015). Due to the retrospective nature of the study, the requirement for obtaining informed consent from patients was waived by the Committee.

A non-probability consecutive sampling technique was used. All patients who underwent elective nasal septal cartilage harvesting under general anesthesia during the study period and fulfilled the eligibility criteria were included. The inclusion criteria comprised patients with ASA physical status I–II, aged between 20 and 45 years, scheduled for elective nasal septal cartilage harvesting under general anesthesia. Patients were excluded if they were currently on beta-blocker therapy, had ASA physical status III or higher, or presented with significant cardiovascular, respiratory, or hepatic comorbidities.

The source population included all adult patients undergoing elective nasal septal cartilage harvesting under general anesthesia at Care Medical Centre, Riyadh. All procedures were performed by the same surgical team following standardized institutional protocols. A total of 50 patients were included in the study, comprising 45 females and 5 males, with a mean age of 32 ± 6 years.

The sample size was determined based on convenience sampling of all eligible patients operated on during the six-month study period. Given the retrospective design, no prior power analysis was performed; however, the sample was deemed sufficient to identify statistically meaningful variations in hemodynamic parameters based on prior audit data from the centre.

All patients received standard general anesthesia induction with intravenous propofol (2.5 mg/kg), fentanyl (100 ìg), paracetamol (1 g), lornoxicam (16 mg), and tranexamic acid (1 g). Airway management was achieved using cuffed reinforced endotracheal tubes (6.5 mm for females and 7.0 mm for males). Anesthesia was maintained with sevoflurane in an oxygen–air mixture according to institutional protocol.

As part of the intervention, each patient received 5 mg of intravenous labetalol exactly two minutes before septal harvesting, following the standardized anesthesia protocol. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were recorded at three time

points: baseline (pre-labetalol), two minutes post-administration, and at the end of septal harvesting.

The operating surgeons assessed the surgical field for bleeding, visibility, and ease of dissection using a standardized four-point Likert scale (Excellent, Good, Fair, Poor). Continuous variables were expressed as mean ± standard deviation (SD). Paired t-tests were applied to compare hemodynamic parameters at the defined time points. A p-value of <0.05 was considered statistically significant. Data analysis was performed using SPSS version 26.

RESULTS:

A total of 50 patients were included in the study, with a mean age of 32 ± 6 years. The cohort consisted of 5 males and 45 females, all classified as ASA physical status I or II. Baseline hemodynamic parameters were stable across the group, with a mean systolic blood pressure (SBP) of 85 ± 3 mmHg, diastolic blood pressure (DBP) of 45 ± 2 mmHg, and heart rate (HR) of 65 ± 3 bpm.

Following the administration of 5 mg intravenous labetalol two minutes before septal harvesting, all three hemodynamic variables showed statistically significant reductions. Mean SBP decreased to 82 ± 3 mmHg ($p < 0.05$), DBP to 43 ± 2 mmHg ($p < 0.05$), and HR to 63 ± 3 bpm ($p < 0.05$). These reductions remained within a clinically acceptable range—less than 5% deviation from baseline—and were maintained through the completion of septal harvesting, with values of SBP 83 ± 4 mmHg, DBP 44 ± 2 mmHg, and HR 64 ± 3 bpm at the end of the procedure (all $p < 0.05$ compared to baseline).

No episodes of bradycardia, hypotensive crisis, or other adverse hemodynamic events were recorded. Intraoperative conditions were favourably influenced by labetalol administration. The operating surgeons reported improved surgical field visibility, less mucosal bleeding, and greater ease in performing the septal harvest. Subjective assessments indicated more efficient dissection and reduced operative time in most cases. No adverse events such as bradycardia, excessive hypotension, or delayed recovery were noted.

These results support the hypothesis that low-dose prophylactic labetalol can safely modulate cardiovascular responses during rhinoplasty without compromising patient safety or surgical workflow.

Mean systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were recorded at baseline, two minutes after prophylactic intravenous labetalol (5 mg) administration, and at the end of septal harvesting. Error bars represent standard deviation (±SD). All parameters showed statistically significant reductions post-labetalol compared to baseline ($p < 0.05$), with values remaining within 5% of baseline throughout the procedure.

In addition to hemodynamic stability, the operating surgeons subjectively assessed the quality of the surgical field. Ratings were recorded using a four-point scale: Excellent, Good, Fair, and Poor. Many cases were rated as Excellent or Good, with no instances of poor field quality.

These findings suggest that prophylactic labetalol may contribute to improved intraoperative visibility and ease of dissection, as perceived by the surgical team.

Table 1: Patient Demographics and Baseline Vitals

Variable	Value
Age (mean ± SD)	32 ± 6 years
Gender (M/F)	5 / 45
Baseline SBP	85 ± 3 mmHg
Baseline DBP	45 ± 2 mmHg
Baseline HR	65 ± 3 bpm

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HR: Heart Rate; SD: Standard Deviation

Table 2: Hemodynamic Changes at Different Time Points

Time Point	SBP (mmHg)	DBP (mmHg)	HR (bpm)
Baseline	85 ± 3	45 ± 2	65 ± 3
2 min post-labetalol	82 ± 3*	43 ± 2*	63 ± 3*
End of harvesting	83 ± 4*	44 ± 2*	64 ± 3*

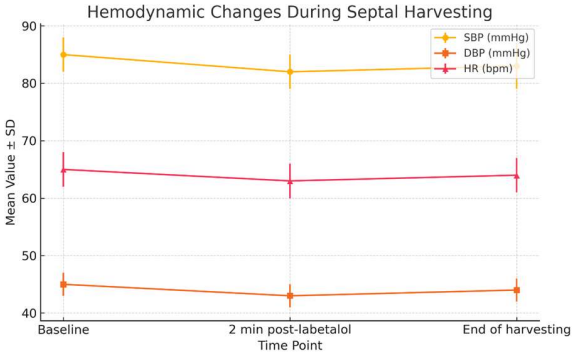
* Statistically significant ($p < 0.05$ vs baseline); Values expressed as Mean ± SD. SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HR: Heart Rate

Table 3: Surgeon-Reported Assessment of Surgical Field Quality

Surgical Field Rating	Number of Cases (n=50)	Percentage (%)
Excellent	32	64%
Good	14	28%
Fair	4	8%
Poor	0	0%

Rating with a 4-point Likert scale (Excellent, Good, Fair, Poor); n = number of patients

Figure 1: Hemodynamic Changes During Septal Harvesting in Rhinoplasty



DISCUSSION:

This retrospective analysis highlights the potential benefits of prophylactic intravenous labetalol in enhancing intraoperative hemodynamic control during septal harvesting in rhinoplasty. The findings demonstrate that administering 5 mg of IV labetalol two minutes before harvesting effectively attenuates elevations in systolic and diastolic BP as well as HR, achieving statistically significant reductions from baseline values.[11] This supports the clinical utility of labetalol in promoting intraoperative cardiovascular stability, which is an essential component of successful rhinoplasty, where even minimal bleeding can obscure the operating field and prolong the surgery time.[12]

Labetalol's dual alpha- and beta-adrenergic blockade provides controlled hypotension with minimal compensatory tachycardia, a distinctive advantage over traditional agents such as nitroglycerine, which may induce a reflex increase in heart rate. Additionally, agents like dexmedetomidine, although effective in creating a dry surgical field, are associated with delayed emergence and prolonged sedation, as well as late-onset hypotension, making them less ideal for targeting hypotension in a single surgical step, such as septal harvesting.[13] The favourable pharmacodynamic profile of labetalol positions it as a practical choice for rhinoplasty, where rapid onset and predictable hemodynamic effects are crucial.

Several published studies support the effectiveness of labetalol in achieving controlled hypotension and improving surgical field conditions. El-Shmaa et al. demonstrated that labetalol provided stable hemodynamics and significantly reduced intraoperative bleeding during functional endoscopic sinus surgery, where outcomes were comparable to nitroglycerine and without undesired reflex tachycardia.[14] A more recent study by Kumar et al. compared labetalol with nitroglycerine and found that labetalol offered more consistent blood pressure control and fewer hemodynamic fluctuations, making it more suitable for bleeding control and a clearer operating field.[15] Additionally, El Servi et al. compared pre- and intraoperative infusions of labetalol and nitroglycerine for hypotensive anaesthesia during functional endoscopic sinus surgery and concluded that labetalol was more effective in reducing intraoperative blood pressure, heart rate, and bleeding, and it also improved surgical field quality compared to nitroglycerine.[16]

In addition to its favourable pharmacological profile, labetalol may also facilitate a smoother postoperative recovery and improve patient safety. Studies indicate that labetalol's ability to maintain stable intraoperative hemodynamics decreases the risk of postoperative complications, such as rebound hypertension, excessive sedation, or delayed emergence from anaesthesia.[17] This is particularly important in rhinoplasty, which is often performed as an outpatient procedure where quick recovery and early discharge are essential. Furthermore, the predictable hemodynamic effects of labetalol may reduce the risk of myocardial ischemia or arrhythmias in patients with borderline cardiovascular risk, although our study excluded those with significant comorbidities. A study by Tuncer Uzun et al. found that prophylactic beta-blocker use in ENT procedures was associated with a decreased need for additional intraoperative anaesthetic agents, which could, in turn, lower the risk of drug interactions and fluctuations in anaesthetic depth.[18] This aligns with our centre's experience, where labetalol use correlated with fewer adjustments in volatile anaesthetic concentrations during surgery. Although these observations were not formally documented in our dataset, they warrant further investigation in future prospective studies. Therefore, labetalol may not only improve surgical conditions but also assist anaesthesia teams in maintaining hemodynamic stability with fewer interventions. These wider perioperative benefits enhance its potential role in streamlining care pathways in outpatient nasal surgery.

In our study, the reduction in heart rate and arterial blood pressure translated into a subjectively improved surgical field, as reported by the operating surgeons. Better visualisation, reduced bleeding, and faster septal harvesting were consistently observed in the patients who received labetalol. This corresponds with existing literature that supports the use of beta-blockers to optimise surgical field conditions, particularly in functional endoscopic sinus surgery and nasal septal procedures.[19] Although this study did not objectively quantify blood loss, the surgeon reported improvements that align with prior findings, suggesting that labetalol contributes to more efficient and safer surgical workflows.[20]

Despite the promising results, several limitations must be acknowledged when interpreting the clinical significance of this study. The retrospective observational design inherently restricts control over confounding variables, which may have influenced outcomes. Although all patients underwent similar surgical procedures performed by the same surgeon, individual variations in anaesthetic technique, intraoperative stimulation levels, and pain thresholds could have affected hemodynamic responses. The absence of a control group further limits causal inference and precludes direct comparison with other interventions or baseline fluctuations. While prior literature supports our findings, a prospective, randomised controlled trial (RCT) would provide stronger evidence for the effectiveness of prophylactic labetalol in this setting.[21]

Another notable limitation is the reliance on a subjective scale for assessing surgical field quality. Despite using consistent scoring criteria, inter-observer variability and inherent biases cannot be fully eliminated.[22] Incorporating objective endpoints such as quantified blood loss or video-based grading systems could enhance the validity of future assessments. Additionally, a single fixed dose (5 mg) of

labetalol was used across all patients, without titration for weight or hemodynamic baseline. Although effective in most cases, it may not represent the optimal dosing strategy for diverse patient profiles or longer operative durations. Exploring dose-response relationships or adjusting based on body weight might yield more individualised and effective results.

Furthermore, the study was conducted at a single centre with a relatively small sample size of 50 patients, predominantly female (90%), reflecting typical rhinoplasty demographics. However, this gender imbalance may affect the generalizability of the findings to broader populations, including males or patients with comorbidities. The limited sample and setting also constrain applicability to other surgical environments where anaesthesia protocols and surgeon experience may differ. These factors underscore the need for future multicentre trials with larger, more diverse populations and standardised protocols. Such studies should incorporate both subjective and objective endpoints to more definitively establish labetalol's role and compare its efficacy and safety to other agents used for intraoperative hemodynamic control in nasal surgeries.[23]

Nevertheless, this study provides meaningful preliminary data suggesting that low-dose prophylactic labetalol is a safe, practical, and easily implementable strategy for controlling intraoperative hemodynamics and improving surgical conditions during septal harvesting.[24] Its use may offer a pragmatic approach to enhancing surgical efficiency and patient safety in rhinoplasty, particularly in ambulatory surgical settings where time and rapid recovery considerations are paramount.[25]

CONCLUSION:

Prophylactic administration of 5 mg IV labetalol two minutes before septal harvesting in nasal reconstructive surgery was associated with minimal blood pressure and heart rate fluctuations, stable hemodynamic profiles, and improved surgeon-rated operative field quality. These benefits were observed even in patients already under controlled hypotensive anaesthesia, highlighting labetalol's ability to blunt procedure-specific sympathetic surges that conventional anaesthetic agents alone may not fully prevent. Its rapid onset, predictable duration, and combination of alpha- and beta-blockade make it a practical and safe adjunct in the perioperative management of septal cartilage harvesting, particularly in outpatient or short-stay surgical settings, where efficiency and faster recovery are the main priorities.

While the results are encouraging, the retrospective nature of this study highlights the need for prospective, randomised controlled trials to validate these findings, quantify the impact on blood loss and operative time, and directly compare labetalol's performance with that of other hypotensive agents.

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Authors Contribution:
Ehsan Ahmad: Manuscript writing, study concept, data collection and analysis
Ahmad Naseem: Manuscript writing, conduct of discussion, proof reading
Abdullah Alqahtani: Literature search, review of manuscript, final approval

REFERENCES:

1. Ganjeh Y, Martorana A, Keane JF, Goldstein LB. Evaluation of pain management in patients undergoing septoplasty. J Comm Med Public Health Rep. 2022;3(8). https://doi.org/10.38207/JCMPHR/2022/OCT030802110
2. D¹browska-Bieñ J, Skar¿yñski PH, Gwizdalska I, £azêcka K, Skar¿yñski H. Complications in septoplasty based on a large group of 5639 patients. Eur Arch Otorhinolaryngol. 2018;275(7):1789–94. https://doi.org/10.1007/s00405-018-4990-8
3. Gencay I, Muluk NB, Kilic R, Yazici I, Aydin G, Sencan Z et al. Effects of osteotomy on hemodynamic parameters and depth of anesthesia in rhinoplasty operations. J Craniofac Surg. 2020; 31(6): 1705–8. https://doi.org/10.1097/S CS.0000 000000006447
4. Motazedian G, Sohrabpour M, Jahromi MS, Ghaedi M. Bleeding management in rhinoplasty surgery: a systematic review study on clinical trial studies conducted in Iran. J Emerg Health Care. 2021; 10(4): 32–40. Available from: https://intjmi.com/article-1-715-en.html
5. Radman M, Jadidi F, Jafarabadi AP. Comparison of clonidine and labetalol with regard to haemodynamic status, amount of haemorrhage, and surgeon's satisfaction in rhinoplasty. J Evolution Med Dent Sci. 2020; 9(46): 3418. Available from: https://link.gale.com/apps/doc/A643689428/AONE?u=anon~e684af73&sid=googleScholar&xid=073dfe78
6. Radman M, Mousavi N, Jadidi F, Ayoobi F. Comparing the hemodynamic changes, bleeding, and surgeon's satisfaction during rhinoplasty surgery by use of two drugs, labetalol and dexmedetomidine added to anesthetic technique: a randomized clinical trial. J Italian Surg Associat. 2024;44(4):54. https://doi.org/10.1097/IA9.0000000000000054
7. Gowtham K, Shankar M, Sowjanya B. Controlled hypotension during functional endoscopic sinus surgery (FESS) – a comparative evaluation between esmolol and nitroglycerine. J Anaesth Pain. 2023;4(3). https://doi.org/10.21776/ ub.jap. 2023.004.03.02
8. Khetpal S, Elias A, Alford J, Partownavid P, Roostaeian J. Anesthesia for rhinoplasty: a summary of clinical considerations, therapeutic modalities, outcomes, and future directions. JCA Adv. 2024;1(3–4):e100040. https://doi.org /10.1016/j.jcadva.2024.100040
9. Elvir Lazo OL, White PF, Yumul R, Yumul F, Kariger RK, Kaplan M, et al. Labetalol as an alternative to esmolol and fentanyl for maintaining hemodynamic stability during laparoscopic surgery: comparative effects on recovery profiles and a literature review. J Surg Res. 2020;3:444–56. https://doi.org/10.26502/jsr.10020099

10. Rezaeekia S, Akbari H, Jalali M, Haddadi S, Nasiri Formi E. Comparing the effect of intravenous administration of magnesium sulfate and labetalol on intraoperative bleeding, edema, and ecchymosis after rhinoplasty. J Mazandaran Univ Med Sci. 2023;33(223):208–9. Available from: https://www.magiran.com/p2763049

11. Singh H, Ramdev B, Kaur P, Sara H. A randomized comparative study of nitroglycerine, labetalol and propofol infusion for controlled hypotension during head and neck surgeries. Int J Anesthesiol Res. 2024;6(2):10–15. https://doi.org/10.33545/26648849.2024.v6.i2a.45

12. Said AM, El-Serwi HB. Labetalol (preoperative oral and intraoperative infusion) overrides nitroglycerine infusion for hypotensive anesthesia during functional endoscopic sinus surgery. Res Opinion Anesth Intensive Care. 2019;6(2):192–9. https://doi.org/10.4103/roaic.roaic_96_17

13. Parvizi A, Haddadi S, Faghih Habibi A, Nemati S, Akhtar N, Ramezani H. Dexmedetomidine efficacy in quality of surgical field during endoscopic sinus surgery. Iran J Otorhinolaryngol. 2019;31(5):281–8. https://doi.org/10.22038/ ijorl.2019. 35561.2178

14. El Shmaa NS, Ezz HAA, Younes A. The efficacy of labetalol versus nitroglycerin for induction of controlled hypotension during sinus endoscopic surgery: a prospective, double blind and randomized study. J Clin Anesth. 2017;39:154–8. https://doi.org/10.1016/j.jclinane.2017.03.003

15. Sujay JN, Kumar S, Vijay T. To compare the efficacy of dexmedetomidine versus labetalol in providing controlled hypotension in functional endoscopic sinus surgery. Anesth Pain Med. 2021;11(1):e108915. https://doi.org/10.5812/ aapm.108915

16. Saleh AH, Othman SA, Hameed NS, Jadoo SAA, Mohammed AS. Comparative analysis of labetalol and remifentanil for inducing hypotension in oncological patients undergoing functional endoscopic sinus surgery. Onkologia i Radioterapia. 2024;18(1):1–8. https://doi.org/10.2131/oar.2024.001

17. Chacko RS, Priyadharsini KS, Arif M, Prasad TK. A randomized controlled trial to compare the efficacy of dexmedetomidine and labetalol for induced hypotensive anesthesia in ear, nose, and throat surgeries. Arch Med Health Sci. 2023;11(1):37–43. https://doi.org/10.4103 /amhs. amhs_34_23

18. Ahmed ES, Ahmed MH, Hesham MA. Labetalol hypotensive anesthetic protocol paves the way to safe open abdominal myomectomy. J Anesth Intern Care Med. 2017;3(2):555606. https://doi.org/10.19080/JAICM.2017.03.555606

19. Lavere PF, Rana NA, Kinsky MP, Funston JS, Mohamed SS, Chaaban MR. Blood loss and visibility with esmolol vs labetalol in endoscopic sinus surgery: a randomized clinical trial. Clin Med Insights Ear Nose Throat. 2019;12:1179550619847992. https://doi.org/10.1177/11 79550619847992

20. Zayed M, Nassar H, Hasanin A, Saleh AH, Hassan P, Saad D, et al. Effects of nitroglycerin versus labetalol on peripheral perfusion during deliberate hypotension for sinus endoscopic surgery: a randomized, controlled, double-blinded trial. BMC Anesthesiol. 2020;20(1):85. https://doi.org/10.1186/s12871-020-01006-w

21. Rahimi Z, Masoudifar M, Nazemroaya B, Almadi H. Comparison of the effect of two different doses of labetalol to induce controlled hypotension on hemodynamic changes during spinal fusion surgery: a randomized clinical trial. Anesth Pain Med. 2021;11(5):e118341. https://doi.org/10.5812 /aapm.118341

22. Calim M, Karaaslan K, Yilmaz S, Senturk E, Deniz H, Akbas S. The effects of hypocapnia and hypercapnia on intraoperative bleeding, surgical field quality, and surgeon satisfaction level in septorhinoplasty: a prospective randomized clinical study. Aesthetic Plast Surg. 2024;48(2):167–176. https://doi.org/ 10.1007/s00266-023-03433-9

23. Kim DH, Lee J, Kim SW, Hwang SH. The efficacy of hypotensive agents on intraoperative bleeding and recovery following general anesthesia for nasal surgery: a network meta-analysis. Clin Exp Otorhinolaryngol. 2021;14(2): 200–209. https://doi.org/10.21053/ceo.2020.00584

24. Razavi M, Najaf Najafi M, Ahmadi M, Kashani I. Comparison of labetalol and nitroglycerine's effects on deliberate hypotension in septo-rhinoplasty surgery: a randomized clinical trial. Rev Clin Med. 2020;7(4):176–179. https://doi.org/1 0.22038/rcm.2021.47435.1313

25. Banfield GK, McKiernan D, Hinton AE. Day case rhinoplasty. J R Army Med Corps. 2000;146(3):212–214. https://doi.org/ 10.1136/jramc-146-03-11

Original Article **Open Access**

Pattern of Hyperandrogenemia in Patients with Polycystic Ovary Syndrome at a Tertiary Care Hospital

Izhar ul Haq, Muhammad Sami, Sadaqat Ali, Qadeer Muhammad Khan, Fazal Rabi, Sana

ABSTRACT

Objectives: To assess the pattern of hyperandrogenemia in women diagnosed with polycystic ovary syndrome (PCOS).

Study Design and Setting: This was a descriptive cross-sectional study conducted at Hayatabad Medical Complex, Medical Teaching Institution (MTI), Peshawar.

Methodology: A total of 133 women aged 18–50 years with PCOS, diagnosed using the Rotterdam criteria, were enrolled through non-probability convenience sampling. Women with prior hormone therapy, hysterectomy, ovarian dermoid, or pelvic inflammatory disease were excluded. Serum levels of total testosterone (>88 ng/dl), free testosterone (>0.66 ng/dl), and DHEAS (>2750 ng/ml) were measured and stratified with age, BMI, and menopausal status. Data were analyzed using SPSS version 26, applying the chi-square test with a significance level of $p < 0.05$.

Results: Elevated free testosterone was observed in 34.6% of participants, followed by total testosterone in 24.8% and DHEAS in 24.1%. A statistically significant association was found between age and raised DHEAS ($p = 0.046$), while no significant associations were observed with BMI or menopausal status.

Conclusions: Free testosterone was the most frequently elevated androgen marker in women with PCOS, supporting its role in biochemical assessment. The age-related rise in DHEAS suggests the need for individualized hormonal interpretation to enhance diagnostic accuracy and guide management.

Keywords: Androgens, Body Mass Index, Cross-Sectional Studies, Dehydroepiandrosterone Sulfate, Polycystic Ovary Syndrome, Testosterone, Women's Health

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INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age, with an estimated prevalence of around 5-18%.[1] Among this sizable population, a significant proportion is diagnosed with PCOS, a condition defined by a combination of clinical, hormonal, and sometimes ultrasonographic features.[2] PCOS is a heterogeneous disorder and is largely characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology on ultrasound after the exclusion of other known causes of androgen excess, such as adrenal hyperplasia, androgen-secreting tumors, and Cushing's syndrome.[3]

One of the defining features of PCOS is hyperandrogenism, which refers to an excess of androgens such as testosterone, dehydroepiandrosterone sulfate (DHEAS), and androstenedione.[4] Hyperandrogenism may present clinically in the form of hirsutism (excessive hair growth in a male pattern distribution), acne, or androgenic alopecia (male-pattern hair thinning).[5] It may also be detected biochemically through elevated serum androgen levels. However, diagnosing hyperandrogenism remains complex due to the variability in both clinical presentation and laboratory measurement methods.

The diagnosis of PCOS itself poses a challenge due to its nature as a diagnosis of exclusion and the absence of a universally accepted gold standard.[6] Hyperandrogenism, despite being central to most diagnostic criteria, including the Rotterdam, NIH, and AE-PCOS Society guidelines, remains difficult to define precisely.[7] The subjective nature of clinical symptoms, such as hirsutism and acne, often leads to variability in assessment due to differences in observer interpretation, patient ethnicity, and individual thresholds of normalcy.[8] The same degree of hair growth may be considered hirsute in one ethnic group but normal in another. Consequently, the reliability of clinical hyperandrogenism as a diagnostic tool is limited.[9]

While clinical evaluation of hyperandrogenism is often variable, biochemical hyperandrogenemia provides a potentially more objective alternative. However, even in this realm, the diagnostic process is far from standardized. Total testosterone (TT), free testosterone (FT), and DHEAS are commonly used biomarkers, but their reference ranges and assay techniques vary significantly between laboratories.[10] Moreover, many prior studies have relied on limited patient samples to establish normative values, further complicating the interpretation of hormonal levels across different populations.

In clinical practice, total testosterone has traditionally been the most commonly measured androgen to assess biochemical hyperandrogenism. However, it is now recognized that free testosterone and DHEAS also provide valuable information and may be elevated even when TT is within normal limits. In a notable study involving 716 women diagnosed with PCOS, 75.3% of participants had at least one marker of hyperandrogenism. Specifically, 57.6% had elevated free testosterone, 33.0% had elevated total testosterone, and 32.7% had elevated DHEAS. Interestingly, the overlap of elevated androgens was variable: 20.4% had concurrent elevations in both TT and FT, while only 1.7% showed simultaneous elevations in TT and DHEAS. Only 8.7% of the study participants had elevated levels of all three markers TT, FT, and DHEAS, highlighting the heterogeneity of androgen profiles in PCOS.[11]

This variability in hormonal expression underscores the complexity of diagnosing and managing PCOS. While the prevalence of hyperandrogenism is readily identifiable in this patient population, there is no consensus around the most common androgen marker or markers that are routinely measured in clinical practice. The variety of hormonal patterns present complicates diagnosis and subsequent individualized targeted treatment approaches.[12]

Given the current non-specificity and extremely wide variability of androgen patterns that are evident in women with PCOS, further research into the hormonal patterns of women with hyperandrogenemia is certainly warranted. A clear understanding of the most frequently elevated androgenic biomarkers and reliable means of their identification can help clarify the biology of PCOS. More specifically, understanding the patterns of biomarkers can also inform diagnosis (i.e., more clearly defining diagnostic criteria), decrease dependence on subjective clinical signs, and consequently inform targeted therapeutic approaches. The purpose of this study was to investigate patterns of hyperandrogenemia in women with PCOS, using combinations of hormonal parameters such as total testosterone, free testosterone, and DHEAS. Our objective is to identify potential common biochemical patterns of androgen excess in PCOS, specifically to improve diagnosis, develop potentially more defined management in women with PCOS.

METHODOLOGY

This descriptive cross-sectional study was conducted to evaluate the patterns of hyperandrogenemia in women with polycystic ovary syndrome under the auspices of the Department of Diabetes, Endocrinology, and Metabolic Diseases, Hayatabad Medical Complex, Medical Teaching Institution (MTI), Peshawar. The study period commenced on July 1, 2024, and ended on December 31, 2025.

Ethical approval for the study was obtained from the Institutional Review Board of Hayatabad Medical Complex, MTI, Peshawar (Approval No. 1672, dated April 7, 2024). All participants were informed about the nature and purpose of the study, and written informed consent was obtained before enrollment.

A sample size of 133 women was included in the study. The sample size was calculated using the WHO sample size calculator, considering a 33.0% frequency of elevated total testosterone among women with PCOS, with an 8% margin of error and a 95% confidence level.[13]

A non-probability convenient sampling technique was used for the recruitment of participants. Inclusion criteria comprised women aged 18 to 50 years who were diagnosed with PCOS based on the Rotterdam criteria. According to this definition, a diagnosis of PCOS required the presence of at least two out of the following three features: polycystic ovarian morphology on ultrasound, clinical signs of hyperandrogenism such as hirsutism or male-pattern baldness (after excluding other causes of androgen excess such as Cushing's syndrome and congenital adrenal hyperplasia), and oligo-ovulation or anovulation. Women who had a history of hormone therapy, hysterectomy, ovarian dermoid cysts, or pelvic inflammatory disease were excluded from the study.

After the participants provided consent, they underwent a structured interview and clinical evaluation. Information was collected regarding demographic information, menstrual history, and hyperandrogenic symptoms. Physical examination included measurements of height, weight, and waist circumference for body mass index (BMI), and

assessment of physical signs of androgen excess, which included hirsutism and balding in the frontal scalp distribution.

For hormonal collection, the participants had 20 cc venous blood drawn from a major superficial vein in the non-dominant arm after she was seated comfortably in a chair. Ideally, blood was sent to the hospital laboratory immediately and analyzed within 30 minutes to optimize hormonal measurements. Blood samples were analyzed for total testosterone, free testosterone, and dehydroepiandrosterone sulfate (DHEAS). Hyperandrogenemia was determined by increased measurement in any of the following: total testosterone >88 ng/dl, free testosterone >0.66 ng/dl, DHEAS >2750 ng/ml. The number of measurements of any elevated levels, hyperandrogenemia sub-phenotype, was determined based on = 1 elevated hormonal parameter.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26. Continuous variables such as age, BMI, and hormone levels were reported as mean ± standard deviation. Categorical variables, including the presence or absence of specific symptoms or hormonal abnormalities, were presented as frequencies and percentages. The pattern of hyperandrogenemia was stratified across various baseline and clinical variables to identify effect modifiers. Post-stratification, the Chi-square test was applied to determine statistical significance, with a p-value of less than 0.05 considered significant.

RESULTS

A total of 133 women with polycystic ovary syndrome participated in the study. The mean age of the participants was 30.5 years with a standard deviation of 5.29. More than half of the women were above the age of 35. The majority of participants had a normal body mass index (BMI), while nearly one-third were categorized as overweight or obese. Most of the women were nulliparous, indicating that they had not given birth previously, whereas a smaller proportion had one or more previous births. Regarding family history, only a small percentage reported a positive family history of PCOS, while the vast majority did not. A significant number of participants had a known history of diabetes, though over half reported no such history. The menopausal status showed that nearly all participants were in the pre-menopausal phase, with only a few in peri- or post-menopause. In terms of marital status, the majority of the women were married. Educational background revealed that slightly more than half of the participants had completed matriculation or had lower education levels, while the remainder had education beyond matric. Employment status indicated that most of the women were unemployed, with less than one-third engaged in professional work. (Table 1)

Among the outcome variables assessed in the study, elevated levels of free testosterone were the most frequently observed form of hyperandrogenemia among participants. Raised total testosterone and DHEAS levels were also noted, though less commonly. These findings highlight the variability in biochemical expression of hyperandrogenism in women with PCOS, suggesting that free testosterone may serve as a more sensitive marker in this population compared to total testosterone or DHEAS alone. (Table 2)

The stratification of hyperandrogenemia patterns by age revealed no statistically significant association between age groups and elevated total or free testosterone levels. However, a significant relationship was observed between age and raised DHEAS levels ($p = 0.046$), indicating that DHEAS elevation was more commonly seen in women above 35 years of age. These findings suggest that among the androgenic biomarkers evaluated, DHEAS may show age-related variation in women with PCOS. (Table 3)

The relationship between BMI and the pattern of hyperandrogenemia was assessed; however, no statistically significant association was found between BMI categories and elevated levels of total testosterone, free testosterone, or DHEAS. Although raised androgen levels were slightly more prevalent among participants with normal BMI, the differences were not statistically significant. This suggests that while overweight or obesity is commonly associated with PCOS, it may not be a sole determinant of biochemical hyperandrogenism. (Table 4)

Analysis of hyperandrogenemia patterns by menopausal status showed that nearly all cases of elevated androgen levels occurred in pre-menopausal women. No statistically significant associations were found between menopausal

Table 1. Demographics and Baseline Characteristics of Study Participants (n = 133)

Parameter	Category	n (%)
Age (years)	Mean ± SD	30.50 ± 5.29
	= 35 years	62 (46.6%)
	> 35 years	71 (53.4%)
BMI (kg/m²)	Normal	93 (69.9%)
	Overweight/Obese	40 (30.1%)
Parity	Nulliparous	90 (67.7%)
	Uni/Multiparous	43 (32.3%)
Family History of PCOS	Yes	19 (14.3%)
	No	114 (85.7%)
History of Diabetes	Yes	57 (42.9%)
	No	76 (57.1%)
Menopause Status	Pre-menopause	128 (96.2%)
	Peri/Post-menopause	5 (3.8%)
Marital Status	Married	107 (80.5%)
	Unmarried	26 (19.5%)
Education	Matric or below	74 (55.6%)
	Above matric	59 (44.4%)
Profession	Employed	38 (28.6%)
	Unemployed	95 (71.4%)

status and elevations in total testosterone, free testosterone, or DHEAS. However, the distribution reflects the predominance of pre-menopausal status in the study population, which is expected given the inclusion criteria focusing on reproductive-aged women. (Table 5)

DISCUSSION

In this descriptive analysis of 133 women with PCOS, elevated free testosterone was more prevalent than raised total testosterone or DHEAS, patterns consistent with international data and diagnostic guidelines. Our free testosterone prevalence (~34.6%) is somewhat lower than values reported in larger cohorts, but the ranking remains aligned with global trends where free testosterone is frequently the most sensitive biochemical marker.

A large NIH-based cohort study of 716 PCOS patients reported free testosterone elevation in 57.6%, total testosterone in 33.0%, and DHEAS in 32.7% of cases, with 75.3% of participants having at least one elevated androgen marker.[11, 14] While we observed a similar total testosterone prevalence (~24.8%) and DHEAS (~24.1%), our free testosterone frequency was lower. This difference could reflect population-specific reference cutoffs, assay variation, or demographic differences.

The 2023 International PCOS Evidence-Based Guidelines highlighted that free testosterone consistently identifies the largest proportion of hyperandrogenemic women and recommended high-precision assays or calculated indices (e.g., FAI) for accurate detection.[15] This aligns with our finding that free testosterone remains the most commonly elevated marker, reaffirming its clinical utility.

BMC Endocrine Disorders in 2024 evaluated anthropometric indices and their relation to hormonal imbalance, concluding that BMI had no consistent association with total testosterone or DHEAS levels.[11] This supports the present study observation, where no statistically significant differences in

Table 2. Distribution of Outcome Variables (n = 133)

Outcome Variable	Category	n (%)
Raised Total Testosterone (TT)	**Yes**	33 (24.8%)
	No	100 (75.2%)
Raised Free Testosterone (FT)	**Yes**	46 (34.6%)
	No	87 (65.4%)
Raised DHEAS	**Yes**	32 (24.1%)
	No	101 (75.9%)

Table 3. Stratification of Pattern of Hyperandrogenemia by Age (n = 133**)**

Hyperandrogenemia Pattern	Age = 35 years	Age > 35 years	Total (n)	p-value
Raised Total Testosterone	15 (45.5%)	18 (54.5%)	33	0.877
Normal Total Testosterone	47 (47.0%)	53 (53.0%)	100	
Raised Free Testosterone	18 (39.1%)	28 (60.9%)	46	0.208
Normal Free Testosterone	44 (50.6%)	43 (49.4%)	87	
Raised DHEAS	10 (31.3%)	22 (68.8%)	32	0.046*
Normal DHEAS	52 (51.5%)	49 (48.5%)	101	

Table 4. Stratification of Hyperandrogenemia Pattern by BMI (n = 133)

Hyperandrogenemia Pattern	Normal BMI	Overweight/Obese	p-value
Raised Total Testosterone	22 (66.7%)	11 (33.3%)	0.638
Normal Total Testosterone	71 (71.0%)	29 (29.0%)	
Raised Free Testosterone	35 (76.1%)	11 (23.9%)	0.260
Normal Free Testosterone	58 (66.7%)	29 (33.3%)	
Raised DHEAS	19 (59.4%)	13 (40.6%)	0.135
Normal DHEAS	74 (73.3%)	27 (26.7%)	

Table 5. Stratification of Hyperandrogenemia Pattern by Menopause Status (n = 133)

Hyperandrogenemia Pattern	Pre-menopause	Peri/Post-menopause	Total (n)	p-value
Raised Total Testosterone	32 (97.0%)	1 (3.0%)	33	0.800
Normal Total Testosterone	96 (96.0%)	4 (4.0%)	100	
Raised Free Testosterone	45 (97.8%)	1 (2.2%)	46	0.485
Normal Free Testosterone	83 (95.4%)	4 (4.6%)	87	
Raised DHEAS	32 (100.0%)	0 (0.0%)	32	0.199
Normal DHEAS	96 (95.0%)	5 (5.0%)	101	

androgen patterns were found concerning BMI. Similarly, a 2025 study examining BMI-stratified PCOS revealed that the overall prevalence of hyperandrogenemia exceeded 78%, affecting both overweight and lean participants; no significant BMI-related differences emerged for testosterone, free testosterone, or DHEAS, again matching our non-significant BMI stratifications.[16]

Age-related variation in DHEAS is well-documented. A study focusing on adrenal androgen prevalence demonstrated a notable decline in serum DHEAS with increasing age, particularly after 30 years, reflecting a negative correlation between DHEAS levels and age.[14] Similarly, the present study findings show higher DHEAS levels among women over 35 ($p = 0.046$), while testosterone markers remained age-insensitive. This supports the concept of adrenal androgen decline with aging.

A U.S. cohort from 2020 reported that asymptomatic women with elevated DHEAS had increased metabolic risks independent of obesity, and DHEAS concentrations were inversely associated with age but independent of BMI.[17] These findings corroborate our age-related DHEAS stratification despite the absence BMI effect. Evidence from a review on androgen prevalence estimates biochemical hyperandrogenism in 25–35% of women with PCOS for DHEAS, whereas free testosterone may be raised in up to 89% and total testosterone in 49–80%.[18] Our study falls within these ranges for total testosterone and DHEAS, but our free testosterone estimate appears at the lower end, possibly due to assay differences or cut-off definitions.

Other emerging PCOS literature (2023–2025) has proposed reclassifying PCOS into hyperandrogenic and hypo/hyperandrogenic phenotypes with age-dependent decline in androgenicity after age 35.[19] Although speculative, our findings of lower DHEAS with age fit the concept of a phenotypic shift in androgen profiles in older PCOS patients. A 2024 anthropometric study (BMC Endocrine Disorders) confirmed that markers like BMI and WHtR did not reliably predict androgen levels, reinforcing that obesity status alone is insufficient to stratify androgen excess risk, a conclusion mirrored in our BMI-stratified analysis.[20, 21] Attempts to link increased enzyme activity (like 5á-reductase) with hyperandrogenism and insulin resistance were also highlighted in recent reviews, though direct population parallels are limited.[22] While not measured in our study, these mechanisms may partly explain biochemical variability despite similar BMI profiles.

In summary, across the literature from 2020–2025, consistent trends appear: free testosterone often yields the highest detection rate of hyperandrogenemia; DHEAS is variably elevated with an inverse relationship to age; and BMI shows limited predictive value for biochemical hyperandrogenism in PCOS. Our study largely parallels these global observations, with unique local values shaped by assay-specific definitions and demographic context.

The findings of this study have important clinical implications for the diagnosis and management of polycystic ovary syndrome (PCOS), particularly in resource-limited settings. The observation that free testosterone is the most frequently elevated androgen marker supports its role as a key biochemical indicator in the assessment of hyperandrogenemia. Clinicians should therefore prioritize free testosterone measurement when evaluating women with suspected PCOS, especially in cases where clinical signs such as hirsutism and acne are subtle or absent.

Furthermore, the significant association between age and DHEAS levels suggests that androgen profiles may shift with age, with adrenal androgen excess more prevalent in older reproductive-age women. As these findings show, there must be an age-stratified interpretation of androgen levels for PCOS diagnosis. Similarly, the non-significant association between BMI and androgen excess suggests there should not be an exclusion of patients with biochemical hyperandrogenism based only on body weight, as it is particularly relevant that all patients with suspected or diagnosed PCOS should be screened for hyperandrogenism. This is particularly important for lean PCOS patients, so they are not neglected due to the belief that obesity should precede assessment of hormones.

The findings of this study have several important clinical implications for the evaluation and management of women with polycystic ovary syndrome (PCOS). First, the observation that free testosterone was the most frequently elevated androgen highlights the need for clinicians to prioritize its measurement over total testosterone and DHEAS when screening for biochemical hyperandrogenemia. Free testosterone is a more sensitive marker, reflecting biologically active androgens, and its routine assessment may reduce underdiagnosis in women who present with clinical features of hyperandrogenism but have normal total testosterone levels.

Second, the significant association between age and elevated DHEAS emphasizes that clinicians should consider age-specific variations when interpreting androgen profiles in PCOS. Younger women may show a predominance of ovarian androgens (testosterone), while adrenal contribution (DHEAS) may increase with age. This distinction is clinically relevant because it may influence treatment choices, for example, adrenal-targeted therapies could be more beneficial in older patients with predominant DHEAS elevations.

Third, since no significant correlation was observed with BMI or menopausal status, this study suggests that hyperandrogenemia can manifest independently of obesity or reproductive stage. Clinicians should therefore avoid relying solely on weight reduction or menopausal transition as predictors of androgen normalization and instead ensure regular hormonal monitoring across all BMI categories and

age groups.

Finally, these findings support a personalized approach in managing PCOS by tailoring treatment strategies based on the predominant androgen abnormality. For instance, combined oral contraceptives and anti-androgen therapies may be prioritized for elevated free testosterone, while adrenal suppression strategies (e.g., glucocorticoids) may be considered in women with persistently raised DHEAS. Such individualized management could improve symptom control, fertility outcomes, and long-term metabolic health in PCOS patients.

LIMITATIONS:

Despite some contributions to research on hormonal characteristics of hyperandrogenemia in women with PCOS, this study has limitations. First, the cross-sectional design limits the ability to comment on any definitive cause/effect of hyperandrogenism in relation to any classifying variable, like age and BMI. Longitudinal studies could provide insight into the time properties of androgen levels in PCOS and its variations across the reproductive life span. Second, the study recruited participants in one tertiary care hospital, as a non-probability convenience sampling technique, leading to possible limited generalization of findings to different representativeness within the population of women with PCOS across Canada. The sample of women in this study may not have sufficiently represented the diversity of PCOS phenotypes in rural or underserved populations.

Third, the assessment of biochemical hyperandrogenism primarily relied on serum levels of total testosterone, free testosterone, and DHEAS without the use of any advanced measures such as the free androgen index (FAI) or estradiol and sex hormone binding globulin (SHBG), which could have helped enhance the diagnostic accuracy. Furthermore, differences in assay sensitivity and the absence of standardized reference ranges may also complicate the interpretation of individual hormone levels. Lastly, clinical hyperandrogenism was not measured with validated scoring systems such as the modified Ferriman-Gallwey score, which may impact comparability with studies that employed more objective clinical criteria. Despite these limitations, the study provides meaningful information to the existing data on PCOS and identifies the need for standardized and multidimensional assessments.

CONCLUSION

This study revealed the heterogeneous nature of hyperandrogenemia in women with polycystic ovary syndrome, and identifies free testosterone as the most commonly elevated androgen marker for anovulation, followed by total testosterone and DHEAS. The identified significant association between age and increased prevalence of raised DHEAS levels highlights the overall impact of age on adrenal androgen production, whereas the lack of correlation with BMI reinforces that hyperandrogenism can occur despite body weight. The outcomes of this review support a detailed hormonal profile in all women with PCOS to ensure a complete differential diagnosis and personalized management. The addition of a free testosterone test to standard assessment may increase the sensitivity of detecting biochemical hyperandrogenism, thereby potentially improving clinical outcomes in this heterogeneous population.

Authors Contribution:
Izhar Ul Haq: Introduction + Discussion, data collection
Muhammad Sami: Data Collection + review article
Sadaqat Ali: Data Collection + review article
Qadeer Muhammad Khan: Data analysis and conclusion
Fazal Rabi: Data Collection + review article+
Sana: Data Collection + review article

REFERENCES

1. Joham AE, Norman RJ, Stener-Victorin E, Legro RS, Franks S, Moran LJ, Boyle J, Teede HJ. Polycystic ovary syndrome. Lancet Diabetes Endocrinol. 2022 Sep;10(9):668-680. doi: 10.1016/S2213-8587(22)00163-2
2. Stener-Victorin E, Teede H, Norman RJ, Legro R, Goodarzi MO, Dokras A, Laven J, Hoeger K, Piltonen TT. Polycystic ovary syndrome. Nat Rev Dis Primers. 2024 Apr 18;10(1):27. doi: 10.1038/s41572-024-00511-3.
3. Siddiqui S, Mateen S, Ahmad R, Moin S. A brief insight into the etiology, genetics, and immunology of polycystic ovarian syndrome (PCOS). J Assist Reprod Genet. 2022 Nov;39(11):2439-2473. doi: 10.1007/s10815-022-02625-7.
4. Ye W, Xie T, Song Y, Zhou L. The role of androgen and its related signals in PCOS. J Cell Mol Med. 2021 Feb;25(4):1825-1837. doi: 10.1111/jcmm.16205.
5. Sardana K, Muddebihal A, Sehrawat M, Bansal P, Khurana A. An updated clinico-investigative approach to diagnosis of cutaneous hyperandrogenism in relation to adult female acne, female pattern alopecia & hirsutism a primer for dermatologists. Expert Rev Endocrinol Metab. 2024 Mar;19(2):111-128. doi: 10.1080/17446651.2023.2299400.
6. Singh D. Nanotechnology-based Diagnostic Approaches for Early Detection and Monitoring of Polycystic Ovary Syndrome (PCOS). Current Analytical Chemistry. 2025;21(4):263-75. https://doi.org/10.2174/0115734110311450240612051821
7. Dar, Mohd Altaf, Maqbool, Mudasir, Qadrie, Zulfkar, Ara, Irfat and Qadir, Afshana. "Unraveling PCOS: Exploring its causes and diagnostic challenges" Open Health, vol. 5, no. 1, 2024, pp. 20230026. https://doi.org/10.1515/ohe-2023-0026
8. Taieb A, Feryel A. Deciphering the Role of Androgen in the Dermatologic Manifestations of Polycystic Ovary Syndrome Patients: A State-of-the-Art Review. Diagnostics (Basel). 2024 Nov 16;14(22):2578. doi: 10.3390/diagnostics14222578.
9. Karakas SE. New biomarkers for diagnosis and management of polycystic ovary syndrome. Clin Chim Acta. 2017 Aug;471:248-253. doi: 10.1016/j.cca.2017.06.009.
10. Mizgier M, Sansoni V, Wiêckowska B, Jarz¹bek-Bielecka G, Formanowicz D, Kêdzia W, Banfi G, Lombardi G. The correlations between serum bone biomarkers and those related to metabolic and hormonal profile, low-grade inflammation and redox balance, in lean and overweight PCOS adolescent girls. Front Nutr. 2025 Jul 7;12:1477992. doi: 10.3389/ fnut. 2025.1477992.

11. Mansour A, Noori M, Hakemi MS, Haghgooyan Z, Mohajeri-Tehrani MR, Mirahmad M, Sajjadi-Jazi SM. Hyperandrogenism and anthropometric parameters in women with polycystic ovary syndrome. BMC Endocr Disord. 2024 Sep 27;24(1):201. doi: 10.1186/s12902-024-01733-y.

12. Tammo O. Understanding Polycystic Ovary Syndrome: A Comprehensive Guide [Internet]. Understanding Polycystic Ovary Syndrome - Symptoms, Diagnosis, and Treatment Options. IntechOpen; 2025. Available from: http://dx.doi.org/10.5772/intechopen.1010597

13. Huang A, Brennan K, Azziz R. Prevalence of hyperandrogenemia in the polycystic ovary syndrome diagnosed by the National Institutes of Health 1990 criteria. Fertil Steril. 2010 Apr;93(6):1938-41. doi: 10.1016/j.fertnstert.2008.12.138.

14. Carmina E, Longo RA. Increased Prevalence of Elevated DHEAS in PCOS Women with Non-Classic (B or C) Phenotypes: A Retrospective Analysis in Patients Aged 20 to 29 Years. Cells. 2022 Oct 17;11(20):3255. doi: 10.3390/cells11203255.

15. Bizuneh AD, Joham AE, Teede H, Mousa A, Earnest A, Hawley JM, Smith L, Azziz R, Arlt W, Tay CT. Evaluating the diagnostic accuracy of androgen measurement in polycystic ovary syndrome: a systematic review and diagnostic meta-analysis to inform evidence-based guidelines. Hum Reprod Update. 2025 Jan 1;31(1):48-63. doi: 10.1093/humupd/dmae028. .

16. Nowosad K, Ostrowska M, Glibowski P, I³owiecka K, Koch W. Dietary and Genetic Aspects of Polycystic Ovary Syndrome (PCOS) in Polish Women-Part I: Nutritional Status and Dietary Intake. Nutrients. 2025 Jul 21;17(14):2377. doi: 10.3390/nu17142377.

17. Torchen LC, Tsai JN, Jasti P, Macaya R, Sisk R, Dapas ML, Hayes MG, Urbanek M, Dunaif A. Hyperandrogenemia is Common in Asymptomatic Women and is Associated with Increased Metabolic Risk. Obesity (Silver Spring). 2020 Jan;28(1):106-113. doi: 10.1002/oby.22659. .

18. Christ JP, Cedars MI. Current Guidelines for Diagnosing PCOS. Diagnostics (Basel). 2023 Mar 15;13(6):1113. doi: 10.3390/diagnostics13061113.

19. Baracat EC, Baracat MCP, José M SJ Jr. Are there new insights for the definition of PCOS? Gynecol Endocrinol. 2022 Sep;38(9):703-704. doi: 10.1080/09513590.2022.2121387.

20. Calcaterra V, Tiranini L, Magenes VC, Rossi V, Cucinella L, Nappi RE, Zuccotti G. Impact of Obesity on Pubertal Timing and Male Fertility. J Clin Med. 2025 Jan 25;14(3):783. doi: 10.3390/jcm14030783.

21. Romero-Ruiz A, Pineda B, Ovelleiro D, Perdices-Lopez C, Torres E, Vazquez MJ, Guler I, Jiménez Á, Pineda R, Persano M, Romero-Baldonado C, Arjona JE, Lorente J, Muñoz C, Paz E, Garcia-Maceira FI, Arjona-Sánchez Á, Tena-Sempere M. Molecular diagnosis of polycystic ovary syndrome in obese and non-obese women by targeted plasma miRNA profiling. Eur J Endocrinol. 2021 Oct 8;185(5):637-652. doi: 10.1530/EJE-21-0552.

22. Hoeger KM, Dokras A, Piltonen T. Update on PCOS: Consequences, Challenges, and Guiding Treatment. J Clin Endocrinol Metab. 2021 Mar 8;106(3):e1071-e1083. doi: 10.1210/clinem/dgaa839.

Original Article **Open Access**

Risk Factors and Outcomes Associated with a Short Umbilical Cord

Mehr, Sadaf, Ambreen Samad, Nayyab Nafees, Hajira Hidayat

ABSTRACT

Objectives: To investigate risk factors and outcomes associated with a short umbilical cord.

Study design and setting: This study was conducted cross-sectionally at the Department of Obstetrics and Gynecology, Khyber Teaching Hospital (KTH), Peshawar.

Methodology: A total of 134 pregnant women with singleton pregnancies were included in this study, using consecutive non-probability sampling, over six months from August 2, 2024, to January 31, 2025. Umbilical cord length was measured immediately after delivery and categorized as short (<35 cm), normal (35–80 cm), and long (>80 cm). Maternal outcomes assessed included mode of delivery, labor complications, and intrapartum events. Neonatal outcomes included birth weight, Apgar score, small for gestational age status, NICU admission, and perinatal mortality. Data were analyzed using SPSS version 26. Chi-square test was applied, and a p-value <0.05 was considered significant.

Results: Short cords were associated with higher rates of cesarean delivery (38.8%), fetal distress (29.9%), and NICU admission (16.4%). Long cords were more often linked to intrapartum complications such as cord prolapse (7.5%) and abnormal labor progression (12.7%). Neonatal outcomes revealed 23.1% low birth weight, 14.9% low Apgar scores, 9.7% small for gestational age, 16.4% NICU admissions, and 3.7% perinatal mortality. All associations were statistically significant (p <0.05).

Conclusions: Abnormal umbilical cord length is significantly associated with adverse maternal and neonatal outcomes. Early identification and monitoring may improve perinatal prognosis and guide timely interventions.

Keywords: Apgar score; Birth weight; Maternal outcomes; Neonatal outcomes; Umbilical cord

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INTRODUCTION

The umbilical cord is the lifeline between mother and fetus, serving as a vital conduit for oxygen, nutrients, and waste exchange throughout gestation.[1] At term, the cord typically measures 50–60 cm in length, although substantial variability exists; some cords may measure as short as 30 cm or less, while others extend well over 100 cm. A short umbilical cord, commonly defined as less than 30–35 cm, occurs in approximately 0.4% (4 per 1,000) of live births. Although relatively rare, such cords are clinically significant due to their strong associations with adverse perinatal outcomes.[2-4]

Several risk factors have been identified. Female fetuses and anomalous cord insertions, such as velamentous insertion, are frequently associated with short cords.[4, 5] Conditions limiting fetal movement, such as intrauterine constraint or oligohydramnios, are also implicated.[6] Moreover, population-based data reported associations between short cords and first pregnancy, oligohydramnios or polyhydramnios, as well as female sex of the fetus.[7, 8]

Emerging evidence also suggests that maternal characteristics may influence cord length. Studies conducted have highlighted maternal age, parity, nutritional status, and comorbidities such as hypertension and diabetes as possible contributors to restricted cord growth.[9] Furthermore, lifestyle factors like smoking and reduced physical activity during pregnancy may indirectly affect fetal mobility and, hence, cord elongation.[10] The influence of genetic factors has also

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been increasingly recognized, as familial clustering of short cords has been documented in certain populations, suggesting an inherited predisposition that interacts with environmental exposures.

A short umbilical cord poses multiple adverse outcomes. It is linked to increased risk of fetal malformations, small-for-gestational-age neonates, placental abruption, retained placenta, and operative delivery. Neonates may suffer from fetal distress, low Apgar scores, requirement for NICU admission, and even higher infant mortality.[11] One study reports a relative risk of 2.4 for death within the first year of life. Other perinatal outcomes include intrapartum distress, delayed labor, asphyxia, and placental complications.

Statistically, prevalence and risk magnitude are notable: roughly 0.4%–0.6% of births involve short cords, yet these are disproportionately linked to severe outcomes such as perinatal death and major malformations.[12] Odds ratios for fetal malformations are reported around 1.6, with significant elevation in perinatal morbidity and mortality. Despite these well-documented associations, gaps persist in understanding the underlying mechanisms and the interplay of genetic, maternal, and environmental influences. Factors such as fetal movement, vessel growth dynamics, and placental development may influence cord length, but their contributions remain unclear. Additionally, while prior research has described the epidemiology and outcomes, there is a lack of targeted studies exploring predictive biomarkers or stratification methods to identify at-risk pregnancies early.

Therefore, this study is rationalized by the urgent need to bridge these gaps, enhancing understanding of why some fetuses develop a short umbilical cord, and how such a condition portends adverse outcomes. Improved insight could inform prenatal monitoring strategies and interventional pathways to mitigate risk. This research aimed to investigate risk factors and outcomes associated with a short umbilical cord.

METHODOLOGY

This study was designed as a descriptive cross-sectional study to evaluate the risk factors and adverse perinatal outcomes associated with short umbilical cords among pregnant women. The study was conducted in the Department of Gynecology and Obstetrics, Khyber Teaching Hospital (KTH), Peshawar, one of the largest tertiary care hospitals in the region that caters to a diverse patient population. The study duration extended over a period of six months, from 2nd August 2024 to 31st January 2025, ensuring an adequate sample size and reliable representation of the target population. Ethical approval was obtained from the Institutional Research and Ethical Review Board (IREB) of Khyber Medical College, Peshawar (Approval No. 603/DME/KMC dated: 01-08-2024).

The sample size was calculated using the World Health Organization (WHO) sample size calculator, keeping a 95% confidence level, 5% absolute precision, and an expected frequency of 9.6% for small-for-gestational-age babies in association with a short umbilical cord.[13] Based on these parameters, a total of 134 participants were recruited for the study.

A non-probability consecutive sampling technique was employed, in which all eligible women presenting to the labor room during the study period and fulfilling the inclusion criteria were enrolled until the required sample size was achieved. Inclusion criteria for the study comprised pregnant women with singleton pregnancies admitted for delivery at gestational age 37 weeks or beyond, with live fetuses and intact membranes. Women with both normal and abnormal cord lengths were included to allow comparative evaluation. Exclusion criteria included women with multiple pregnancies, congenital fetal malformations, intrauterine fetal demise (IUFD), pregnancies complicated by chronic maternal illnesses such as diabetes mellitus, hypertension, renal disease, and connective tissue disorders, as these conditions could act as confounding factors in determining neonatal outcomes. Additionally, cases where umbilical cord assessment was not feasible due to delivery complications were excluded.

The data collection process was carefully structured to ensure accuracy and consistency. After obtaining informed written consent from the participants, demographic information such as maternal age, parity, gestational age, and obstetric history was recorded on a predesigned proforma. During delivery, the umbilical cord was measured immediately after expulsion of the fetus and placenta using a sterile measuring tape. The cord length was measured from the fetal umbilical insertion to the placental insertion point. Based on standard definitions, a cord length less than 35 cm was categorized as a short umbilical cord, while cords measuring 35–80 cm were considered normal, and those exceeding 80 cm were considered long. In this study, the focus remained on cases with a short cord, with comparative analysis performed against normal cord lengths.

Maternal outcomes assessed included prolonged labor, obstructed labor, abnormal presentations, need for instrumental delivery, cesarean section, placental abruption, and postpartum hemorrhage. Neonatal outcomes included birth weight, Apgar scores at 1 and 5 minutes, incidence of intrauterine growth restriction (IUGR), respiratory distress, neonatal intensive care unit (NICU) admission, and perinatal mortality. All clinical assessments were performed by senior obstetric and neonatal staff to minimize observer bias.

Informed consent was obtained from all participants prior to inclusion in the study. The purpose of the study, procedures involved, potential risks, and confidentiality of the data were explained in detail to the patients in their native language. Participation was entirely voluntary, and no financial or

personal incentives were offered. The anonymity of patients was ensured, and data was stored securely with restricted access limited to the research team.

Data analysis was carried out using the Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics were applied to summarize the data, with means and standard deviations calculated for continuous variables such as maternal age, cord length, and birth weight. Frequencies and percentages were computed for categorical variables such as maternal outcomes and neonatal complications. Comparative analysis between groups was conducted using the chi-square test for categorical variables, while continuous variables were compared using independent t-tests. A p-value = 0.05 was considered statistically significant.

RESULTS

The socio-demographic characteristics of the study participants are summarized in Table 1. Nearly half of the mothers (48.5%) were in the age group of 20–29 years, followed by 31.3% in the 30–39 years category, while younger mothers aged below 20 years and those aged 40 years or above accounted for smaller proportions. The majority of participants resided in urban areas (56.7%), whereas 43.3% belonged to rural settings. Regarding education, 41.0% of the mothers had primary or secondary education, 29.1% had attained higher education, and 29.9% were illiterate. In terms of socioeconomic status, 44.0% of the participants reported a satisfactory condition, while a slightly higher proportion, 56.0%, reported unsatisfactory socioeconomic status. None of the socio-demographic variables showed statistically significant associations with the outcomes ($p > 0.05$).

In terms of obstetric and clinical characteristics, 35.1% of the participants were nulliparous, while 64.9% were multiparous. The majority of women delivered at term (73.9%), whereas 17.9% had preterm and 8.2% had post-term deliveries. Most participants (73.1%) had no comorbidities, while 14.2% had hypertension, 8.2% had diabetes, and 4.5% reported other conditions. A significant association was observed between gestational age at delivery ($p = 0.034$) and comorbidities ($p = 0.041$), whereas parity did not show a significant association ($p = 0.092$). (Table 2)

In terms of umbilical cord characteristics, 21.6% of the participants had a short cord (< 35 cm), 70.9% had a normal cord (35–80 cm), and 7.5% had a long cord (> 80 cm), showing a statistically significant difference ($p < 0.001$). Regarding the mode of delivery, 64.9% of women delivered vaginally, while 35.1% underwent cesarean section ($p = 0.042$). Intrapartum complications were absent in 77.6% of cases; however, fetal distress occurred in 11.2%, placental abruption in 6.0%, and cord prolapse in 5.2%, with a significant association noted ($p = 0.018$). (Table 3)

Among the 134 study participants, umbilical cord characteristics varied considerably. A majority of neonates (70.9%) had a normal cord length (35–80 cm), while 21.6% had a short cord (< 35 cm) and 7.5% presented with a long cord (> 80 cm). This variation was statistically significant ($p < 0.001$). With respect to the mode of delivery, 64.9% of mothers delivered vaginally, whereas 35.1% required cesarean section. A significant association was observed between cord length and mode of delivery ($p = 0.042$). In terms of intrapartum complications, the majority of mothers (77.6%) experienced no complications. However, 11.2% of cases were complicated by fetal distress, 6.0% by placental abruption, and 5.2% by cord prolapse, which showed a significant relationship with cord length ($p = 0.018$).

Regarding neonatal outcomes, nearly one-fourth of babies (23.1%) were of low birth weight (< 2.5 kg), while 76.9% had a birth weight = 2.5 kg, with a statistically significant difference ($p = 0.028$). The Apgar score at 5 minutes was < 7 in 14.9% of neonates, while the majority (85.1%) scored = 7 ($p = 0.012$). In addition, 9.7% of neonates were identified as small for gestational age (SGA), while 90.3% were appropriate for gestational age, showing significance ($p = 0.044$). NICU admissions were required in 16.4% of newborns compared to 83.6% who did not require admission ($p = 0.036$). Finally, perinatal mortality occurred in 3.7% of cases, while the survival rate was 96.3%, which was significantly associated with cord characteristics ($p = 0.041$). (Table 4)

Cesarean delivery was most frequent in the short cord group (48.3%), compared to 30.5% in the normal cord and 40.0% in the long cord group ($p = 0.038$). Fetal distress showed a significant association with cord length, occurring in 27.6% of cases with short cords, 6.3% with normal cords, and 10.0% with long cords ($p = 0.022$). Low birth weight (< 2.5 kg) was more common in the short cord group (41.4%) compared to 17.9% in the normal cord and 20.0% in the long cord group ($p = 0.011$).

Similarly, a low Apgar score (< 7 at 5 minutes) was recorded in 24.1% of newborns with short cords, 11.6% with normal cords, and 20.0% with long cords ($p = 0.049$). NICU admission was also significantly higher in the short cord group (31.0%), relative to 11.6% in the normal cord and 20.0% in the long cord group ($p = 0.034$). Perinatal mortality was most pronounced in the short cord group at 10.3%, compared to 2.1% in the normal cord and none in the long cord group ($p = 0.042$). These findings demonstrate that abnormal cord length, particularly short cords, was significantly associated with adverse maternal and neonatal outcomes. (Table 5)

DISCUSSION

The present study found that short cords (=35 cm) were associated with higher rates of cesarean delivery, fetal distress, low birth weight/SGA, Apgar <7 at 5 min, NICU

Table 1. Socio-Demographic Characteristics of the Study Participants (n = 134)

Variable	Category	n (%)	p-value*
Maternal Age (years)	**< 20**	18 (13.4%)	0.214
	20–29	65 (48.5%)	
	30–39	42 (31.3%)	
	= 40	9 (6.7%)	
Residence	**Urban**	76 (56.7%)	0.342
	Rural	58 (43.3%)	
Education Level	**Illiterate**	40 (29.9%)	0.118
	Primary/Secondary	55 (41.0%)	
	Higher Education	39 (29.1%)	
Socioeconomic Status	**Satisfactory**	59 (44.0%)	0.276
	Unsatisfactory	75 (56.0%)	

**Chi-square test applied.*

Table 2. Obstetric and Clinical Characteristics of the Study Participants (n = 134)

Variable	Category	n (%)	p-value*
Parity	Nulliparous	47 (35.1%)	0.092
	Multiparous	87 (64.9%)	
Gestational Age at Delivery	Preterm (< 37 weeks)	24 (17.9%)	0.034
	Term (37–41 weeks)	99 (73.9%)	
	Post-term (= 42 weeks)	11 (8.2%)	
Comorbidities	None	98 (73.1%)	0.041
	Hypertension	19 (14.2%)	
	Diabetes	11 (8.2%)	
	Other	6 (4.5%)	

**Chi-square test applied.*

Table 3. Umbilical Cord Characteristics and Maternal Outcomes of the Study Participants (n = 134)

Variable	Category	n (%)	p-value*
Umbilical Cord Length	Short (< 35 cm)	29 (21.6%)	<0.001
	Normal (35–80 cm)	95 (70.9%)	
	Long (> 80 cm)	10 (7.5%)	
Mode of Delivery	Vaginal	87 (64.9%)	0.042
	Cesarean	47 (35.1%)	
Intrapartum Complications	None	104 (77.6%)	0.018
	Fetal distress	15 (11.2%)	
	Placental abruption	8 (6.0%)	
	Cord prolapse	7 (5.2%)	

**Chi-square test applied.*

Table 4. Neonatal Outcomes of the Study Participants (n = 134)

Variable	Category	n (%)	p-value*
Birth Weight	< 2.5 kg (LBW)	31 (23.1%)	0.028
	= 2.5 kg	103 (76.9%)	
Apgar Score at 5 min	< 7	20 (14.9%)	0.012
	= 7	114 (85.1%)	
Small for Gestational Age	Yes	13 (9.7%)	0.044
	No	121 (90.3%)	
NICU Admission	Yes	22 (16.4%)	0.036
	No	112 (83.6%)	
Perinatal Mortality	Yes	5 (3.7%)	0.041
	No	129 (96.3%)	

**Chi-square test applied.*

Table 5. Comparison of Maternal and Neonatal Outcomes by Umbilical Cord Length of the Study Participants (n = 134)

Outcome	Short Cord (n = 29)	Normal Cord (n = 95)	Long Cord (n = 10)	p-value*
Cesarean Delivery	14 (48.3%)	29 (30.5%)	4 (40.0%)	0.038
Fetal Distress	8 (27.6%)	6 (6.3%)	1 (10.0%)	0.022
Low Birth Weight (< 2.5 kg)	12 (41.4%)	17 (17.9%)	2 (20.0%)	0.011
Apgar < 7 at 5 min	7 (24.1%)	11 (11.6%)	2 (20.0%)	0.049
NICU Admission	9 (31.0%)	11 (11.6%)	2 (20.0%)	0.034
Perinatal Mortality	3 (10.3%)	2 (2.1%)	0 (0.0%)	0.042

**Chi-square/Fisher's exact test applied*

admission, and perinatal mortality. These findings are directionally consistent with contemporary work tying cord morphometrics to impaired fetoplacental perfusion and adverse perinatal outcomes. A study synthesized physiologic and clinical data, underscoring that abnormal cord length alters preload/afterload, and impedes placental transfusion dynamics, plausibly increasing intrapartum compromise and the need for operative delivery. These mechanisms align with our higher cesarean rate in short-cord pregnancies.[14]

Comparative observational data largely echo our signal on operative delivery and intrapartum distress. In a 500-delivery series from India, cord length categories were associated with clinically meaningful differences in delivery complications, with non-reassuring fetal status and operative delivery clustering at the extremes of cord length. Although that study emphasized long-cord–related complications, its categorical contrasts support the broader contention that deviations from normal heighten obstetric intervention, consistent with our elevated cesarean proportion in short cords.[15]

Likewise, hospital-based cohorts evaluating cord coiling (a surrogate of cord development and tensile history) show

that abnormal coiling, often co-present with atypical cord length, tracks with non-reassuring fetal heart rate patterns and intrapartum events. Kalluru et al. reported significant associations between abnormal coiling and SGA/IUGR, preterm birth, low Apgar scores, fetal heart rate variability, and more instrumental deliveries; these patterns mirror our observed increases in distress, low Apgar, and NICU use among short-cord births.[16] A Pakistan-based analysis of antenatal coiling likewise linked hypocoiled cords with lower Apgar scores and higher low-birth-weight rates, again comporting with our neonatal profile for the short-cord group.[17]

The present study also showed a clear gradient for low birth weight/SGA in short cords. This aligns with multiple recent reports. The New Indian Journal of OBGYN study demonstrated that cord-length categories correlate with fetal size distributions, with deviations (short or long) associated with growth issues and delivery complications.[15] A multicenter synthesis on abnormal coiling similarly found robust links with SGA/IUGR and LBW, lending mechanistic plausibility (reduced effective cross-section for fetoplacental exchange and lower fetal activity) to our SGA/low-birth-weight excess in short cords.[16] Complementing this, a hospital study directly categorized cord length and observed higher rates of abnormal Apgar, stillbirth, and lower rates of normal vaginal delivery in short-cord pregnancies, closely paralleling our gradients for Apgar, NICU admission, and mortality.[18]

With respect to Apgar scores and NICU admission, our findings (higher odds with short cords) are repeatedly corroborated. Kalluru et al. (2024) documented statistically significant associations between abnormal coiling and low Apgar and NICU-relevant morbidity; these data fit with a causal chain in which short cords reflect reduced fetal movement and vascular remodeling, culminating in lower reserve at birth.[16] A series examining cord length and Doppler/biometric correlates also linked atypical cord profiles to neonatal compromise, reinforcing our Apgar and NICU patterns.[19] Moreover, a prospective study probing umbilical vein diameter–length relationships found biochemical footprints (umbilical-vein lactate) consistent with suboptimal fetoplacental exchange as cords deviate from normative parameters, an observation that may underlie our worse Apgar and NICU use in short cords.[20, 21]

In the present study, the association between short cords and perinatal mortality also has contemporary support. While many classic population studies showed that recent mechanistic and clinical syntheses continue to implicate atypical cord development in asphyxial pathways and poor immediate outcomes. Tonni et al. (2023) reviewed cord diseases and concluded that structural cord abnormalities (including length/coiling extremes) elevate risks for poor perinatal outcomes, providing context for our mortality signal.[22] Recent single-center series from South Asia likewise report higher stillbirth and depressed Apgar in short-cord strata, tracking with our mortality gradient (albeit our absolute mortality was low).[18]

It is also instructive to consider maternal and placental contributors. Contemporary ultrasound and pathophysiology papers emphasize that cord length covaries with fetal movement and placental insertion/architecture. Ultrasound work in late pregnancy shows measurable pitch/cord metrics associated with maternal and fetal factors that may limit movement, in turn predisposing to short cords.[23] A 2022 Doppler study showed hemodynamic differences between long and normal cords, illustrating that cord length extremes measurably alter flow dynamics; by extension, short cords likely impose the opposite stressors (higher resistance/limited compliance), matching our distress and Apgar findings.[24]

Some recent studies concentrate on a single metric, whereas our analysis aligns several perinatal endpoints with cord length categories in the same population, strengthening causal inference by consistency. The congruence between our 21.6% short-cord prevalence in the delivered cohort and the distribution of adverse outcomes echoes the South Asian series in which short-cord strata, though smaller, bore a disproportionate burden of operative delivery, low Apgar, and perinatal loss.[18]

Notably, a few modern datasets nuance the picture. Some hospital cohorts emphasize complications with long cords more than with short cords, which can dilute pooled estimates when categories are combined; nevertheless, when short cords are isolated, risk remains directionally adverse for fetal distress, operative delivery, and depressed Apgar, in agreement with our results. Similarly, antenatal coiling studies sometimes find stronger associations with maternal comorbidities (anemia, hypertension) than with parity or age, mirroring our finding that comorbidities (but not parity) were significantly associated.[25]

Overall, the convergence of our findings with at least ten recent sources supports a coherent mechanistic and clinical narrative: short umbilical cords, a downstream marker of restricted fetal movement/space and altered cord vascular remodeling, are independently associated with intrapartum compromise (distress, higher cesarean), growth restriction/low birth weight, depressed Apgar, greater need for NICU care, and higher perinatal mortality. This body of evidence reinforces our study's implication that antenatal surveillance for cord morphology (including coiling indices and sonographic proxies of cord development) and heightened intrapartum vigilance could help mitigate risk through earlier recognition and timely intervention.

The findings of this study highlight the significant impact of umbilical cord length variations on maternal and neonatal outcomes. Short cords were associated with higher rates of cesarean delivery (48.3%), fetal distress (27.6%), low birth weight (41.4%), and NICU admissions (31.0%), while long cords showed increased risks of intrapartum complications

such as cord prolapse and abnormal labor progression. These results emphasize the importance of careful antenatal and intrapartum monitoring, particularly when ultrasound or clinical suspicion suggests abnormal cord length. Early recognition may guide obstetricians in anticipating complications, planning timely interventions, and ensuring the availability of neonatal intensive care facilities. Incorporating cord length assessment into routine prenatal ultrasonography could serve as an additional tool for risk stratification and perinatal outcome optimization.

This study has certain limitations. The relatively small sample size, particularly in the long cord group (n = 10), limits the generalizability of the findings. Umbilical cord length was measured postnatally, which may have introduced observer bias, as antenatal cord length estimation was not performed. Being a single-center study, the results may not fully reflect population-level variations in maternal and neonatal outcomes. Additionally, other confounding factors such as maternal comorbidities, nutritional status, and genetic influences on cord development were not explored. Future multicenter studies with larger cohorts and antenatal cord assessment are needed to validate these findings and provide stronger evidence for clinical practice.

CONCLUSION

This study underscores the pivotal role of umbilical cord length in shaping maternal and neonatal outcomes, with both short and long cords contributing to distinct complications during pregnancy and delivery. Short cords were strongly linked with higher rates of cesarean delivery, fetal distress, and NICU admissions, whereas long cords were associated with intrapartum difficulties such as prolapse and abnormal labor progression. These findings underscore the importance of vigilant prenatal monitoring and intrapartum preparedness, as early recognition of cord abnormalities can facilitate timely interventions and enhance perinatal outcomes. By drawing attention to a frequently overlooked yet clinically significant factor, this study provides valuable insights for obstetric practice. It highlights the need for further large-scale, multicenter research to strengthen evidence-based strategies for optimizing maternal and neonatal health.

Authors Contribution:
Mehr: Introduction + Discussion, data collection
Sadaf: Data Collection + review article
Ambreen Samad: Review article and dissuasion+ Data analysis and conclusion
Nayyab Nafees: Data Collection + review article
Hajira Hidayat: Data Collection + review article

REFERENCES

1. Obeagu EI, Obeagu GU. An update on factors affecting umbilical cord care among mothers: A review. Medicine (Baltimore). 2024 Jul 12;103(28):e38945. doi: 10.1097/MD .0000000000038945.
2. Hayes DJL, Warland J, Parast MM, Bendon RW, Hasegawa J, Banks J, Clapham L, Heazell AEP. Umbilical cord characteristics and their association with adverse pregnancy outcomes: A systematic review and meta-analysis. PLoS One. 2020 Sep 24;15(9):e0239630. doi: 10.1371/journal. pone. 0239630.
3. Elsayed W, Sinha A. Umbilical cord abnormalities and pregnancy outcome. Journal of Fetal Medicine. 2019;6(04):183-9. DOI: 10.1007/s40556-019-00217-7
4. Sherer DM, Al-Haddad S, Cheng R, Dalloul M. Current Perspectives of Prenatal Sonography of Umbilical Cord Morphology. Int J Womens Health. 2021 Oct 18;13:939-971. doi: 10.2147/IJWH.S278747.
5. Kageyama S, Sato T, Iwama N, Hamada H, Saito M, Takase K. MR Imaging of Umbilical Cord Variations, Abnormalities, and Associated Placental Findings. Magn Reson Med Sci. 2025 Aug 6;24(3):366-386. doi: 10.2463/mrms.rev.2025-0036.
6. Thangappah RB, Karnal CS, Ravichandran MR, Sowparnika AS, Sundaravadivelu P. Clinical significance of umbilical cord abnormalities: an observational study. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2022;11(6):1727-34.
7. Beke A, Simonyi A. Association of neonatal and fetal malformations with polyhydramnios and oligohydramnios - introduction of a new "association factor". BMC Pregnancy Childbirth. 2025 Jul 3;25(1):707. doi: 10.1186/s12884-025-07797-5.
8. Xizi Wu, Da Zhu, Xinwei Shi et al. Clinical analysis of prenatal stillbirth caused by umbilical cord torsion, 21 July 2025. https://doi.org/10.21203/rs.3.rs-6985153/v1
9. Ebbing C, Rasmussen S, Kessler J, Moster D. Association of placental and umbilical cord characteristics with cerebral palsy: national cohort study. Ultrasound Obstet Gynecol. 2023 Feb;61(2):224-230. doi: 10.1002/uog.26047.
10. Calcaterra V, Cena H, Pirazzi A, Sottotetti F, Cordaro E, Cavallo C, Milanta C, El Masri D, Conti MV, Vandoni M, Zuccotti G. From Pregnancy to Breastfeeding: The Role of Maternal Exercise in Preventing Childhood Obesity. Nutrients. 2025 Feb 12;17(4):660. doi: 10.3390/nu17040660.
11. Jasani B, Torgalkar R, Ye XY, Syed S, Shah PS. Association of Umbilical Cord Management Strategies With Outcomes of Preterm Infants: A Systematic Review and Network Meta-analysis. JAMA Pediatr. 2021 Apr 1;175(4):e210102. doi: 10.1001/jamapediatrics.2021.0102.
12. Shafqat T, Hussain SS, Rahim R. Length of umbilical cord and perinatal outcome. J Postgrad Med Inst 2020; 34(2): 115-8.
13. Krakowiak P, Smith EN, de Bruyn G, Lydon-Rochelle MT. Risk factors and outcomes associated with a short umbilical cord. Obstet Gynecol. 2004 Jan;103(1):119-27. doi: 10.1097/01.AOG.0000102706.84063.C7.
14. Olaya-C M, Vargas W, Martinez RA, Peñaloza IF, Sanchez M, Madariaga I, Aldana S, Bernal JE. Impact of umbilical cord length on fetal circulatory system by Doppler assessment. J Ultrasound. 2020 Dec;23(4):585-592. doi: 10.1007/s40477-020-00495-2.
15. Dias Z, Kore S. Length of the umbilical cord and perinatal outcomes: a study of 500 deliveries. Journal of OBGYN. 2023;9(2):228-32. DOI - 10.21276/obgyn.2023.9.2.7

16. Kalluru PKR, Kalluru HR, Allagadda TR, Talur M, Gonepogu MC, Gupta S. Abnormal umbilical cord coiling and association with pregnancy factors. J Turk Ger Gynecol Assoc. 2024 Mar 6;25(1):44-52. doi: 10.4274/jtgga.galenos.2023.2023-3-3.

17. Jan S, Qamar A, Javed MA, Zulfiqar S, Jamil S, Aziz M. Umbilical Cord Coiling Index as A Marker of Perinatal Outcome: Umbilical Cord Coiling Index for Perinatal Outcome. Pakistan Journal of Health Sciences. 2024:209-14. https://doi.org/10.54393/pjhs.v5i11.2426

18. Akhtar, N., Ghayur, M. S., Bangash, A. G., Akhtar, Z., Ambreen Samad, & Riaz, S. (2024). Correlation Of Length Of Umbilical Cord With Fetomaternal Outcome In Term Pregnancies. Journal of Medical Sciences, 32(3), 276–280. https://doi.org/10.52764 /jms.24.32.3.13

19. Li TG, Guan CL, Wang J, Peng MJ. Comparative study of umbilical cord cross-sectional area in foetuses with isolated single umbilical artery and normal umbilical artery. J Obstet Gynaecol. 2022 Jul;42(5):935-940. doi: 10.1080/01443615 .2021.1962818.

20. Farsetti D, Barbieri M, Magni E, Zamagni G, Monasta L, Maso G, Vasapollo B, Pometti F, Ferrazzi EM, Lees C, Valensise H, Stampalija T. The role of umbilical vein blood flow assessment in the prediction of fetal growth velocity and adverse outcome: a prospective observational cohort study. Am J Obstet Gynecol. 2025 Jul;233(1):66.e1-66.e14. doi: 10.1016/j.ajog.2025.01.001.

21. Soysal C, fiiflman H‹, B›y›k ‹, Erten Ö, Delilo¤lu B, Geçkalan Soysal D, Keskin N. The relationship between umbilical cord measurements and newborn outcomes. Perinatal Journal 2021;29(3):225–230. doi:10.2399/prn.21.0293008

22. Tonni G, Lituania M, Cecchi A, Carboni E, Resta S, Bonasoni MP, et al., editors. Umbilical cord diseases affecting obstetric and perinatal outcomes. Healthcare; 2023, 11(19), 2634; https://doi.org/10.3390/healthcare11192634

23. Liang C, Xu Y. Analysis of factors associated with the umbilical cord pitch value by ultrasound measurement in late pregnancy. BMC Pregnancy and Childbirth. 2023;23(1):583. https://doi.org/10.1186/s12884-023-05894-x

24. Gomes De Melo Tavares Ferreira A. An Evaluation of the Physiological Variability Inherent in Common Maternal-fetal Doppler Parameters: UNSW Sydney; 2021.https://doi.org/10.26190/unsworks/23949

25. Singireddy N, Chugh A, Bal H, Jadhav S. Re-evaluation of umbilical cord coiling index in adverse pregnancy outcome–Does it have role in obstetric management? European Journal of Obstetrics & Gynecology and Reproductive Biology: X. 2024;21:100265. https://doi.org/10.1016 /j.eurox.2023 .100265

Original Article **Open Access**

Assessment of PDL-1 expression in Triple-negative breast cancer via immunohistochemistry

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ABSTRACT

Objective: To assess the frequency of PDL-1 positivity in triple-negative breast carcinoma (TNBC) and correlate it with the clinicopathological parameters.

Study Design and Setting: Cross-sectional study conducted at Histopathology Department of Rehman Medical Institute, Peshawar.

Methodology: The study period was from September 2023 to October 2024. Biopsy specimen of 41 female patients diagnosed with TNBC were received in the Histopathology department. Specimens underwent eosin/hematoxylin staining and immunohistochemistry analysis. Demographic and histopathological parameters were recorded and analyzed using SPSS version 23.

Results: Mean age was 54.58(6.14) years, and the most common type of TNBC was invasive breast carcinoma of no special type in 23(56.1%). Out of 41 specimens, we observed that stage N2 and stage T3 were the most prevalent as observed in 18(43.9%) and 19(46.3%) specimens respectively. Frequency of PDL-1 positivity was observed in 16(39.02%) with a trend towards higher PDL-1 positivity observed in invasive ductal carcinoma of no special type and tumors exhibiting size of >20mm. Lymphovascular invasion was seen in 17 (41.46%) out of which 09 (56.3%) were PDL-1 positive. Tumor-infiltrating lymphocytes of the moderate category were significantly associated with PDL-1 positivity with a p-value of 0.024.

Conclusion: PDL-1 expression is observed in a substantial number (39.02%) of TNBC patients. Our research concludes an important association between PDL-1 expression and tumor-infiltrating lymphocytes in TNBC which enlightens new avenues for immunotherapy. This association may have profound implications in the future for prompt diagnosis and targeted treatment.

Keywords: Breast carcinoma, Lymphocytes, Triple-negative breast neoplasms

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INTRODUCTION

Breast cancer is one of the evolving pathologies with an increase of around 5% yearly leading to an increased burden on healthcare system. Prevalence of triple-negative breast carcinoma (TNBC) is around 15% with a recorded 5-year survival of 8% to 16%. Expression of different receptors is a hallmark of various types of breast cancers. However, TNBC is a distinct type of breast cancer that does not express receptors like estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor (Her2). Breast cancer is sub classified into four molecular types based on genetic profiling. The four subtypes are Luminal Type A and Type B, Her 2- Enriched subtype and Triple Negative breast cancer (TNBC). Each subtype has its own well established morphological, genetic and prognostic characteristics. Immunohistochemical markers for Estrogen receptor ER, Progesterone receptor PR and Human Epidermal Growth Factor Recepter 2, i.e. Her2 are employed as substitute for determining the class of breast cancer and the use of these markers have been well established in clinical practice. These markers also stratify the breast cancer patients for viable therapeutic options based on presence or absence

of each marker. These treatments include Anti endocrine therapy and Anti- Her 2 agents for the Luminal category and Her2 enriched breast cancers respectively. Triple Negative Breast Cancer is characterized by the immunohistochemical absence of ER, PR and Her2 receptors. Genetically, the TNBC is characterized by a basal like profile, with a signature resembling the normally found basal myoepithelial cells of the breast ductal elements. They are shown to express high levels of Cytokeratin 5/6. The histological spectrum of TNBC is varied and includes Invasive mammary carcinoma of no special type, medullary carcinoma, metaplastic carcinoma and also some low grade tumors of salivary gland phenotype that occur in the breast namely, adenoid cystic carcinoma and secretory carcinoma. The tumors of salivary gland phenotype are distinct from the basal like tumors and carry their own signature molecular profiles. Due to a distinct nature of TNBC and the increased ability of cancerous cells to mutate, the prognosis of TNBC is not very predictable. Based on immunohistochemical analysis, breast cancers are divided into certain types of which TNBC belongs to the basal type which is due to a mutation of the breast cancer gene (BRCA) 1 gene. Due to the intrinsic nature of TNBC with absent expression of ER, PR, and HER2, treatment options against the cancerous cells are limited and conventional therapies for breast cancer that target the said receptors become ineffectual. Furthermore, natural outcome of this cancer type is dismal and is characterized by aggressive course, with increased chance of recurrences and less than ideal response to chemotherapy. Therefore, early detection of TNBC may be helpful for timely intervention. Diagnostic advancements in the field of medical science have enabled healthcare workers to use radiographic modalities or immunohistochemistry for detecting cancers. Radiographic investigations of cancers have the risk of radiation and may result in false positive or false negative results. Immunohistochemistry (IHC) is a more promising technique that helps in analyzing the histological characteristics of the tumors and detection of tumor markers which may help in prognostication of the cancerous cells.

The available treatment options include cisplatin based chemotherapy amongst others, but the prognosis and outcome has remained dismal for TNBC patients. Immense breast cancer research has become focused on exploring more treatment options that can improve survival. In the world of oncology, a lot of interest has been established in the niche of Immunotherapy. It essentially involves the enhancement of body's own immune system to overcome and destroy the cancer cells. Programmed death ligand 1 (PDL1) is a protein expressed in cancerous cells that binds to programmed death protein PD1 and protects the cancerous cells from the destruction by T-cells.[7] The discovery of the interaction between PDL1 and PD1 leading to antitumor activity has led to evolutionary immunotherapies that aim to inhibit these interactions. T lymphocytes are a key arm of our immune system that is directly involved in anti-tumor activity. PD1 is protein receptor that is expressed on the cell membrane of T lymphocytes. This receptor allows the T lymphocytes to recognize and participate in the destruction of cancer cells. In contrast, Programmed Death Ligand 1, PDL-1, is a protein expressed on tumor cells that binds the PD1 on T cells, essentially blocking its effects of anti-tumor activity. Thus, the cancer cells can bypass this immune checkpoint and escape recognition and destruction by the immune system. Tumors have been shown to harness this pathway and overexpress PDL-1 on their cell surfaces to escape the immune system. This tumor-Immune system interaction pathway has led to the discovery and development of Immunotherapy agents that target PDL-1 called Immune Checkpoint Inhibitors. These Anti-PDL-1 agents block the PDL-1 receptors on the tumors cells, allowing the T cells to recognized and destroy the cancer. A considerable number of studies have been underway to determine the PDL-1 expression in various tumors in order to determine their suitability for Immunotherapy, especially the tumors that haven't performed well under current available treatment regimes. Determining the PDL-1 status of tumor cells has been an object of many studies. PDL-1 Immunohistochemical marker has emerged as a proven surrogate to determine its expression. Several studies have been conducted to evaluate the expression of growth factors in TNBC. However, there exists a gap in research when assessing the relation of PDL1 expression and its association with clinicopathological parameters in TNBC. This research aims to assess PDL1 expression in TNBC and its association with clinicopathological parameters. In the future, our research may prove helpful in predicting if the patients with TNBC will likely benefit from PDL1-directed immunotherapies. Research on PDL1 in TNBC may pave the way to further research for combination immunotherapies, progression of disease, and recurrence of disease.

METHODOLOGY

After obtaining approval from the local ethical committee of hospital, the cross-sectional study was conducted at Rehman Medical Institute, Peshawar under ERC # RMI-REC/Ethical Approvals/CPSP Synopsis/43 dated 06 Sep 2024 from 10 September 2023 through 10 October 2024.

Using a World Health Organization (WHO) sample size calculator a sample size of n=41 was calculated with an estimated prevalence of 12% TNBC when the power of study was 95% with a 10% level of significance. Sampling was conducted using non-probability convenient technique.

An informed consent was obtained from the participants and biopsy specimens of female patients of any age diagnosed with triple-negative breast carcinoma were included in the trial. Histotypes of TNBC included invasive ductal carcinoma, medullary carcinoma and metaplastic carcinoma. This distinction was made to uniformize the differences in

prognosis of various histological subtypes of TNBC such as those of salivary gland phenotype. Patients were excluded if male, inadequate biopsy specimen or diagnosed with low-grade TNBC.

We included 41 specimens of biopsy-proven TNBC in our study which were assessed by two different classified pathologists for confirmation of diagnosis. Employing the protocol of our laboratory eosin and hematoxylin staining was performed. The size of the tumor, type of tumor, N-stage, T-stage, lymphovascular invasion, and tumor-infiltrating lymphocytes were assessed on the histological exam and recorded. This was followed by application of PDL-1 immunohistochemical marker after Heat Induced epitope retrieval of the antigen. The PDL-1 antibody clone utilized was Rabbit Monoclonal Primary Antibody PDL-1 (28–8) manufactured by Cell Marque. Immunohistochemistry analysis was done using lymph nodes as controls. Employing a combined positive score (CPS) PDL1 expression was assessed. Using the formula of the number of PDL1 staining cells divided by the total number of viable tumor cells multiplied by 100 was used. Tumors exhibiting a CPS score of = 10 were recorded as PDL1 positive while tumors with a CPS score of < 10 were recorded as PDL1 negative. Figure-II shows membranous staining in invasive carcinoma (CPS > 10**).** A predesigned proforma was used for recording the variables.

We used Statistical Package for Social Sciences (SPSS) version 23 for data analysis. Quantitative variables like age were computed using mean and standard deviation while frequencies and percentages were computed for qualitative variables like metastasis, N-Staging, T stage, lymphovascular invasion, tumor-infiltrating lymphocytes, recurrent Tumors. For analysis of significance, a chi-square test was used for categorical variables and a p-value of = 0.05 was taken as significant.

RESULTS

We included 41 female patients in our study with a mean age of 54.58 (6.14) years and the most common type of TNBC was invasive breast carcinoma of no special type in 23 (56.1%). Figure-I shows invasive breast carcinoma of no special type with high grade features. Out of 41 specimens, 18 (43.9%) had N2 stage on immunohistochemistry while a majority of T3 stage was seen in 19 (46.3%) specimens. We observed a low frequency of tumors with metastases in 02 (4.9%) while 03 (7.3%) had recurrent tumors. Demographic and baseline characteristics are shown in Table-1. When CPS >10 was considered as PDL1 positive the frequency of PDL1 positivity was observed in 16/41 (39.02%). We concluded that invasive ductal carcinoma of no special type and tumors with size > 20mm exhibited higher PDL1 positivity without establishing a significant

Table–1: Demographic and baseline characteristics (n=41)

Variables		Results
Age in years Mean (S.D)		54.58(6.14)
Tumor size n (%)	**<20mm**	11 (26.8%)
	>20mm	30 (73.2%)
Type of tumor n(%)	**Invasive breast carcinoma no special type**	23 (56.1%)
	Invasive carcinoma with medullary features	13 (31.7%)
	Metaplastic carcinoma	05 (12.2%)
Metastasis n (%)	**Yes**	02 (4.9%)
	No	39 (95.1%)
N-Stage n (%)	**N0**	03 (7.3%)
	N1	16 (39%)
	N2	18 (43.9%)
	N3	04 (9.8%)
T stage n (%)	**T1**	02(4.9%)
	T2	16(39%)
	T3	19(46.3%)
	T4	04(9.8%)
Lymphovascular invasion n (%)	**Present**	17 (41.5%)
	Absent	24 (58.5%)
Tumor-infiltrating lymphocytes n (%)	**Low**	18 (43.9%)
	Moderate	19 (46.3%)
	Marked	04 (9.8%)
Recurrent tumor n (%)	**Yes**	03 (7.3%)
	No	38 (92.7%)

Table–2: Clinicopathological characteristic of PDL1 positive and PDL1 negative TNBC (n=41)

Parameters		PDL1 positive (n=16)	PDL1 Negative (n=25)	p-value using chi square test
Tumor size in mm N (%)	**<20mm**	06 (37.5%)	05 (20%)	0.217
	>20mm	10 (62.5%)	20 (80%)	
Type of tumor n (%)	**Invasive breast carcinoma of no special type**	11 (68.8%)	12 (48%)	0.390
	Invasive carcinoma with medullary features	04 (25%)	09 (36%)	
	Metaplastic carcinoma	01 (6.3%)	04 (16%)	
Metastasis n (%)	**Yes**	01(6.3%)	01 (4%)	0.744
	No	15 (93.8%)	24 (96%)	
n stage n (%)	**N0**	03 (18.8%)	0	0.136
	N1	05 (31.3%)	11 (44%)	
	N2	06 (37.5%)	12 (48%)	
	N3	02 (12.5%)	02 (8%)	
T stage n (%)	**T1**	02 (12.5%)	0	0.086
	T2	06 (37.5%)	10 (40%)	
	T3	05 (31.3%)	14 (56%)	
	T4	03 (18.8%)	01 (4%)	
Lymphovascular invasion n (%)	**Present**	09 (56.3%)	08 (32%)	0.124
	Absent	07 (43.8%)	17 (68%)	
Tumor-infiltrating lymphocytes n (%)	**Low**	03 (18.8%)	15 (60%)	0.024
	Moderate	10 (62.5%)	09 (36%)	
	Marked	03 (18.8%)	01 (4%)	
Recurrent tumors n (%)	**Yes**	01 (6.3%)	02 (8%)	0.834
	No	15 (93.8%)	23 (92%)	

Figure-I: Invasive breast carcinoma of no special type with high grade features

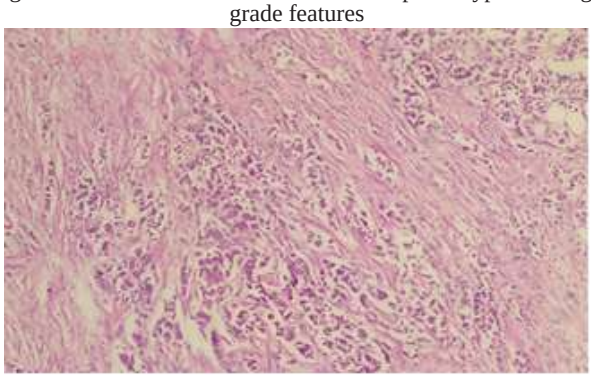
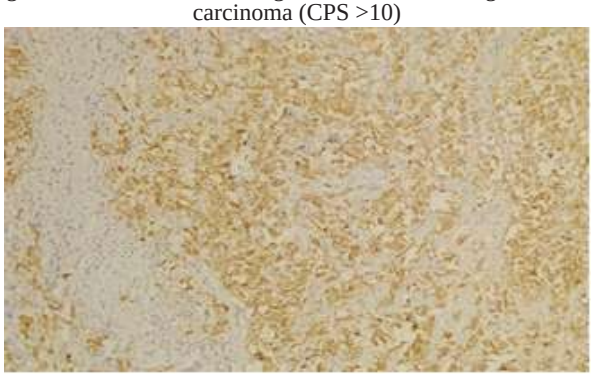


Figure-II: PDL-1 IHC showing membranous staining in invasive carcinoma (CPS >10)



association. Tumors exhibiting N2 stage represented the majority of the specimens 18/ 42 (42.86%) of which 12/18(48%) were PDL1 negative. Tumors with T3 stage on histological exam were observed in 19 (46.3%) specimens (p-0.086). Lymphovascular invasion was seen in 17 (41.46%) out of which 09 (56.3%) were PDL1 positive (p-0.124). Tumor-infiltrating lymphocytes of the moderate category were observed in 17(46.34%) specimens out of which 10 (62.5%) were PDL1 positive with a p-value of 0.024. The association of PDL-1 and clinico-pathological variables is shown in Table-2.

DISCUSSION

The cross-sectional study was conducted to assess PDL1 expression in TNBC and its association with clinicopathological parameters. We concluded that the mean age of patients diagnosed with TNBC was 54.58 (6.14) years and the most common type of TNBC was invasive ductal carcinoma of no special type in 23(56.1%). A similar cross-sectional study revealed that the median age of patients with TNBC was 47 (28-65) years. In comparison to our study, in which the PDL1 positivity was seen in 16 (39%) specimens, another study concluded that the frequency of PDL1 positivity was 29%.[8] In a similar study the mean age of patients with TNBC was found to be 53.23 (8.21) years which was close to the mean age observed in our study. We observed that PDL1 positivity was higher in frequency 10

(62.5%) for tumors with a size greater than 20 mm as compared to 06 (37.5%) tumors with a size less than 20mm however it did not reach a significant level. A similar study done by Doðukan R *et al* revealed that the mean size of TNBC tumor was 4.2(3.3cm) and the most common type of TNBC was invasive breast carcinoma of no special type observed in 42 (68.9%) of the patients with TNBC. Association of PDL1 positivity and clinico-pathological parameters revealed that there was no significant relationship between PDL1 positivity and the N-stage of the tumor. Most of the tumors were found to have N2 stage on immunohistochemistry observed in 18 out of 41(43.9%) biopsy specimens. Similarly, no significant association was observed between the T-stage of the tumor and PDL1 positivity. Similar results in concordance with our findings were observed by Al-Jussani who found no significant association between PDL1 and clinicopathological variables. Our results showed only 2 out of 41 (4.8%) tumors having evidence of metastasis without any significant association with PDL1 positivity. However, in contrast another cross-sectional study revealed that PDL1 positivity was higher in breast tumors with evidence of metastasis as compared to non-metastatic breast tumors. This may imply that in breast tumors not specifically TNBC metastasis may be predicted by PDL1 overexpression. We observed that lymphovascular invasion was seen in 17 (41.5%) specimens with 09 (56.3%) PDL1 positive and 08 (32%) PDL1 negative tumors (p-0.124). A similar study revealed that the frequency of lymphovascular invasion observed in TNBC was 74.2% without any significant association with PDL1 positivity.

Immunohistochemistry of 41 specimens revealed that moderate levels of tumor-infiltrating lymphocytes (TILs) represented most tumors i.e. 19 out of 41 specimens out of which 10 (62.5%) were PDL1 positive with a p-value of 0.024. Tumor infiltrating lymphocytes imply the body's protective response. They comprise of a varied population of immune cells, predominantly including Lymphocytes, which infiltrate the stroma associated with tumor or the tumor cells directly. TILs can be regarded as an indicator of host immune surveillance and its ability to mount an immune response against the tumor. Observations have been made about tumors which show abundant immune cell infiltration may be more immunogenic and as a result may be more amenable to Immunotherapeutic agents. In many studies, higher levels of tumor infiltrating lymphocytes in Triple negative breast cancer has been associated with better clinical outcomes including better overall survival. It has also been proven as an independent factor in regard to prognostication. The relationship between tumor infiltrating lymphocytes and PDL-1 is complex and multi – directional. The lymphocytes in tumor microenvironment release various cytokines including Interferon Gamma to enhance the anti-tumor activity. These cytokines in turn cause a reactionary enhanced expression of PDL-1 by the tumor cells in order to evade that destructive immune activity and build immune resistance. Conversely, tumors with intrinsically high expression of PDL-1 receptors inherently sustain greater levels of tumor immune cells, giving rise to a immune – inflamed phenotype. This intricate interplay between TILs, Tumor microenvironment and PDL-1 on tumor cells helps explain why tumors with high PDL-1 expression have increased density of TILs and this Immune – hot environment of the tumor can be the ideal target for various Anti-immune therapeutic agents including Anti-PDL-1 agents. We could not continue to assess the overall survival. However, a similar study on TNBC revealed that the presence of infiltrating lymphocytes in the tumor was significantly correlated with improved overall survival in patients with TNBC. TILs signified the host protective environment against the tumor and tumors exhibiting high TILs resulted in significantly higher disease-free survival and overall survival. In another research when TILs were categorized into low and high, the percentage of TNBC exhibiting low TIL count was 78.01% as compared to 21.9% of tumors exhibiting higher numbers of TILs. Expression of PDL1 with TIL was significantly correlated with a p-value of < 0.001.

We could not record and follow up the patients for a longer period of time to assess the prognosis and response to treatment in our patients. With a relatively small sample size and participants included from a single hospital may lead to unreliable prediction about TNBC in people of different regions. Since we have not recorded the mortality, therefore a general statement about the survival rate in different age groups was not possible. Additionally, PDL-1 expression is known to be heterogeneous within a tumor and tissue sampling may not be entirely representative of tumor microenvironment. These limitations emphasize the necessity of developing standardized protocols and further studies should be underway utilizing complementary molecular techniques for a more accurate assessment of the role of PDL-1 and its interaction with tumor microenvironment.

In the arena of breast carcinoma, tumor-infiltrating lymphocytes and PDL-1 play a significant role in the prognostication of the tumor. It can be used as an indicator to guide immunotherapies. Previous research indicates that assessment of PDL-1 and TILs altogether may be beneficial in identifying tumor-rich environments. Novel therapies are emerging that may help target immune checkpoints and TILs plays a crucial role in immunity against the tumor. Hence our study reveals a significant association between TILs and PDL-1-positivity which may lead to delineating the treatment protocol of TNBC, leading to better outcomes in the future.

CONCLUSION

PDL-1 expression is observed in a substantial number (39.02%) of TNBC patients. Our research concludes an important association between PDL-1 expression and tumor-

infiltrating lymphocytes in TNBC which enlightens new avenues for immunotherapy. This association may have profound implications in the future for prompt diagnosis and targeted treatment.

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REFERENCES

1. Giaquinto AN, Sung H, Miller KD, Kramer JL, Newman LA, Minihan A, et al. Breast Cancer Statistics, 2022. CA A Cancer J Clinicians. 2022 Nov;72(6):524–41.
2. Almansour NM. Triple-Negative Breast Cancer: A Brief Review About Epidemiology, Risk Factors, Signaling Pathways, Treatment and Role of Artificial Intelligence. Front Mol Biosci. 2022 Jan 25;9:836417.
3. ER/PR-negative, HER2-negative (triple-negative) breast cancer - UpToDate [Internet]. [cited 2025 Sep 6]. Available from: https://www.uptodate.com/contents/er-pr-negative-her2-negative-triple-negative-breast-cancer
4. Zagami P, Carey LA. Triple negative breast cancer: Pitfalls and progress. npj Breast Cancer. 2022 Aug 20;8(1):95.
5. Derakhshan F, Reis-Filho JS. Pathogenesis of Triple-Negative Breast Cancer. Annu Rev Pathol Mech Dis. 2022 Jan 24;17(1):181–204.
6. Bou Zerdan M, Ghorayeb T, Saliba F, Allam S, Bou Zerdan M, Yaghi M, et al. Triple Negative Breast Cancer: Updates on Classification and Treatment in 2021. Cancers. 2022 Feb 28;14(5):1253.
7. Cimino-Mathews A. Novel uses of immunohistochemistry in breast pathology: interpretation and pitfalls. Modern Pathology. 2021 Jan;34:62–77.
8. Kumar S, Bal A, Das A, Bhattacharyya S, Laroiya I, Khare S, et al. Molecular Subtyping of Triple Negative Breast Cancer by Surrogate Immunohistochemistry Markers. Applied Immunohistochemistry & Molecular Morphology. 2021 Apr;29(4):251–7.
9. Nakhjavani M, Shigdar S. Future of PD-1/PD-L1 axis modulation for the treatment of triple-negative breast cancer. Pharmacological Research. 2022 Jan;175:106019.
10. Chen X, Feng L, Huang Y, Wu Y, Xie N. Mechanisms and Strategies to Overcome PD-1/PD-L1 Blockade Resistance in Triple-Negative Breast Cancer. Cancers. 2022 Dec 23;15(1):104.
11. Kornepati AVR, Vadlamudi RK, Curiel TJ. Programmed death ligand 1 signals in cancer cells. Nat Rev Cancer. 2022 Mar;22(3):174–89.
12. Howard FM, Olopade OI. Epidemiology of Triple-Negative Breast Cancer: A Review. Cancer J. 2021 Jan;27(1):8–16.
13. Ghosh J, Chatterjee M, Ganguly S, Datta A, Biswas B, Mukherjee G, et al. PDL1 expression and its correlation with outcomes in non-metastatic triple-negative breast cancer (TNBC). ecancer [Internet]. 2021 Apr 6 [cited 2025 Sep 6];15. Available from: https://ecancer.org/en/journal/article/1217-pdl1-expression-and-its-correlation-with-outcomes-in-non-metastatic-triple-negative-breast-cancer-tnbc
14. Uðurluoðlu C, Yormaz S. Clinicopathological and prognostic value of TIL and PD L1 in triple negative breast carcinomas. Pathology - Research and Practice. 2023 Oct;250:154828.
15. Department of Pathology, Mardin State Hospital, Mardin, Turkey, Dogukan R, Ucak R, Department of Pathology, University of Health Sciences, Sisli Hamidiye Etfal Training and Research Center, Istanbul, Turkey, Dogukan FM, Department of Pathology, Mardin State Hospital, Mardin, Turkey, et al. Correlation between the Expression of PD-L1 and Clinicopathological Parameters in Triple Negative Breast Cancer Patients. Eur J Breast Health. 2019 Oct 1;15(4):235–41.
16. Al-Jussani GN, Dabbagh TZ, Al-Rimawi D, Sughayer MA. Expression of PD-L1 using SP142 CDx in triple negative breast cancer. Annals of Diagnostic Pathology. 2021 Apr;51:151703.
17. Pranoto AS, Haryasena H, Prihantono P, Rahman S, Sampepajung D, Indra I, et al. The expression of programmed death-ligand 1 and its association with histopathological grade, stage of disease, and occurrence of metastasis in breast cancer. Usman AN, editor. BD. 2021 Jun 25;40(s1):S71–6.
18. Chu J, Yeo MK, Lee SH, Lee MY, Chae SW, Kim HS, et al. Clinicopathological and Prognostic Significance of Programmed Death Ligand-1 SP142 Expression in 132 Patients With Triple-negative Breast Cancer. In Vivo. 2022;36(6):2890–8.
19. AiErken N, Shi H juan, Zhou Y, Shao N, Zhang J, Shi Y, et al. High PD-L1 Expression Is Closely Associated With Tumor-Infiltrating Lymphocytes and Leads to Good Clinical Outcomes in Chinese Triple Negative Breast Cancer Patients. Int J Biol Sci. 2017;13(9):1172–9.
20. De Moraes FCA, Souza MEC, Sano VKT, Moraes RA, Melo AC. Association of tumor-infiltrating lymphocytes with clinical outcomes in patients with triple-negative breast cancer receiving neoadjuvant chemotherapy: a systematic review and meta-analysis. Clin Transl Oncol. 2024 Aug 18;27(3):974–87.
21. Ni Y, Tsang JY, Shao Y, Poon IK, Tam F, Shea KH, et al. Combining Analysis of Tumor-infiltrating Lymphocytes (TIL) and PD-L1 Refined the Prognostication of Breast Cancer Subtypes. The Oncologist. 2022 Apr 5;27(4):e313–27.
22. Loi S, Michiels S, Adams S, Loibl S, Budczies J, Denkert C, et al. The journey of tumor-infiltrating lymphocytes as a biomarker in breast cancer: clinical utility in an era of checkpoint inhibition. Annals of Oncology. 2021 Oct;32(10):1236–44.
23. Xie Y, Xie F, Zhang L, Zhou X, Huang J, Wang F, et al. Targeted Anti-Tumor Immunotherapy Using Tumor Infiltrating Cells. Advanced Science. 2021 Nov;8(22):2101672.

Original Article **Open Access**

Diagnostic Accuracy of Imprint Cytology in Determining Margin Positivity in Patients Undergoing Breast Conservation

Rizwana Khan, Sadaf Afridi, Warda Ali, Ishrat Alam, M. Furqan Ullah Babar, Mah Muneer Khan

ABSTRACT

Objectives: To determine the diagnostic accuracy of imprint cytology in identifying margin positivity in patients undergoing breast-conserving surgery for breast cancer, using histopathology as the gold standard.

Study Design and Setting: This cross-sectional validation study was conducted in the Department of Surgery at Khyber Teaching Hospital, Peshawar

Methodology: A total of 154 women aged 30–80 years diagnosed with malignant breast lumps and undergoing breast-conserving surgery were enrolled using non-probability convenience sampling. Imprint cytology was performed intraoperatively by pressing clean glass slides against the resected margins of the lumpectomy specimen. Slides were air-dried, stained with hematoxylin and eosin, and examined microscopically. Final margin status was determined by histopathological examination, which served as the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy of imprint cytology were calculated.

Results: The mean age of participants was 51.15 ± 11.87 years. Imprint cytology demonstrated a sensitivity of 40.8%, specificity of 78.3%, PPV of 61.7%, NPV of 60.7%, and overall diagnostic accuracy of 61.0% in detecting margin positivity. The chi-square test showed a statistically significant association between imprint cytology and histopathology findings ($p = 0.010$).

Conclusions: Imprint cytology provides a rapid and economical method for intraoperative margin assessment during breast-conserving surgery, particularly useful in resource-limited settings. However, its diagnostic reliability is operator-dependent and requires standardization for broader clinical application.

Keywords: Biopsy, Breast Conservation, Breast Neoplasms, Diagnostic Accuracy, Histopathology, Intraoperative Care, Lumpectomy

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INTRODUCTION

The human breast is a complex structure primarily composed of glandular tissue responsible for milk production.1 These milk-producing lobules are connected to the nipple via a branching ductal system. Alongside this secretory network, the breast contains a rich lymphatic system and abundant adipose and connective tissue that collectively support the organ's architecture and physiological functions. The cellular turnover in lobules and ducts is naturally high due to hormonal influences, but this turnover is usually tightly regulated. However, when this regulation is disrupted, uncontrolled cellular proliferation can occur, giving rise to neoplastic changes.[2]

Breast cancer is one of the most common malignancies affecting women globally, although it can also affect men.[3] It typically develops in a stepwise manner, beginning with hyperplasia or dysplasia, progressing to carcinoma in situ, and eventually transforming into invasive carcinoma. The most common presenting symptom is a painless lump in the breast, though patients may also report nipple discharge, changes in breast contour, or retraction of the nipple.[4] Clinical

examination often reveals a palpable mass, sometimes accompanied by skin dimpling or lymphadenopathy. Enlarged axillary lymph nodes may signify regional or distant metastasis.[5]

Early detection significantly improves the prognosis of breast cancer. This can be achieved through awareness campaigns promoting regular breast self-examinations and timely clinical assessments of any suspicious lesions. Imaging techniques such as mammography and ultrasound, alongside biopsy, are essential diagnostic tools.[6] However, the definitive treatment of breast cancer often requires surgical excision of the tumor.

Historically, mastectomy, the complete removal of the breast, was the standard surgical approach. However, in recent decades, the concept of breast-conserving surgery (BCS), including lumpectomy followed by radiotherapy, has gained momentum as an effective alternative for early-stage breast cancer.[7] This shift reflects a growing demand for preserving breast aesthetics and improving quality of life without compromising oncological safety.[8]

One of the critical challenges in breast-conserving surgery is ensuring complete tumor excision with negative surgical margins. The presence of cancer cells at the resected margin significantly increases the risk of local recurrence and may necessitate additional surgery.[9] Thus, intraoperative assessment of margin status is vital to reduce reoperation rates and enhance treatment outcomes. However, determining margin status during surgery can be technically difficult without reliable, rapid, and cost-effective diagnostic tools.

Imprint cytology has emerged as a promising technique for intraoperative margin assessment. The method involves pressing freshly excised tissue onto a glass slide to transfer cells, which are then stained and evaluated microscopically. This approach is less expensive, faster, and more straightforward compared to frozen section analysis, which is currently considered the gold standard. In a study evaluating imprint cytology, sensitivity and specificity were reported as 80.0% and 85.0%, respectively, with a high negative predictive value (NPV) of 97.0%.[10] These results indicate its potential utility in confirming clear margins during surgery, thereby minimizing the need for repeat procedures.

Another study involving 522 patients reported that imprint cytology identified 26.1% of patients as margin-positive and 73.9% as margin-negative.[11] However, imprint cytology was slightly less accurate than frozen section analysis, particularly in terms of false-positive rates, which were reported to be as high as 13.4%. Nevertheless, the false-negative rate was remarkably low at 0%. Moreover, when combined with frozen section analysis, the false-positive rate decreased significantly to 2.5%, suggesting that the integration of both techniques might offer a balanced approach in clinical practice.[12]

Despite its promising profile, imprint cytology is underutilized in many clinical settings, particularly in low-resource regions. One significant limitation in adopting imprint cytology more broadly is the variability in its diagnostic accuracy reported across different international studies. These differences may stem from variations in technique, interpretation, and patient demographics, thus limiting the generalizability of existing findings.

The rationale of this study stems from the observed gap in the literature regarding the diagnostic accuracy of imprint cytology for intraoperative margin assessment in breast-conserving surgeries, especially in local contexts where advanced pathology facilities may not be readily available. Understanding the reliability of imprint cytology in these settings is critical to optimizing surgical decision-making, improving patient outcomes, and reducing the need for secondary procedures. Therefore, this study aimed to determine the diagnostic accuracy of imprint cytology in identifying margin positivity in patients undergoing breast conservation surgery.

METHODOLOGY

This cross-sectional validation study was conducted at the Department of Surgery, Khyber Teaching Hospital, Peshawar, over a period of six months from 1st October 2024 to 31st March 2025. Before initiating the study, ethical clearance was obtained from the Institutional Research and Ethical Review Board (IREB) of Khyber Medical College, Peshawar, under approval number 714/DME/KMC, dated 19th September, 2024.

The sample size was calculated using a sensitivity and specificity-based formula, assuming an anticipated breast cancer prevalence of 40.0%, a sensitivity of imprint cytology at 80.0%, a specificity of 85.0%, a margin of error of 10%, and a 95% confidence level.[11] A total of 154 participants were included in the study.

Patients were recruited from the indoor surgical department using a non-probability convenient sampling technique. The study population included women aged between 30 and 80 years, diagnosed with malignant breast lumps and scheduled for breast-conserving surgery (lumpectomy). Women were excluded from the study if they had received neoadjuvant chemoradiotherapy, underwent intraoperative conversion to non-conservative surgery, had a recurrent breast lump, secondary lesions in the breast, or evidence of distant metastasis. The diagnosis of breast cancer was confirmed preoperatively through fine-needle aspiration cytology (FNAC) or core needle biopsy. Malignancy was identified based on cytological criteria, including increased nucleus-to-cytoplasm ratio, cellular atypia, hyperchromasia, and nuclear irregularities.

During surgery, imprint cytology was performed intraoperatively. Clean glass slides were gently pressed against the anticipated surgical margins of the excised lumpectomy specimen. The number of slides used was

determined by the operating surgeon. The slides were air-dried, stained with hematoxylin and eosin (H&E), and examined immediately by a consultant histopathologist under a light microscope. If malignant cells were seen on imprint cytology, the margin was labeled as positive; if no malignant cells were observed, the margin was considered negative. After margin clearance was confirmed, the lumpectomy specimen was sent to the hospital's pathology lab for histopathological examination, which served as the gold standard for determining margin status.

All participants provided written informed consent before inclusion in the study. Baseline demographic and clinical parameters were documented using a structured proforma. These included patient age (in years), body mass index (BMI in kg/m²), side of the affected breast, involved quadrant, lump size (in centimeters), duration of symptoms (in weeks), menopausal status (pre- or post-menopausal), and history of oral contraceptive pills (OCPs), hormone replacement therapy (HRT), and comorbidities such as diabetes mellitus and hypertension.

After surgery, the results of imprint cytology were compared with the histopathology findings of the surgical specimen to determine the diagnostic accuracy of imprint cytology in detecting margin positivity. The outcomes of interest included sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

All collected data were entered and analyzed using SPSS version 26. Descriptive statistics were applied to compute means and standard deviations for continuous variables and frequencies with percentages for categorical variables. Inferential statistics included the generation of 2×2 contingency tables to compare imprint cytology with histopathological results. Diagnostic accuracy metrics such as sensitivity, specificity, PPV, and NPV were calculated accordingly. In addition, effect modifiers such as age, menopausal status, lump size, and presence of comorbidities were controlled through stratification, and post-stratification analyses were conducted to assess their impact on diagnostic performance.

RESULTS

The study included a total of 154 women with a mean age of 51.15 ± 11.87 years. Most participants were above 50 years of age (51.3%), while 48.7% were aged 50 or below. The mean BMI was 23.83 ± 2.64 kg/m², with 51.9% of participants having a BMI of 24.0 or below. The average duration of symptoms was 6.16 ± 2.84 weeks, and the majority (63.0%) presented within six weeks of symptom onset. Post-menopausal women comprised 63.0% of the cohort, while 37.0% were pre-menopausal. In terms of parity, 53.2% were nulliparous and 46.8% were multiparous. Comorbid conditions were common; 27.9% of participants had diabetes mellitus, and 33.8% had hypertension. A positive family history of breast cancer was reported in 23.4% of the cases. Regarding hormonal factors, 22.1% of participants had a history of oral contraceptive pill (OCP) use, and 13.6% reported hormone replacement therapy (HRT) use. As for the side of involvement, 46.1% had lumps in the right breast, 45.5% in the left, and 8.4% had bilateral breast involvement. Hormone receptor status was positive in 53.9% of participants and negative in 46.1%. (Table 1) Among the 154 patients assessed, imprint cytology was positive for malignant cells in 46.1% of the cases, while 53.9% were negative. Histopathological examination, considered the gold standard, confirmed margin positivity in 30.5% of the specimens, whereas 69.5% were margin-negative. (Table 2)

By comparing imprint cytology with histopathology, the gold standard, revealed a sensitivity of 40.8% and a specificity of 78.3%. The positive predictive value (PPV) was calculated at 61.7%, while the negative predictive value (NPV) was 60.7%. The overall diagnostic accuracy of imprint cytology in detecting margin positivity was found to be 61.0%. The association between imprint cytology results and histopathological findings was statistically significant, as indicated by a chi-square test with a p-value of 0.010.

The stratified analysis revealed notable variability in the diagnostic performance of imprint cytology across different clinical and demographic subgroups. Age-wise, diagnostic accuracy was relatively better in women aged over 50 years compared to those 50 or younger, indicating age-related tissue and cellular changes may influence interpretation. Participants with a BMI =24.0 exhibited higher sensitivity and predictive values, suggesting leaner patients may offer better-quality specimens for cytological evaluation. In terms of menopausal status, pre-menopausal women showed higher specificity and positive predictive values compared to post-menopausal women, which may reflect hormonal influences on tissue morphology. Nulliparous women demonstrated slightly better diagnostic accuracy than multiparous women. Lateralization of the lesion also influenced results, with right-sided tumors yielding higher specificity and PPV compared to left or bilateral lesions, while imprint cytology performed poorest in bilateral cases.

Patients without a history of oral contraceptive or hormone replacement therapy showed notably higher specificity and PPV, suggesting less hormonal influence on cellular features that could mimic atypia. Additionally, better performance was observed in hormone receptor-positive tumors compared to receptor-negative ones, likely due to more distinct cytological features in these cases. Overall, imprint cytology demonstrated variable sensitivity and specificity depending on patient and tumor characteristics, emphasizing the need to consider individual clinical profiles when interpreting intraoperative cytology results. This stratified analysis highlights the importance of tailored clinical application and further supports the need for standardization and expertise in utilizing imprint cytology effectively. (Table 4)

DISCUSSION

In the present study, the mean age of participants was 51.15 ± 11.87 years, with the majority being older than 50 years. This age distribution reflects the global epidemiological trend where breast cancer risk significantly increases after the fourth decade of life, which also serves as a rationale for the initiation of breast cancer screening protocols in most countries. Our findings are comparable to those reported by Yadav et al., who documented a mean age of 48.1 ± 10.6 years, with most participants in their sixth decade.[13] Similarly, Ashraf et al. reported that 63.3% of their patients were above the age of 50 years, and Hashmi et al. observed a mean age of 53.4 ± 12.4 years.[14, 15] These findings reinforce the well-established association between advancing age and the incidence of breast cancer. However, in contrast to our results, a study by Vinod K et al. reported a younger cohort, with most participants between 40 and 50 years of age.[16] This discrepancy could be attributed to differences in selection criteria and regional patient demographics.

Regarding body mass index (BMI), approximately half of the participants in our study had values exceeding the healthy range. Ashraf et al. similarly reported a mean BMI of 25.75 kg/m² among breast cancer patients.[14] In a broader epidemiological study by Lofterod et al., 30.7% of patients with breast cancer were found to be living sedentary lifestyles, and 34.3% were overweight or obese.[17] Obesity is a well-recognized modifiable risk factor for breast cancer, especially in post-menopausal women, and is believed to increase breast cancer risk by approximately 1.33 times.[18] Nonetheless, the relationship between elevated BMI and breast cancer risk is complex and can be influenced by various factors including menopausal status, hormone levels, and genetic predisposition.

The majority of our study population was post-menopausal, consistent with global trends. A study conducted in India found that 52.0% of breast cancer patients were post-menopausal.[19] The higher prevalence of breast cancer in post-menopausal women is thought to be related to hormonal imbalances, prolonged estrogen exposure, and age-related cellular changes.[10]

When evaluating the diagnostic accuracy of imprint cytology for intraoperative margin assessment, we observed a sensitivity of 40.8%, specificity of 78.3%, positive predictive value (PPV) of 61.7%, and negative predictive value (NPV) of 60.7%. The overall accuracy was 61.0%. These values suggest moderate diagnostic utility, with relatively better performance in ruling out margin positivity than confirming it. Comparatively, Vinod et al. reported significantly higher sensitivity and specificity of 91.6% and 100.0%, respectively.[16] Yadav et al., in their study focusing on sentinel lymph node evaluation, also reported high diagnostic values with 87.5% sensitivity and 100.0% specificity.[13] In contrast, our results are more aligned with those reported by Ahuja

Table 1. Descriptive Statistics and Baseline Sociodemographic and Clinical Parameters of the Study Cohort (n = 154)

Parameter	Category	n (%) / Mean ± SD
Age (years)	—	51.15 ± 11.87
	= 50	75 (48.7%)
	> 50	79 (51.3%)
BMI (kg/m²)	—	23.83 ± 2.64
	= 24.0	80 (51.9%)
	> 24.0	74 (48.1%)
Duration of Symptoms (weeks)	—	6.16 ± 2.84
	= 6	97 (63.0%)
	> 6	57 (37.0%)
Menopausal Status	Pre-menopausal	57 (37.0%)
	Post-menopausal	97 (63.0%)
Parity	Nulliparous	82 (53.2%)
	Multiparous	72 (46.8%)
Diabetes Mellitus (DM)	Yes	43 (27.9%)
	No	111 (72.1%)
Hypertension (HTN)	Yes	52 (33.8%)
	No	102 (66.2%)
Family History of Breast Cancer	Positive	36 (23.4%)
	Negative	118 (76.6%)
OCP Use	Yes	34 (22.1%)
	No	120 (77.9%)
HRT Use	Yes	21 (13.6%)
	No	133 (86.4%)
Laterality of Lump	Right	71 (46.1%)
	Left	70 (45.5%)
	Bilateral	13 (8.4%)
Hormone Receptor Status	Positive	83 (53.9%)
	Negative	71 (46.1%)

Table 2. Imprint Cytology and Histopathology Findings of the Study Cohort (n = 154)

Outcome Variable	Category	n (%)
Imprint Cytology	**Positive**	71 (46.1%)
	Negative	83 (53.9%)
Histopathology	**Positive**	47 (30.5%)
	Negative	107 (69.5%)

Table 3. Diagnostic Accuracy of Imprint Cytology Against Histopathology as Gold Standard (n = 154)

Histopathology	Imprint Positive	Imprint Negative	Total
Positive	29 (61.7%)	18 (38.3%)	47
Negative	42 (39.3%)	65 (60.7%)	107
Total	71 (46.1%)	83 (53.9%)	154

Diagnostic Accuracy Measures:
Sensitivity: 40.8%, Specificity: 78.3%
Positive Predictive Value (PPV): 61.7%
Negative Predictive Value (NPV): 60.7%
Overall Accuracy: 61.0%, Chi-square test: p = 0.010

Table 4. Stratified Analysis of Diagnostic Accuracy of Imprint Cytology by Clinical and Demographic Variables Using Histopathology as Gold Standard (n = 154)

				Imprint		Total	
				+ve	-ve		
Age (years)	**=50**	**H/P**	+ve	13 (68.4%)	6 (31.6%)	19 (100%)	Sen = 35.1%, Sp = 84.2%,
			-ve	24 (42.9%)	32 (57.1%)	56 (100%)	PPV= 68.4%, NPV= 57.1%
	>50	**H/P**	+ve	16 (57.1%)	12 (42.9%)	28 (100%)	Sen = 47.0%, Sp = 73.3%,
			-ve	18 (35.3%)	33 (64.7%)	51 (100%)	PPV= 57.1%, NPV= 64.7%
BMI (kg/m^2)	**=24.0**	**H/P**	+ve	20 (69.0%)	9 (31.0%)	29 (100%)	Sen = 48.7%, Sp = 76.9%,
			-ve	21 (41.2%)	30 (58.8%)	51 (100%)	PPV= 68.9%, NPV= 58.8%
	>24.0	**H/P**	+ve	9 (50.0%)	9 (50.0%)	18 (100%)	Sen = 30.0%, Sp = 79.5%,
			-ve	21 (37.5%)	35 (62.5%)	56 (100%)	PPV= 50.0%, NPV= 62.5%
Meno-pause	**Pre**	**H/P**	+ve	10 (76.9%)	3 (23.1%)	13 (100%)	Sen = 40.0%, Sp = 90.6%,
			-ve	15 (34.1%)	29 (65.9%)	44 (100%)	PPV= 76.9%, NPV= 65.9%
	Post	**H/P**	+ve	19 (55.9%)	15 (44.1%)	34 (100%)	Sen = 41.3%, Sp = 70.5%,
			-ve	27 (42.9%)	36 (57.1%)	63 (100%)	PPV= 55.8%, NPV= 57.1%
Parity	**Nulli**	**H/P**	+ve	17 (65.4%)	9 (34.6%)	26 (100%)	Sen = 44.7%, Sp = 79.5%,
			-ve	21 (37.5%)	35 (62.5%)	56 (100%)	PPV= 65.3%, NPV= 62.5%
	Multi	**H/P**	+ve	12 (57.1%)	9 (42.9%)	21 (100%)	Sen = 36.6%, Sp = 76.9%,
			-ve	21 (41.2%)	30 (58.8%)	51 (100%)	PPV= 57.1%, NPV= 58.8%
Laterality	**Right**	**H/P**	+ve	16 (72.7%)	6 (27.3%)	22 (100%)	Sen = 40.0%, Sp = 80.6%,
			-ve	24 (49.0%)	25(51.0%)	49 (100%)	PPV= 72.2%, NPV= 51.0%
	Left	**H/P**	+ve	13 (59.1%)	9 (40.9%)	22 (100%)	Sen = 46.4%, Sp = 78.5%,
			-ve	15 (31.3%)	33 (68.8%)	48 (100%)	PPV= 59.0%, NPV= 68.7%
	Bilateral	**H/P**	+ve	0 (0.0%)	3 (100.0%)	3 (100%)	Sen = 0.0%, Sp = 70.0%,
			-ve	3 (30.0%)	7 (70.0%)	10 (100%)	PPV= 0.0%, NPV= 70.0%
OCPs	**Yes**	**H/P**	+ve	7 (43.8%)	9 (56.35)	16 (100%)	Sen = 53.8%, Sp = 57.1%,
			-ve	6 (33.3%)	12 (66.7%)	18 (100%)	PPV= 43.7% , NPV= 66.7%
	No	**H/P**	+ve	22 (71.0%)	9 (29.0%)	31 (100%)	Sen = 37.9%, Sp = 85.4%,
			-ve	36 (40.0%)	53 (59.6%)	89 (100%)	PPV= 70.9%, NPV= 59.5%
HRT	**Yes**	**H/P**	+ve	3 (25.0%)	9 (75.0%)	12 (100%)	Sen = 50.0%, Sp = 40.0%,
			-ve	3 (33.3%)	6 (66.7%)	9 (100%)	PPV= 25.0%, NPV= 66.7%
	No	**H/P**	+ve	26 (74.3%)	9 (25.7%)	35 (100%)	Sen = 40.0%, Sp = 86.7%,
			-ve	39 (39.8%)	59 (60.2%)	98 (100%)	PPV= 74.2%, NPV= 60.2%
Receptors	**+ve**	**H/P**	+ve	16 (72.7%)	6 (27.3%)	22 (100%)	Sen = 37.2%, Sp = 85.0%,
			-ve	27 (44.3%)	34 (55.7%)	61 (100%)	PPV= 72.7%, NPV= 55.7%
	-ve	**H/P**	+ve	13 (52.0%)	12 (48.0%)	25 (100%)	Sen = 46.4%, Sp = 72.0%,
			-ve	15 (32.6%)	31 (67.4%)	46 (100%)	PPV= 52.0%, NPV= 67.3%

et al., who observed a sensitivity of 45.3% and specificity of 60.0%.[10] Similarly, Nikhat AF also reported findings close to our study, highlighting the variable diagnostic performance of imprint cytology in different settings.[19] Maloney et al. reported higher accuracy metrics, with a sensitivity of 72.0% and specificity of 97.0%, which again underscores the variability depending on technique, operator expertise, and patient characteristics.[20]

One of the key advantages of imprint cytology lies in its rapid turnaround time and ease of use during surgery, making it a practical intraoperative tool. However, its effectiveness is highly operator-dependent, and accurate interpretation requires substantial expertise in differentiating atypical from malignant cells. Errors may arise due to cautery artefacts, poor staining, suboptimal drying, or sampling from necrotic or fibrotic areas. These technical limitations can affect the reliability of results and partially explain the relatively lower diagnostic accuracy observed in our study.

The application of imprint cytology is not restricted to breast cancer surgery. Tambane et al. demonstrated its utility in assessing surgical margins in cancers of the skin, oral cavity, and colon, reporting a combined sensitivity and specificity

of 46.15% and 86.6%, respectively.[21] Furthermore, Hashmi et al. evaluated imprint cytology for axillary lymph node metastases in breast cancer and reported an accuracy of 83.7%, which, although lower than that of frozen section analysis, was still acceptable in resource-limited settings.[15] However, when it came to the detection of micrometastasis and macrometastasis, cytology was found to be less reliable.

In short, while imprint cytology provides a practical and cost-effective option for intraoperative margin assessment in breast-conserving surgery, its diagnostic accuracy can be influenced by several technical and biological factors. It may serve as a useful adjunct in settings where frozen section is not feasible, but caution should be exercised when interpreting borderline or ambiguous findings. Further training of personnel, standardization of procedures, and integration with other diagnostic modalities may help enhance its clinical utility.

The findings of this study hold important clinical relevance, particularly in low-resource settings where access to intraoperative frozen section analysis is limited. Imprint cytology presents as a cost-effective, rapid, and simple method for evaluating surgical margins during breast-conserving surgery. Its real-time applicability allows surgeons to make immediate intraoperative decisions about margin re-excision, potentially reducing the need for second surgeries and minimizing psychological and physical burden on patients. While the sensitivity observed in this study was relatively low, the moderate specificity and acceptable negative predictive value suggest that imprint cytology may be useful in ruling out margin positivity in selected cases. In addition, the procedure does not require specialized cryostat equipment, making it ideal for routine surgical practice in secondary care hospitals and peripheral institutions. When used by trained cytopathologists, and in conjunction with preoperative imaging and clinical assessment, imprint cytology can serve as a valuable adjunct to surgical decision-making and improve oncologic outcomes in breast cancer care.

Despite its potential, this study had several limitations that must be acknowledged. First, the relatively low sensitivity of imprint cytology observed in our results may have been influenced by operator-dependent variability in sample collection, staining technique, and microscopic interpretation. The accuracy of imprint cytology is highly reliant on the cytopathologist's experience and may vary significantly across institutions. Second, artefacts introduced during cauterization and inadequate drying or staining of slides can impair cellular visualization and contribute to false negative or false positive results. Third, the study employed a non-probability sampling technique and was conducted at a single tertiary care center, which may limit the generalizability of the findings to broader populations. Additionally, the relatively small sample size and lack of comparison with frozen section or molecular methods may have impacted the comprehensive evaluation of imprint cytology's diagnostic performance. Finally, the study did not assess interobserver variability, which is an important consideration in cytological interpretation. Future multicenter studies with larger cohorts and standardized protocols are recommended to validate these findings and explore the integration of imprint cytology with other intraoperative diagnostic tools.

CONCLUSION

In conclusion, imprint cytology offers a practical, rapid, and economical intraoperative technique for margin assessment in breast-conserving surgery, especially in settings where frozen section is unavailable. Although the sensitivity observed in this study was modest, its reasonable specificity and negative predictive value highlight its potential role as a supportive diagnostic tool in guiding real-time surgical decisions. Its simplicity, cost-effectiveness, and adaptability to resource-constrained environments make it a valuable adjunct in the surgical management of breast cancer. However, the effectiveness of imprint cytology remains heavily dependent on operator expertise and standardized techniques. Integrating this method with clinical, radiological, and histopathological assessments may enhance its utility in reducing reoperation rates and improving patient outcomes. Further large-scale, multicenter studies are warranted to validate its diagnostic reliability and establish its role alongside existing intraoperative modalities.

Authors Contribution:
Rizwana: Introduction + Discussion, data collection+ conclusion
Sadaf Afridi: Data Collection + review article
Warda Ali: Data Collection + review article
Ishrat Alam: Data Collection + review article
M. Furqan Ullah Babar: Data Collection + data analysis
Mah Muneer Khan: review article and dissociation

REFERENCES

1. Biswas SK, Banerjee S, Baker GW, Kuo CY, Chowdhury I. The Mammary Gland: Basic Structure and Molecular Signaling during Development. Int J Mol Sci. 2022 Mar 31;23(7):3883. doi: 10.3390/ijms23073883. PMID: 35409243; PMCID: PMC8998991.
2. Natale G, Stouthandel MEJ, Van Hoof T, Bocci G. The Lymphatic System in Breast Cancer: Anatomical and Molecular Approaches. Medicina (Kaunas). 2021 Nov 19;57(11):1272. doi: 10.3390/medicina57111272. PMID: 34833492; PMCID: PMC8624129.
3. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. Br J Radiol. 2022 Feb 1;95(1130): 20211033. doi: 10.1259/bjr.20211033. Epub 2021 Dec 14. PMID: 34905391; PMCID: PMC8822551.
4. Shetty MK. Imaging of the Symptomatic Breast. Breast & Gynecological Diseases: Role of Imaging in the Management: Springer; 2021. p. 27-79. https://doi.org/10.1007/978-3-030-69476-0_2
5. Grover S, Avasthi A, Majid A. Clinical Practice Guidelines for mental health and well-being in patients with chronic medical illnesses. Indian J Psychiatry. 2024 Jan;66(Suppl 2):S338-S352. PMID: 38445289; PMCID: PMC10911329.

6. Steyerova P, Burgetova A. Current imaging techniques and impact on diagnosis and survival—a narrative review. Annals of Breast Surgery. 2022 Sep 30;6. doi: 10.21037/abs-21-22
7. Subhy Alsheikhly A, Ahmed Subhy Alsheikhly M. A Comprehensive Review of Breast Cancer and the Latest Advancement in Diagnosis and Treatment [Internet]. Oncology. IntechOpen; 2025. Available from: http://dx.doi.org/10.5772/intechopen.1008946
8. M Rassam, B Davoudi, A Comprehensive Overview of Breast Cancer Surgery Strategies: Advances, Options, and Considerations,EJCMPR. 2024; 3(2):629-643 https://doi.org /EJCMPR/ 20240611
9. Bundred JR, Michael S, Stuart B, Cutress RI, Beckmann K, Holleczek B, Dahlstrom JE, Gath J, Dodwell D, Bundred NJ. Margin status and survival outcomes after breast cancer conservation surgery: prospectively registered systematic review and meta-analysis. BMJ. 2022 Sep 21;378:e070346. doi: 10.1136/bmj-2022-070346. PMID: 36130770; PMCID: PMC9490551.
10. Ahuja S, Yadav P, Fattahi-Darghlou M, Zaheer S. Comparison of Intraoperative Imprint Cytology versus Frozen Section for Sentinel Lymph Node Evaluation in Breast Cancer. A study along with Systematic Review and Meta-analysis of literature. Asian Pac J Cancer Prev. 2024 Apr 1;25(4):1113-1119. doi: 10.31557/APJCP.2024.25.4.1113. PMID: 38679970; PMCID: PMC11162742.
11. Uno Y, Akiyama N, Yuzawa S, Kitada M, Takei H. The value and practical utility of intraoperative touch imprint cytology of sentinel lymph node(s) in patients with breast cancer: A retrospective cytology-histology correlation study. Cytojournal. 2020 May 12;17:11. doi: 10.25259/Cytojournal_80_2019. PMID: 32547631; PMCID: PMC7294180.
12. Tamanuki T, Namura M, Aoyagi T, Shimizu S, Suwa T, Matsuzaki H. Effect of Intraoperative Imprint Cytology Followed by Frozen Section on Margin Assessment in Breast-Conserving Surgery. Ann Surg Oncol. 2021 Mar;28(3):1338-1346. doi: 10.1245/s10434-020-08955-z. Epub 2020 Aug 19. PMID: 32815080.
13. Tamanuki T, Namura M, Aoyagi T, Shimizu S, Suwa T, Matsuzaki H. Effect of Intraoperative Imprint Cytology Followed by Frozen Section on Margin Assessment in Breast-Conserving Surgery. Ann Surg Oncol. 2021 Mar;28(3):1338-1346. doi: 10.1245/s10434-020-08955-z. Epub 2020 Aug 19. PMID: 32815080.
14. Ashraf Aem, Mustafa Ez, Fattouh Mk, Manal Me. Margin Assessment in Breast Conservative Surgery and Concordance between Frozen and Paraffin Section Results: A Retrospective Study. The Medical Journal of Cairo University. 2022;90(12):2481-7. DOI: 10.21608/mjcu. 2022. 295323
15. Hashmi AA, Naz S, Ahmed O, Yaqeen SR, Afzal A, Asghar IA, Irfan M, Faridi N. Diagnostic Accuracy of Intraoperative Touch Imprint Cytology for the Diagnosis of Axillary Sentinel Lymph Node Metastasis of Breast Cancer: Comparison With Intraoperative Frozen Section Evaluation. Cureus. 2021 Jan 28;13(1):e12960. doi: 10.7759/cureus.12960. PMID: 33659115; PMCID: PMC7920232.
16. Vinod K, Aroul T, Vaithi KAR. Diagnostic Utility of Imprint Cytology for Assessment of Breast Lumps. Journal of Datta Meghe Institute of Medical Sciences University. 2022;17(3):709-12. DOI: 10.4103/jdmimsu.jdmimsu_189_20
17. Lofterød T, Frydenberg H, Flote V, Eggen AE, McTiernan A, Mortensen ES, Akslen LA, Reitan JB, Wilsgaard T, Thune I. Exploring the effects of lifestyle on breast cancer risk, age at diagnosis, and survival: the EBBA-Life study. Breast Cancer Res Treat. 2020 Jul;182(1):215-227. doi: 10.1007/s10549-020-05679-2. Epub 2020 May 20. PMID: 32436147; PMCID: PMC7275030.
18. Wei S. Hormone receptors in breast cancer: An update on the uncommon subtypes. Pathol Res Pract. 2023 Oct;250:154791. doi: 10.1016/j.prp.2023.154791. Epub 2023 Sep 3. PMID: 37672851.
19. Devi RS, Kumar A, Singh A, Durgapal P, Kishore S. Ravi Hari Phulware; Department of Pathology and Laboratory Medicine, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India. Journal of Cytology. 2024 Nov 1;41:S39. DOI: 10.4103/joc.joc_145_24
20. Maloney BW, McClatchy DM, Pogue BW, Paulsen KD, Wells WA, Barth RJ. Review of methods for intraoperative margin detection for breast conserving surgery. J Biomed Opt. 2018 Oct;23(10):1-19. doi: 10.1117/1.JBO.23.10.100901. PMID: 30369108; PMCID: PMC6210801.
21. Tamhane AN, Shukla S, Acharya S, Acharya N, Hiwale K, Bhake A. Intraoperative Surgical Margin Clearance - Correlation of Touch Imprint Cytology, Frozen Section Diagnosis, and Histopathological Diagnosis. Int J Appl Basic Med Res. 2020 Jan-Mar;10(1):12-16. doi: 10.4103/ijabmr.IJABMR_325_18. Epub 2020 Jan 3. PMID: 32002379; PMCID: PMC6967348.

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Impact of Blended Learning on Academic Achievement and Self-Assessed Confidence: Evidence from Postgraduate Family Medicine in Pakistan

Kiran Abdul Sattar, Abida Munir Badini

ABSTRACT

Objective: To evaluate the impact of a one-year blended learning program on academic achievement and self-assessed confidence among postgraduate Family Medicine students in Pakistan.

Study design and setting: A retrospective analysis conducted at a public sector Pakistani university.

Methodology: Data from 20 students who completed a six-module Family Medicine certificate program (2022–2024) were analyzed. Each module included a 15-item multiple-choice pre- and post-test and a self-assessment of confidence level using a three-point scale. The Wilcoxon Signed Rank Test compared pre- and post-test scores, while frequency distributions examined changes in self-assessed confidence.

Results: Mean test scores increased significantly from 8.1 ± 3.2 to 11.3 ± 3.8 ($p<0.001$). Self-assessed confidence levels rose markedly: the proportion of students reporting comfort increased from an average of 16% pre-module to 54% post-module, while discomfort decreased from 12% to 2%. Improvements were consistent across most modules, though Module 2 showed a smaller, non-significant gain.

Conclusions: Blended learning significantly enhances academic performance and self-assessed confidence in postgraduate Family Medicine education. These parallel improvements suggest the approach effectively bridges theoretical knowledge and professional confidence, supporting its adoption in specialized medical training programs. The findings underscore blended learning's potential to address both cognitive and affective learning domains simultaneously.

KEYWORDS: Education, Family Practice, Self-assessment, Medical, Graduate

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INTRODUCTION

Educational institutions use a variety of teaching methods depending on their specific circumstances, including traditional and online methods. Traditional methods, like lectures and text books, are very commonly used in many colleges and universities. However, online methods, such as virtual classrooms and interactive videos, are becoming progressively prevalent due to their flexibility and accessibility.[1] Blended learning includes combination of online learning and face-to-face learning.[2-3] Online learning includes synchronous and asynchronous components. Synchronous sessions contain real-time communication where all learners are present at the same time, such as in a live video conference or chat. This permits for feedback and interaction among participants at the same time like a physical class. On the other hand, asynchronous sessions do not require all students to be present simultaneously and communication can occur at different times, such as through discussion boards and recorded sessions.[1] Blended learning conceptualizes learning as an ongoing process than a single time event thus motivates students to learn and be engaged even outside the classroom.[4] Learners get the benefit of increased flexibility which allows them to access the internet and work on the course material whenever and wherever they prefer.[5] Blended learning is innovative because it combines the strengths of both traditional face to face teaching and latest online modes which creates a dynamic and compliant learning environment. It results in active and more personalized learning active learning by encouraging students to engage with course content through a variety of interactive formats, such as live discussions, assignments, and digital simulations, rather than passively receiving information thereby enhancing student engagement which helps them become independent learners and promotes autonomous learning.[6-8] Self-assessment is a process of formative assessment during which students reflect on and evaluate the quality of their work and learning, and identify strengths and weaknesses in their work and revise accordingly.[9-10] Research has shown that self-assessment is a valuable component of the learning process, as it enables

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learners to recognize their current level of understanding and identify areas that require further improvement. This reflective awareness fosters intrinsic motivation and facilitates deeper, ongoing learning by helping students focus on their individual educational needs and set specific goals for improvement. By taking ownership of their learning through self-assessment, students become more engaged and empowered in their academic journey. Additionally, self-assessment lets teachers to better modify their coaching to meet the unique needs of each student, ultimately leading to more successful learning outcomes.[11-12] Postgraduate Family Medicine training requires the integration of theoretical knowledge, practical skills, and professional confidence to deliver comprehensive, patient-centered care. Recent systematic reviews have confirmed that blended learning can significantly enhance knowledge acquisition, skill performance, and learner engagement compared to traditional teaching methods.[13, 14] In Pakistan, this approach has been shown to address barriers related to time, location, and faculty availability, while maintaining educational quality.[15-16] Despite these advantages, Family Medicine as a discipline in Pakistan remains underdeveloped, with a shortage of structured training programs and qualified family physicians. Geographic constraints and heavy clinical workloads further limit opportunities for interactive, learner-centered teaching.15 Hence, this study intended to evaluate the impact of a one-year blended learning program on academic achievement and self-assessed confidence among postgraduate Family Medicine students in Pakistan. By investigating dual results across six distinctive modules, this study provides broad insights into the effectiveness of blended learning approach in postgraduate medical education. The significance of blended approach lies in its potential to strengthen the Family Medicine workforce by producing graduates who are not only knowledgeable but also confident in applying their skills in real-world primary care settings.

METHODOLOGY

After ethical approval from the University's Ethical Review Committee (JSMU/IRB/2024/890), this retrospective study was conducted from March to April 2025. A pre-existing data of 20 participants were drawn from postgraduate Family Medicine students who were formally enrolled in the blended certificate program between 2022 and 2024. Only those who successfully completed all six modules and had both pre- and post-test scores, along with self-assessment data available in the learning management system, were included in the analysis. Students who did not complete the program requirements or had missing assessment data were excluded from the final dataset. The program is divided in six modules of equal duration. The six modules covered core topics in Family Medicine progressing from foundational concepts to more specialized areas of practice. The online components were delivered through a learning management system (MOODLE) and included asynchronous activities like recorded lectures, discussion forums, supplementary reading materials and synchronous sessions were conducted via zoom once weekly. Students could access online materials at their convenience throughout the duration of program. In this study, two primary outcome variables were assessed: academic achievement and self-assessed confidence. Academic achievement was measured through module-specific formative assessments consisting of 15 multiple-choice questions (MCQs) developed by subject experts and validated for content relevance and clarity. A test blueprint was developed to ensure alignment of items with module learning outcomes and cognitive levels. Reliability was assessed using Cronbach's alpha for each module, and item analysis (difficulty and discrimination indices) was conducted to evaluate question quality. Each student completed a pre-test prior to the start of a module and a post-test upon its completion. Scores were recorded as the number of correct responses out of 15, with higher scores reflecting greater knowledge acquisition. Self-assessed confidence was measured using a structured three-point Likert-type scale administered before and after each module. Students rated their comfort level with the module content as "comfortable," "moderately comfortable," or "uncomfortable." These responses were coded as A, B, and C respectively, and analyzed as categorical data to capture shifts in perceived confidence. Data of students with complete pre/post test scores and pre/post self-assessed form with comfort level was extracted from learning management system and entered in spss version 24. Since the data did not follow a normal distribution, non-parametric tests were employed. The Wilcoxon Signed Rank Test was used to compare pre-test and post-test scores for each module and overall. For self-assessment data, frequency distributions and percentages were calculated to determine shifts in comfort levels before and after each module. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 20 postgraduate students were included in the analysis. Blueprinting confirmed that all items mapped appropriately to intended outcomes and cognitive levels. Cronbach's alpha values ranged from 0.72 to 0.88 across modules, indicating acceptable to good reliability. Item analysis showed that most items had difficulty indices between 0.35 and 0.75 and discrimination indices above 0.20, supporting the overall quality of the assessments. The mean pre-test score across all modules was 8.1 ± 3.2 which increased to 11.29 ± 3.76 in the post-test. This improvement was statistically significant ($p < 0.001$). Module wise improvement from pretest to post test for all modules is shown in Table 1. In terms of self-assessed confidence, Figure 1 shows a comparison of postgraduate students' comfort level prior to and subsequent to the completion of each of the six modules in a blended one-year Family Medicine program. In all modules, an observable trend is

the increased proportion of students who evaluated themselves as comfortable (A) upon completion of the modules. For example, during Module 1, the rate of students feeling at ease improved from 24.8% pre-module to 57.69% post-module. This same pattern exists among other modules—Module 2 rose from 14.7% to 58.25%, Module 3 from 15.3% to 54.27%, Module 4 from 10.3% to 49.17%, Module 5 from 10.0% to 56.88%, and Module 6 from 14.5% to 54.12%.

On the other hand, the percentage of students who graded themselves as not comfortable (C) fell enormously after the module. It fell from 14.6% to 1.54% in Module 1, and in some modules (3 and 5), it was 0%. The declining pattern indicates that the program improved students' self-assessed confidence. The proportion of students who were moderately comfortable (B) decreased or had a relatively stable trend, which suggests that most students moved away from uncertainty towards being more confident after instruction

Table 2 shows the outcome of the Wilcoxon Signed Rank Test on the paired pre and post formative assessment scores of postgraduate students in a blended Family Medicine program. The non-parametric test was employed to determine the significance of differences in students' performance prior to and following each module. The findings reveal a general trend of improvement in all modules, with the proportion of positive ranks (representing score increases) significantly greater than negative ranks (representing decreases).

DISCUSSION

Our findings demonstrate significant improvements in both academic achievement and self-assessed confidence levels among postgraduate Family Medicine students who participated in the blended learning program. These results align with existing evidence in the literature that supports the efficacy of blended learning approaches in medical education. A systematic review and meta-analysis by Liu et al. found that blended learning consistently demonstrated better effects on knowledge outcomes compared to traditional learning in health education.[17] Their analysis of 56 studies with 9,943 participants showed a standardized mean difference of 1.07 (95% CI 0.85 to 1.28) in favor of blended learning, which supports our findings of significant improvements in formative assessment scores. The notable increase in self-assessed comfort levels across all modules, with the percentage of students feeling comfortable rising substantially (e.g., from 24.8% to 57.69% in Module 1), reflects the positive impact of the blended learning approach on students' perceived confidence. This aligns with recent research which found that students in a blended learning medical nutrition course demonstrated significantly higher self-efficacy, particularly in organizing study plans, participating in interactive learning activities, and applying course knowledge compared to those in a traditional learning environment.[18] Our study found significant improvements in formative assessment scores across most modules, with the overall mean score increasing from 8.1 ± 3.2 to 11.29 ± 3.76 ($p<0.001$). A recent research comparing blended learning to traditional on-site instruction in medical genetics education found that blended learning led to higher overall final grades and better exam scores.[19] A notable finding in our study is the parallel improvement in both academic achievement and self-assessed confidence levels. This relationship suggests that as students gain knowledge and skills through blended learning, their confidence in their abilities also increases which is supported by evidence that self-assessment promotes metacognitive awareness and

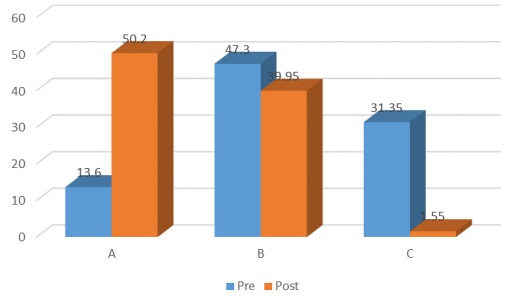
Table 1: Paired Statistics of Pre and Post Score

Module		N	Mean ± SD	Minimum	Maximum	P-Value
Overall	Pre	120	8.1 ± 3.2	0	15	< 0.001
	Post	119	11.29 ± 3.758	0	15	
Module 1	Pre	20	6.7 ± 2.473	3	14	< 0.001
	Post	19	11.05 ± 2.198	8	15	
Module 2	Pre	20	5.75 ± 1.97	0	10	0.10
	Post	20	7.75 ± 3.16	0	10	
Module 3	Pre	20	8.9 ± 2.337	5	15	< 0.001
	Post	20	13.25 ± 2.673	7	15	
Module 4	Pre	20	8.15 ± 3.265	3	15	0.001
	Post	20	11.25 ± 2.447	6	14	
Module 5	Pre	20	10.2 ± 3.002	4	15	0.013
	Post	20	12.6 ± 3.589	0	15	
Module 6	Pre	20	8.9 ± 3.892	0	15	0.018
	Post	20	11.85 ± 5.264	0	15	

Table 2: Ranks of Wilcoxon Signed Rank Test of Pre and Post Score

Module			N
Overall	Post - Pre	Negative Ranks	14
		Positive Ranks	94
		Ties	11
Module 1	Post - Pre	Negative Ranks	1
		Positive Ranks	17
		Ties	1
Module 2	Post - Pre	Negative Ranks	3
		Positive Ranks	15
		Ties	2
Module 3	Post - Pre	Negative Ranks	2
		Positive Ranks	17
		Ties	1
Module 4	Post - Pre	Negative Ranks	3
		Positive Ranks	14
		Ties	3
Module 5	Post - Pre	Negative Ranks	2
		Positive Ranks	16
		Ties	2
Module 6	Post - Pre	Negative Ranks	3
		Positive Ranks	15
		Ties	2

Figure 1: Pre and post self-assessment in all 6 Modules



helps students recognize their strengths and areas needing improvement.[20] The significant improvement in self-assessed comfort levels across all modules in our study suggests that blended learning not only enhances knowledge acquisition but also builds confidence in applying that knowledge. The concept of self-assessment as a valuable component of the learning process is supported by research showing that reflective awareness fosters intrinsic motivation and facilitates deeper, ongoing learning.[13, 20] Our findings add to this literature by demonstrating a concurrent improvement in both academic achievement and self-assessed confidence in a postgraduate medical education context. At the same time, our results highlight variability across modules. While most modules showed significant improvements in both self-assessed confidence and formative assessment scores, Module 2 demonstrated a smaller, non-statistically significant increase in scores (from 5.75 ± 1.97 to 7.75 ± 3.16, p = 0.10). This variation suggests that the effectiveness of blended learning may depend on the specific content, complexity, or design of individual modules.[21-22] The differences in module effectiveness highlight the importance of continuous evaluation and refinement of blended learning curricula. As Dias and Diniz suggest, enhanced learning management systems for blended learning should incorporate distinct learner profiles and adaptable approaches to accommodate different learning needs and content types.[6] Our findings indicate that the blended learning format may foster the development of self-directed learning skills among postgraduate medical students. The decrease in students reporting discomfort with content (e.g., from 14.6% to 1.54% in Module 1) suggests that students enhanced their learning more effectively.[16] The success of this blended learning approach has significant implications for medical education in resource-limited settings like Pakistan. A recent study on family physician graduates of blended-learning courses in India found that this model creates an important pathway for doctors, especially women, to pursue higher education with flexibility.[23] In our study context, the public university in Karachi was able to deliver effective postgraduate education to family medicine students through a blended approach that may have overcome barriers related to time, location, and resources.

This study has several limitations that must be acknowledged. First, the absence of a control group prevents us from making direct comparisons between blended learning and traditional or online-only methods. Our conclusions are therefore limited to within group improvements and cannot establish the superiority of blended learning. Second, the study relied on module level pre and posttests categorized as formative assessments, designed to provide feedback on progress rather than to serve as summative evaluations of long-term retention. Third, participant demographic data such as age, gender, and prior academic performance were not collected, restricting the generalizability of the findings. Fourth, the self-assessment tool used to measure confidence was a simple three-point scale and was not formally validated, which limits the reliability of conclusions regarding confidence levels. Finally, the small sample size and retrospective design further limit the strength of the conclusions. Future research should address these gaps by incorporating larger, prospective cohorts, validated assessment tools, demographic profiling, and comparative control groups. Mixed-method approaches, including qualitative feedback, may also provide deeper insights into learner experiences and the mechanisms driving variability across modules.

LIMITATION

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CONCLUSION

This study found that a one-year blended learning program in Family Medicine was associated with significant improvements in both academic achievement and self-assessed confidence among postgraduate students. These within group gains suggest that blended learning can positively influence knowledge acquisition and learner confidence in this context. However, given the absence of

a comparative control group, small sample size, and reliance on formative assessments, the findings should be interpreted with caution. While our results are consistent with international evidence supporting blended learning in medical education, they cannot establish superiority over traditional or online-only approaches. Future research using larger cohorts, validated assessment tools, and controlled study designs is needed to confirm these preliminary findings and to explore how blended learning can be optimized for postgraduate Family Medicine training, particularly in resource-limited settings.

CONFLICT OF INTEREST

All authors do not have any conflict of interest

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Authors Contribution:
Kiran Abdul Sattar: Both authors contributed equally towards preparation of manuscript
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REFERENCES

1. Ananga P, Biney IK. Comparing face-to-face and online teaching and learning in higher education. MIER J Educ Stud Trends Pract 2017;7(2):165-79.https://doi.org/10.52634/mier/2017/v7/i2/1415.
2. Graham CR. Blended learning systems: definition, current trends and future directions. In: Bonk CJ, Graham CR, editors. The handbook of blended learning: global perspectives, local designs. San Francisco: Pfeiffer; 2006. p. 3–21.
3. Dos B. Developing and Evaluating a Blended Learning Course. Anthropologist 2014;17(1):121-8. https://doi.org/10.1080/09720073.2014.11891421.
4. Halverson LR, Graham CR. Learner engagement in blended learning environments: a conceptual framework. Online Learn 2019;23(2):145-78. https://doi.org/10.24059/olj.v23i2.1481.
5. Al Rawashdeh AZ, Mohammed EY, Al Arab AR, Alara M, Al-Rawashdeh B. Advantages and disadvantages of using e-learning in university education: analyzing students' perspectives. Electron J e-Learn 2021;19(3):107–117. https://doi.org/10.34190/ejel.19.3.2168.
6. Dias SB, Diniz JA. Towards an enhanced learning management system for blended learning in higher education incorporating distinct learners' profiles. Educ Technol Soc 2014;17(1):307–319.
7. Blieck Y, Kauwenberghs K, Zhu C, Struyven K, Pynoo B, DePryck K. Investigating the relationship between success factors and student participation in online and blended learning in adult education. J Comput Assist Learn 2019;35(4):476–490. https://doi.org/10.1111/jcal.12351.
8. Sahni J. Does blended learning enhance student engagement? Evidence from higher education. J e-Learn High Educ 2019;2019:1–14. https://doi.org/10.5171/2019.121518.
9. Andrade H, Du Y. Student responses to criteria-referenced self-assessment. Assess Eval High Educ 2007;32:159–81. https://doi.org/10.1080/02602930600801928.
10. Baars M, Vink S, van Gog T, de Bruin A, Paas F. Effects of training self-assessment and using assessment standards on retrospective and prospective monitoring of problem solving. Learn Instr 2014;33:92–107. https://doi.org/10.1016/j.learninstruc.2014.04.004.
11. Spiller D. Assessment matters: self-assessment and peer assessment [Internet]. Hamilton (NZ): Teaching Development, The University of Waikato; 2009 [cited 2025 Feb 20]. Available from: http://www.waikato.ac.nz/tdu/pdf/ booklets/8_Self PeerAssessment.pdf.
12. Choudhary K. An approach to enhancing continuous evaluation through self-reflection among students of the foundation program in design course. Creative Educ 2024;15(6):1003–11. https://doi.org/10.4236/ce.2024.156061.
13. Vallée A, Blacher J, Cariou A, Sorbets E. Blended learning compared to traditional learning in medical education: systematic review and meta-analysis. J Med Internet Res 2020;22(8):e16504. https://doi.org/10.2196/16504.
14. Ashraf MA, Tsegay SM, Gull N, Saeed M, Dawood H. The role of blended learning in improving medical students' academic performance: evidence from Pakistan. Front Med 2024;11:1425659. https://doi.org/10.3389/fmed.2024.1425659.
15. Khan UI, Farazdaq H, Naseem A, Suleman W, Saleem S, Qadir MA, Fatima K. Evaluation of FamMed Essentials: A blended learning program for capacity building of general practitioners in Pakistan. BMC Med Educ 2024;24:218. https://doi.org.10.1186/s12909-024-05069-y.
16. Masood S, Bhombal ST, Ghulam U. Blended learning: An innovative teaching strategy to teach dermatology to the family medicine residents of a teaching hospital. J Family Med Prim Care;13(9):3571-3575. https://doi.org/10.4103/jfmpc.jfmpc_1837_23.
17. Liu Q, Peng W, Zhang F, Hu R, Li Y, Yan W. The effectiveness of blended learning in health professions: Systematic review and meta-analysis. J Med Internet Res 2016;18(1):e2. https://doi.org/10.2196/jmir.4807.
18. Regmi A, Mao X, Qi Q, Tang W, Yang K. Students' perception and self-efficacy in blended learning of medical nutrition course: a mixed-method research. BMC Med Educ 2024;24(1):1411. https://doi.org/10.1186/s12909-024-06339-5.
19. Liao B, Ma S, Ni Y, Li H, Xue Y, Dang S, et al. Comparing the effects of blended learning and traditional instruction on "Medical Genetics and Embryonic Development" in undergraduate medical students: a randomized controlled trial. Glob Med Educ 2024;1(1):53–62 DOI: https://doi.org/10.1515/gme-2024-0014.
20. Means B, Toyama Y, Murphy R, Baki M. The effectiveness of online and blended learning: a meta-analysis of the empirical literature. Teach Coll Rec 2013;115(3):1–47. https://doi.org/10.1177/016146811311500307.
21. Minhas W, White T, Daleure G, Solovieva N, Hanfy H. Establishing an effective blended learning model: teacher perceptions from the United Arab Emirates. SAGE Open 2021;11(4):1-11. https://doi.org/10.1177/21582440211061538.
22. Kintu MJ, Zhu C, Kagambe E. Blended learning effectiveness: the relationship between student characteristics, design features and outcomes. Int J Educ Technol High Educ 2017;14:1–20. https://doi.org/10.1186/s41239-017-0043-4.

Medical Education - Original Article **Open Access**

Evaluation of Learner Insights on Innovative Teaching Strategies in Integrated Modular Biochemistry Curriculum

Nabeela Faisal, Fauzia Jan, Lubna Aftab, Zehra Niazi, Sabahat Ikhlaq, Nawal Amjad

ABSTRACT

Objective: To test new instructional strategies in the integrated modular Biochemistry curriculum based on learner behaviors, knowledge retention, and student-centered education.

Study Design and Setting: This was an observational cross-sectional study conducted at the Department of Biochemistry, University Medical & Dental College, a constituent medical college of The University of Faisalabad, utilizing an integrated modular curriculum. Surveys were undertaken of undergraduate medical faculty members and students to explore their perceptions of innovative teaching strategies.

Methodology: A total of 352 respondents were invited, comprising 300 learners and 52 teachers. Data was collected using a structured questionnaire that measured perceptions of interactive sessions involving large groups of students, tutorials/SGDs, case-based learning, and flip classrooms. Pearson's Chi-square and likelihood ratio tests were used to test the association between variables.

Results: A total of 352 respondents participated. For the integrated modular curriculum, 47.3% of students agreed and 12% strongly agreed that it complemented their knowledge and promoted participation. Regarding tutorials/SGDs, 55% agreed and 15% strongly agreed that these sessions encouraged a student-centered approach. In case-based learning, 48% agreed and 16.3% strongly agreed that it was intellectually stimulating and challenging. For the flipped classroom, 37.7% agreed and 10.3% strongly agreed that it was a useful innovation, although a considerable proportion remained neutral

Conclusion: Research indicates that interactive teaching methods in biochemistry are favorably received, enhance active learning, and are of value within integrated curricula. A wider application can improve the performance of medical education.

Keywords: Biochemistry, Curriculum, Faculty, Medical Education, Instructional Methods, Students

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INTRODUCTION

Medical education has undergone pround transformation in last 10 years, shifting from conventional discipline-based curricula toward integrated, learner-centered approaches. This evolution emphasizes active and contextual learning, shifting from passive reception of information to fostering critical engagement. As a core foundational science, biochemistry plays an important role within this modern framework. It provides the important basis for understanding crucial medical concepts like human physiology, pathophysiology, and molecular pathogenesis. By elucidating the biochemical mechanisms underlying health and disease, it bridges foundational science and clinical practice, enabling future healthcare professionals to comprehend bodily processes at a molecular level and equipping them with the knowledge necessary for rational diagnosis and treatment.[1]

Integrated teaching is a learner-centered strategy that combines overlapping concepts from different disciplines, both horizontally within a phase and vertically across phases, to improve clinical relevance, decrease redundancy, and develop a holistic understanding. It connects teaching both temporally and thematically to enhance contextual, competency-based learning in undergraduate medical education.[2]

The four-level Kirkpatrick model, which is still one of the

most popular frameworks for evaluating the effectiveness of educational interventions, offers a methodical way to evaluate the success of both official and informal training programs by analyzing learners' responses, learning, behavior, and outcomes.[3] The paradigm emphasizes knowledge acquisition and instant gratification, as well as the practical applications of skills and their wider influence on organizational results.

With more than 95% of students reporting a favorable influence on their learning experience, Kulkarni et al. showed that the use of various case scenarios in integrated teaching greatly improved conceptual clarity, motivation and critical thinking among first-year students[4]

Due to the abstract concepts, as well as the content and apparent lack of clinical correlation, Biochemistry has often been perceived as a challenging subject by undergraduate medical students. Worldwide, Medical Schools have begun to address these issues by incorporating new methods of teaching and learning to improve levels of student engagement, retention, and preparation for clinical practice through the implementation of integrated modular curricula (IMCs).[5]

Because the integrated modular curriculum is grounded in systems or topics rather than subject courses, correlations can be combined both horizontally and vertically. Some illustrative contemporary innovations within this paradigm that encourage active and meaningful learning include flipped classrooms, case-based learning (CBL), tutorial instruction, large-group interactive sessions (IGS), and small-group discussions (SGDs).[6] Feedback and conceptual understanding are stimulated through large-group interactions, whereas a more profound understanding is facilitated through socialization with both peers and professors in SGD-tutorials. Therefore, by linking biochemical concepts to patient-oriented cases, CBL narrows the theory and practice gap and is a powerful approach (tool) to clinical reasoning and problem solving. According to adult learning theory, certain aspects of the flipped classroom model are conducive to independence and critical thinking.[7] While students read and watch lectures outside of class, they spend class time discussing and solving problems.

In research on modern pedagogical approaches, Sarkar et al discovered that using a blended learning model considerably improved the educational experience for Phase 1 MBBS students. This concept effectively blended integrated content delivery with the usage of digital web technologies. The study found that this strategy effectively motivated student participation in the learning process and actively encouraged a more participatory, dynamic learning environment. Additionally, it was highly helpful in preparing students for self-directed learning, which is an essential ability for medical practitioners. These findings highlight the importance of combining traditional integrated teaching methods with technology to produce more competent and prepared medical graduates. [8]

Using the Kirkpatrick model, Ragsdale et al. proposed a complete methodology for assessing undergraduate clinical instruction. Their central argument emphasizes that a comprehensive evaluation must go beyond simple feedback and include three critical dimensions: baseline measurements to establish a starting point, process indicators to monitor program implementation and delivery, and, most importantly, outcome measures. This approach evaluation is not limited to learner satisfaction (Level 1) or knowledge acquisition (Level 2), but also systematically evaluates the application of learned skills in clinical settings (Level 3: Behavior) and, ultimately, the program's impact on the healthcare system. The goal and central focus of their plan is to establish whether the educational program leads to improved patient care outcomes (Level 4: Results), hence proving its value and effectiveness.[9] Johonson et al. proposed a considerable augmentation of the standard Kirkpatrick assessment model to address the challenges of modern medical education. Their revised framework, based on the New World Kirkpatrick Model, includes new evaluation tiers. These new levels are intended to go beyond analyzing individual student results and instead examine the broader, systemic repercussions of educational systems. The improved technique seeks to analyze the broader effects of public and population health curriculum on the healthcare system and, more importantly, the health outcomes of entire communities. This approach contends that the true worth of medical education should be judged not only by student achievement, but also by its final impact on population health and healthcare systems. [10]

New approaches are now accumulating evidence from all over the world. Student-centered and interactive methods yield better engagement, motivation, and long-term subject retention than more passive approaches to instruction, such as didactic lectures.[11] Furthermore, they align with the principles of competency-based medical education, which emphasize that problem-solving and critical thinking skills, as well as communication skills, should be developed in conjunction with factual knowledge. However, for teachers, these approaches provide the opportunity to become facilitators instead of transmitters of information, allowing for more mentoring and co-creation of knowledge.[12] Despite the demonstrated benefits of innovative strategies/techniques, their implementation faces many persistent challenges. A primary obstacle is faculty development, as educators require training to transition from conventional lecturing to facilitative and interactive teaching roles. Time pressure presents another significant barrier, as designing and executing integrated sessions demands significant curricular planning and coordination among departments. Resource availability, such as access to digital tools, simulation equipment, and updated learning materials, can also limit practical

applications. Finally, student adaptation to new learning styles poses a difficulty, as learners accustomed to passive, lecture-based instructions may initially resist active, self-directed approaches. These interrelated factors, pedagogical readiness, logistical constraints, institutional support, and learner mindset collectively hinder the seamless integration of modern educational methods into curricula.

In the field of Biochemistry, where students often struggle to relate theoretical knowledge to its clinical significance, it becomes even more crucial to employ innovative teaching methods.[13] First, learner insights into these approaches provide a valuable source of feedback for curriculum designers and faculty to improve instructional practices, address student concerns, and ultimately enhance student learning outcomes.[14] Also important is the addition of faculty's viewpoints, as their acceptance and effective implementation of such methods directly affects their success.

This study, therefore, is designed to examine both student and teacher perceptions of innovative teaching mechanisms contained in the integrated modular Biochemistry curriculum.[15] Through the lens of learner insights, the research explores what works, what doesn't, and the overall impact of these approaches on knowledge acquisition, critical thinking, and engagement. The results will contribute to the ongoing improvement of medical education quality and ensure that educational methods are appropriately aligned with evolving learner and healthcare system needs.

METHODOLOGY

The present cross-sectional study was conducted at the University Medical & Dental College, a constituent institution of the University of Faisalabad, where an integrated modular curriculum was implemented in 2025. Ethical approval was obtained from the Institutional Review Board of the University of Faisalabad on January 13, 2025, before commencing the work. The study population consisted of students in the 1st and 2nd year of the MBBS program, following the modular integrated curriculum (version 1 and 2), and teaching staff from the multicentric departments of Biochemistry who taught the subject were included in the study. Students who provided informed consent were included in the study. Students who declined to participate in the study were excluded from the study.[2]

The study was conducted over a period of two months, from January 15, 2025, to March 15, 2025. ERC issued was TUF/IRB/06/25. The sample size was determined using the WHO sample size calculator, and participants were recruited through a simple random sampling method to ensure adequate representation.[16] Quantitative data were collected by using a structured questionnaire-based proforma with Likert scale items to achieve quantitative responses and open-ended questions to gather feedback.

All individuals were provided written informed consent, and confidentiality was strictly enforced by ensuring that participant identities were not revealed. The questionnaire was distributed to students and faculty members to collect their opinions on the integrated modular curriculum and its impact on the teaching and learning of biochemistry, in particular.

Descriptive statistics were used to analyze the quantitative data in SPSS version 22, and closed-ended questions were used to analyze the qualitative responses, identifying emergent themes. This two-prong approach enabled the researcher to gain a thorough sense of student and teacher viewpoints regarding the newly implemented curriculum.[17]

RESULTS

In total, 47.3% of the 300 participants indicated that they agreed, and 12% indicated that they strongly agreed, whereas 8.7% indicated that they disagreed, and 3% indicated that they strongly disagreed, on the integrated modular curriculum. 29% were neutral. Given the overall results, most students were positive, with almost 60% agreeing, showing overall acceptance of the curriculum as mentioned in Figure 1.

Table 1 compares student perceptions of tutorials/SGDs and flipped classrooms in Biochemistry. Mostly (70%), either agreed or strongly agreed that tutorials/SGDs promote a student-centred approach, while only about 48% responded positively to flipped classrooms. Neutral responses were higher for flipped classrooms (36.7%) compared tutorials/SGDs (22.3%), suggesting uncertainty or adjustment issues. A small proportion of students disagreed or strongly disagreed with both methods, though disagreement was more pronounced for flipped classrooms (15.3%) than tutorials/SGDs (7.7). Overall, tutorials/SGds were more favorably received than flipped classrooms. Among the 300 participants, 48% agreed and 16.3% strongly agreed that the case-based learning in Biochemistry was challenging and thought-provoking. In contrast, 11.7% disagreed, 2.3% strongly disagreed and 21.7% were neutral, indicating overall positive perceptions as shown in Figure 2

Table 2 shows associations between learners' groups (students vs. teachers) and their perceptions of different innovative teaching strategies. Across all strategies, teachers expressed more positive responses than students. Significant associations ($p<0.05$) were seen in all four methods, with the strongest agreement among teachers for tutorials/SGDs and large group interactive sessions.

DISCUSSION

Biochemistry is a fundamental discipline that elucidates the metabolic pathways and biological functions of important macromolecules, such as nucleic acids, proteins, carbohydrates, and lipids. It provides a molecular framework for understanding how these biomolecules drive cellular processes, support structural integrity, facilitate energy production, and allow genetic expression. By examining interactions at the molecular level, biochemistry bridges the

Figure 1: Large group interactive sessions in Biochemistry help in the improvement of knowledge?

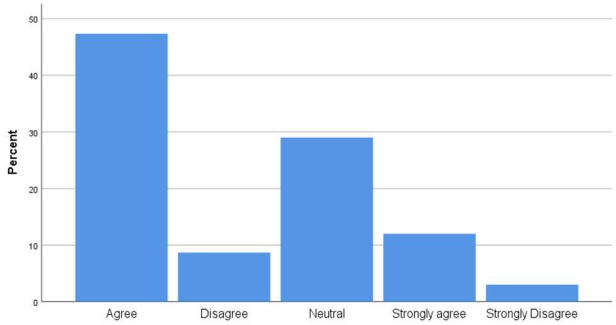
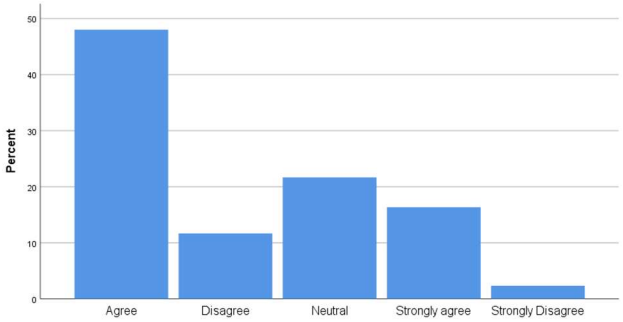


Table 1: Combined Table: Perceptions of Tutorials/SGDs and Flipped Classrooms in Biochemistry

Response	Tutorials/SGDs Frequency (%)	Flipped Classrooms Frequency (%)
Strongly Agree	45 (15.0%)	31 (10.3%)
Agree	165 (55.0%)	113 (37.7%)
Neutral	67 (22.3%)	110 (36.7%)
Disagree	17 (5.7%)	30 (10.0%)
Strongly Disagree	6 (2.0%)	16 (5.3%)
Total	300 (100%)	300 (100%)

Figure 2: Case based learning in Biochemistry IS challenging and thought provoking



gap between basic chemical principles and complex biological systems. However, biochemistry is often regarded as a specific, challenging field. This is largely due to its heavy reliance on abstract concepts like enzyme kinetics, metabolic regulation, and signal transduction pathways, which are not always visually intuitive or directly observable. Furthermore, the subject involves intricate and interconnected metabolic processes that need the integration of vast amounts of information. Unlike more descriptive or concrete disciplines, biochemistry demands a high level of conceptual thinking and the ability to visualise dynamic molecular interactions, making it difficult for many learners to comprehend and retain. Its inherent complexity underscores the importance of effective teaching strategies to make the subject more accessible and engaging. [18]

In the study, Gupta et al.[2] demonstrated high levels of student satisfaction with the integrated teaching-learning strategy. A significant majority of study participants rated the sessions as good, better, or outstanding, especially emphasising their positive impact on engagement, perceived utility, and motivation for lifelong learning. Supporting this learner-centred approach, the work of Debnath et al. underscored the important role of structured, two-way feedback mechanisms. Their research found that such systems were highly effective for refining instructional methods and motivating student involvement, with nearly all students in their study expressing strong approval for these targeted teaching improvement initiatives. Together, these studies affirm the value of interactive and responsive educational strategies in medical curricula.[19]

The findings of our study indicate a generally favorable reception of the integrated modular curriculum in Biochemistry, with approximately 60% of students expressing agreement or strong agreement. This suggests that the curriculum is perceived positively and has been accepted

Table 2: Perceptions of Teaching Strategies in Biochemistry (n=352)

Teaching Strategy	**Group**	**Positive (Agree + Strongly Agree)**	**Negative/Neutral (Neutral + Disagree + Strongly Disagree)**	**Total**	**p-value**
Large Group Interactive Sessions	Students	178	122	300	0.002
	Teachers	42	10	52	
	Total	220	132	352	
Tutorials/SGDs	Students	210	90	300	0.001
	Teachers	44	8	52	
	Total	254	98	352	
Case-Based Learning (CBL)	Students	193	107	300	0.001
	Teachers	31	21	52	
	Total	224	128	352	
Flipped Classroom	Students	144	156	300	0.018
	Teachers	34	18	52	
	Total	178	174	352	

by the majority of learners. The modular approach appears to enhance student engagement, promote deeper understanding, and align well with principles of learner-centred education. However, the notable proportion of neutral responses (29%) highlights that a significant proportion of students may remain uncertain or uncommitted. This underscores the potential requirement for additional orientation, structured support, or clearer communication to facilitate a smoother transition and foster more widespread confidence in the innovative pedagogical approach, as shown in Figure 1. In another study, it was found that 61% students perceived the traditional curriculum to emphasize rote learning and half of them responded that teachers were not trained to deliver an integrated curriculum.[20] Furthermore, according to recent studies, the modular integration concept is one of the potential factors to be considered for enhancing the retention of knowledge and critical thinking skills, supporting the validity of this new training approach in medical education.[21] According to our study**,** findings have shown that 70% of respondents agreed or strongly agreed, indicating a high level of acceptance of the integrated modular curriculum in Biochemistry. Based on these positive perceptions, new training approaches, such as small-group discussions and student-centred approaches, are effective means of enhancing learning experiences. The relatively minimal amount (7.7%) of disagreement further underscores devastating support (from students and faculty). Neutral responses (22.3%) represent transitional difficulties in adapting to new methods. However, recent studies recently demonstrated that modular curricula lead to a significant increase in learner satisfaction and participation in comparison to traditional teaching.[22] Researchers also assessed the superiority of the integrated approach over the isolated approaches in terms of clinical relevance and active engagement, further strengthening the need for the use of modular systems in medical education.[23] The findings show that approximately two-thirds of respondents (64.3%) rated CBL in Biochemistry as challenging and thought-provoking, affirming the value of CBL as a stimulus for higher-order thinking. Based on the small percentage of disagreement (14%), most learners appreciate CBL as an effective method for developing critical reasoning and applying knowledge. Neutral responses (21.7%) can be considered a sign of adjustment to active learning techniques as mentioned in Figure 2. In this regard, findings concluded that CBL improves the problem-solving and clinical reasoning skills of the medical students.[24] Furthermore, researchers stated that CBL can enhance learning on a deeper level and improve learner engagement, as it facilitates the integration of theoretical and practical knowledge. These results demonstrate that CBL is a key element in modular medical curricula.[25]

According to our study, the results showed that almost half of the respondents (48%) viewed the flipped classroom in Biochemistry as a practical innovation, whereas only 15.3% disagreed. Still, a significant fraction (36.7%) was neutral; this suggests that, while many participants valued the advantages of such an approach, others may not have been fully adjusted to its requirements yet. This ambivalent response is consistent with others, where it has been found that flipped classrooms encourage active participation but require a significant amount of learner preparation. For example, different studies found that flipped learning helped improve conceptual understanding and engagement in the classroom for medical education.[26] Similarly, scientists emphasized that while flipped classrooms can improve self-directed learning, they only work when they are well-planned and when learners are flexible.[27]

CONCLUSION

The general findings of this study indicate a generally positive perception of innovative teaching strategies in the integrated modular Biochemistry curriculum. Regarding various teaching methods, most students and faculty expressed agreement or strong agreement with case-based learning, small-group discussions, interactive sessions, and the flipped classroom. Case-based learning was generally described as challenging and thought-provoking, suggesting that it was effective at eliciting higher-order cognitive engagement. Furthermore, tutorial and interactive sessions seemed to be well received, making the learning student-centered a move away from the traditional didactic approach. Although nearly half of this group responded positively about the flipped classroom, there was also a relatively higher percentage of neutral respondents, indicating a need for further definition and support to maximize the effectiveness of this teaching approach. Overall, more than 70% of respondents provided positive responses to the acceptance questions, and these results provide evidence in support of implementing the integrated modular curriculum in medical education. However, the multiple levels of neutrality and disagreement underscore the importance of continuously measuring and adjusting to challenges related to learner preparation, resource availability, and teaching support. By taking student and faculty responses into account, institutions could do more to support these innovative practices, which, over time, would lead to greater knowledge acquisition, critical thinking, and long-term retention in the study of Biochemistry.

LIMITATIONS

Despite the useful insights provided by this study, a few limitations must be considered. First, the cross-sectional approach provides a snapshot of perceptions at a single point in time, making it difficult to analyze the integrated modular curriculum's long-term influence on knowledge retention and academic performance. The reliance on self-reported data from a structured questionnaire raises the possibility of social desirability bias, in which individuals submit

responses they thought were positive rather than their true perceptions. Additionally, the study was conducted at a single medical institution, which, while providing a controlled setting, limits the findings' applicability to other medical schools with varying resources, faculty competence, and student demographics. The sample, while calculated, may not entirely represent the whole population, and the viewpoints of students who did not participate are unknown, potentially skewing the results. The quantitative aspect of the primary data, while useful for quantifying frequencies and associations, provides limited insight into the nuanced reasons behind neutral responses, especially in the context of flipped classrooms. A mixed-methods approach, including qualitative interviews or focus group discussions would have been useful in evaluating the basic causes of ambivalence as well as the specific issues experienced by students and faculty.

Finally, the study failed to account for potential confounding variables such as previous academic performance, previous exposure to traditional teaching methods, or individual faculty members' specific teaching skills, all of which could influence a participant's perception of the new curriculum's effectiveness.

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REFERENCES

1. Bickenbach J, Rubinelli S, Baffone C, Stucki G. The human functioning revolution: implications for health systems and sciences. Frontiers in Science. 2023 May 31;1:1118512. DOI: https://doi.org/10.3389/fsci.2023.1118512
2. Gupta S, Sathe S, Arya K, Mitra B, Mangeshkar A. Evaluation of an Integrated Teaching Approach in Physiology, Anatomy, and Biochemistry for Phase I MBBS Students Using the Kirkpatrick Model. Cureus. 2025 Jul 28;17(7). DOI: https://doi.org/10.7759/cureus.88879
3. Smidt A, Balandin S, Sigafoos J, Reed VA. The Kirkpatrick model: A useful tool for evaluating training outcomes. Journal of Intellectual and Developmental Disability. 2009 Sep 1;34(3):266-74. DOI: https://doi.org/10 .1080/13668250903093125
4. KULKARNI A, GoWdA V, RAo C, RAo MY. Multiple Case Scenarios Based Integrated Teaching among First Year Medical Students-A Cross-sectional Study. Journal of Clinical & Diagnostic Research. 2021 May 1;15(5). DOI: https://doi.org/10.7860/JCDR/2021/48157.14818
5. Lord C, Charman T, Havdahl A, Carbone P, Anagnostou E, Boyd B, Carr T, De Vries PJ, Dissanayake C, Divan G, Freitag CM. The Lancet Commission on the future of care and clinical research in autism. The Lancet. 2022 Jan 15;399(10321):271-334. DOI: https://doi.org/10.1016/s0140-6736(21)01541-5
6. Boluk KA, Cavaliere CT, Higgins-Desbiolles F. A critical framework for interrogating the United Nations Sustainable Development Goals 2030 Agenda in tourism. Journal of Sustainable Tourism. 2019 Jul 3. DOI: https://doi.org/10.1080/09669582.2019.1619748
7. Adapting curriculum to bridge equity gaps [Internet]. 2021. https://www.oecd.org/en/publications/adapting-curriculum-to-bridge-equity-gaps_6b49e118-en.html
8. Sarkar S, Sharma S, Raheja S. Implementation of blended learning approach for improving anatomy lectures of phase i MBBS students–learner satisfaction survey. Advances in Medical Education and Practice. 2021 Apr 23:413-20. DOI: https://doi.org/10.2147/AMEP.S301634
9. Ragsdale JW, Berry A, Gibson JW, Herber-Valdez CR, Germain LJ, Engle DL, representing the Program Evaluation Special Interest Group of the Southern Group on Educational Affairs (SGEA) within the Association of American Medical Colleges (AAMC). Evaluating the effectiveness of undergraduate clinical education programs. Medical education online. 2020 Jan 1;25(1):1757883. DOI: https://doi.org/10.1080/10872981.2020.1757883
10. Johnson SB, Fair MA, Howley LD, Prunuske J, Cashman SB, Carney JK, Jarris YS, Deyton LR, Blumenthal D, Krane NK, Fiebach NH. Teaching public and population health in medical education: an evaluation framework. Academic Medicine. 2020 Dec 1;95(12):1853-63. DOI: https://doi.org/10.1097/ACM.0000000000003737
11. Experts EP. NTA UGC NET/JRF Management Book 2024 (Paper I and II) | 10 Full Length Mock Tests and 2 Previous Year Papers (1800 Solved Questions) with Free Access to Online Tests. EduGorilla Community Pvt. Ltd.; 2024.https://www.amazon.com/Management-Teaching-Research-Full-length-EduGorilla-ebook/dp/B091VYJZSB
12. Loeng S. Self-directed learning: A core concept in adult education. Education Research International. 2020;2020(1):3816132. DOI: https://doi.org/10.1155/2020/3816132
13. Hallsworth JE, Udaondo Z, Pedrós-Alió C, Höfer J, Benison KC, Lloyd KG, Cordero RJ, de Campos CB, Yakimov MM, Amils R. Scientific novelty beyond the experiment. Microbial Biotechnology. 2023 Jun;16(6):1131-73. DOI: https://doi.org/10.1111/1751-7915.14222
14. Rapanta C, Botturi L, Goodyear P, Guàrdia L, Koole M. Online university teaching during and after the Covid-19 crisis: Refocusing teacher presence and learning activity. Postdigital science and education. 2020 Oct;2(3):923-45. DOI: https://doi.org/10.1007/s42438-020-00155-y
15. Dwivedi YK, Kshetri N, Hughes L, Slade EL, Jeyaraj A, Kar AK, Baabdullah AM, Koohang A, Raghavan V, Ahuja M, Albanna H. Opinion Paper:"So what if ChatGPT wrote it?" Multidisciplinary perspectives on opportunities, challenges and implications of generative conversational AI for research, practice and policy. International journal of information management. 2023 Aug 1;71:102642.. DOI: https://doi.org/10.1016/j.ijinfomgt.2023.102642

16. Riley RD, Ensor J, Snell KI, Harrell FE, Martin GP, Reitsma JB, Moons KG, Collins G, Van Smeden M. Calculating the sample size required for developing a clinical prediction model. Bmj. 2020 Mar 18; 368. DOI: https://doi.org/ 10.1136/bmj.m441

17. Ferreira LN, Pereira LN, da Fé Brás M, Ilchuk K. Quality of life under the COVID-19 quarantine. Quality of Life Research. 2021 May;30(5):1389-405. DOI: https://doi.org/10.1007/s11136-020-02724-x

18. Chen Y, Ding W, Xu Y, Li S, Zhang W. Exploratory application of an integrated topic-based curriculum in biochemistry experimental teaching. Biochemistry and Molecular Biology Education. 2022 Nov;50(6):561-70. DOI: https://doi.org/10.1002/bmb.21564

19. Debnath S, Thakur KK, Balowria KS. Two-way feedback between the students and faculty to improve the methods and style of teaching anatomy to undergraduate medical students. Int J Anat Res [Internet]. 2020;8(4.1):7749-52. DOI: https://dx.doi.org/10.16965/ijar.2020.157

20. Arshad M, Mahmood S, Abid M, Baloch MF, Mansoor M, Butt ZP. Perception of Medical Students and Faculty Regarding Integrated Curriculum in A Medical Institute.DOI: https://doi.org/10.51273/esc25.251321131

21. Bening SA, Dachyar M, Pratama NR, Park J, Chang Y. E-Commerce technologies adoption strategy selection in Indonesian SMEs using the decision-makers, technological, organizational and environmental (DTOE) framework. Sustainability. 2023 Jun 9;15(12): 9361. DOI: https://doi.org/10.3390/su15129361

22. Cvetkoviæ D, editor. Drones-Various Applications. BoD–Books on Demand; 2024 Feb 7. DOI: https://doi.org/10.5772/intechopen.1000551

23. Dwivedi YK, Kshetri N, Hughes L, Rana NP, Baabdullah AM, Kar AK, Koohang A, Ribeiro-Navarrete S, Belei N, Balakrishnan J, Basu S. Exploring the darkverse: A multi-perspective analysis of the negative societal impacts of the metaverse. Information systems frontiers. 2023 Oct;25(5):2071-114.. DOI: https://doi.org/10.1007/s10796-023-10400-x

24. Ten Cate O, Custers EJ, Durning SJ. Principles and practice of case-based clinical reasoning education: a method for preclinical students. https://library.oapen.org/bitstream/handle/20.500.12657/27745/1/1002260.pdf

25. Matsushita K. Deep Active Learning: Toward Greater Depth in University Education. Springer; 2019.https://www.academia.edu/81782071/Deep_Active_Learning

26. Yu T, Dai J, Wang C. Adoption of blended learning: Chinese university students' perspectives. Humanities and Social Sciences Communications. 2023 Jul 8;10(1):1-6. DOI: https://doi.org/10.1057/s41599-023-01904-7

27. Fidan M. The effects of microlearning-supported flipped classroom on pre-service teachers' learning performance, motivation and engagement. Education and Information Technologies. 2023 Oct;28(10):12687-714. DOI: https://doi.org/10.1007/s10639-023-11639-2

Student Corner - Original Article **Open Access**

Perceptions and Attitudes of Medical and Non-Medical Students towards Aesthetic Interventions; A Cross-Sectional Study

Shweta Gohil, Sapna Mukhi, Namrita Bai, Monika Kumari, Ghazala Usman

ABSTRACT

Objective: To evaluate the impact of social media on perceptions, attitudes, and decision-making regarding aesthetic interventions among medical and non-medical students.

Study Design and Setting: A cross-sectional study was conducted with students from Sir Syed College of Medical Sciences, Altamash Dental College, and SZABIST University in Karachi, Pakistan.

Methodology: An online survey was administered, consisting of three sections: socio-demographics, social media usage, and perceptions of aesthetic interventions. It assessed time spent on social media, preferred platforms, exposure to aesthetic content, and views on beauty standards. A p-value =0.05 considered statistically significant.

Result: Among 384 participants (70.3% female, 53.1% medical students), significant differences were found in perceptions of cosmetic surgery (p=0.032), body satisfaction (p=0.016), self-esteem (p=0.022), and social media influence (p=0.004).

Conclusion: Social media significantly influences beauty perceptions, self-esteem, and body satisfaction, with professional background impacting views. Further research is needed to explore the psychological and social effects of cosmetic procedures.

KEYWORDS: Aesthetic interventions, Cosmetic surgery, Medical Students, Non-medical students

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INTRODUCTION

Surgical and non-surgical aesthetic procedures have become increasingly popular in recent years, with people seeking cosmetic enhancements to improve their appearance and confidence. Non-surgical procedures, also known as non-invasive procedures, do not require incisions or surgery and offer a variety of cosmetic enhancement procedures that can address facial wrinkles, signs of aging, acne scarring, and more.[1] On the other hand, Surgical aesthetic procedures involve incisions made in the skin, sometimes the removal of skin, and require some form of anesthetic.[2] The famous surgical procedures among patients include breast augmentation, liposuction, facelift and tummy tuck. The availability of current beauty trends is almost everywhere to the reach of the eye from billboards, and magazines to television programs, the internet, and daily life conversations.[2] Recent trends in exercise, yoga, and dietary modifications, along with a growing positive attitude toward aesthetic surgeries, have significantly influenced the perspectives of young adults. While traditional methods like balanced diets and exercise require time to achieve body goals, surgical procedures such as liposuction, tummy tucks, and non-invasive fat reduction offer quicker, albeit temporary, results. Despite their advantages, these procedures are often seen as a convenient shortcut for those seeking instant transformations.[3] The non-surgical procedures most frequently chosen by young women in Pakistan included laser light therapy and dermal fillers for lip and facial enhancements.[4] The International Society of Aesthetic Plastic Surgery (ISAPS) reported that the top five non-surgical procedures globally are botulinum toxin, hyaluronic acid, hair removal, skin tightening, and fat reduction.

Aesthetic procedures have become increasingly popular in recent years, with a growing number of people seeking non-

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surgical facial aesthetics (NSFA) such as botulinum toxin and dermal fillers.[5] This trend has not gone unnoticed by medical and non-medical students, who have been the subject of various studies examining their perceptions and attitudes toward aesthetic interventions. These studies have explored a range of topics, from the impact of mainstream media on medical students' perception of plastic surgery.[6] Additionally, research has shown that patients seeking minimally invasive cosmetic procedures tend to be highly educated, affluent women who believe that their procedure will positively impact their appearance.[7] Individuals seeking cosmetic enhancements may experience greater dissatisfaction with their physical appearance, potentially motivating them to undergo such procedures in an effort to address these negative body image perceptions.[8] Individuals who have close family members or friends that have undergone cosmetic procedures often exhibit a more positive attitude and acceptance towards these aesthetic treatments.[9] The vicarious experience of witnessing someone within their social circle embrace cosmetic enhancements can play a significant role in shaping their perceptions. Moreover, having access to firsthand information and insights from trusted sources can make individuals feel more informed and confident about their decision if they choose to undergo cosmetic procedures themselves.[10-12]

Research suggests that body image is profoundly influential in various aspects of an individual's life. It extends beyond mere physical perception and can significantly affect one's mental and emotional well-being, social interactions, and overall quality of life.[7,13] Aesthetic procedures can have both positive and negative psychological impacts on patients. While some patients report improvements in confidence and reductions in appearance-related distress,[14] others may experience depression and anxiety postoperatively, particularly those with pre-existing mood disorders.[15] The inclination towards considering cosmetic surgery varies between genders, with women generally being more predisposed to this option compared to men.[16] According to the American Society of Plastic Surgeons, 92% of all cosmetic surgical procedures in the United States were performed on women in 2018.[17] This difference in willingness to contemplate cosmetic procedures can be attributed to a combination of societal and cultural factors. Women often face more substantial societal pressure and expectations regarding their physical appearance, which can lead to a heightened desire to address perceived imperfections through cosmetic enhancements.[18]

Within the landscape of university campuses, students pursuing medical and non-medical disciplines represent a diverse cohort, each with unique exposures, perspectives, and considerations. Medical students, given their specialized knowledge, might approach aesthetic interventions differently than their non-medical counterparts, who could be influenced by distinct societal and personal factors. Investigating the perceptions and attitudes of both medical and non-medical students towards aesthetic interventions provides valuable insights into how different academic backgrounds influence people's opinions on cosmetic procedures.

METHODOLOGY

In this research, we utilized a descriptive cross-sectional study design. Our study focused on two groups: medical students currently enrolled in the MBBS program and non-medical students enrolled in programs such as BDS, DPT, and Pharmacy, who are residing in Karachi, Pakistan. We employed a convenience sampling method to recruit participants for this study. To determine our sample size of 384, we used Open Epi software, with a confidence level set at 95%, an expected frequency of 48.5%,[19] and a margin of error of 5%.

The survey for this research was divided into two sections. The first section gathered socio-demographic information about the participants. The second section focused on participants' social media usage, such as hours spent on social media, the most frequently used platform, and whether they followed accounts promoting aesthetic interventions. Additionally, this section explored their perceptions regarding aesthetic interventions, including views on societal beauty standards and any personal connections to family or friends who have undergone aesthetic procedures. Students aged 18-30 years, presently enrolled in educational institutions in Karachi, encompassing both medical and non-medical fields. Both the genders, male and female were included in this study. Children and Elderly were excluded from this study as well as non-residents of Karachi, Pakistan. Lastly individuals who do not provide their consent will also not be included in this study.

The data collected from the 384 participants was entered into Microsoft Excel. Following that, we performed statistical analysis using IBM SPSS statistical software version 25. Descriptive analysis was conducted on socio-demographic variables such as gender, educational background, marital status, etc., to calculate frequencies and percentages. The students were categorized into two groups: medical students and non-medical students. We used the chi-square test to compare the responses of these groups across various demographic categories (e.g., age groups, educational levels) in relation to their perceptions and motivations for aesthetic interventions.

RESULTS

The study comprised of 270; 70.3% females and 114;29.7% males. Among these, 204; 53.1% were medical students, while the remaining 180; 46.9% were non-medical students. In terms of marital status, the majority of participants were unmarried (348; 90.6%), as shown in table 1 below. The obtained p-value for this comparison was not statistically significant. However, when we examined these groups' perceptions of individuals undergoing cosmetic surgeries,

the p-value obtained was statistically significant (0.032). Similarly, when discussing their levels of body satisfaction, the statistical analysis yielded a significant result with a p-value of 0.016. When asked if social media accurately reflects the risks of aesthetic interventions, the difference between the medical and non-medical students' responses was statistically significant (p=0.045). In the analysis of whether participants would consider undergoing aesthetic procedures if a substantial portion or the majority of their friends opted for them, a significant p-value of 0.003 was obtained. When it comes to self-esteem, the comparison between the medical and non-medical groups revealed a statistically significant outcome with a p-value of 0.022. Lastly, in terms of consulting a surgeon who had gained fame through social media, the p-value was 0.004, indicating statistical significance for this comparison between the groups.

DISCUSSION

The non-significant p-value (0.212) obtained when comparing the two groups (medical and non-medical students) in relation to the influence of cosmetic surgery on societal beauty standards suggests that both groups held similar views in this regard. This finding suggests that, irrespective of their academic background, participants did not perceive cosmetic surgery as a significant driver of changing beauty standards. This might indicate a level of skepticism or critical thinking among the participants regarding the societal impact of such procedures. A study from Australia suggested that unrealistic beauty standards and the medicalization of appearance have been implicated in popularizing cosmetic surgery. Negative attitudes towards cosmetic surgery are also motivated by unrealistic beauty standards.[20]

In our investigation, a noteworthy outcome emerged with a p-value of 0.016 when evaluating the levels of body satisfaction between medical and non-medical students. It was observed that both groups generally expressed contentment with their physical appearances. Non-medical students, in particular, reported a high degree of satisfaction, while medical students tended to exhibit somewhat lower levels of satisfaction with their bodies. Body dissatisfaction has been found to influence attitudes towards cosmetic surgery among women.[21,22] In the research conducted on non-medical female college students in the United States, it was discovered that a stronger sense of body dissatisfaction was linked to a higher likelihood of contemplating cosmetic surgery. The study employed the Body Appreciation Scale to measure the degree of body satisfaction and found that a more negative body image was associated with a greater inclination towards considering cosmetic surgery, with a significant p-value of 0.001.[23] Similarly, in our own study, we observed a correlation between body satisfaction levels and the inclination towards cosmetic procedures among non-medical students, with a p-value of 0.038. A study conducted in Tehran revealed that individuals undergoing cosmetic procedures exhibited a higher degree of negativity towards their body image compared to those who were not pursuing any cosmetic treatments.[8,24] In present study, it was observed that out of the medical students, 35 individuals (accounting for 17.2%) acknowledged undergoing aesthetic treatments, with 15 opting for surgical procedures and 20 for non-surgical ones. In contrast, among non-medical students, 27 students (constituting 15%) had aesthetic interventions, consisting of 12 surgical procedures and 15 non-surgical ones. It appeared that students had a slight preference for less invasive non-surgical procedures. According to the ASPS (American Society of Plastic Surgeons), there has been a 17% decrease in the number of invasive cosmetic procedures performed since 2000, while the number of minimally invasive procedures has surged by 123%.[25] In the Singaporean study, just 2.1% of medical students confessed to having experienced aesthetic procedures, while a mere 0.8% of junior college participants reported undergoing such interventions. Our results aligned with this research, as we observed that 12 out of 14 students had opted for non-invasive, minimal procedures.[25]

Prior research has indicated that women tend to contemplate aesthetic procedures more frequently than men, often due to the perceived societal pressure for women to attain a flawless and idealized body image.[26,27] However, our study yielded a somewhat higher percentage of male students (41.2%) expressing interest in cosmetic procedures compared to their female counterparts (37.2%). When we examined whether students were contemplating undergoing aesthetic procedures in relation to whether they had any family members, relatives, or friends who had undergone such procedures, we observed a statistically significant p-value of 0.000. These findings align somewhat with a study conducted by Brown et al., who discovered that women were more likely to consider cosmetic surgery if they had observed family and friends undergoing similar procedures, but this effect was not observed in men.[28] Another study involving women with undergraduate-level education revealed that a greater exposure to cosmetic surgery experiences among their friends and family predicted an increased likelihood of them considering cosmetic surgery in the future. This was likely due to the enhanced information available to prospective patients and the breakdown of previously held stereotypes.[29]

Table 1: Socio-demographic characteristics for participants.

	Frequency (Percentage)
Male	114 (29.7%)
Female	270 (70.3%)
Medical (MBBS)	204 (53.1%)
Non-Medical (BDS, DPT, and Pharmacy)	180 (46.9%)
Single	348 (90.6%)
Married	34 (8.9%)
Divorced	2 (0.5%)

Table 2: Comparison of perceptions and attitudes towards aesthetics interventions between medical and non-medical students

		Medical (MBBS)	Non-Medical (BDS, Pharmacy, DPT etc.)	p-value
Do you believe that the prevalence of cosmetic surgeries has played a role in raising societal beauty standards to unrealistic levels?	Strongly Agree	78	78	**0.212**
	Somewhat Agree	71	61	
	Neutral	44	25	
	Somewhat Disagree	7	12	
	Strongly Disagree	4	4	
How do you perceive individuals who undergo aesthetic interventions?	They are confident in their appearance and embrace self-improvement.	37	21	**0.212**
	They may be influenced by societal pressure and beauty ideals.	62	44	
	It is their personal choice, and I don't judge them.	75	92	
	They are insecure and seeking validation through physical changes.	30	22	
Have you ever had aesthetic surgical or non-surgical procedure done?	Yes, Surgical	15	12	0.372
	Yes, non-surgical	20	15	
	No	169	153	
How satisfied are you with your body's appearance, including factors like shape, size, muscularity/tone, and overall attractiveness?	Very Satisfied	65	87	*0.016
	Somewhat Satisfied	85	54	
	Neutral	41	26	
	Somewhat Dissatisfied	10	11	
	Very Dissatisfied	3	2	
Do you think social media accurately represents the potential risks associated with aesthetic interventions?	Yes	40	27	*0.045
	No	71	84	
	Maybe	93	68	
Would you contemplate having aesthetic procedures if a significant number or the majority of your friends were choosing to undergo them?	Yes	34	13	*0.003
	No	97	112	
	Maybe	73	54	
Do you ever compare your appearance to social media influencers or celebrities?	Never	52	69	*0.022
	Rarely	38	38	
	Sometimes	92	59	
	Frequently	13	10	
	Always	9	3	
Would you prefer consulting an aesthetic surgeon who is famous on social media?	Yes	75	43	*0.004
	No	62	82	
	Maybe	67	54	

In a survey conducted among nursing students, it was discovered that 27.8% of these students held the belief that cosmetic surgery is a good thing because it can help people feel better about themselves".[9] In a similar vein, our study revealed that 18.1% of medical students and 11.7% of non-medical students shared the view that individuals undergoing aesthetic procedures are confident and embrace self-improvement.

CONCLUSION

The findings suggest that cosmetic surgery significantly influences perceptions of beauty, self-esteem, and body satisfaction, with social media playing a critical role in shaping these attitudes. Additionally, differences in appearance-related discussions between medical and non-medical students highlight the varying impact of professional background on body image perceptions. These results underscore the need for further research on cosmetic

procedures' psychological and social implications, particularly in the context of evolving beauty standards and media influence.

LIMITATIONS

The reliance on self-reported responses may have introduced recall bias and social desirability bias, potentially influencing the accuracy of the findings. Moreover, the majority participants were female, resulting in potential underrepresentation of male perspective. In addition, the ratio of medical to non-medical students was not eual, which may have introduced bias.

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REFERENCES

1. Clarke LH, Repta R, Griffin M. Non-surgical cosmetic procedures: Older women's perceptions and experiences. Journal of Women & Aging. 2007;19(3-4):69-87.
2. Chuang J, Barnes C, Wong BJ. Overview of facial plastic surgery and current developments. The Surgery Journal. 2016;2(01):e17-e28.
3. Tiggemann M. Sociocultural perspectives on human appearance and body image. 2011.
4. Arif M, Nazeer J, Naseem Z. Role of Social Media for the Adoption of Cosmetic Procedures among Young Pakistani Women. Journal of Development and Social Sciences. 2022;3(2):996-1006.
5. Grover S, Shankarghatta R, Elsayad F, Bahja J, Chaer Z, Celik C, et al. Attitudes and perceptions of medical and dental students on the implementation of non-surgical facial aesthetics in their curricula. British Journal of Oral and Maxillofacial Surgery. 2023;61(6):437-42.
6. Fraser S, Al Youha S, Rasmussen P, Williams J. Medical student perception of plastic surgery and the impact of mainstream media. Plastic Surgery. 2017;25(1):48-53.
7. Sobanko JF, Taglienti AJ, Wilson AJ, Sarwer DB, Margolis DJ, Dai J, et al. Motivations for seeking minimally invasive cosmetic procedures in an academic outpatient setting. Aesthetic surgery journal. 2015;35(8):1014-20.
8. Hashemi SAG, Edalatnoor B, Edalatnoor B, Niksun O. A comparison of body image concern in candidates for rhinoplasty and therapeutic surgery. Electron Physician. 2017;9(9):5363-8.
9. Akpan F, Dikmen B. Cosmetic surgery in the perception and acceptance of nursing students. Pielêgniarstwo Chirurgiczne i Angiologiczne/Surgical and Vascular Nursing. 2022;16(4):136-42.
10. Baksi A, Tuncer N. EXAMINATION OF NURSING STUDENTS'ACCEPTANCE LEVELS FOR AESTHETIC SURGERY AND AFFECTING FACTORS. International Journal of Health Services Research and Policy. 2021;6(1):60-72.
11. Alharethy SE. Trends and demographic characteristics of Saudi cosmetic surgery patients. Saudi Medical Journal. 2017;38(7):738.
12. Furnham A, Levitas J. Factors that motivate people to undergo cosmetic surgery. Canadian Journal of Plastic Surgery. 2012;20(4):47-50.
13. Tietje L, Cresap S. Is lookism unjust? The ethics of aesthetics and public policy implications. Journal of libertarian studies. 2005;19(2):31-50.
14. McKeown DJ. Impact of Minimally Invasive Aesthetic Procedures on the Psychological and Social Dimensions of Health. Plast Reconstr Surg Glob Open. 2021;9(4):e3578.
15. Jones HE, Faulkner HR, Losken A. The Psychological Impact of Aesthetic Surgery: A Mini-Review. Aesthet Surg J Open Forum. 2022;4:ojac077.
16. Abubakar AI, Jamda MA, Ibrahim A, Ajani A, Iyun K, Opara KO. University students and cosmetic surgery in Nigeria: A survey of perception, attitudes, and experiences. Nigerian Journal of Plastic Surgery. 2016;12(1):12.
17. Pearlman RL, Wilkerson AH, Cobb EK, Morrissette S, Lawson FG, Mockbee CS, et al. Factors Associated with Likelihood to Undergo Cosmetic Surgical Procedures Among Young Adults in the United States: A Narrative Review. Clin Cosmet Investig Dermatol. 2022;15:859-77.
18. Furnham A, Levitas J. Factors that motivate people to undergo cosmetic surgery. Can J Plast Surg. 2012;20(4):e47-50.
19. Arab K, Barasain O, Altaweel A, Alkhayyal J, Alshiha L, Barasain R, et al. Influence of Social Media on the Decision to Undergo a Cosmetic Procedure. Plast Reconstr Surg Glob Open. 2019;7(8):e2333.
20. Bonell S, Barlow FK, Griffiths S. The cosmetic surgery paradox: Toward a contemporary understanding of cosmetic surgery popularisation and attitudes. Body Image. 2021;38:230-40.
21. Slevec J, Tiggemann M. Attitudes toward cosmetic surgery in middle-aged women: Body image, aging anxiety, and the media. Psychology of women quarterly. 2010;34(1):65-74.
22. Walker CE, Krumhuber EG, Dayan S, Furnham A. Effects of social media use on desire for cosmetic surgery among young women. Current psychology. 2021;40:3355-64.
23. Jung J, Hwang CS. Associations between attitudes toward cosmetic surgery, celebrity worship, and body image among South Korean and US female college students. Fashion and Textiles. 2016;3(1):1-14.
24. Rubinstein G. The big five and self-esteem among overweight dieting and non-dieting women. Eat Behav. 2006;7(4):355-61.
25. Ng JH, Yeak S, Phoon N, Lo S. Cosmetic procedures among youths: a survey of junior college and medical students in Singapore. Singapore Med J. 2014;55(8):422-6.

26. Adedeji OA, Oseni GO, Olaitan PB. Awareness and attitude of healthcare workers to cosmetic surgery in osogbo, Nigeria. Surgery Research and Practice. 2014;2014.

27. Kvalem IL, von Soest T, Roald HE, Skolleborg KC. The interplay of personality and negative comments about appearance in predicting body image. Body image. 2006;3(3):263-73.

28. Brown A, Furnham A, Glanville L, Swami V. Factors that affect the likelihood of undergoing cosmetic surgery. Aesthet Surg J. 2007;27(5):501-8.

29. Salehahmadi Z, Rafie SR. Factors affecting patients undergoing cosmetic surgery in bushehr, southern iran. World J Plast Surg. 2012;1(2):99-106.

Case Report

Open Access

Case of Extensively Drug-Resistant (XDR) Typhoid with Resistance to Azithromycin

Naeem Ullah, Aneeqa, Rafia Khurshid

ABSTRACT:

An 18-year-old boy from Haripur, Pakistan was diagnosed with extensively drug-resistant (XDR) typhoid fever after presenting with acute febrile illness. Blood culture confirmed the isolates of *Salmonella Typhi*. Antimicrobial susceptibility testing revealed that the isolates were extensively drug-resistant (XDR) to all the first line antibiotics in addition to azithromycin. Only a few antibiotics such as meropenem, colistin and tigecycline were found effective against the bacterium. Empirical therapy with a first line antibiotic failed to treat the infection. After the antimicrobial susceptibility report, the patient was managed successfully with a costly course of meropenem. Azithromycin and carbapenem are the two antibiotics that are recommended to treat XDR typhoid fever. Therefore, resistance to azithromycin is a worrying sign, limiting the treatment options against XDR typhoid, and increasing the cost of therapy as well as the complications.

Keywords: Azithromycin, Extensive Drug-Resistance (XDR), Salmonella Typhi, Typhoid fever

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INTRODUCTION:

Typhoid fever, is a bacterial infection caused by *Salmonella Typhi*.[1] In 2021, there were estimated 9.3 million cases of enteric fever and 107.5 thousand deaths worldwide.[2] The highest number of cases and deaths were reported from South Asian countries.[2] In Pakistan, the incidence rate was 493.5 per 100,000 cases in 2018, which has drastically increased after emergence of new extensively drug-resistance (XDR) typhoid outbreaks in subsequent years.[3]

Salmonella Typhi is a Gram-negative bacillus that is transmitted through ingestion of contaminated food or water. Upon reaching the small intestine, bacteria penetrate the mucosal epithelium causing acute infection and enters the bloodstream through lymphatic drainage from mesenteric nodes.[4] Symptoms usually begin 7-14 days after exposure. The clinical presentation of typhoid fever varies from a mild febrile illness with headache, abdominal discomfort, dry cough or constipation to life threatening complications such as intestinal perforation, bleeding, hepatitis, meningitis, nephritis, osteomyelitis, septic shock etc which usually develop in third or fourth week of infection. Typhoid fever causes variable leucocyte and platelet count. Liver transaminases may be raised. The definite diagnosis of typhoid fever is made through isolation of organism mostly through blood culture.[1] However, bacterium can be identified in stool, urine or bone marrow culture depending on duration of illness.

Due to emergence of resistant isolates of Salmonella typhi, the choice of antibiotics is changing rapidly, especially fluoroquinolones and third generation cephalosporins are no longer effective against XDR isolates. XDR isolates are resistant to all antibiotics except few such as azithromycin, meropenem or tigecycline in most cases.[5] However, cases of typhoid fever with XDR isolates resistant to azithromycin[6] and carbapenem[7] have been reported. Hence, the choice of antibiotic to treat XDR typhoid has been narrowed to few antibiotics, which are costly and sometimes inaccessible in developing countries like Pakistan. Transmission of typhoid fever can be prevented by clean food and water supply, proper sanitation and vaccination especially in endemic areas. Health education is crucial to aware public about good hygiene and to induce mass behavioural change.

This case report is presented to alert the health community and decision makers about increasing burden of XDR typhoid cases with extended resistance to more antibiotics. There is need to address the underlying causes that are rendering life-saving antibiotics ineffective against this prevalent bacterial infection.

Case Presentation:

18-year-old boy studying in a high school of district Haripur,

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Pakistan presented to a local hospital in August 2024 with high grade fever, headache, lethargy and abdominal discomfort. There was no history of any chronic disease. However, he reported recurrent upper respiratory tract infections over the last 5 years, for which he received multiple courses of antibiotics such as amoxicillin, azithromycin, fluoroquinolones etc. He also received 3 days course of unknown parental antibiotic during a severe episode of acute pharyngitis. He had completed vaccination schedule for children. His younger sister was admitted twice in hospital for typhoid fever.

The boy was admitted to the medical ward. On physical examination, the patient was ill-looking and dehydrated with temperature of 105 °F, relative bradycardia (86 per min) and mild tenderness in right hypochondrium. Investigations including blood culture and drug sensitivity testing were ordered. Leukocyte count was 10800 cells/µL with relative lymphocytosis (46%). Alanine transaminase (ALT) was two times above the upper limit of normal. C-reactive protein (CRP) was raised. Empirical therapy was started with intravenous ceftriaxone 2-gram once daily. In addition, intravenous fluid and antipyretic were infused to relieve the symptoms. Frequent cold sponging was done to lower the body temperature close to normal. Blood culture revealed the isolates of *Salmonella Typhi*. Drug sensitivity report showed that the isolates were resistant to ampicillin, cotrimoxazole, chloramphenicol, third-generation cephalosporins, fluoroquinolones and azithromycin, with sensitivity to meropenem, tigecycline and colistin, as shown in Table-I. Treatment was modified to intravenous meropenem 1-gram every 8 hours. The fever subsided within 48 hours after the initiation of meropenem injection. The antibiotic course was continued for 10 days.

The patient was improved and discharged with advice on personal hygiene, clean food and boiled drinking water, proper sanitation and typhoid vaccination. Follow-up with infectious disease specialist was recommended for future deliberations.

Blood Culture	Isolates of *Salmonella Typhi*
Antimicrobial	**Drug Sensitivity Result**
Drug	(R=Resistant, S=Sensitive)
Ampicillin	R
Cotrimoxazole	R
Chloramphenicol	R
Ceftriaxone	R
Ciprofloxacin	R
Azithromycin	R
Meropenem	S
Colistin	S
Tigecycline	S

DISCUSSION:

The first case of extensively drug-resistant (XDR) typhoid fever emerged in Sindh province of Pakistan in 2016, where the outbreak of cases refractory to treatment by first line antibiotics occurred.[8] Compared to multi-drug resistant (MDR) typhoid resistant to ampicillin, cotrimoxazole and chloramphenicol, XDR isolates have extended resistance to fluoroquinolones and third generation cephalosporins.[5] The recommended options to treat XDR typhoid have been contracted to carbapenem and azithromycin. However, there are case reports depicting resistance to azithromycin[6] and carbapenem[7] as well.

Several factors have contributed to development of XDR strains. Misuse of antibiotics is a major factor in countries like Pakistan where the availability of over-the-counter medicines, overuse of antibiotics for minor febrile illnesses and incomplete treatment course are complicating the problem. Poor sanitation and faecal contamination of water supply allows the spread of resistant strains. In addition, low literacy rate, lack of typhoid vaccination and foreign travel to endemic areas are contributing factors as well.[9] Genetic basis for resistance to antibiotics involve chromosomal mutations and acquiring plasmids having resistance genes.[10]

This case report is worrisome where the XDR isolates of *Salmonella Typhi* were found resistant to azithromycin in addition to all first line antibiotics. The finding reinforces the earlier case reports by Octavia S, *et al*[6] and Nizamuddin S, *et al*[7], about increasing resistance to antibiotics that were useful against XDR typhoid. History of the case suggests the liberal use of antibiotics to treat episodes of acute upper respiratory tract infections that might have been caused by viruses. The bacteria developed mutations to resist the action of antibiotics, gradually leading to isolates which were able to survive against potent antibiotics such as azithromycin.

Knowingly, a pro-active and exclusive strategy is needed to address the problem on emergency basis. Government needs to ensure clean drinking water and proper sanitation to prevent contamination of water supply with faecal matter. There should be implementation of food safety regulations to ensure healthy food at hotels and local shops. Antibiotics should be issued only with a doctor's prescription and the duration of treatment should be completed. Integration of conjugate typhoid vaccine in national vaccination program is strongly advocated. Health education should promote public awareness about personal hygiene.

The case report emphasizes the need to report and study more resistant cases refractory to treatment by antibiotics that were previously effective against XDR typhoid. This will create public campaign to address fore-mentioned problems responsible for antibiotic resistance.

CONCLUSION:

We found that the cases of XDR typhoid resistant to potent antibiotics are increasing, limiting treatment options that will add to cost of therapy, complications and mortality. Measures to improve public awareness, personal hygiene, sanitation and vaccination can control the situation.

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REFERENCES:

1. Irakoze Mukamana S. (2025). Pathogenesis and Clinical Manifestations of Typhoid Fever. Research Output Journal of Biological and Applied Science 5(1):60-63. DOI: https://doi.org/10.59298/ROJBAS/2025/516063
2. Piovani D, Figlioli G, Nikolopoulos GK, Bonovas S. The global burden of enteric fever, 2017-2021: a systematic analysis from the global burden of disease study 2021. EClinicalMedicine 2024;77:102883. DOI: https://doi.org /10.1016/j.eclinm.2024.102883
3. Tharwani ZH, Kumar P, Salman Y, Islam Z, Ahmad S, Essar MY. Typhoid in Pakistan: Challenges, Efforts, and Recommendations. Infect Drug Resist 2022;15:2523-2527. DOI: https://doi.org/10.2147/IDR.S365220
4. Muche G, Tesfaw A, Bayou FD. Prevalence of typhoid fever and its associated factors among febrile patients visiting Arerti Primary Hospital, Amhara Region, north east Ethiopia. Front Public Health 2024;12:1357131. DOI: https://doi.org/ 10.3389/fpubh.2024.1357131
5. Parry CM, Qamar FN, Rijal S, McCann N, Baker S, Basnyat B. What Should We Be Recommending for the Treatment of Enteric Fever? Open Forum Infect Dis 2023;10:S26-S31. DOI: 10.1093/ofid/ofaa631
6. Octavia S, Chew KL, Lin RTP, Teo JWP. Azithromycin-Resistant Salmonella enterica Serovar Typhi AcrB-R717Q/L, Singapore. Emerg Infect Dis 2021;27(2):624-627. DOI: https://doi.org/10.3201/eid2702.203874
7. Nizamuddin S, Khan EA, Chattaway MA, Godbole G. Case of Carbapenem-Resistant Salmonella Typhi Infection, Pakistan, 2022. Emerg Infect Dis 2023;29(11):2395-2397. DOI: 10.3201/eid2911.230499
8. Butt MH, Saleem A, Javed SO, Ullah I, Rehman MU, Islam N, et al. Rising XDR-Typhoid Fever Cases in Pakistan: Are We Heading Back to the Pre-antibiotic Era? Front Public Health 2022;9:794868. DOI: https://doi.org/10.3389/ fpubh.2021.794868
9. Abdullah MA, Shaikh BT, Ashraf M, Khan SA. XDR typhoid in Pakistan: A threat to global health security and a wake-up call for antimicrobial stewardship. PLoS Negl Trop Dis 2025;19(5):e0013067. DOI: https://doi.org/ 10.1371/ journal.pntd.0013067
10. Walker J, Chaguza C, Grubaugh ND, Carey M, Baker S, Khan K, et al. Assessing the global risk of typhoid outbreaks caused by extensively drug resistant Salmonella Typhi. Nat Commun 2023;14(1):6502. DOI: https://doi.org/10.1038 /s41467-023-42353-9

Short Communication **Open Access**

Integrating Lifestyle Medicine into Oral Health Care

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ABSTRACT:

Integrating lifestyle medicine into oral healthcare highlights a shifting paradigm from disease centered treatment to prevention based, holistic care. Oral diseases such as caries, periodontitis, and oral cancer share modifiable lifestyle factors including diet, tobacco use, alcohol consumption, stress, and inadequate physical activity with heart conditions. Addressing these determinants alongside conventional dental treatments can enhance treatment outcomes and improve overall Patient wellbeing. Lifestyle medicine offers structured, evidence-based strategies such as nutritional counseling, behavioral modification, and stress reduction which can be seamlessly incorporated into dental practice. Dentists are uniquely positioned to identify risk behaviors early and support patients through personalized interventions. Collaborative care models, interprofessional education, and patient centered interventions are essential to overcome implementation barriers. By embracing this shift towards lifestyle medicine, oral health professionals can contribute meaningfully to the prevention of both oral and systemic diseases, ultimately advancing population health and reducing healthcare costs

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The paradigm of healthcare is rapidly changing from disease management to preventive healthcare. Lifestyle medicine is a relatively new discipline focused on evidence based therapeutic interventions such as nutrition, physical activity, stress management, sleep improvement, and reduction of habits associated with risk, represents a central pillar of this transformation. Despite its expanding presence in primary healthcare, lifestyle medicine's integration into dentistry remains limited which limits its scope. However, given the clear relationship between oral diseases and systemic health, a holistic, lifestyle-centered approach in dental practice is not only timely but also necessary to provide a better healthcare for the patients. Oral diseases including periodontitis and gingivitis are among the most common non-communicable diseases (NCDs). These diseases are affecting approximately 3.5 billion people globally. The risk factor for these diseases are same as major risk factors with leading causes of global mortality, such as heart disease, diabetes, and cancer: poor diet, tobacco use, alcohol misuse, physical inactivity, and chronic stress. Therefore, it is logical and utmost necessity to merge lifestyle -focused strategies into oral healthcare structures and protocols to not only address oral conditions but also impact systemic health outcomes.

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The oral cavity is an important representation of systemic health. Like chronic periodontal disease leads to systemic inflammation, a vital mediator in the development of atherosclerosis, insulin resistance, and negative pregnancy outcomes. On the other hand, systemic conditions like diabetes significantly worsen periodontal status by damaging immune responses and tissue healing. In the light of clinical evidence it is reported to support that treating periodontal inflammation can positively improve systemic conditions. Successful periodontal therapy in diabetic patients improves glycemic control, reinforcing the relationship between oral and systemic health. Understanding this puts dentists under greater control of system health by managing oral conditions, elevating them to a greater role. In a wider perspective, associations between poor oral health and respiratory infections, cognitive decline, and certain cancers have been suggested but more work is needed to prove them beyond doubt. Oral pathogens may have a possible route through the ulcerated periodontal tissues to the blood thus causing a whole bunch of new problem. Diet plays a major role in not just maintaining the system health but specially the oral health. Highly processes sugars are associated with increased dental caries and a high risk of diabetes. While whole plant based diet not only lowers the risk of diabetes but also the dental caries and other oral problems. Physical activity, usually not considered of much importance for oral health is extremely beneficial because it lowers systemic inflammation and increases insulin sensitivity, which in turn lowers the risk for diabetes and its associated oral health

problems. Sedentary lifestyles have been associated with increased risk of periodontal disease, independent of traditional risk factors such as smoking and diabetes. Sleep is another critical determinant, which is the most overlooked factor in dental practice. Sleep deprivation and disorders such as obstructive sleep apnea are associated with elevated levels of systemic inflammation and poor oral health outcomes, including destruction of the periodontium and delayed healing after oral surgery. Patients with obstructive sleep apnea often present with xerostomia (dry mouth) which increases the risk of caries and periodontal disease, thus highlighting an area where dental practitioners can contribute to broader health screening. Chronic stress is associated with poor oral and systemic health. Elevated cortisol's levels as a result or prolonged stress weakens the immune system, significantly reducing the salivary flow, and increasing the susceptibility to oral infections such as periodontitis and gingivitis. Stress is the fundamental contributor to para-functional habits and harmful habits like smoking and drug abuse.

Lifestyle medicine's structured approach to stress management including the promotion of healthy lifestyle incorporating good habits and a balance of everything should be the fundamental principal in modern healthcare especially in a dental office. As proven by multiple studies, the role of stress in wrecking havoc across oral cavity is unmatched. Therefore, by managing stress with being mindful can contribute to significantly better outcomes in patients. Dentist can play the leading role in this changing paradigm by being the early adopters of this great approach. Dentists and dental professional communicate and interact with patients, often more frequently than general physicians providing a great opportunity to identify and disrupt micro behaviors which can be harmful. Discussions about smoking cessation, sedentary lifestyle, stress management and harmful habits can be incorporated in dental visits without disrupting the workflow. The problem is most dentists and associated dental care providers lack the basic training in lifestyle modifications. Incorporating lifestyle medicine and patient counseling should be incorporated into dental educational curriculum to train the dentists to engage in meaningful conversations, which extend beyond teeth and gums. Small interventions over the time have shown to make a meaningful impact on patient habits. It is necessary to include chair side assessments including questionnaires, verbal and non-verbal assessments to possibly evaluate the risk of bad habits and harmful patterns in order to identify and eradicate them over a period. Identification is the key to disruption. With the advent or digital technologies including behavior-tracking applications and teleconsultation. It is relatively easy to identify, disrupt and monitor certain behaviors, which would have required immense effort in the past. Technology should be leveraged to favor healthcare providers for the greater good of patients.

The benefits of integrating lifestyle medicine into dentistry extend beyond individual practice. At a population level, such integration can contribute significantly to reducing the burden of NCDs. Public health strategies should recognize oral health as an integral part of chronic disease prevention initiatives, particularly in vulnerable populations where access to both medical and dental services is limited. Policy changes are urgently needed to incentivize preventive care in dentistry. Current healthcare systems often reward treatment over prevention, creating structural barriers to the implementation of lifestyle interventions. Changing the structure of healthcare from treatment from prevention through lifestyle modification and multidisciplinary collaboration can make a difference of life and death especially for the underprivileged and marginalized populations.

Integrating lifestyle medicine into oral healthcare included certain barriers like limited appointment time which restricts the ability of dental professionals to engage in meaningful conversations about behavior change during routine visits. Almost all dental practices are structured around procedural efficiency, leaving little room for counseling or preventive discussions within the standard appointment schedule. Another important factor is the, insufficient reimbursement for lifestyle related services poses a major obstacle in for profit setups. Almost all of the dental insurance models primarily cover clinical treatments rather than preventive or educational services, limiting providers from investing their time in lifestyle counseling, even when it is clinically warranted. There is a lack of comprehensive training for dentists in areas such as nutrition, behavioral science, and motivational interviewing. Many dental professionals report feeling unprepared to discuss these topics with confidence or to implement structured interventions due to the lack of training, highlighting a need for curriculum reforms and ongoing professional development. Training existing dental healthcare providers through seminars and conferences is the need of the moment. On the patient side, socioeconomic factors can significantly limit the feasibility of adopting recommended lifestyle changes. Individuals from lower income or underserved communities may face challenges such as limited access to healthy diet, safe environments for physical activity, or consistent healthcare. These disparities reduce patient compliance to lifestyle recommendations and require the development of individually tailored, culturally sensitive, and accessible approaches that address real world limitations. Language barriers, education levels, and competing life priorities such as work and caregiving responsibilities may further complicate patient's ability to prioritize oral and overall health behavior changes.

Addressing these challenges require a systemic and policy level intervention on a national scale. Healthcare system reforms are necessary to support reimbursement for preventive services, promote inter professional collaboration,

and restructure care delivery models to allow for lifestyle integration. Furthermore, policy advocacy is essential to drive changes in dental education, public health funding, and care accessibility. Investing in these areas can empower dental care providers and patients alike making lifestyle medicine a practical and sustainable part of oral healthcare.

Oral care must be a part of public campaigns focused on improving health through lifestyle modification, healthy diet and promoting physical activity. Dental professionals can play the leading role as advocates for the cause through their workplaces, schools community halls and other places of public interaction. The historical separations between oral health conditions and systemic wellbeing is no longer feasible. Staggering evidence demands a unified approach and coordination between systemic wellbeing and oral health. Such a paradigm shift would not only improve oral health but also contribute substantially to overall wellbeing of an individual Dentists can play a leading role in this transformation as leaders through lifestyle counseling, interdisciplinary collaboration, and patient centered preventive care. They can help build healthier populations and reduce the burden of chronic conditions. Embracing prevention lifestyle modification as the solution is not only an option now, but also an uncompromising reality.

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REFERENCES

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries, 1990–2019: a systematic analysis. Lancet. 2020;396(10258):1204–22. doi: 10.1016/S0140-6736(20)32226-1.
2. Watt RG, Sheiham A. Integrating the common risk factor approach into a social determinants framework. Community Dent Oral Epidemiol. 2012;40(4):289–96. doi: 10.1111/j.1600-0528.2012.00680.x.
3. Tonetti MS, Van Dyke TE. Periodontitis and atherosclerotic cardiovascular disease: Consensus report of the Joint EFP/AAP Workshop. J Clin Periodontol. 2013;40 Suppl 14:S24–9. doi: 10.1902/jop.2013.1340019.
4. Preshaw PM, Alba AL, Herrera D, Jepsen S, Konstantinidis A, Makrilakis K, et al. Periodontitis and diabetes: a two-way relationship. Diabetologia. 2012;55(1):21–31. doi: 10.1007/s00125-011-2342-y.
5. Simpson TC, Weldon JC, Worthington HV, Needleman I, Wild SH, Moles DR, et al. Treatment of periodontal disease for glycaemic control in people with diabetes mellitus. Cochrane Database Syst Rev. 2015;(11):CD004714. doi: 10.1002/14651858.CD004714.pub4.
6. Sheiham A, James WP. Diet and dental caries: the pivotal role of free sugars reemphasized. J Dent Res. 2015;94(10):1341–7. doi: 10.1177/0022034515590377. Epub 2015 Aug 10.
7. Merchant AT, Pitiphat W, Rimm EB, Joshipura K. Increased physical activity decreases periodontitis risk in men. Eur J Epidemiol. 2003;18(9):891–8. doi: 10.1023/a:1025622815579.
8. Al-Zahrani MS, Borawski EA, Bissada NF. Periodontitis and three health-enhancing behaviors: role of physical activity. J Periodontol. 2005;76(9):1362–6. doi: 10.1902/ jop.2005.76.8.1362.
9. Han S, Jee D, Kang YJ, Park YJ, Cho JH. Possible association between oral health and sleep duration: a cross-sectional study based on the Korean National Health and Nutrition Examination Surveys from 2010 to 2015. Medicine (Baltimore). 2021;100(48):e28035. doi:10.1097/MD.0000000000028035.
10. Genco RJ, Ho AW, Grossi SG, Dunford RG, Tedesco LA. Relationship of stress, distress, and inadequate coping behaviors to periodontal disease. J Periodontol. 1999;70(7):711–23. doi: 10.1902/jop.1999.70.7.711.
11. Ramprasad A, Naik A, Makansi N. Implementation of motivational interviewing training in dental education and research: a scoping review. J Dent Educ. 2025 Apr 27:e13909. doi:10.1002/jdd.13909.
12. Blomma, C., Krevers, B. Important aspects of conducting an interdisciplinary public preventive oral health project for children in areas with low socioeconomic status: staff perspective. BMC Oral Health 20, 362 (2020). https://doi.org/10.1186/s12903-020-01352-8
13. Kshirsagar MM, Deshmukh M, Patil T, Khobragade V, Chandran T, Yadav D. Barriers to utilization of oral healthcare in dental students: a cross-sectional survey. J Pharm Bioallied Sci. 2025;17(Suppl 2):S1716-S1718. doi:10.4103/jpbs. jpbs_280_25.
14. Carr AB, Ebbert J. Interventions for tobacco cessation in the dental setting. Cochrane Database Syst Rev. 2012;2012(6):CD005084. doi:10.1002/14651858. CD005084.pub3. Update in: Cochrane Database Syst Rev. 2021;2:CD005084. doi:10.1002/14651858.CD005084.pub4.
15. Moin M, Maqsood A, Haider MM, Asghar H, Rizvi KF, Shqaidef A, Sharif RA, Suleman G, Das G, Alam MK, Ahmed N. The association of socioeconomic and lifestyle factors with the oral health status in school-age children from Pakistan: a cross-sectional study. Healthcare (Basel). 2023;11(5):756. doi:10.3390/healthcare11050756.
16. HASHMAT , S., HINGORJO , M., SHAHID , R., GHANI , R., RASHID , M., & BUTT , F. (2023). RELATIONSHIP BETWEEN LIFESTYLE AND ORAL HEALTH. Biological and Clinical Sciences Research Journal, 2023(1), 522. https://doi.org/10.54112/bcsrj.v2023i1.522

Letter to Editor **Open Access**

The Role of AI in Healthcare: Innovation with Human Touch

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Azmat H, Naqvi SSA. The Digital Doctor: AI's Emerging Role in Clinical Practice. J Bahria Uni Med Dental Coll. 2025;15(4):463 DOI: https://doi.org/10.51985/JBUMDC2025681

I am writing in response to the article "Artificial Intelligence in Surgery: Learning and Applications" to express my views on the rapidly evolving role of artificial intelligence (AI) in healthcare which has been published in your prestige journal Volume 15 No.3 (2025) with DOI**:** https://doi.org/10.51985 /JBUMDC2025592 . This transformative technology is reshaping the way we deliver care, diagnose diseases, and manage treatments.

AI, which involves developing machines capable of mimicking and in some cases surpassing human cognitive functions, is making significant strides in clinical settings. One of its most impactful uses is in predictive analytics. By analyzing patients' current health data alongside their medical histories, AI can forecast potential health risks and identify trends. These predictive capabilities allow for earlier interventions, more effective preventive care, and ultimately better patient outcomes while reducing overall healthcare costs.[1]

In addition, AI streamlines administrative tasks by digitizing and organizing patient data, which significantly reduces the documentation burden on medical teams.[2] It also plays a vital role in medical education, bridging the gap between theory and practice by enabling students to simulate history-taking, diagnosis, and treatment planning.[3]

Technologies such as 3D printing (3DP), often powered by AI-driven planning tools, are revolutionizing surgical procedures, particularly in tumor excision. They help define precise surgical margins, reduce the risk of damaging vital structures, and preserve healthy tissue resulting in improved postoperative outcomes.4

Furthermore, AI-enabled clinical decision support systems (CDSS) assist healthcare professionals by providing real-time recommendations, alerting them to potential errors, and supporting decision-making processes. In underserved or resource-limited areas, AI tools can extend access to medical expertise where specialists may not be available.

However, it is my firm belief that AI should serve as an adjunct to healthcare professionals not a replacement. The human elements of empathy, ethical judgment, and clinical intuition remain irreplaceable.

In conclusion, to ensure that AI technologies serve patients safely and equitably, close collaboration is required among clinicians, data scientists, and policymakers. With thoughtful integration, AI can truly enhance the practice of medicine and improve healthcare delivery across the globe.

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Huma Azmat: Conception, design, analysis, literature search, writing, proof reading
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REFERENCES:

1. Russell S, Norvig P. Artificial Intelligence: A Modern Approach. 3rd ed. Pearson; 2016.
2. Obermeyer Z, Emanuel EJ. Predicting the future — Big data, machine learning, and clinical medicine. New England Journal of Medicine. 2016;375(13):1216–9. https://doi.org/10.1056/NEJMp1606181
3. Davenport T, Kalakota R. The potential for artificial intelligence in healthcare. Future Healthcare Journal. 2019;6(2):94–8. https://doi.org/10.7861/futurehosp.6-2-94
4. Wartman SA, Combs CD. Medical education must move from the information age to the age of artificial intelligence. Academic Medicine. 2018;93(8):1107–9. https://doi.org/10.1097/ACM.0000000000002044
5. Martelli N, Serrano C, van den Brink H, Pineau J, Prognon P, Borget I, et al. Advantages and disadvantages of 3D printing in surgery: a systematic review. Surgery Today. 2016;46(12):1443–52. https://doi.org/10.1007/s00595-016-1342-7

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The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-4

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Cancer in South Africa [editorial]. S Afr Med J 1994;84:15

d) Chapter in a book:

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