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## EDITORIAL

## NOVEL APPROACHES TO COMBAT ANTIMICROBIAL RESISTANCE IN DEVELOPING COUNTRIES

Raja Kamran Afzal, Ali Khalid

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Antimicrobial resistance (AMR) is an emerging public health crisis whose threat to present-day antimicrobial efficacy and global progress in the control of infectious diseases has rapidly escalated. It presents as an even graver situation in developing countries, whose underdeveloped healthcare infrastructure, limited laboratory capacity, weak regulation in antimicrobial prescription and consumption, as well as restricted access to novel antimicrobials accelerates selection and proliferation of multidrug resistant organisms. Traditional methods such as the use of surveillance systems, infection prevention and control, and antimicrobial stewardship are vital but are insufficient by themselves. We must advance beyond incremental changes to the problem of the increasing AMR crisis, instead committing to the use of novel and locally appropriate solutions. This change is enabled by quick and low-cost diagnostics that circumvent poor laboratory infrastructure which leads to empirical wide-spectrum antibiotic prescription. Rapid and cost-effective diagnostics such as loop-mediated isothermal amplification (LAMP), lateral flow immunoassays and low cost molecular platforms can all be deployed to facilitate identification of the target pathogen as well as its susceptibility pattern at the bedside.<sup>1</sup> Establishment and reinforcement of sentinel laboratory networks; integration of genomic surveillance; and creation of a centralised repository for AMR data are also critical for tracking resistance patterns and informs interventions. Likewise, antimicrobial stewardship programs are also facing the challenge to adapt to the resource-limited settings and can overcome them through rational

application of interventions, as described.<sup>2</sup> Evidence based rational interventions include restrictive antimicrobial formularies, ongoing audit-and-feedback and syndrome specific treatment algorithms designed based on local antibiograms. Integration of electronic decision support platforms in hospital information systems can aid in oversight of prescriptions without use of infectious diseases specialists; it would be impossible for a small cohort of ID specialists to adequately oversee and influence prescriptions in limited resource countries.<sup>3</sup> Mobile diagnostic tools and concise prescribing guideline local in context can equip health practitioners to combat the crisis through judicious antimicrobial prescription and can be more scalable solutions for curbing the problem of its overuse. Investment in new therapeutic avenues is as essential since the current pipeline for antimicrobials remains slim. Biologics like bacteriophage therapy, endolysins, bacteriocins and antimicrobial peptides are proving effective for Gram-negative multidrug resistant infections, and are best suited for immunocompromised and hospital-acquired conditions.<sup>4</sup> Production of these biologics would require development of specific local strain libraries and established production methods; they also require specific regulatory frameworks. Monoclonal antibodies directed at key virulence factors can supplement existing antibiotics, a form of passive immunisation. However, developing countries are best suited for such innovative approaches because of their high burden of disease and biodiversity of pathogens, if they establish effective regulatory mechanisms. Lastly, collaboration across sectors is vital for the sustainability of the crisis management system. AMR does not exist solely in human health; antibiotics are heavily used in veterinary practice, fish farming and agriculture, driving selection and spread. The adoption of a One Health approach, integrating the surveillance data from human, animal and environmental sources, would provide a holistic approach to containing the spread of resistant organisms.<sup>1</sup> Strategies to include vaccination of

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livestock, a phased ban on non-therapeutic use of antibiotics, and surveillance of environmental sites for resistant genes can aid significantly in reducing selection pressures. In summary, an approach to tackling the AMR crisis in developing countries should incorporate state-of-the-art diagnostics, novel therapeutics, optimized

antimicrobial stewardship, and multi-sectoral partnership. By utilizing their strengths and coordinating with their peers globally, developing countries can greatly influence global efforts to mitigate AMR, as well as create sustainable model approaches applicable in their specific contexts.

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## BRIDGING THE GAP IN HEPATOCELLULAR CARCINOMA DETECTION: EVALUATING LI-RADS WITH MRI

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### ABSTRACT

**Objectives:** This study aimed to determine diagnostic accuracy of the LI-RADS (Liver Imaging Reporting and Data System) using magnetic resonance imaging (MRI) for detecting Hepatocellular carcinoma (HCC) in cases of liver cirrhosis diagnosed to have hepatic nodules  $\leq 20$  mm, using histopathology as the reference.

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

**Place and Duration of Study:** Department of Radiology, Holy Family Hospital, Rawalpindi. Study duration was from 25-03-2024 till 24-01-2025

**Patients and Methods:** After ethical approval, 170 consecutive eligible patients underwent multiphasic gadolinium-enhanced abdominal MRI on a 1.5 Tesla system (33 mT/m gradient), with LI-RADS interpretation by a consultant radiologist. All patients also underwent ultrasound-guided percutaneous fine needle biopsy, and histopathology served as the gold standard. Data were analyzed using SPSS 20, with diagnostic performance assessed via a  $2 \times 2$  contingency table, and stratification applied to evaluate the impact of effect modifiers on diagnostic accuracy.

**Results:** A total of 170 patients (53% males, 47% females) were included, with mean age  $45.28 \pm 11.67$  years, BMI  $30.38 \pm 2.33$  kg/m<sup>2</sup>, cirrhosis duration  $7.93 \pm 2.46$  months, and nodule size  $11.25 \pm 5.25$  mm; HCC was identified in 60% by LI-RADS. Diagnostic performance showed sensitivity 60.78%, specificity 95.58%, PPV 95.38%, NPPV 61.90%, and accuracy 74.70%.

Stratified accuracy was similar by age ( $<40$ : 75.38%,  $>40$ : 73.53%) and sex (males 74.44%, females 75%), but higher with BMI  $>27$  kg/m<sup>2</sup> (76.69% vs. 71.64%) and cirrhosis duration  $>10$  months (83% vs. 70.94%); accuracy was 77.02% for nodules  $<10$  mm and 72.91% for  $>10$  mm. Overall, LI-RADS shows high specificity but moderate sensitivity, with better performance in higher BMI and longer cirrhosis duration.

**Conclusion:** This study demonstrates Li-RADS with MRI to have high diagnostic accuracy for detection of hepatocellular carcinoma. Standardization of reports of CT and MRI with LI-RADS improves consistency, reduces errors, and enhances patient management. It also supports nationwide data collection, enabling future research and AI-driven analysis in HCC diagnostics.

**Keywords:** Diagnostic Accuracy, Hepatocellular Carcinoma, Liver Imaging Reporting and Data System, Magnetic Resonance Imaging

### INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary liver malignancy that typically arises in background of

preexisting chronic liver disease. The individuals with chronic hepatitis B hepatitis C infections are considered high-risk. Diagnosing HCC may be challenging and frequently necessitates the usage of multiple imaging-techniques. Ideally, the tumors measuring approximately 2 cm should be identified early to allow access to the full range of therapeutic options.

However, as the specific symptoms are often subtle or absent, HCC is often identified at an advanced stage.<sup>1</sup> Hence, median survival once HCC is diagnosed is limited to approx. 6-20 months.<sup>2</sup> HCC is a primarily tumor that originates from liver, that typically arises in

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chronic liver disease cases. Treating physicians often face diagnostic difficulties, and several imaging modalities have to be obtained for each case.<sup>3</sup>

The most commonly used imaging modalities for diagnosing HCC include ultrasound, CT, MRI, and angiography. A characteristic imaging appearance on one of these tests, along with an elevated serum alpha-fetoprotein (AFP) level, is typically adequate for confirming the diagnosis. Helical CT is generally preferred by radiologists due to the high cost and longer acquisition time associated with standard MRI scans.<sup>4</sup> However, MRI is useful in patients with renal insufficiency and patients allergic to the dye or contrast material used in CT scan. MRI is especially useful when CT findings are inconclusive, particularly in a liver with significant nodularity, as it can more accurately distinguish dysplastic nodules from HCC. Additionally, MRI outperforms CT in differentiating vascular pathologies, including the hemangiomas, and areas of focal fat from hepatocellular carcinoma.<sup>5</sup>

The LI-RADS system designed and formulated by American College of Radiology (ACR), provides a standardized framework for interpreting CT and MRI in case having liver cirrhosis or those that carry certain other risk factors that may contribute to HCC (Figure I). This study aimed to evaluate diagnostic accuracy of LI-RADS while being applied to MRI in order to diagnose the hepatocellular carcinoma. LI-RADS may be utilized as a standardized diagnostic and prognostic tool, helping to minimize under- or over-reporting while also aiding in the monitoring of follow-up cases.

The LI-RADS aims to achieve several long-term goals, including the creation of a standardized imaging

terminology, the definition of criteria for interpreting the image, the unification of radiological report structure and content, the establishment of minimum technical standards, and the development of a formal system for data collection.<sup>6</sup> The successful implementation of these goals is anticipated to strengthen communication between radiologists and clinicians. This will also decrease the inconsistencies and errors in image interpretation, ensure the comprehensive reporting, reduce the incidence of suboptimal imaging studies, and promote effective monitoring of outcomes, performance evaluation, quality assurance, research, and meta-analysis.<sup>7</sup>

LI-RADS encompasses a complete range of hepatic lesions extending from benign lesions, to potentially cancerous and definitive malignancy amongst the cirrhotic or cases at risk of HCC.<sup>8</sup> This system incorporates the imaging diagnostics beyond vascularity to assess the probability of HCC and includes specific criteria for identifying vascular invasion.<sup>9</sup> In addition, LI-RADS being intended to be useful for radiology consultants, regardless of them being expert in liver related imaging, and can be applied both in tertiary liver centers and other settings, as well as in daily clinical evaluation of their patients and also for research purposes. It offers generalized guidance on CT or MRI interpretation, along with the rationale of this being recommended. The LI-RADS criterion are structured for facilitation of organized and standardized imaging interpretation and reporting of at-risk cases for HCC.<sup>10</sup>

The purpose of this study is to evaluate the role of LI-RADS in standardizing liver imaging interpretation and reporting to improve diagnostic accuracy,

| CT/MRI Diagnostic Table                                                                                                                                                |       |         |      |                |              |      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|---------|------|----------------|--------------|------|
| Arterial phase hyperenhancement (APHE)                                                                                                                                 |       | No APHE |      | APHE (not rim) |              |      |
| Observation size (mm)                                                                                                                                                  |       | < 20    | ≥20  | <10            | 10-19        | ≥ 20 |
| <b>Count major features:</b> <ul style="list-style-type: none"> <li>• "Washout" (not peripheral)</li> <li>• Enhancing "capsule"</li> <li>• Threshold growth</li> </ul> | None  | LR-3    | LR-3 | LR-3           | LR-3         | LR-4 |
|                                                                                                                                                                        | One   | LR-3    | LR-4 | LR-4           | LR-4<br>LR-5 | LR-5 |
|                                                                                                                                                                        | ≥ Two | LR-4    | LR-4 | LR-4           | LR-5         | LR-5 |



Observations in this cell are categorized LR-4, except:  
 ·LR-5g, if ≥ 50% diameter increase in < 6 months (equivalent to OPTN 5A-g)  
 LR-5us, if "washout" and visibility at screening ultrasound (per AASLD HCC criteria)

**Figure I: Overview of all the LI-RADS categories based on MRI.**

communication, and overall clinical outcomes.

## PATIENTS AND METHODS

This was a descriptive cross-sectional study. The study set-up was Radiology Department, Holy Family Hospital (HFH) Rawalpindi. Study duration was 25<sup>th</sup> March 2024 till 24<sup>th</sup> Jan 2025, and was conducted after ethical approval (ERB# 4826/RTH/RWP). Data were collected using non-probability, consecutive sampling. Sample size was calculated as per 95% confidence level, with a desired precision of 10% for sensitivity and 4% for specificity, and an HCC prevalence of 64.15%. LI-RADS MRI as 65.40% and 96.40% in diagnosing HCC,<sup>11</sup> estimated sample size was 170. Cirrhotic patients aged 25-65 years, of both genders with hepatic nodules  $\leq$  20 mm on ultrasonography (well circumscribed, hypo echoic lesions) and duration of cirrhosis  $>$ 3 months were included, while the patients in whom contrast agent (Gadolinium) is contraindicated (e.g. acute or chronic renal failure), already taking chemotherapy for hepatic neoplasm, contraindicated for MRI studies (having MRI incompatible prosthesis or implant) and noncooperative patients were excluded from the study.

Total 170 consecutive patients referred to dept. of radiology HFH, Rawalpindi, who fulfilled inclusion criteria were inducted for study. Written informed consent was obtained for each study participant. Multiphasic gadolinium enhanced Abdominal MRI was performed on all patients. The 1.5 Tesla MRI system was used having 33 mT/m gradient strength. MRI examinations were performed with a phased-array body coil. Patient was in supine position during imaging which increased the ratio of signal-to-noise. Intravenous Gadolinium 0.5 mmol/L was used in all patients. The LI-RADS results with magnetic resonance imaging (MRI) were reported by a radiology consultant having experience of  $\geq$  5 years after the fellowship. The presence or absence of hepatocellular carcinoma was documented as outlined in the operational definition (Fig 1).<sup>12</sup> All patients subsequently underwent percutaneous ultrasound guided fine needle biopsy in the designated ward, and the histopathology report of the specimen was obtained from the hospital's central laboratory. The findings from the LI-RADS using MRI were compared with histopathology results. Data on age, gender, duration of cirrhosis, BMI, and hepatic nodule size were collected using a specified study proforma.

The analysis of study data was conducted via SPSS version 20.0. The mean values along with standard

deviations were calculated for age, BMI, total duration of liver cirrhosis and size of hepatic nodule size. Regarding gender and the presence or absence of hepatocellular carcinoma, frequencies and percentages were computed. A 2 $\times$ 2 contingency table was used to calculate the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of LI-RADS with MRI in diagnosing hepatocellular carcinoma in hepatic nodules  $\leq$  20 mm in cirrhotic patients, using histopathological diagnosis as gold standard. The effect modifier variables (i.e., age, gender, body mass index, total duration since liver cirrhosis, nodule size of HCC) were addressed via stratification and diagnostic accuracy was then calculated post-stratification.

## RESULTS

Amongst 170 cases, it was observed that the mean age was  $45.28 \pm 11.67$  (range: 25-65) years. The BMI (kg/m<sup>2</sup>) was calculated as  $30.38 \pm 2.33$  (27-34) kg/m<sup>2</sup>. It was observed that the duration of cirrhosis was  $7.93 \pm 2.46$  (4-12) months. The size of hepatic nodule (mm) was  $11.25 \pm 5.25$  (5-20) mm. Of the total patients, 90(52.9%) were male and 80(47.10%) were female cases.

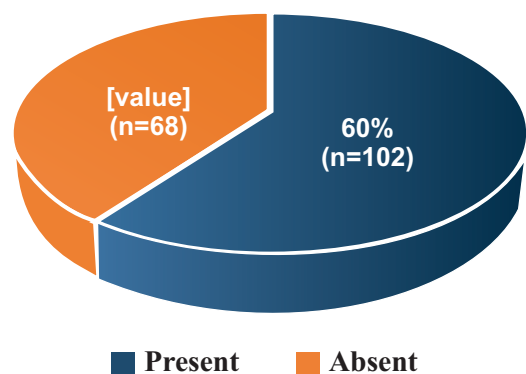
Hepatocellular carcinoma on LI-RADS was present in 102 (60%) and absent in 68 (40%) patients (Figure-II). The sensitivity of hepatocellular carcinoma was calculated at 60.78%, with a specificity of 95.58%. The PPV was 95.38%, the NPV was 61.90%, while overall diagnostic accuracy was 74.70% (Table-II). By stratification of age, the diagnostic accuracy of hepatocellular carcinoma was 75.38% in below forty years age group while in forty years and above age group the diagnostic accuracy was 73.53%. The diagnostic accuracy of hepatocellular carcinoma was 74.44% in males while in females the diagnostic accuracy was 75%. In patients with BMI  $<$ 27 kg/m<sup>2</sup> the diagnostic accuracy of HCC was determined to be 71.64% while in patients with BMI  $>$  27 kg/m<sup>2</sup> the diagnostic accuracy was 76.69%. In patients with duration of cirrhosis  $<$ 10 months the diagnostic accuracy of HCC was 70.94% while in patients with cirrhosis  $>$ 10 months the diagnostic accuracy was 83.01%. In patients with size of hepatic nodule  $<$ 10 mm the diagnostic accuracy of hepatocellular carcinoma was 77.02% while in patients with size of hepatic nodule  $>$ 10 mm the diagnostic accuracy was 72.91%.

## DISCUSSION

This study reports mean age of HCC cases to be 45 years,

indicating that hepatocellular carcinoma (HCC) affects a relatively younger population in our setting. In contrast, data from the United States shows a significantly higher median age of HCC diagnosis,

which is 64 years. This disparity may be due to differences in risk factors, including prevalent hepatitis B



**Figure II: The distribution of Hepatocellular carcinoma on LI-RADS (n = 170).**

**Table I: Hepatocellular carcinoma on LI-RADS and on histopathology (n = 170)**

| Hepatocellular carcinoma on LI-RADS                                                                                                                                                                   | Hepatocellular carcinoma on histopathology |                     | Total |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|---------------------|-------|
|                                                                                                                                                                                                       | Yes                                        | No                  |       |
| Yes                                                                                                                                                                                                   | TP= 62 <sup>a</sup>                        | FP= 3 <sup>b</sup>  | 65    |
| No                                                                                                                                                                                                    | FN= 40 <sup>c</sup>                        | TN= 65 <sup>d</sup> | 105   |
| Total                                                                                                                                                                                                 | 102                                        | 68                  | 170   |
| <b>Sensitivity 60.78%; Specificity 95.58%;<br/>           PPV (Positive predictive value) 95.38%; NPPV<br/>           (Negative predictive value) 61.90%<br/>           Diagnostic accuracy 74.7%</b> |                                            |                     |       |

and hepatitis C infected cases in our population, leading to earlier onset of liver disease and subsequent HCC development. These findings highlight the need for early screening and surveillance programs tailored to the local demographics.<sup>13</sup>

This study has included approx. equal number of male (53%) and female (47%) patients. Research has highlighted significant gender-based disparities in incidence, severity, prognostic outcome of HCC. The varying epidemiological distribution of factors

contributing to damaging the liver and role of sex hormones could be underlying reasons to these disparities. Men are observed to have HCC at earlier age as compared to women. Though the exact mechanism is not clear, however protective mechanism of estrogens is suggested for this gender disparity.<sup>14</sup> Our study included equal number of males and female cases and LI-RADS demonstrated the diagnostic accuracy that was consistent when comparing the genders i.e., 74.44% in males Vs. 75% in females with HCC. This concludes that LI-RADS is applicable equally in both the genders.

The mean duration of cirrhosis observed in this study was 7 months, with cases ranging from as early as 4 months to up to a year. The transition from cirrhosis to hepatocellular carcinoma varies significantly depending on the underlying cause of liver disease. Factors such as viral hepatitis, disease associated with alcohol use and metabolic disorder influence the rate of progression, highlighting the necessity for diligent monitoring and early identification strategies in high-risk patients. A Hyderabad based study conducted by Attari SA et al found HCC in 7.2 % of HCV positive case undergoing the liver biopsy.<sup>15</sup> A study by Philip et al demonstrated that in their HCC patients, cirrhosis was observed approx. 10 years before HCC was diagnosed.<sup>16</sup> In contrast, our patients reported a much shorter duration of diagnosed cirrhosis. This may be due to delayed diagnosis resulting from a lack of routine screening, limited access to healthcare facilities, or inadequate imaging, particularly among underprivileged populations. The diagnostic accuracy of LI-RADS was notably higher (83%) in patients with cirrhosis of longer duration, as opposed to those with cirrhosis lasting less than 10 months (70.9%). This suggests that prolonged disease progression may lead to more distinct imaging characteristics, improving LI-RADS performance in HCC detection.

The mean size of hepatic nodule (mm) was 11.25 mm in our cases at presentation. The minimum size of nodule was 5 mm and maximum 20 mm. With respect to the size of hepatic nodule, the diagnostic accuracy of hepatocellular carcinoma was 77% for nodules less than 10 mm size, while for nodule >10 mm the diagnostic accuracy was 73%. This supports the need for an active diagnostic work-up, even for nodules smaller than 10 mm, if the ultimate aim is to diagnose HCC at earliest possible stage.<sup>17</sup>

In the present study, the diagnostic accuracy of the Liver Imaging Reporting and Data System (LI-RADS) was

found to be 74.7%, suggesting a reasonably good performance in differentiating hepatocellular carcinoma (HCC) from other hepatic lesions. This finding aligns with previously published literature, though there is some variability in reported diagnostic accuracy rates. For example, Ling et al. reported a higher diagnostic accuracy of 86% in their cohort, along with good inter-observer agreement.<sup>18</sup> This suggests that LI-RADS can be a reliable tool in clinical practice when applied consistently. However, inter-observer variability remains a concern in some studies. Kiri et al. found only moderate inter-observer agreement, and they attributed this variability to potential confounding factors such as elevated body mass index (BMI) and the presence of steatohepatitis. These factors may obscure lesion characteristics and complicate image interpretation, thereby reducing the diagnostic precision of LI-RADS.

Additional studies support this notion of variability in LI-RADS performance. Davenport et al.<sup>19</sup> reported that LI-RADS improves standardization in liver lesion reporting, however the accuracy and consistency of interpretations can vary depending on the radiologist's experience and patient-specific factors such as liver parenchymal changes.

Similarly, Barth BK et al.<sup>20</sup> found that although LI-RADS categories generally correlate well with histopathologic findings, discrepancies can still occur, particularly in atypical cases or in patients with concurrent liver pathologies.

Taken together, these studies underscore both the strengths and limitations of LI-RADS. While it offers a structured and standardized approach for the evaluation of hepatic lesions in at-risk populations, its diagnostic performance can be influenced by patient-related factors, radiologist expertise, and image quality. Continued efforts toward radiologist training, protocol optimization, and potential refinements in LI-RADS criteria are essential to improve accuracy and reduce inter-observer variability.

Most LI-RADS research is based on Western

populations, with minimal studies validating its accuracy in Pakistani patients with diverse genetic, environmental, and viral hepatitis-related risk factors. Additionally, many radiology centres don't routinely use LI-RADS, leading to inconsistent reporting and diagnosis of HCC across different hospitals and regions. Many radiologists and clinicians lack formal training in LI-RADS, affecting its adoption and proper utilization. LI-RADS, a standardized tool, is non-invasive and minimizes misdiagnosis by categorizing hepatic nodules systematically, preventing unnecessary biopsies or delayed treatments. Hence, implementing LI-RADS widely can significantly improve liver cancer management and outcomes for our patients.

## CONCLUSION

This study demonstrates Li-RADS with MRI to have high diagnostic accuracy for detection of hepatocellular carcinoma. Standardization of reports of CT and MRI with LI-RADS improves consistency, reduces errors, and enhances patient management. It also supports nationwide data collection, enabling future research and AI-driven analysis in HCC diagnostics.

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**Source of funding:** none

### Authors' Contribution

Zahida Khanum: Conception of study/Designing/ Planning, Experimentation/Study Conduction, Analysis/Interpretation/ Discussion, Manuscript Writing  
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# FACILITATORS AND BARRIERS TO EVIDENCE-BASED PRACTICE AMONG NURSES WORKING IN SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN

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## ABSTRACT

**Objective:** The objective of this study was to identify and explore the facilitators and barriers influencing the adoption and implementation of Evidence-Based Practice among nurses working at Sheikh Zayed Hospital in Rahim Yar Khan.

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

**Place and duration of study:** This study was conducted from 23 November 2024 to 30 May 2025 at Sheikh Zayed Hospital, Rahim Yar Khan.

**Patients and Methods:** This study included non-probability convenient sampling technique to recruit 300 registered nurses with over one year of experience. Data were collected via a structured questionnaire adapted from an Evidence-Based Practice competency tool, approved by the Institutional Review Board. Quantitative data were analyzed using mean and standard deviation, while qualitative variables were analyzed using frequency and percentage in SPSS-27, ensuring informed consent and participant confidentiality.

**Results:** This study primarily surveyed female (94.7%) and married (68.7%) Registered Nurses (85%) with diverse educational backgrounds. A large proportion of nurses valued Evidence-Based Practice, with 73.7% believing it improves patient care decisions, 65.7% that it leads to better outcomes, and 68% willing to implement it. While nurses perceived strong organizational support (86.7%), significant barriers to implementation were identified, including a lack of confidence in research evaluation (44%), limited time (66.7%), inadequate access to published research (77%), and concerns about research reliability (95.7%).

**Conclusion:** Nurses perceive organizational support and have a good appreciation for Evidence-Based Practice, yet there are still many practical obstacles to overcome.

Addressing the lack of confidence in research evaluation, time constraints, and limited access to reliable research is crucial to fully integrate EBP into nursing practice and improve patient outcomes.

**Keywords:** Evidence based practice, Knowledge, Nurses, Organizational support, Pakistan

## INTRODUCTION

Nurses are an important part of healthcare structure, playing key role to improve quality of patient care.<sup>1</sup> Nursing serves as foundation of global healthcare framework, In Nursing Evidence based practice (EBP) is

essential part in providing high quality patient care.<sup>2</sup> Traditionally, the focus of nurses is health promotion, disease prevention and changing the behavior of individual with respect to their health. Nurses have multidisciplinary knowledge and experience of health promotion in their nursing practice.<sup>3</sup>

The presence of nurses is essential in clinical trial team as they can support clinical activities and also responsible for coordination and management of research activities.<sup>4</sup> The involvement of clinical research Nurses (CRNs) is considered to improve quality of clinical practice and patient centered care in clinical trial. Nursing research is crucial part to nursing profession and essential for continuing advancement to

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promote optimal nursing care.<sup>5</sup> Evidence based practice is defined as union of best available resources with clinical expertise and patient values to inform decision making in healthcare.<sup>6</sup>

High quality nursing care is emerging need in current health care structure and this demand is spreading globally. Evidence based practice in nursing involve providing holistic quality care based on the current research and knowledge rather than following traditional methods and seniors, personal beliefs and advice from college. EBP has multiple advantages. Enhancing the nurses' ability to make decisions, think critically, and serve patients with clinical experience is one way to advance their intellectual capability.<sup>7</sup>

Various researches show that nurses don't have complete knowledge about EBP. Nurses don't have broad range of abilities to formulate a question at work, analyze, critically evaluate and intervene to improve patient care. There is shortage of nurses in hospitals.<sup>7</sup> Due to shortage of staff and high patient ratio patient quality of care is compromised. For knowledge development, evidence synthesis is important but this is top down process. Knowledge is generated by few, synthesized by small group and disseminated to the large number of staff providing direct care. Those who are the recipient of knowledge may not be the same individuals who posed the original question.<sup>8,9</sup>

The objective of this study was to identify and explore the facilitators and barriers influencing the adoption and implementation of Evidence-Based Practice among nurses working at Sheikh Zayed Hospital in Rahim Yar Khan.

## PATIENTS AND METHODS

This observational cross-sectional study took place at Sheikh Zayed Hospital, a 1000-bed tertiary care facility in Rahim Yar Khan, Pakistan, which also serves patients from nearby areas like Rajanpur and Sadiqabad from 23 Nov 2024 to 30 May 2025. Ethical approval for the study was granted by the Institutional Review Board of Sheikh Zayed Medical College on November 22, 2024, under reference number 156/IRB/SZMC/SZ.

Using the formula for a cross-sectional study, the sample size was determined. The recommended sample size was determined to be 300 based on a 95% confidence level, a 5% margin of error, and a prior prevalence of 73.4% reported by Abu-Baker, et al. in a study on evidence-based practice among nurses in Jordan.<sup>10,11</sup>

Using a non probability convenient sampling technique, data were collected by the researchers themselves through a structured questionnaire, adapted from an 83-variable EBP competency questionnaire with domains covering working times, facilitators, and barriers to EBP. Inclusion criteria comprised registered nurses and head nurses with over one year of ward experience who provided informed consent, while student nurses, doctors, paramedics, and those on leave were excluded. Participants were briefed on research objectives and assured of voluntary participation and data confidentiality.

Data were organized and analysed using SPSS-27, with mean and standard deviation for quantitative variables (age, years of experience) and frequency and percentage for qualitative variables (demographics, research details, EBP barriers and facilitators).

## RESULTS

The results showed that the majority of respondents were female (94.7%) and married (68.7%). Most participants were Registered Nurses (85%), while 15% were Head Nurses. Regarding education, 52% held General Nursing qualifications, 45.3% had a BSN, and 2% MSN (Table I). A large proportion of nurses valued EBP, with 73.7% indicating it improves patient care decisions, 65.7% believing it leads to better outcomes, and 68% expressing willingness to implement it in their practice (Table II). Furthermore, 77% perceived EBP as enhancing professional autonomy. Organizational support was reported by 86.7% of participants, and 91.7% confirmed the existence of an EBP committee, while 90.7% stated that research findings were easily accessible (Figure-1). Despite this support, 44% lacked confidence in evaluating research articles, and 66.3% felt uncomfortable searching databases. Time constraints were commonly cited, with 66.7% reporting insufficient time to review and apply evidence, and 91.7% indicating difficulty in testing new ideas. Additionally, 77% noted inadequate access to published nursing research, 88.3% observed limited communication with researchers, and 95.7% questioned the reliability of research findings (Figure 2).

### Research Engagement:

Only 32% of the participants reported taking a formal research course. Engagement with research activities was moderate, with 35% of participants never publishing in academic journals and 30% publishing only occasionally. Regarding evidence-based

**Table I: Demographic profile of the participants.**

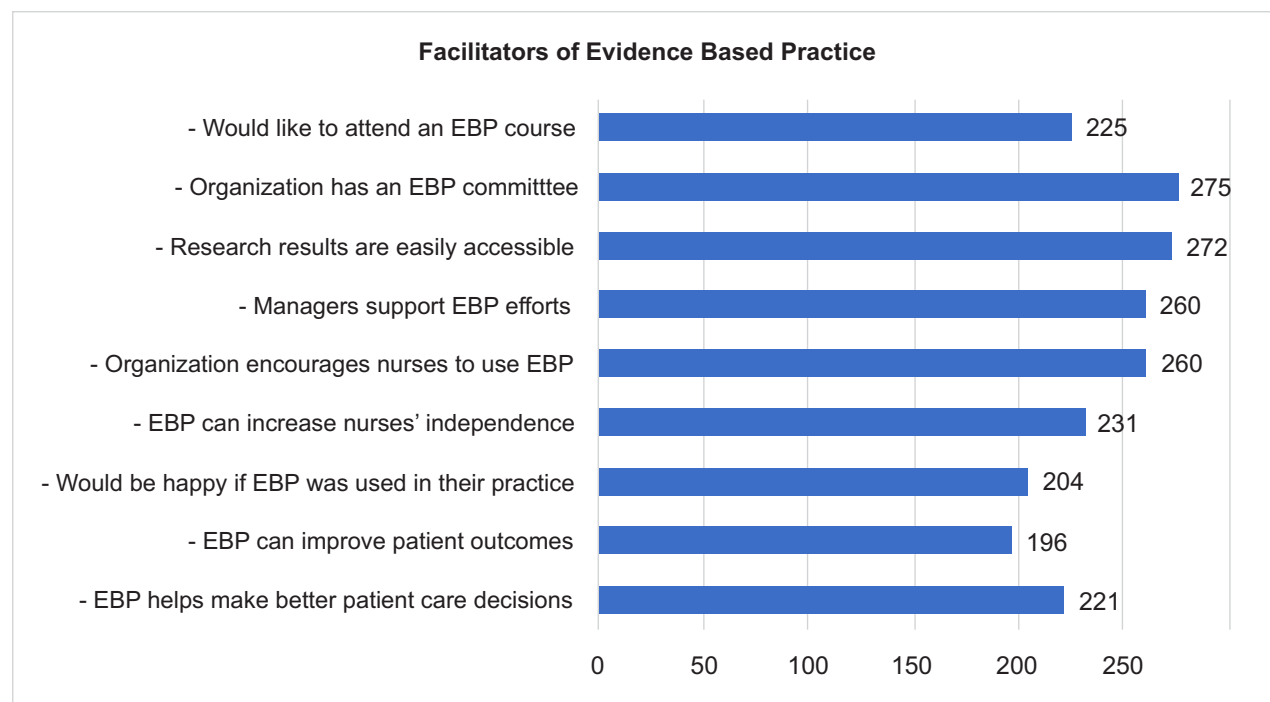
| CATEGORY                             | Frequency (No.) | Percentage (%) |
|--------------------------------------|-----------------|----------------|
| <b>Gender</b>                        |                 |                |
| Female                               | 284             | 94.70          |
| Male                                 | 16              | 5.30           |
| <b>Marital Status</b>                |                 |                |
| Married                              | 206             | 68.70          |
| Single                               | 92              | 30.70          |
| <b>Current Position</b>              |                 |                |
| Registered Nurse                     | 255             | 85.00          |
| Head Nurse                           | 45              | 15.00          |
| <b>Highest Level of Education</b>    |                 |                |
| BSN (Bachelor of Science in Nursing) | 136             | 45.30          |
| General Nursing                      | 156             | 52.00          |
| MSN (Master of Science in Nursing)   | 6               | 2.00           |

information sources, 31% relied on online databases such as PubMed and Google Scholar, while 16.2% used institutional guidelines. Only a small proportion (4.9%) reported seeking guidance from colleagues or mentors. Regular engagement with research-related activities was limited. For instance, 35% of participants reported sometimes reading academic papers, while 28.3% sometimes accessed websites for research. Notably, 22% never accessed research websites, and 18.3% never read academic papers.

**Table II- Research engagement among nurses**

| RESEARCH ENGAGEMENT                                         | Frequency (n) | Percentage (%) |
|-------------------------------------------------------------|---------------|----------------|
| <b>Taken a Research Course</b>                              |               |                |
| Yes                                                         | 96            | 32.00          |
| No                                                          | 204           | 68.00          |
| <b>Primary Resources for Evidence-Based Information</b>     |               |                |
| Online Databases                                            | 88            | 31.00          |
| Institutional Guidelines                                    | 46            | 16.20          |
| Colleagues/Mentors                                          | 14            | 4.90           |
| <b>Publish in Journal</b>                                   |               |                |
| Never                                                       | 105           | 35.00          |
| Rarely                                                      | 91            | 30.30          |
| Sometimes                                                   | 90            | 30.00          |
| <b>Regularly Read Papers Published in Academic Journals</b> |               |                |
| Never                                                       | 55            | 18.30          |
| Rarely                                                      | 97            | 32.30          |
| Sometimes                                                   | 105           | 35.00          |
| <b>Present/Attend Academic Conferences</b>                  |               |                |
| Never                                                       | 47            | 15.70          |
| Rarely                                                      | 81            | 27.00          |
| Sometimes                                                   | 118           | 39.30          |
| <b>Regularly Access Websites to Read Research Papers</b>    |               |                |
| Never                                                       | 66            | 22.00          |
| Rarely                                                      | 81            | 27.00          |
| Sometimes                                                   | 85            | 28.30          |

Perceptions of organizational support for EBP were mixed. Only 8% of participants noted the presence of an EBP committee within their organization, and collaboration with universities on research projects was

**Figure 1: Facilitators of Evidence Based Practice among nurses**

limited. Furthermore, access to institutional resources was inadequate, with participants reporting limited library access to relevant journals. Reward systems for using research findings were minimal, and structural support for integrating EBP into routine practice appeared insufficient.

### DISCUSSION:

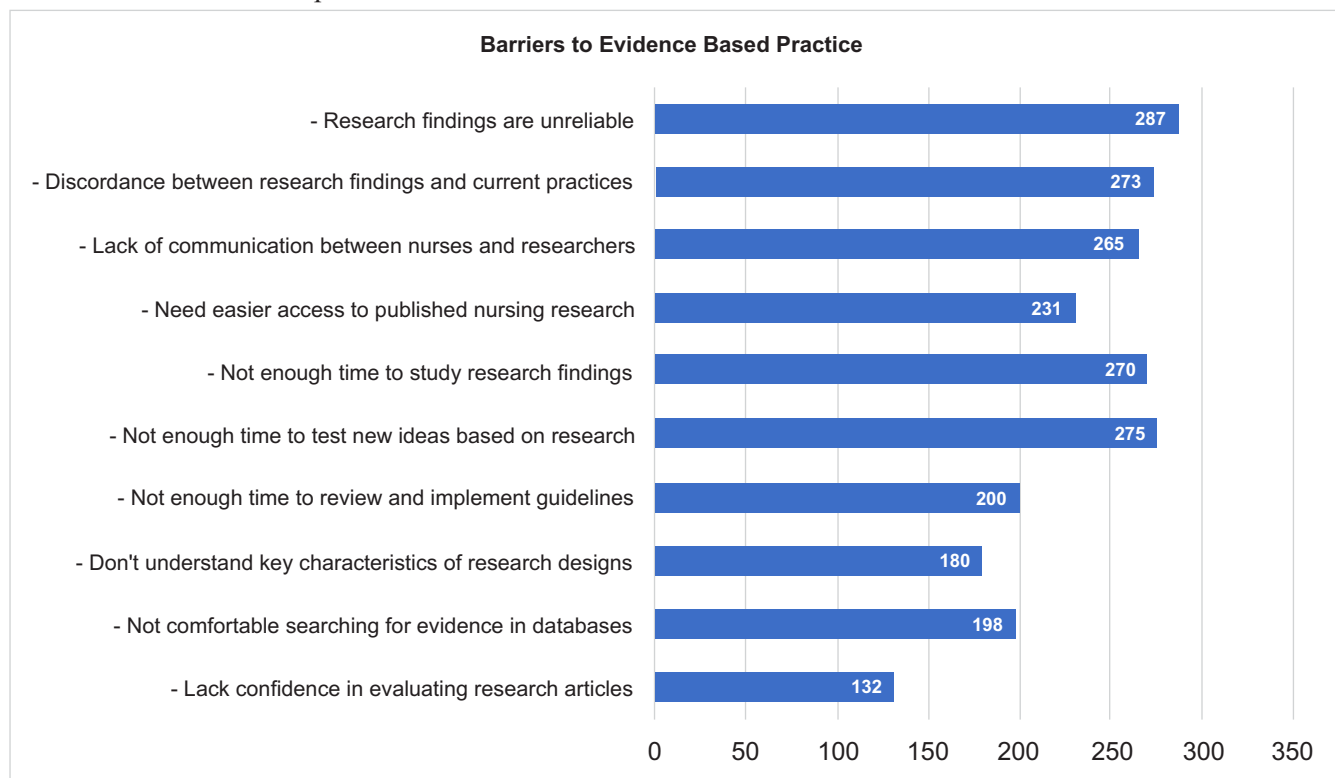
This study, which included 300 nurses from Sheikh Zayed Hospital, provides a comprehensive demographic profile and insights into their use of evidence-based practice (EBP). Table 1 indicates that the majority of our participants were married (68.7%), female (94.7%), and registered nurses (85%). General nursing qualifications accounted for the largest educational group (52%), followed by BSN (45.3%), and MSN degrees (2%) were the least common. In contrast to studies on Spanish nurses, where males were marginally more prevalent (57.1%) in EBP studies<sup>12, 13</sup>, this demographic mix, especially the large percentage of female nurses, is noteworthy.

One important area for improvement is highlighted by our findings on prior EBP knowledge. Only 32% of our nurses had completed a formal research course, highlighting a significant deficiency in basic EBP training. Approximately two-thirds (65.3%) of nurses were confirmed to have prior EBP information and

instructions on how to use electronic resources in an earlier survey, which stands in stark contrast to this.<sup>14, 15</sup>

Just 4.9% of nurses in our survey sought advice from mentors or colleagues, whereas 31% of nurses mainly relied on internet databases for evidence-based information. Additionally, 35% of participants never published in scholarly publications, and 30% only infrequently did so, indicating a lack of engagement with research dissemination. Likewise, 22% of our participants had never visited a research website, and 18.3% had never regularly read scholarly papers. This is consistent with a thorough survey of US registered nurses that found that 77% had never received instruction on how to use electronic health records, and 58% had never accessed research publications to support clinical practice.<sup>16, 17</sup>

Important facilitators and barriers to the adoption of EBP were also discovered by our investigation. Our findings show substantial organizational support for the notion that EBP should be a core part of professional nursing training. Majority of nurses believed that management supported their EBP efforts and that their organization promoted the usage of EBP. Additionally, 91.7% of respondents stated that their company had an EBP committee, and 90.7% said that study findings were readily available. The vast majority of nurses also had



**Figure 2: Barriers to Evidence Based Practice among nurses**

favorable opinions about EBP, with 77% saying it boosts nurses' freedom and 73.7% saying it helps them make better decisions about patient care. A sizable portion (75%) also said that they wanted to learn more, saying they would like to take an EBP course. In contrast, a study carried out in the Amhara region revealed limited effectiveness of support for research provided.<sup>18</sup>

Time restrictions and certain knowledge/skills deficiencies are the main causes of the substantial hurdles that still exist in spite of these facilitators. Ninety percent of our participants claimed they lacked sufficient time to review research findings, and 91.7% claimed they lacked the time to test novel concepts derived from research. This is consistent with the Amhara study's findings, which showed that time constraints were cited by all participants as a hindrance to the adoption of EBP.<sup>18</sup> In a similar vein, 66.7% of respondents said they did not have enough time to review and apply the recommendations.

Important skills and knowledge gaps were also revealed by the fact that 60.3% of nurses in our study did not comprehend the essential features of research designs, and 66.3% of nurses were uncomfortable looking for evidence in databases. A lack of contact between nurses and researchers was mentioned by 88.3% of respondents, and 77.7% of respondents said they needed easier access to published nursing research. Remarkably, 95.7% of respondents thought research conclusions were untrustworthy, and 91% thought there was a discrepancy between them and existing behaviors. These numbers highlight a significant obstacle in putting research into practice. More than 54% of clinical nurses in the US who participated in a survey said they had never heard of "Evidence-Based Practice," which is consistent with the knowledge gaps on research topics that our study found.<sup>19</sup>

Our research revealed that online databases (31%) and institutional guidelines (16.2%) are the main sources of evidence-based knowledge when it comes to clinical practice decisions. The results also points out that nurses, mentors, and coworkers regularly attend conferences and visit websites to read research publications, even though only 4.9% of them asked for advice from their peers. This is consistent with results from other researches in which participants listed the internet, social media apps, head nurse and clinician peer experience, and educational seminars and conferences as their main sources of information.<sup>20,21</sup>

## CONCLUSION

Nurses perceive organizational support and have a good appreciation for Evidence-Based Practice, yet there are still many practical obstacles to overcome.

Addressing the lack of confidence in research evaluation, time constraints, and limited access to reliable research is crucial to fully integrate EBP into nursing practice and improve patient outcomes. The primary barrier to evidence-based practice, according to nurses, is deficiencies in knowledge and skills as well as time and resource constraints.

## LIMITATIONS

Cross sectional study design, convenient sampling and small sample size are the limitations of our study. Although we used a validated tool to assess Evidence Based Practice among nurses using self-reported questionnaires, might have introduced possibility of erroneous or socially acceptable answers. Furthermore, the data were collected only from the nurses of Sheikh Zayed Hospital Rahim Yar Khan and the nurses from the other regions were not included. As a result, the findings may not accurately reflect the opinions of staff nurses in other cities and their generalizability may be impacted.

## RECOMMENDATIONS

To improve the generalizability of the results and investigate the factors impacting nurses' evidence-based practice efforts at several time points, future study with a more rigorous design—that is, longitudinal—is advised. It is advised to use the probability sampling technique with a larger sample size involving multi-centers to enhance generalizability.

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Qurat ul Ain Mustafa: Manuscript Writing, Critical Review, Material Analysis

Nida Jameel: Manuscript Writing, Critical Review, Material Analysis

Rimsha Fatima: Manuscript Writing, Critical Review, Material Analysis

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# FREQUENCY AND OUTCOMES OF ACUTE KIDNEY INJURY IN PATIENTS PRESENTING WITH ACUTE HEART FAILURE AT A CARDIAC CENTRE IN KARACHI

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## ABSTRACT

**Objectives:** To determine the frequency of acute kidney injury (AKI) in patients with acute heart failure (AHF) and evaluate its association with in-hospital mortality.

**Patients and Methods:** This cross-sectional study was conducted over six months at Tabba Heart Institute, Karachi. A total of 121 consecutive patients aged 40–80 years admitted with AHF were enrolled. Patients with acute coronary syndromes, sepsis, arrhythmias, or major non-cardiac comorbidities were excluded. AKI was defined as a  $\geq 0.3$  mg/dL increase in serum creatinine within 48 hours of admission. Demographic, clinical, and socioeconomic variables were recorded. Primary outcomes were the frequency of AKI and in-hospital mortality.

**Results:** Nineteen patients (15.7%) developed AKI. Patients with AKI had a higher prevalence of urban residence (100% vs 80.4%,  $p=0.035$ ), dyslipidemia (73.7% vs 44.1%,  $p=0.018$ ), and reported lower family income (73.7% vs 34.3%,  $p=0.001$ ) compared to non-AKI patients. In-hospital mortality was higher in the AKI group (42.1% vs 20.6%,  $p=0.044$ ). Univariate logistic regression showed an odds ratio (OR) for mortality with AKI of 3.05 (95% CI 1.03–9.05,  $p=0.044$ ). After adjustment, the adjusted OR was 3.21 (95% CI 0.73–14.18,  $p=0.124$ ).

**Conclusion:** AKI occurred in approximately one-sixth of patients hospitalized with AHF and was associated with higher unadjusted in-hospital mortality. Socioeconomic factors, particularly low income and urban residence, were linked to AKI risk, underscoring the need for targeted preventive strategies in high-risk subgroups.

**Keywords:** Acute heart failure, Acute kidney injury, In-hospital mortality, Pakistan, Socioeconomic status.

## INTRODUCTION

Heart failure (HF) is a rapidly growing public health issue, with rising prevalence driven by an aging population and improved post-myocardial infarction and HF survival.<sup>1</sup> This burden is intensified by the bidirectional relationship between cardiac and renal dysfunction, in which acute or chronic impairment in one organ precipitates dysfunction in the other, a phenomenon known as cardiorenal syndrome.<sup>2,3</sup> AKI, in particular, is a critical event in this interplay, as it can accelerate progression to end-stage renal disease and is a powerful predictor of poor outcomes.<sup>4</sup>

The reported incidence of AKI in AHF varies widely, from 9% to 43%, with consistent evidence linking it to higher in-hospital and one-year mortality rates.<sup>5-7</sup> For AHF cases with AKI, hospital death stands at about 10.8%, with extended stays and higher expenses.<sup>8</sup> Studies from Spain noted 13% AKI in AHF inpatients, while in a Pakistani study, Bhatti et al. observed an in-hospital mortality rate of 7.4% in HF patients who developed AKI.<sup>9,10</sup>

Despite growing evidence on worsening renal function in AHF, the precise frequency of acute AKI and its impact on in-hospital mortality remain underexplored in local settings. Understanding the local burden of AKI in acute heart failure is important because it may complicate fluid management, worsen hemodynamic instability, and limit treatment options, thereby worsening patient outcomes.<sup>11</sup> This study aims to determine the frequency of AKI in AHF and assess its association with in-hospital mortality, with the goal of informing targeted prevention strategies, optimizing care quality, and guiding resource allocation for high-risk patients.

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## PATIENTS AND METHODS

This cross-sectional study was conducted at the Coronary Care Unit of Tabba Heart Institute, Karachi, over a six-month period from 1<sup>st</sup> March 2025 to 1<sup>st</sup> August 2025, following approval from the Institutional Review Board of Tabba Heart Institute (OHRP Reg. No. IORG000786; Approval No. THI/IRB/SQ/12-03-2025/119). The required sample size was calculated to be 121 patients using the WHO sample size calculator, assuming a 13% prevalence of AKI among patients with AHF, a 6% margin of error, and a 95% confidence level. Participants were recruited using a non-probability consecutive sampling technique. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, and written informed consent was obtained from all participants prior to data collection.<sup>12</sup>

### Inclusion and exclusion criteria

Patients aged 40–80 years, of either gender, presenting with new-onset or acutely decompensated heart failure requiring hospitalization were eligible. We did not restrict enrollment based on the etiology of cardiomyopathy. Patients with stable or chronic coronary artery disease presenting with acute heart failure not triggered by an acute ischemic event were included.

Patients were excluded if they presented with acute coronary syndromes [ST-Elevation Myocardial Infarction (STEMI), non-ST-Elevation Myocardial Infarction (NSTEMI)], or unstable angina). Additional exclusion criteria were: sepsis, diarrhea, pulmonary hypertension, pericardial disease, significant arrhythmias (bradyarrhythmias or tachyarrhythmias), stroke, asthma, and chronic obstructive pulmonary disease.

### Data collection

Data were extracted from the hospital's electronic health records. All patients were informed about the risk, benefit and purpose of the study prior to taking written informed consent. Demographic information (age, gender, residence, education level, occupation, family income), comorbidities (diabetes mellitus type II, hypertension, dyslipidemia), smoking status, laboratory findings, and hospital course were recorded. Serum creatinine and urine output were noted, and AKI was defined according to KDIGO criteria as an increase in serum creatinine of  $\geq 0.3$  mg/dL within 48 hours of admission or from the most recent available baseline.<sup>13</sup>

The primary outcome was in-hospital mortality.

### Data analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 27. Age was categorized into two groups (40–60 years and 61–80 years). All variables including age group, gender, residence, comorbidities, smoking status, socioeconomic indicators, presence of AKI, and in-hospital mortality were summarized as frequencies and percentages.

Group comparisons between AKI and non-AKI patients were performed using the chi-square test or Fisher's exact test. Variables with  $p \leq 0.05$  in univariate analysis were entered into logistic regression to assess the association between AKI and in-hospital mortality, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Multivariate regression was not performed due to quasi-complete data separation. A two-tailed  $p$ -value of  $\leq 0.05$  was considered statistically significant.

## RESULTS

A total of 121 patients with AHF were included in the analysis. Most were aged 61–80 years (68.6%) and male (50.4%). The majority resided in urban areas (83.5%). The most common comorbidities were dyslipidemia (48.8%), diabetes mellitus type II (27.3%), hypertension (26.4%), and current smoking (37.2%). AKI occurred in 19 patients (15.7%). The in-hospital mortality rate was 24.0% (Table I).

### Comparison between AKI and non-AKI groups

Patients with AKI were more likely to reside in urban areas compared to those without AKI (100% vs. 80.4%;  $p = 0.035$ ). Dyslipidemia was more frequent in the AKI group than in the non-AKI group (73.7% vs. 44.1%;  $p = 0.018$ ). A lower family income ( $< \text{PKR } 75,000$ ) was observed more commonly in patients with AKI (73.7% vs. 34.3%;  $p = 0.001$ ). Interestingly, none of the patients in the AKI group had diabetes mellitus or hypertension. This unexpected finding may reflect the small sample size, selection pattern, or chance rather than a true absence of association. Compared to 31.4% and 28.4% in the non-AKI group, respectively (both  $p = 0.004$ ). In-hospital mortality was higher in the AKI group (42.1% vs. 20.6%;  $p = 0.044$ ) (Table II).

### Association between AKI and in-hospital mortality

In univariate logistic regression, AKI was associated with in-hospital mortality (OR 3.05; 95% CI 1.03–9.05;  $p = 0.044$ ). After adjusting for age, sex, comorbidities,

and socioeconomic variables, the association was not statistically significant (adjusted OR 3.21; 95% CI 0.73–14.18;  $p = 0.124$ ) (Table III). Multivariate logistic regression could not be performed as the model did not converge due to quasi-complete separation of data; therefore, only univariate results are presented. Quasi-complete separation occurs when a predictor variable perfectly (or almost perfectly) predicts the outcome, resulting in estimation instability and preventing the model from generating reliable coefficients.

## DISCUSSION

In our study, AKI developed in 15.7% of patients hospitalized with AHF, a frequency comparable to previous reports (13–27%).<sup>14,15</sup> AKI was associated with higher in-hospital mortality in our cohort (42.1% vs 20.6%), underscoring the prognostic weight of renal dysfunction in this setting. Interestingly, the mortality observed in our AKI subgroup was substantially higher than that described in both regional and international cohorts. For example, a recent Pakistani study reported an in-hospital mortality of 7.4% among AHF patients with AKI,<sup>10</sup> suggesting that population differences, variations in disease severity at presentation, or disparities in clinical management may partly explain this discrepancy. It may also reflect differences in level of care across tertiary, secondary, private, and public facilities in Pakistan. The adverse prognostic impact of renal impairment is also supported by long-term data, where patients with worsening kidney function consistently experience higher mortality compared with those without impairment.<sup>16</sup> In our analysis, AKI tripled the odds of in-hospital death (OR 3.05, 95% CI 1.03–9.05); however, this association did not remain significant after adjustment, likely reflecting the relatively small number of AKI cases and the confounding influence of comorbidities and socioeconomic status. Nevertheless, the direction and magnitude of the effect support the clinical importance of vigilant renal monitoring and deliberate hemodynamic optimization in this high-risk group, particularly during aggressive decongestion.

One unexpected finding was the complete absence of diabetes mellitus and hypertension among patients who developed AKI, despite these comorbidities being widely recognized risk factors for renal dysfunction in heart failure.<sup>17–18</sup> In contrast, Mullens et al. reported that 44% of patients with worsening renal function had diabetes and 48% had hypertension, compared with 34% and 40%, respectively, among those without renal

impairment, although these differences did not reach statistical significance.<sup>17</sup> Several factors may explain this discrepancy. First, the small number of AKI cases limits statistical inference. Second, our exclusion criteria created a complex selection pattern: removing younger adults (18–40 years) likely enriched the cohort for chronic comorbidities, whereas excluding Acute Coronary Syndrome (ACS) patients may have reduced the prevalence of such comorbidities among those presenting with acute hemodynamic compromise. Third, all patients in the AKI group were urban dwellers, whereas roughly one-fifth of non-AKI patients lived in non-urban areas, suggesting potential environmental or healthcare-access differences that merit further investigation. Finally, contextual factors, including heightened medical awareness and health-seeking behavior in our urban cohort, may have contributed to the observed pattern. In sum, institutional selection, sampling characteristics, and comorbidity prevalence likely influenced this unexpected finding.

Socioeconomic disadvantage also correlated with AKI in our cohort, as patients with lower monthly income (< PKR 75,000) were significantly more likely to have AKI or experienced AKI (73.7% vs 34.3%,  $p = 0.001$ ). This finding is consistent with population-based data from the UK, where social deprivation was linked to higher AKI incidence (adjusted OR up to 1.79) and poorer survival after first AKI (adjusted HR 1.20).<sup>19</sup> These results suggest that socioeconomic inequities may not only increase AKI risk but also worsen outcomes, underscoring the importance of targeted preventive strategies in resource-limited settings.

We observed a higher prevalence of dyslipidemia among patients with AKI. Although direct evidence in AHF is limited, data from CKD populations provide relevant insights. Khandelwal et al. reported dyslipidemia in 73.8% of pediatric CKD patients, associated with endothelial dysfunction and vascular injury, while Malla et al. highlighted similar pro-atherogenic lipid changes as a common complication of CKD. These findings suggest that dyslipidemia-related vascular injury may also contribute to renal dysfunction in AHF.<sup>20,21</sup>

Our findings also have implications for the management of AHF. The clinical challenge lies in balancing the need for aggressive decongestion against the risk of renal hypoperfusion and electrolyte imbalance. In our setting, where late presentation and advanced disease at admission are common, this balance may be even harder

to achieve, potentially contributing to the observed AKI incidence. Importantly, emerging data suggest that targeted pharmacologic strategies may help break this vicious cycle. Sodium-Glucose Cotransporter-2 inhibitors, even when combined with Renin-Angiotensin-Aldosterone System (RAAS) blockers, have not been shown to increase AKI risk and may confer renal protection by improving hemodynamic stability.<sup>22</sup> Similarly, RAAS antagonism in sepsis-induced AKI has been associated with reduced renal injury and improved survival, while sacubitril/valsartan has demonstrated favorable renal and cardiovascular outcomes in CKD without compromising safety.<sup>23-24</sup> Combination approaches that address hemodynamic, metabolic, and inflammatory pathways are increasingly recognized as synergistic.<sup>25</sup> Yet, despite consistent benefits of Guideline-Directed Medical Therapy (GDMT) in HF patients with and without CKD, real-world data show that CKD patients remain undertreated, including in our local context where SGLT2 inhibitor use is limited.<sup>26-27</sup> Together, these findings highlight how AKI not only complicates therapy but also perpetuates suboptimal GDMT use, reinforcing a cycle of worse HF and CKD outcomes.

There are several limitations to our study. It was conducted at a single cardiac center, which limits generalizability to other settings, especially rural or less-resourced hospitals. The cross-sectional design prevented assessment of long-term outcomes, and the use of non-probability sampling may have introduced selection bias. AKI was defined solely by serum creatinine which may have underestimated its incidence, and although our sample size was calculated to capture the expected AKI prevalence adequately, the low event rate still precluded multivariate analysis and may have limited our ability to identify independent predictors with confidence. Moreover, our cohort included only hospitalized patients with AHF, which may have excluded individuals managed in the outpatient setting with milder disease, potentially limiting the applicability of our findings across the full spectrum of HF severity. Although acute coronary syndromes were excluded, thereby reducing the likelihood of patients undergoing coronary angiography, the potential contribution of contrast-induced nephropathy cannot be entirely ruled out. Finally, by excluding patients with overlapping acute conditions such as myocardial infarction and severe arrhythmias, our cohort may not fully represent the spectrum of real-world AHF presentations.

Our findings emphasize the need for early identification

and prevention of AKI in AHF, particularly among socioeconomically disadvantaged patients, and highlight the importance of developing integrated, protocol-driven strategies that mitigate renal complications while optimizing heart failure therapy. In clinical practice, this approach includes optimizing volume status, closely monitoring renal function during HF treatment, and tailoring therapy to individual risk profiles to reduce mortality. Future multicenter studies with larger and more inclusive samples, broader AKI definitions, and longitudinal follow-up could further clarify the complex interplay between cardiac and renal dysfunction in acute settings.

## CONCLUSION

In this study, AKI occurred in approximately one in six patients hospitalized with acute heart failure and was associated with significantly higher in-hospital mortality. AKI was more common among patients with dyslipidemia and lower socioeconomic status, highlighting the interplay between metabolic and social determinants of health in acute cardiac care.

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**DISCLAIMER:** None

## Conflict Of Interest

The authors declare no conflicts of interest related to this study. No financial or personal relationships with other individuals or organizations have influenced the conduct or reporting of this research.

## ETHICAL STATEMENT

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.<sup>12</sup> The study protocol was approved by the Institutional Review Board of Tabba Heart Institute (OHRP Reg. No. IORG000786; Approval No. THI/IRB/SQ/12-03-2025/119). Written informed consent was obtained from all participants prior to data collection.

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**Table I: Baseline characteristics of the study cohort (N = 121)**

| Variable                             | n (%)      |
|--------------------------------------|------------|
| <b>Age group</b>                     |            |
| 40–60 years                          | 38 (31.4)  |
| 61–80 years                          | 83 (68.6)  |
| <b>Gender</b>                        |            |
| Male                                 | 61 (50.4)  |
| Female                               | 60 (49.6)  |
| <b>Residence</b>                     |            |
| Urban                                | 101 (83.5) |
| Rural                                | 20 (16.5)  |
| <b>Comorbidities</b>                 |            |
| Diabetes mellitus                    | 33 (27.3)  |
| Hypertension                         | 32 (26.4)  |
| Dyslipidemia                         | 59 (48.8)  |
| Smoking                              | 45 (37.2)  |
| <b>Socioeconomic characteristics</b> |            |
| Family monthly income < PKR 75,000   | 49 (40.5)  |
| Family monthly income ≥ PKR 75,000   | 72 (59.5)  |
| Employed                             | 53 (43.8)  |
| Unemployed                           | 68 (56.2)  |
| <b>Educational status</b>            |            |
| Illiterate                           | 6 (5.0)    |
| Primary                              | 48 (39.7)  |
| Secondary                            | 37 (30.6)  |
| Higher                               | 30 (24.8)  |
| <b>Clinical outcomes</b>             |            |
| Acute kidney injury (AKI)            | 19 (15.7)  |
| In-hospital mortality                | 29 (24.0)  |

Abbreviations: AKI, acute kidney injury;  
PKR, Pakistani Rupees.

**Table II: Baseline characteristics and outcomes according to AKI status (N = 121)**

| Characteristic        | AKI (n = 19) | No AKI (n = 102) | p-value |
|-----------------------|--------------|------------------|---------|
| Age ≥ 61 years        | 78.9%        | 66.7%            | 0.290   |
| Male gender           | 47.4%        | 51.0%            | 0.772   |
| Urban residence       | 100.0%       | 80.4%            | 0.035*  |
| Diabetes mellitus     | 0.0%         | 32.4%            | 0.004*  |
| Hypertension          | 0.0%         | 31.4%            | 0.004*  |
| Dyslipidemia          | 73.7%        | 44.1%            | 0.018*  |
| Smoking               | 31.6%        | 38.2%            | 0.582   |
| Income < 75,000 PKR   | 73.7%        | 34.3%            | 0.001*  |
| Employed              | 47.4%        | 43.1%            | 0.733   |
| In-hospital mortality | 42.1%        | 20.6%            | 0.044*  |

\*Statistically significant at  $p < 0.05$ .

Abbreviations: AKI, acute kidney injury;  
PKR, Pakistani Rupees.

**Table III: Unadjusted and adjusted predictors of in-hospital mortality among patients with AHF (N = 121)**

| Variable                                                                 | Unadjusted OR (95% CI) | p-value  | Adjusted OR (95% CI) | p-value |
|--------------------------------------------------------------------------|------------------------|----------|----------------------|---------|
| Acute kidney injury                                                      | 3.05 (1.03–9.05)       | 0.044*   | 3.21 (0.73–14.18)    | 0.124   |
| Age group (61–80 years vs 40–60 years)                                   | 1.02 (0.99–1.05)       | 0.172    | 1.03 (0.99–1.06)     | 0.154   |
| Male sex                                                                 | 0.82 (0.35–1.93)       | 0.648    | 0.73 (0.23–2.28)     | 0.591   |
| Diabetes mellitus                                                        | 1.51 (0.66–3.44)       | 0.331    | 0.89 (0.30–2.65)     | 0.838   |
| Hypertension                                                             | 0.88 (0.39–1.96)       | 0.753    | 0.62 (0.20–1.95)     | 0.417   |
| Dyslipidemia                                                             | 0.76 (0.27–2.11)       | 0.597    | 0.47 (0.12–1.79)     | 0.270   |
| Smoking                                                                  | 0.98 (0.38–2.53)       | 0.963    | 0.91 (0.28–2.91)     | 0.876   |
| Occupational status (employed vs unemployed)                             | 7.12 (2.39–21.21)      | <0.001** | 7.91 (2.38–26.28)    | 0.001** |
| Income category (less than vs more than PKR. 75000)                      | 1.11 (0.63–1.94)       | 0.720    | 0.87 (0.42–1.79)     | 0.705   |
| Education level (illiterate vs primary vs secondary vs higher education) | 1.04 (0.62–1.75)       | 0.888    | 1.22 (0.65–2.29)     | 0.532   |

\*Statistically significant at  $p < 0.05$ , \*\*Statistically significant at  $p < 0.01$ .

Abbreviations: AHF, acute heart failure; AKI, acute kidney injury; CI, confidence interval; OR, odds ratio; PKR, Pakistani Rupees.

**Authors' Contributions:**

Cheena Kumari: Conception of study / Designing / Planning, Experimentation / Study Conduction, Analysis / Interpretation / Discussion, Manuscript Writing

Khursheed Hassan: Conception of study / Designing / Planning, Critical Review

Naimat Ullah Junejo: Experimentation / Study Conduction, Analysis / Interpretation / Discussion, Manuscript Writing

Abdul Sami: Experimentation / Study Conduction, Manuscript Writing

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# INTRA-OPERATIVE INSTILLATION OF STEROIDS INJECTIONS (DEXAMETHASONE) DURING CAESAREAN SECTION TO REDUCE EARLY AND LATE POST-OPERATIVE MORBIDITY

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## ABSTRACT

**Objective:** To evaluate whether intra-operative intra-peritoneal instillation of dexamethasone reduces immediate and late post-operative morbidity following caesarean section.

**Study Type:** Interventional comparative study

**Place and Duration of Study:** Tertiary care hospital in Pakistan from 12 January 2020 to 22 December 2022.

**Patients & Methods:** A total of 400 women undergoing elective caesarean section were recruited, divided equally into four categories: primigravida and those with 1, 2, or 3 previous caesarean sections. Within each group, 50 patients received intra-peritoneal dexamethasone (3 ml), and 50 served as controls. Post-operative pain was assessed at 6–12 hours, 12–24 hours, and on the first post-operative day. Early mobilization, oral intake, and overall well-being were also recorded. A subgroup of 41 women returning for repeat caesarean section one year later were evaluated for intra-operative adhesions.

**Results:** Patients who received dexamethasone reported fewer pain complaints and required less additional analgesia compared with controls. On the first post-operative day, additional pain relief was needed in 30–40% of controls versus 12–16% of those receiving dexamethasone. Early mobilization was achieved by 66–76% of the dexamethasone group versus 36–44% of controls. Oral intake and overall well-being were also better in the dexamethasone group. At follow-up, more patients in the intervention group were comfortable at home, and fewer adhesions were noted in women who had received dexamethasone during prior surgery.

**Conclusion:** Intra-peritoneal instillation of dexamethasone during caesarean section is associated with reduced post-operative pain, earlier recovery, and less morbidity.

**Keywords:** Adhesions, Caesarean section, Dexamethasone

## INTRODUCTION

Gynecological and obstetric surgeries, particularly caesarean section, are among the most frequently performed operative procedures worldwide. Although advances in surgical techniques and peri-operative care

have improved patient outcomes, post-operative complications remain a major source of maternal morbidity and healthcare burden.<sup>1</sup> These complications include pain, surgical site infection, ileus, haemorrhage, delayed mobilization, prolonged hospital stays, and intra-abdominal adhesion formation.<sup>2</sup>

Post-operative pain is one of the most common early complications following abdominal and pelvic surgery and has a direct effect on recovery and quality of life. Inadequate pain control delays ambulation, prolongs hospitalization, impairs oral intake, and increases the risk of thromboembolic events and pulmonary complications. In gynecological surgery, tissue trauma and the inflammatory response associated with surgical

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manipulation contribute significantly to post-operative morbidity.<sup>3</sup>

Caesarean section has shown a steady global rise over recent decades. While generally considered safe, repeat caesarean deliveries are associated with increasing operative difficulty and post-operative complications, including haemorrhage, infection, bladder injury, chronic pelvic pain, and adhesions.<sup>4</sup> Studies have demonstrated that adhesions become more prevalent with each subsequent surgery and may increase operative time, blood loss, and technical difficulty in future procedures.<sup>5</sup>

The pathophysiology of post-operative complications is closely related to the inflammatory cascade initiated by tissue injury. Surgical trauma triggers release of cytokines, inflammatory mediators, fibrin deposition, fibroblast proliferation, and vascular permeability changes, all of which contribute to pain, edema, and adhesion formation. These inflammatory processes begin immediately after surgery and are most active during the first postoperative week.<sup>6</sup>

Traditionally, reduction of post-operative morbidity has relied on meticulous surgical technique, including gentle tissue handling, adequate haemostasis, minimization of tissue ischemia, and prevention of infection.<sup>7,8</sup> In recent years, attention has shifted toward pharmacological agents that may modulate the inflammatory response and improve postoperative recovery.<sup>9</sup> Various agents, including non-steroidal anti-inflammatory drugs, corticosteroids, and barrier materials, have been investigated for their role in reducing post-operative complications and adhesion formation.<sup>10,11</sup>

Dexamethasone, a potent corticosteroid with anti-inflammatory and anti-edematous properties, has been widely used in surgical practice to reduce postoperative nausea, vomiting, pain, and inflammatory reactions. Experimental and clinical studies suggest that dexamethasone may also reduce fibrin deposition and fibroblast activity, thereby limiting adhesion formation and improving post-operative recovery.<sup>12</sup>

The objective of the study was to evaluate the effect of intra-operative intraperitoneal instillation of a single dose of dexamethasone during caesarean section and assess its role in reducing post-operative morbidity and improving recovery outcomes.

## PATIENTS AND METHODS

This comparative interventional study was carried out in the operation theatre recovery area, surgical ITC, and

post-operative ward between 12 January 2020 and 22 December 2022 (IERC/OBS/2021/09). A total of 1,335 patients were screened, and 400 who met the inclusion criteria were selected by convenience sampling. The inclusion criteria included patients undergoing elective caesarean section under spinal anaesthesia and primigravida and women with one, two, or three previous caesarean sections.

The exclusion criteria were as follows:

- Patients undergoing caesarean section under general or epidural anaesthesia.
- Women with a previous caesarean section attempting Vaginal Birth After Caesarean (VBAC) or Trial of Labor After Caesarean (TOLAC).
- Women with four or more previous caesarean sections.
- Women with prior gynaecological surgeries such as myomectomy, cystectomy, or laparoscopy.

These patients underwent elective caesarean section.

Patients were divided into four categories, each with 100 participants:

- Category I: Primigravida
- Category II: Previous 1 caesarean section
- Category III: Previous 2 caesarean sections
- Category IV: Previous 3 caesarean sections

Within each category, 50 patients received intra-peritoneal instillation of dexamethasone (3 ml) intra-operatively, sprayed using a 3 cc syringe, while 50 patients served as controls.

Post-operative pain intensity was recorded using a standardised pain score proforma at 6–12 hours, 12–24 hours, and on the first post-operative day in both the surgical ITC and post-operative ward. Hydration with Ringer lactate and injection Falgan (paracetamol) 8-hourly were given as per hospital protocol. Patients who required analgesia beyond the routine pain relief were documented.

On the operative day and first post-operative day, data were also collected regarding postural change, mobility, oral intake (fluids and semi-solids), and overall well-being.

During the second year of the study, 41 patients who presented for repeat caesarean section and had received dexamethasone during their previous operation one year earlier were assessed for the intra-operative intensity of

adhesions.

All data were tabulated, and percentages were calculated. Statistical analysis was performed using SPSS version 22, with results compared between the two groups.

## RESULTS

A total of 400 women were included in the study (100 per category). The results demonstrated significant differences in morbidity between women who received intra-peritoneal dexamethasone (Group II) and those who did not (Group I).

### Pain Complaint (Tables I & II):

- In **Group I**, during the first 6–12 hours, 18% of primigravida and women with one previous caesarean section, 22% with two, and 36% with three caesarean sections reported pain despite routine analgesia.
- In **Group II**, the rates were lower: 10% of primigravida, 14% with one previous section, 10% with two, and 8% with three previous sections.

During 12–24 hours post-operatively:

- **Group I**: 30% of primigravida, 32% with one previous section, 34% with two, and 36% with three

previous sections reported pain.

- **Group II**: 16% of primigravida and those with one previous section, 18% with two, and 14% with three previous sections reported pain.

On the first post-operative day:

- **Group I**: Additional analgesia beyond paracetamol was required by 30% of primigravida, 30% with one previous section, 36% with two, and 40% with three caesarean sections.
- **Group II**: Only 16% of primigravida, 14% with one and two previous sections, and 12% with three caesarean sections required additional pain relief.

### Mobility and Well-Being (Tables III & IV):

- In **Group I**, early postural change was observed in 50% of primigravida, 40% of women with one previous section, and 36% with two or three sections. Early mobilization occurred in 36–44% of women across the groups. Oral intake was resumed in 36–50% of patients.
- In **Group II**, early postural change was more frequent: 64% of primigravida, 68% with one previous section, 72% with two, and 60% with three sections. Early mobilization was achieved in 66–76%

**Table I: Pain complaint in group 1 patients not instilled with intra-operative dexamethasone and routine pain relief injections during post-operative period**

| Serial No. | Category             | Pain complaint during first 6-12 hours post-operatively<br>n=50 | Pain complaint during 12 - 24 hours post-operatively<br>n=50 | Pain complaint during first post-operative day<br>n=50 |
|------------|----------------------|-----------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------|
| 1.         | Primigravida         | 9(18%)                                                          | 15(30%)                                                      | 15(30%)                                                |
| 2.         | Previous 1 C section | 9(18%)                                                          | 16(32%)                                                      | 15(30%)                                                |
| 3.         | Previous 2 C section | 11(22%)                                                         | 17(34%)                                                      | 18(36%)                                                |
| 4.         | Previous 3 C section | 9(18%)                                                          | 18(36%)                                                      | 20(40%)                                                |

**Table II: Pain complaint in group II patients instilled with intra-operative dexamethasone and routine pain relief injections during post-operative period**

| Serial No. | Category             | Pain complaint during first 6-12 hours post-operatively<br>n=50 | Pain complaint during 12- 24 hours post-operatively<br>n=50 | Pain complaint during first post-operative day<br>n=50 |
|------------|----------------------|-----------------------------------------------------------------|-------------------------------------------------------------|--------------------------------------------------------|
| 1.         | Primigravida         | 5(10%)                                                          | 8(16%)                                                      | 8(16%)                                                 |
| 2.         | Previous 1 C section | 7(14%)                                                          | 8(16%)                                                      | 7(14%)                                                 |
| 3.         | Previous 2 C section | 5(10%)                                                          | 9(18%)                                                      | 7(14%)                                                 |
| 4.         | Previous 3 C section | 4(8%)                                                           | 7(14%)                                                      | 6(12%)                                                 |

**Table III: Well-being of group I post-operatively without instilled Dexamethasone**

| Serial No. | Category                | Early Postural Change<br>n=50 | Early Mobilization<br>n=50 | Oral Intake<br>n=50 | Up & Above<br>at Home |
|------------|-------------------------|-------------------------------|----------------------------|---------------------|-----------------------|
| 1.         | Primigravida            | 25(50%)                       | 18(36%)                    | 22(44%)             | 45(90%)               |
| 2.         | Previous 1<br>C section | 20(40%)                       | 20(40%)                    | 18(36%)             | 46(92%)               |
| 3.         | Previous 2<br>C section | 18(36%)                       | 19(38%)                    | 25(50%)             | 42(84%)               |
| 4.         | Previous 3<br>C section | 18(36%)                       | 22(44%)                    | 25(50%)             | 44(88%)               |

**Table IV: Well-being of group II patients post-operatively with instilled Dexamethasone**

| Serial No. | Category                | Early Postural Change<br>n=50 | Early Mobilization<br>n=50 | Oral Intake<br>n=50 | Up & Above<br>at Home |
|------------|-------------------------|-------------------------------|----------------------------|---------------------|-----------------------|
| 1.         | Primigravida            | 32(64%)                       | 38(76%)                    | 28(56%)             | 45(90%)               |
| 2.         | Previous 1<br>C section | 34(68%)                       | 36(72%)                    | 30(60%)             | 43(86%)               |
| 3.         | Previous 2<br>C section | 38(72%)                       | 33(66%)                    | 32(64%)             | 44(88%)               |
| 4.         | Previous 3<br>C section | 30(60%)                       | 34(68%)                    | 28(56%)             | 43(86%)               |

of patients, and oral intake resumed in 56–64%.

#### Follow-up:

- In **Group I**, 90% of primigravida, 92% with one previous section, and 84–88% of those with two or three previous caesarean sections reported being well at home.
- In **Group II**, these rates were higher: 95% of primigravida, 86% with one previous section, 88% with two, and 86% with three caesarean sections were comfortable and well at home.

#### DISCUSSION

Our study demonstrated a marked difference in morbidity between patients who did not receive intra-peritoneal dexamethasone and patients who received intra-peritoneal dexamethasone.

Menzies D. emphasized that the best method to prevent adhesions in the future is meticulous surgical technique, though pharmacological agents may also reduce adhesion formation by limiting fibroblast and fibrin deposition.<sup>13</sup> Our study supports this concept, demonstrating that dexamethasone, a widely available and inexpensive pharmacological agent, can be effective in reducing morbidity by attenuating adhesion formation.

Diamond M.P. and Freeman M.L. also emphasized in their study that the clinical implications of post-surgical adhesions should be addressed effectively.<sup>14</sup> They concluded that meticulous surgical techniques remain central to adhesion prevention but highlighted the value of pharmacological adjuncts. They noted that adhesions contribute to increased morbidity and delayed wound recovery.

Similarly, Höckel M. et al. conducted a study in rats and observed that intraperitoneal adhesions decreased with sustained intraperitoneal dexamethasone delivered by a novel therapeutic system. In their study, dexamethasone was sprayed into the peritoneal cavity, and a subsequent second-look laparotomy demonstrated fewer adhesions in the treatment group.<sup>15</sup>

Our results are also comparable to those of Greene A.K. et al., who used the anti-angiogenic COX-2 inhibitor celecoxib intra-operatively and observed reduced post-operative morbidity. They concluded that pain, nausea, and vomiting were significantly decreased in the celecoxib group, leading to earlier recovery.<sup>16</sup>

Rodgers K.E. et al. similarly reported a reduction in adhesion formation with the intraperitoneal administration of various anti-inflammatory agents. They observed reduced pain perception and reduced adhesion intensity, consistent with our findings using

dexamethasone.<sup>17</sup>

Orita H., Girgis W., and Dizerega G.S. also showed prevention of post-surgical peritoneal adhesion formation in rabbits by intraperitoneal ibuprofen instillation. They reported markedly reduced adhesion formation and morbidity in the treatment group, further supporting the potential role of intraperitoneal anti-inflammatory agents.<sup>18</sup>

More recent studies also align closely with our findings. Vandana et al. reported that intra-peritoneal dexamethasone with bupivacaine reduced pain in laparoscopic surgery.<sup>19</sup> Our study similarly demonstrated significant reductions in pain scores after caesarean section, indicating that dexamethasone's analgesic effect is robust across different types of intra-abdominal procedures.

Alkatout et al. and Tanigaki et al. evaluated barrier agents such as 4DryField® PH and other pharmacologic adjuncts for adhesion prevention, reporting improved post-operative recovery and fewer adhesions.<sup>20,21</sup> Compared with these novel but often costly interventions, our study demonstrates that dexamethasone offers a low-cost, widely available option with similar benefits.

Taken together, our findings are consistent with both older experimental work and more recent clinical studies, reinforcing the role of pharmacological

interventions in adhesion prevention and morbidity reduction. Our study contributes unique clinical evidence from a large obstetric cohort, supporting intra-peritoneal dexamethasone as a simple, inexpensive, and effective strategy for improving post-operative outcomes in caesarean section patients.

## CONCLUSION

Intra-operative intra-peritoneal instillation of dexamethasone significantly reduced post-operative pain, facilitated earlier mobilization and oral intake, and improved overall patient well-being. Follow-up data also suggested reduced adhesion-related morbidity.

**Conflicts of Interest:** None

**Funding Sources:** None

**Ethical Statement:** Prior to initiating the study, ethical approval was obtained from the Institutional Review Committee.

## Authors Contribution

Tehreem Yazdani: Conception of study / Designing / Planning, Experimentation / Study Conduction, Facilitated for Reagents / Material Analysis

Shazia Awan: Critical Review

Fareeha Zaheer: Analysis / Interpretation / Discussion

Muhammad Saad Mukhtar: Analysis / Interpretation / Discussion, Manuscript Writing

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# BEYOND THE PANDEMIC: HOW COVID-19 STILL SHAPES DOCTORS' JOB STRESS AND PERFORMANCE

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## ABSTRACT

**Objective:** To investigate the relationship between job stress and job performance among doctors and analyze whether this relationship is moderated by COVID-19.

**Study Design:** Cross sectional analytical study

**Place and duration of study:** Gujranwala Teaching Hospital and Gujranwala Medical College Teaching Hospital, conducted from 1 Nov 2024 to 31 Mar 2025.

**Patients and methods:** A structured online questionnaire was distributed among 212 doctors working in OPDs and Emergency departments, via google forms and personal emails. Convenience sampling was used and ethical approval was obtained (IRB.43/GMC). Validated scale developed by Tessema, M., and Soeters, J was used for measuring job performance, for job stress, scale from Parker and Decotiis and perceived threat of COVID-19 was measured using a modified version of scale from Sinclair and LoCicero. Data were analyzed using SPSS version 24 for descriptives, correlation and moderation effects.

**Results:** The mean stress score in doctors came out to be  $3.48 \pm 0.82$ , mean job performance score  $3.78 \pm 0.48$  and perceived threat of COVID score,  $3.13 \pm 0.65$  all out of 5.00, the high stress score is at lower limit of severe stress level. Job stress showed a negative correlation with job performance and the perceived threat of COVID 19 as a moderator significantly strengthened the negative association.

**Conclusion:** Job stress negatively affects doctor performance, further intensified by perceived threat of COVID-19. Stress management interventions are vital to maintain healthcare performance during pandemics.

**Keywords:** COVID-19, doctors, job performance, job stress, moderating effect

## INTRODUCTION/BACKGROUND

Workplace stress has been a significant occupational health concern in high-income nations since the early 1980s. A study conducted in Germany indicated that both physicians and non-physician staff in general practices reported chronic stress levels that were twice as high compared to other professions.<sup>1</sup> The stress levels documented in the literature tend to increase as we move from primary care hospitals to tertiary care settings.<sup>2</sup> Work-related stress is linked to increased risks of alcohol and drug abuse, strained social relationships, depression,

anxiety, and even suicide among doctors.<sup>3</sup>

Stress negatively impacts a doctor's professional performance by reducing attention span, concentration, and decision-making abilities.<sup>4</sup> It also hampers their ability to build strong physician-patient relationships, which are crucial for providing high-quality patient care.<sup>5</sup> Another consequence of stress could be a decline in work quality, potentially compromising patient safety.<sup>6</sup> A survey of 6,536 physicians involved in direct patient care in the US found that the quality of communication between physicians and patients was negatively affected by physician morale, job stress, time pressure, and work overload.<sup>7, 8</sup> Additionally, another study highlighted a significant effect of high stress levels on various factors like: being a single resident, working in a surgical department, and the lack of breaks during working hours.<sup>9</sup>

The COVID-19 pandemic introduced unprecedented stress to the healthcare system and its workers.<sup>10</sup> While

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COVID-19 led to a global shutdown in a few days, healthcare professionals bravely stepped up to confront the pandemic.<sup>11</sup> The pandemic's impact was felt worldwide, generating immense stress among physicians and other healthcare professionals.<sup>12</sup> Beyond the physical toll of illness and hospitalization, the pandemic also triggered financial difficulties, as well as feelings of fear and isolation, as evidenced by a Chinese study on healthcare workers. This study found that women and frontline healthcare workers were at a heightened risk for depression, anxiety, and insomnia.<sup>13</sup>

In light of these factors, this study aims to fill the critical gap by examining the relationship between job stress and job performance, exploring the role of the COVID-19 pandemic as a moderator of job stress and overall job performance among frontline doctors. Specifically, the study will investigate whether doctors still perceive a lingering threat from COVID-19 even after a substantial period has passed and how this perceived threat influences their functioning capacity. By addressing this overlooked dimension, the study aspires to advance theoretical understanding and provide actionable insights for healthcare administrators and policymakers to design targeted interventions that enhance doctors' resilience, optimize performance and safeguard the quality of patient care in the post-pandemic era. The first hypotheses is that stress negatively influences doctor's job performance, second one is; perceived threat of covid-19 moderates between stress and job performance in such a way that it strengthens the negative relationship.

The purpose of this study is to examine the impact of job stress on frontline doctors' job performance and to investigate whether the perceived threat of COVID-19 strengthens the negative relationship between stress and performance in the post-pandemic context.

## PATIENTS AND METHODS

A cross-sectional analytical study was carried out, with participants selected from Gujranwala Medical College Teaching Hospital (GMCTH) and Gujranwala Teaching Hospital (GTH). The sample size was determined using the formula: Sample size  $n = [DEFFNp(1-p)] / [(d^2/Z^2(1-\alpha/2(N-1)+p*(1-p))]$ . Based on a population of 500 doctors and a previous stress prevalence of 28.3% participants<sup>14</sup>, the sample size was calculated to be 193. To account for potential non-respondents, an additional 10% was added, bringing the total sample size to 212. Non-probability sampling was employed, specifically convenience sampling, due to time

constraints and the sensitive nature of the topic. Ethical approval was granted by the institutional ethical committee of Gujranwala Medical College. The study included doctors working at both major government hospitals in Gujranwala. A structured questionnaire consisting of four sections was used. The first section collected demographic information, followed by a scale measuring job performance, a scale for perceived stress, and a scale for perceived threat from COVID-19. Job performance was assessed using an 8-item employee performance scale developed by Tessema, M., and Soeters, J. (2006).<sup>15</sup> Job stress was evaluated using a 13-item scale from Parker and Decotiis (1983).<sup>16</sup> The perceived threat of COVID-19 was measured using a 13-item scale adapted from Sinclair and LoCicero's (2007)<sup>17</sup> perceived threat of terrorism scale, modified to assess the perceived threat of COVID-19.<sup>18</sup> All the responses were measured on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). Ethical approval of the study was taken from the IRB of Gujranwala Medical college (IRB.43/GMC). Participants were given the questionnaires by hand in OPD and In Patient wards. Others were contacted online and the questionnaires were sent by emails and WhatsApp. Voluntary participation of the participants was done, and the data was kept anonymous. Data were analyzed using SPSS version 24, frequencies and percentages were calculated for categorical data and mean, standard deviations were calculated for continuous variables. Correlation analysis was done using Pearson Correlation and hierarchical moderation analysis was done to check the effect of the moderator.

## RESULTS

Out of 212 participants, 196 respondents filled the forms completely, resulting in a response rate of 92.4%

**Table I: Demographic details of the participants (n=196)**

| Variable               |                   | Percentage | Frequency |
|------------------------|-------------------|------------|-----------|
| <b>Gender</b>          | Male              | 55%        | 108       |
|                        | Female            | 45%        | 88        |
| <b>Age</b>             | 23-36             | 71%        | 140       |
|                        | 37-50             | 27%        | 52        |
|                        | Above 50 years    | 2%         | 4         |
| <b>Marital status</b>  | Married           | 71%        | 140       |
|                        | Unmarried         | 25%        | 48        |
|                        | divorced/widow    | 4%         | 8         |
| <b>Work experience</b> | 11-15 years       | 12%        | 24        |
|                        | 6-10 years        | 41%        | 80        |
|                        | above 20 years    | 2%         | 4         |
|                        | less than 5 years | 45%        | 88        |

n=196

Majority of the participants were males and most of them were young doctors between ages 23 years to 36 years.

**Table-II. Correlation analysis and scale reliability in parentheses**

| Variable                         | 1      | 2     | 3     |
|----------------------------------|--------|-------|-------|
| <b>Job performance</b>           | (.77)  |       |       |
| <b>Job stress</b>                | -.068  | (.94) |       |
| <b>Perceived threat of COVID</b> | .455** | -.178 | (.84) |

Control Variables: age, gender, marital status and clinical experience, n=196, \*p<.05, \*\*p<.01

The mean stress score in doctors came out to be  $3.48 \pm 0.82$ , out of 5.00 which shows quite a considerable amount of stress in doctors. This level is on the lower margin of the severe stress level (3.50–5.00). Mean score for the perceived threat of COVID among doctors came out to be  $3.13 \pm 0.65$ , out of 5.00, showing a considerable level of fear among the participants even though a significant amount of time has passed after the pandemic. Mean job performance score came out to be  $3.78 \pm 0.48$  out of 5.00, which was showing good performance despite considerable stress. When job performance, job stress and perceived threat of COVID scores were compared among the males and females, the difference was statistically insignificant. This showed that almost everyone was affected but still trying to perform in a better way. One-way ANOVA was applied to check any significant difference in these scores among different age groups, marital status or job experience which was also insignificant.

**Table-III. Hierarchical regression for moderation**

| Models                    | M <sub>1</sub> (β) | M <sub>2</sub> (β) |
|---------------------------|--------------------|--------------------|
| <b>Step-1</b>             |                    |                    |
| Job stress                | .010               |                    |
| Perceived threat of COVID | -.135              |                    |
| R <sup>2</sup>            | .032               |                    |
| <b>Step-2</b>             |                    |                    |
| Stress*COVID threat       |                    | .250*              |
| R <sup>2</sup>            |                    | .134               |
| Change in R <sup>2</sup>  |                    | .102               |

Control Variables: age, gender, marital status and clinical experience, n=49, \*p<.05

Correlation analysis among the variables showed that there was a low negative correlation among job stress and job performance but a considerable positive correlation among threat of COVID and stress. COVID

threat also showed low negative correlation with job performance individually.

### Effect of moderator

The hierarchical moderation analysis shows that job stress and perceived threat of COVID-19 do not predict each other in first model. However, the second step includes the interaction term between job stress and perceived threat of COVID-19 (Stress\*COVID threat). The results indicate that the relationship was statistically significant ( $\beta = 0.250$ ,  $p < 0.05$ ), showing that the effect of job stress on job performance was significantly moderated by the perceived threat of COVID-19. Furthermore, the inclusion of the interaction term increased the explained variance among job performance by 10.2% (Change in  $R^2 = 0.102$ ), resulting in a total model  $R^2$  of 0.134. These findings conclude that while job stress and the perceived threat of COVID-19 alone do not directly affect job performance much, their interaction significantly influences performance outcomes.

### DISCUSSION

The study revealed a substantial amount of stress among doctors, consistent with other studies.<sup>19</sup> A multicenter survey involving 1,563 Chinese medical staff revealed stress-related symptoms in 73.4% of participants.<sup>20</sup>

While stress negatively correlates with job performance, our study suggests that doctors can still perform well under stress. This inverse relationship has been reported in multiple studies.<sup>21,22</sup>

Additionally, this study analyzed the moderator effect of perceived threat of COVID-19 on stress- performance relationship, which came out to strengthen the negative relation of stress on job performance. This is in line with studies indicating that healthcare workers' anxiety increased due to the risk of exposure and concerns for their families.<sup>23,24</sup>

While this pandemic shared similar characteristics across different countries, each nation's unique political situations and social infrastructure influence individual behaviors and environment.<sup>25</sup> Healthcare workers need more empathy, cooperation and support from both senior colleagues and peers. It's crucial that they avoid panic, demonstrate teamwork, role model positive behaviors, and help.<sup>26</sup> The findings further highlight the critical role of organizational and peer support in alleviating the impact of stress on healthcare workers' performance. Although a few studies have acknowledged the need for

empathy and cooperation within healthcare teams<sup>27</sup>.

Organizational leaders should communicate clear messages that highlight the importance of clinicians and the collective goal of managing the pandemic together. Work schedules should be structured to ensure physical well-being, adequate rest, and access to rest areas for clinicians working long or multiple shifts. Leaders should offer comprehensive support, provide necessary protective equipment, and plan resource distribution to prepare for future uncertainties. Additionally, mental health support programs should be developed and implemented to better manage stress during challenging situations like pandemics. Extensive research is needed to identify effective interventions that can mitigate the negative effects of stress, especially in the context of ongoing health crises. The limitations of this study include small data size, analysis of other variables affecting job performance e.g., workload, psychological wellbeing, working environment.

## CONCLUSION

This study demonstrates that job stress continues to exert a detrimental effect on doctors' performance, with the perceived threat of COVID significantly intensifying this effect. Despite the long time that has passed since the peak of COVID pandemic, its lingering psychological impact is still evident in frontline doctors. While doctors in this study maintained reasonably good performance

levels, moderation analysis revealed that stress coupled with the perceived threat of COVID-19 further compromised their effectiveness. These findings emphasize the critical need of stress management interventions, organizational support system and resilience building strategies to protect physician wellbeing and healthcare delivery. Addressing these factors is necessary not only to manage this situation but also to prepare healthcare professionals for future crises.

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### Authors' contributions:

Sadia Yaseen: Conception of study / Designing / Planning, Manuscript Writing, Experimentation / Study Conduction, Critical Review, Analysis / Interpretation / Discussion

Hafiz Muhammad Kashif: Conception of study / Designing / Planning, Experimentation / Study Conduction, Analysis / Interpretation / Discussion, Manuscript Writing, Facilitated for Reagents / Material Analysis

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# FREQUENCY AND INDICATIONS OF CAESAREAN-SECTION IN FEMALES UNDERGOING INDUCTION OF LABOR

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## ABSTRACT

**Objective:** To determine the frequency of caesarean section and to identify the common indications leading to caesarean delivery in females undergoing induction of labor.

**Study Design:** A descriptive cohort study

**Place and Duration of Study:** This study was conducted at Hameed Latif Hospital from 05 June 2024 to 20 December 2024.

**Patients and Methods:** Five hundred pregnant women admitted for induction, selected via convenient sampling. Descriptive statistics were applied to analyze both qualitative and quantitative variables, with stratification for effect modifiers such as age and BMI, followed by post-stratification chi-square test.

**Results:** The study revealed that 45.2% of participants underwent caesarean section, while 54.8% achieved vaginal delivery. Prolonged labor was the most prevalent indication for caesarean section (40.1%), followed by fetal distress (29.9%), failed labor (19.8%), and patient refusal of further induction (10.2%). The caesarean section rate was notably elevated in the 31-35 years age group (42.4%) and in women with higher BMI (49.2%).

**Conclusion:** Induction of labor is associated with a moderate risk of caesarean section, particularly in primigravida women and those with an unfavorable cervix. The most common indications for caesarean section include failed induction, fetal distress, and failure to progress. Careful selection of patients and proper monitoring during induction can help reduce the rate of unnecessary caesarean deliveries.

**Keywords:** Body Mass Index, Caesarean Section, Fetal Distress, Labor Induction, Post-Partum Hemorrhage

## INTRODUCTION

Caesarean section (CS), the delivery of a fetus via abdominal and uterine incision after 20 weeks of gestation, presents a complex obstetric challenge. While potentially life-saving in certain situations, CS carries both immediate and long-term risks for the mother and infant.<sup>1</sup> World Health Organization (WHO) recommends a CS rate of 10-15%,<sup>2</sup> yet global rates have been steadily increasing, raising public health concerns, particularly in countries like Pakistan.<sup>3,4</sup>

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There is a greater likelihood of labor induction in primigravida's (49.8%). The rate of caesarean sections is elevated in this group compared to those who have had previous pregnancies. The occurrence of labor induction has steadily risen over time. The percentage ranges from 9.5% to 33.7% of pregnancies each year. In developed nations, this procedure is performed in about 25% of pregnancies.<sup>5</sup> While induction serves as a treatment approach, it is a medical intervention that could result in adverse effects such as higher caesarean delivery rates, postpartum hemorrhage, fetal distress, inefficient prolonged labor, elevated instances of instrumental vaginal delivery, neonatal jaundice, and the immediate care required for the newborn.<sup>6</sup>

Inducing labor involves the artificial stimulation of uterine contractions as a therapeutic intervention before the natural onset of labor, particularly when the advantages of a normal vaginal delivery prevail over the risks associated with prolonging the pregnancy.<sup>7</sup>

Indications for CS are diverse, encompassing fetal factors like distress, cord prolapse, twin, post-term pregnancy, and decreased fetal movement, malpresentation, and macrosomia, as well as maternal factors such as cephalo-pelvic disproportion, dystocia, and antepartum hemorrhage.<sup>8</sup> Increasingly, maternal requests for CS, often driven by a desire to avoid prolonged labor or concerns for fetal well-being, also contribute to the trend.<sup>9</sup>

In Pakistan, CS rates are reportedly high, with some institutions reporting rates up to 40%. The role of labor induction in this context remains debated. While some advocate for induction to reduce CS rates and improve neonatal outcomes, evidence suggests it can also lead to uterine hyperstimulation, operative deliveries, and ultimately CS.<sup>9</sup> The increasing frequency of maternal requests for CS further underscores the need for careful patient selection and a thorough evaluation of the risks and benefits of labor induction. Understanding the frequency of CS and the factors that contribute to it following labor induction is crucial for optimizing obstetric practices and improving maternal and neonatal outcomes.

The purpose of this study was to determine the frequency of caesarean section and to identify the common indications leading to caesarean delivery in females undergoing induction of labor.

## PATIENTS AND METHODS

This retrospective cohort study was conducted from 05 June 2024 to 20 December 2024 after approval from the IRB committee of the Hameed Latif Hospital and Islam Medical College with the Ref. No. HLH/IRB/2024-014 dated 20 April 2024 and Ref. No. IRB-2024-78 dated 25 April 2024 respectively. Sampling technique was convenient sampling, and sample size was 500, which was calculated by G-power software with the effect size 0.1,  $\alpha$  error = 0.27, and power  $(1-\beta) = 0.72$ .

After taking obstetric history and conducting an obstetric examination, patients underwent crucial laboratory tests such as blood grouping and cross-matching, anti-hepatitis C virus antibodies testing, hepatitis B surface antigen testing, complete blood counts, urine analysis, blood glucose level assessments, ultrasounds, and cardiotocography (CTG). Informed consent was obtained from patients. Comprehensive personal details, last menstrual period, and the gestational age (weeks) were recorded. Body Mass Index (BMI) was also calculated.

Labor was induced using Prostaglandins or Misoprostol.

At the time of the initial induction, the Bishop score was  $< 4$  cm. A second dose of induction agents was administered at least 4-6 hour later. Cervical dilation progressed to 10 cm, allowing for vaginal delivery in the majority of patients. However, those who did not achieve full dilation were selected for C-section.

Singleton pregnancy, cephalic presentation, gestational age  $> 37$  weeks, and having evidence supporting indications for induction. After approving the inclusion criteria, selected women were enrolled in the study. Women with malpresentation, premature rupture of membranes, placenta previa, previous myomectomy, and cervical dilatation greater than or equal to 4 cm were excluded. Women who had a history of previous C-sections were also excluded.

## STATISTICAL ANALYSIS

Data analysis was done by using SPSS software version 26. Descriptive statistics were applied to evaluate both categorical and continuous variables. Quantitative variables, including age, BMI, and gestational age, were reported as means and standard deviations. Qualitative variables were represented as frequencies and percentages. Effect modifiers, such as age, diabetes mellitus, hypertension, and BMI, were managed through stratification. The chi-square test was used to check the association between variables. The p-value of  $\leq 0.05$  was considered statistically significant.

## RESULTS

The mean age of women was 32 years with the mean gestational age 38.71 weeks, and their BMI was  $26.3 \pm 3.52$  kg/m<sup>2</sup>. Total of 500, 297 (59.4%) women were primiparous and 203 (40.6%) were multiparous. 310 (62%) women had no abortion history. (Table I)

The most common indication of labor was Post term 213 (42.6%), PROM was second most common indication accounting for 105 (21%) cases, hypertension, GDM and oligohydramnios were less common in our patients but still significant. Women's age was categorized in to 4 categories,  $\leq 25$  years, 26-30 years, 31-35 years and  $> 35$  years. In both groups, most of women belonged to 31-35 years (42.4% v/s 39.7%). In group A, 188 (83.1%) women admitted at 37-38 weeks of gestation and 38 (16.8%) were at 39-40 weeks. Most of women in group A, 111 (49.2%) were obese and in group B, mostly women 120 (43.7%) were overweight.

In 274 (54.8%) women induction was successful done which led to vaginal birth, while 226 (45.2%) had failed induction resulting in emergency CS due to fetal distress

(meconium and cord prolapse were also included) was 29.9%, prolonged labor (40.1%), failed labor (19.8%), and 10.2% patients were refused for induction. (Table II) Out of 226 women, 70% had not post-operative complications, 12.3 % had anemia, 7.9% had Post-Partum Hemorrhage (PPH) and 9.8% had wound infection.

**Table I: Distribution of age, gestational age, BMI, parity, mode of delivery, and indication**

| Characteristics          | (mean $\pm$ S.D) |
|--------------------------|------------------|
| Age (years)              | 32.1 $\pm$ 4.76  |
| Gestational Age (weeks)  | 38.7 $\pm$ 0.38  |
| BMI (kg/m <sup>2</sup> ) | 26.3 $\pm$ 3.52  |
| <b>Parity</b>            | <b>n (%)</b>     |
| Primiparous              | 297 (59.4)       |
| Multiparous              | 203 (40.6)       |
| <b>Previous abortion</b> |                  |
| Yes                      | 120 (24)         |
| No                       | 380 (76)         |
| <b>Mode of delivery</b>  |                  |
| Cesarean                 | 226 (45.2)       |
| Normal                   | 274 (54.8)       |

**BMI**= Body Mass Index

**Table II: Indications of C-Section**

| <b>n=226</b>          | <b>n (%)</b> |
|-----------------------|--------------|
| Prolong labor         | 91 (40.1)    |
| Fetal distress        | 68 (29.9)    |
| Failed labor          | 44 (19.8)    |
| Refusal for induction | 23 (10.2)    |

**Table III: Fetal weight Outcome and APGAR score of Infants**

| <b>Fetal Weight Outcome (grams)</b> | <b>n (%)</b> |
|-------------------------------------|--------------|
| <500                                | 26 (5.2)     |
| 500-2500                            | 265 (53)     |
| > 2500                              | 209 (41.8)   |
| <b>APGAR Score</b>                  |              |
| < 4                                 | 23 (4.6)     |
| 4-6                                 | 106 (21.2)   |
| > 6                                 | 371 (74.2)   |

**APGAR** = Appearance (skin color), Pulse (heart rate), Grimace (reflex irritability), Activity (muscle tone), and Respiration (breathing)

## DISCUSSION

In this study, women who experienced labor induction and subsequently had unplanned caesarean deliveries were examined. This research revealed that the reasons for labor induction had a minimal impact on the increased risk of caesarean delivery after labor induction. The caesarean section rate was 45% in our study which was higher than the WHO criteria. The results suggested that various factors contribute to the CS rates. This rate is considerably greater than those reported in prior research, although some studies indicated even higher rates of C-section, as 69.7% and 48.98%, respectively.<sup>10</sup>

The ages of the women who underwent caesarean delivery in our study ranged from 23 to 35 years, with almost 39% of those falling into the 31-35 age bracket, while 33% were aged 29-30 years. A study reported that C-section rates increased with age. The higher occurrence of caesareans among younger women in our research might be associated with the cultural norm of early marriage prevalent in Pakistan. Jadoon et al. found that caesarean rates increased with age, reporting 26.2% for ages 20-34, 35.9% for those aged 35-40, and 43.1% for individuals over 40.<sup>4</sup>

The frequency of pregestational obesity was 21.4%, and the incidence of CS was 34.8% (33% of which corresponded to elective, 46% to emergency, and 21% to medically necessary CS deliveries). Pregestational obesity increased the risk of CS as well as the risk of elective and emergency CS. The population attributable risk of pregestational obesity for CS was 32%.<sup>11</sup> In our study total of 226 women, 111 (49.2%) were obese and had CS.

At this time, there is no evidence indicating that elective CS is safer than vaginal births; the majority of research suggests that CS comes with higher risks. Therefore, healthcare professionals must promote vaginal delivery as the preferred approach.<sup>12</sup> In our study, most of the women 274 (54.8%) delivered vaginally, and 226 (45.2%) of women had CS.

Moreover, various complications during pregnancy contribute to the increasing rate of CS. According to our data, the leading causes for caesarean sections included fetal distress (including meconium and cord prolapse at 29.9%), prolonged labor (40.1%), and failed labor (19.8%), with 10.2% of patients being denied for dosage. These results align with multiple studies conducted in low- and middle-income nations.<sup>4</sup>

According to Negese K. et al, 90 (24.5%) maternal complications that developed after the CS were significant. The most prevalent complication was surgical site infection (SSI) at 10.3%, followed by anemia (6.5%), postpartum hemorrhage (PPH) (3%), wound dehiscence (3.0%), respiratory tract infection (RTI) (1.10%), fistula (0.3%), and other complications (0.3%) respectively.<sup>13</sup> In our finding 70% had no post-operative complications, 12.3% had anemia, 7.9% had PPH and 9.8% had wound infection.

A study found that out of 38,705 neonates, 98.6% achieved a normal ( $\geq 7$ ) Apgar score, 439 (1.1%) registered an intermediate score (4–6), and 114 (0.3%) received a low score (0–3). The incidences of low and intermediate five-minute Apgar scores were strongly linked to the mode of delivery and poorer neonatal outcomes.<sup>14</sup> In our study regarding the fetal weight, 265 (53%) infants were normal in weight (500-2500 g), and 209 (41.8%) were above 2500 g, 26 (5.2%) were below 500 g. The most of infants, 371 (74.2%) with APGAR score  $>6$ , 161 (21.2%) with 4-6 APGAR score and 23 (4.6%) had  $<4$ .

### LIMITATION

The study acknowledges limitations due to a small sample size, which restricts the generalizability of findings concerning CS trends among Pakistani women.

### CONCLUSION

Induction of labor is associated with a moderate risk of

caesarean section, particularly in primigravida women and those with an unfavorable cervix. The most common indications for caesarean section include failed induction, fetal distress, and failure to progress. Careful selection of patients and proper monitoring during induction can help reduce the rate of unnecessary caesarean deliveries.

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Rabia Javaid: Critical Review

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## HELICOBACTER PYLORI INFECTION AND ANEMIA IN DYSPEPTIC PATIENTS – A CROSS SECTIONAL STUDY

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### ABSTRACT

**Objective:** To determine the association between *Helicobacter pylori* infection and anemia.

**Study Design:** Analytical cross sectional study

**Place and Duration of Study:** Combined Military Hospital Rawalpindi for 6 months from 02 Jan 2025 to 10 Jun 2025.

**Materials and Methods:** After informed consent, demographic and clinical information was obtained in 285 patients. Four cc blood was drawn for complete blood count. Anemia was defined as hemoglobin level < 12 g/dl in women and < 13 g/dl in men. The *Helicobacter pylori* rapid antigen test was done on stool samples. Saline stool preparation was checked for the presence of parasites. Bivariate regression analysis and Chi square tests were conducted to find association amongst variables. P value of < 0.05 was considered statistically significant.

**Results:** Of 285 participants, 113 (39.6%) were male and 172 (60.4%) were female. The *H. pylori* infection was present in 44.9% (128/285) patients and anemia was present in 25.3% (72/285). Among anemic patients, 48/72 (66.7%) were *H. pylori*-positive compared to 80/213 (37.5%) non-anemic patients. *H. pylori* infection was significantly associated with anemia ( $P < 0.001$ ), older age, smoking, and type of water source.

**Conclusion:** *H. pylori* infection was significantly associated with anemia in dyspeptic patients. Older age, smoking, and unsafe water sources were also significantly associated with the infection.

**Keywords:** Anemia, Dyspepsia, *Helicobacter pylori*

### INTRODUCTION

Globally, anemia is a public health issue, it affects about 32.9% of people of all age groups, in developing and developed countries, with Sub-Saharan Africa bearing the greatest burden.<sup>1</sup> It poses serious health risks and also impacts social and economic progress. Anemia weakens the immune system, reduces physical stamina, and negatively affects work productivity in adults.<sup>2</sup>

*Helicobacter pylori* (*H. pylori*) infection is ubiquitous in the world population. Its prevalence is higher in the developing countries 50.8%, as compared to advanced countries 34.7%.<sup>3</sup> *H. pylori* is a spiral shaped flagellated

Gram-negative microaerophilic organism that has evolved to survive in the hostile acidic stomach environment for extended periods and contribute to its natural microbial environment. It can trigger chronic inflammation with conditions like atrophic gastritis, micro-erosions, and gastroduodenal ulcers.<sup>4</sup> It is classified as class I carcinogen by World Health organization (WHO) as it can lead to gastric adenocarcinoma and mucosa associated lymphoid tissue (MALT) lymphoma.<sup>4</sup> *H. pylori* treatment is the standard of care in early stage MALT lymphoma.<sup>5</sup> Despite its association with these conditions, over 80% of those infected do not exhibit any symptoms.<sup>6</sup>

The exact pathway by which *Helicobacter pylori* infection causes iron shortage and/or anemia is not yet completely known. The several proposed processes are: a rise in pH, and drop in ascorbic acid level in stomach secretions both of which impair dietary iron intake, chronic blood loss due to micro-erosions in the gastric lining, the direct uptake of iron by the bacteria and elevated production of hepcidin, a key hormone that

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regulates iron balance by reducing its absorption in the small intestine.<sup>7</sup>

There are many diagnostic tests available to identify *Helicobacter pylori* infection. Non-invasive techniques are <sup>13</sup>C urea-based tests, and the stool antigen test. Polymerase Chain Reaction (PCR) is reserved for research settings and checking antibiotic resistance. In contrast, invasive procedure, such as endoscopy paired with appropriate tissue samples, tend to offer higher diagnostic accuracy.<sup>8</sup>

Despite extensive global research regarding *H pylori* and anemia, there are limited data from the Pakistani population on whether *H. pylori* infection is independently associated with anemia in dyspeptic patients. A study from Quetta reported that among *H. pylori* positive cases, anemia was present in 45% Younus et al., 2025.<sup>9</sup> Another recent Pakistani study found *H. pylori* infection in 64.8% of dyspeptic patients, with significant associations including low hemoglobin levels ( $P = .02$ ) and low socioeconomic status ( $P \leq .01$ ) Shahzad et al., 2025.<sup>10</sup> However, neither study simultaneously examined the role of age, water source, smoking, and anemia together in an analytical cross-sectional design. The objective of this study was to determine the association between *Helicobacter pylori* infection and anemia among dyspeptic patients and also to analyze the effects of confounding variables such as: age, smoking, alcohol intake, residence, educational level, and water source.

## PATIENTS AND METHODS

This analytical cross-sectional study was undertaken in our tertiary care center from Jan 2025 to Jun 2025. Prior approval from the Ethical Committee/Institutional Review Board was taken with reference no. 940. A sample size of 285 patients was obtained using World Health Organization (WHO) calculator; at 5% margin of error, 95% confidence interval (CI), and prevalence of anemia at 24.3%<sup>11</sup>. Non-probability consecutive method was used for patient registration.

The patients having following conditions such as malabsorption, hematemesis, melena, hematuria, heavy menstrual bleeding, gastro duodenal ulcers or celiac, suffering from chronic illness, having history of surgery or recent blood transfusion pregnancy, took antibiotics, proton pump inhibitors, or bismuth compounds within four weeks prior to enrollment were excluded from the study.

Patients gave written consent for participation in the

study and confidentiality of data was maintained. Information on demographic characteristics including age, marital status, gender, tobacco use, education level, household income, and occupation, as well as risk factors linked to anemia, such as nutrition, dietary supplement use, history of parasites, deworming status, alcohol consumption, and whether participants drank boiled water or otherwise, its source, residence and socioeconomic status were included using a structured questionnaire. Following this, for complete blood count (CBC) ethylenediamine tetra-acetic acid (EDTA) vacutainer tubes were used to obtain 4 cc venous blood, and analyzed using automated hematology analyzer. Malaria parasites were identified using thick films examined under  $1000 \times$  magnification, stained with Giemsa stain for 20 minutes.

Sterile collection containers were distributed to participants, along with clear instructions on how to properly obtain around one gram of stool for sampling. *H pylori* in stools was tested by a commercially available rapid antigen kits (Murex) by ICT method with a sensitivity of over 95% and a specificity of 95.7%. Saline stool preparation were used to look for parasites.

Shapiro-Wilk test was used to assess the normal distribution of data. Categorical variables such as gender, educational level, smoking, alcohol intake, residence and water source were presented as percentages and frequencies. As age was not following normal distribution, being a continuous variable mean (SD) and median (IQR) were calculated. Chi square test was employed to check *H pylori* and anemia association in dyspeptic patients. Bivariate analysis of binary logistic regression was utilized for the relationship between *H pylori* and variables as above, with outcomes reported in odds ratio (OR) and 95% confidence interval (CI).  $P$  value of  $< 0.05$  was deemed statistically significant. Statistical Product and Service Solutions (SPSS) version 24 was used for data analysis.

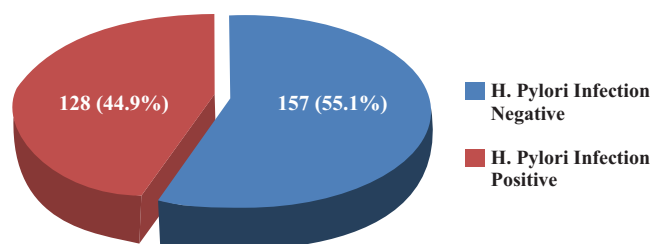
## RESULTS

The study included 285 patients. Of these 172 (60.4%) were female and 113 (39.6%) were male. Patients' mean age was 31.12 (10.12) years and median age was 30 (22-40) years. The study populations' baseline characteristics are shown in Table -I. Malaria thick film examination was negative in all 285 participants, as were stool preparations for parasitemia.

**Table-I: Demographic and Clinical Characteristics of Patients (n = 285)**

| Variables           |                  | Median, IQR  |
|---------------------|------------------|--------------|
| Age (years)         |                  | 30 (22 - 40) |
| n (%)               |                  |              |
| Gender              | Male             | 113 (39.6%)  |
|                     | Female           | 172 (60.4%)  |
| Age (years)         | 18-22            | 74 (26%)     |
|                     | 23-27            | 57 (20%)     |
|                     | 28-32            | 48 (16.8%)   |
|                     | 33-37            | 27 (9.5%)    |
|                     | 38-42            | 30 (10.5%)   |
|                     | >42              | 49 (17.2%)   |
| Educational Level   | None             | 24 (8.4%)    |
|                     | Primary          | 136 (47.7%)  |
|                     | Secondary        | 55 (19.3%)   |
|                     | Higher Education | 70 (24.6%)   |
| Residence           | Rural            | 189 (66.3%)  |
|                     | Urban            | 96 (33.7%)   |
| Smoking             | No               | 237 (83.2%)  |
|                     | Yes              | 48 (16.8%)   |
| Alcohol Intake      | No               | 249 (87.4%)  |
|                     | Yes              | 36 (12.6%)   |
| Water Source        | Piped            | 175 (61.4%)  |
|                     | Spring           | 76 (26.7%)   |
| Boil Drinking Water | Open Water       | 34 (11.9%)   |
|                     | No               | 167 (58.6%)  |
| Anemic Status       | Yes              | 118 (41.4%)  |
|                     | Non-Anemic       | 213 (74.7%)  |
|                     | Anemic           | 72 (25.3%)   |

The H pylori prevalence was 44.9% (128/285), as shown in Figure – 1.

**Figure – 1: H pylori infection prevalence in dyspeptic patients**

*Helicobacter pylori* infection on bivariate analysis, had a statistically significant association with age, water source, smoking and anemia, as shown in Table-III. As compared to patients aged 18-22 years, those aged 28-32 years had greater odds of infection (OR = 2.63, 95% CI [1.07-6.45] P = .034). The association became even stronger in older age groups, with patients aged 38–42 years showing markedly higher odds (OR = 9.54, 95% CI [3.14–29.01] P < .001) and those above 42 years also at elevated risk (OR = 4.67, 95% CI [1.75–12.41] P = .002). Compared to those using piped water, individuals using spring water (OR = 2.75, 95% CI [1.36–5.59] P = .005) or open water sources (OR = 8.35, 95% CI [3.11–22.42] P < .001) had significantly higher odds of carrying infection. Smoking had quite significant association with *H. pylori* infection than non-smokers (OR = 6.47, 95% CI [2.41-17.41] P = .001). Similarly anemic patients had increased odds of *H. pylori* infection as compared to non-anemic patients (OR = 2.73, 95% CI [1.33-5.61] P = .006). In contrast, *H. pylori* infection did not have statistically significant association with: gender, educational level, residence, practice of boiling drinking water, and alcohol intake.

**Table-II: Helicobacter pylori Infection association with Anemia Status among Patients with Dyspepsia (n = 285)**

| Anemic Status | H Pylori Infection |             | Total       | P value |
|---------------|--------------------|-------------|-------------|---------|
|               | Negative           | Positive    |             |         |
| Non-Anemic    | 133 (62.5%)        | 80 (37.5%)  | 213 (74.7%) | < .001  |
| Anemic        | 24 (33.3%)         | 48 (66.7%)  | 72 (25.3%)  |         |
| <b>Total</b>  | 157 (55.1%)        | 128 (44.9%) | 285 (100%)  |         |

Values are presented as n (%). P value from Chi-square test.

**Table III. Bivariate analysis of *H. pylori* infection and variables in dyspeptic patients (n = 285)**

| Variable            |                  | Odds Ratio | 95% CI     | P value |
|---------------------|------------------|------------|------------|---------|
| Gender              | Male             | Ref        |            |         |
|                     | Female           | 0.85       | 0.39-1.81  | .676    |
| Age (years)         | 18-22            | Ref        |            |         |
|                     | 23-27            | 1.57       | 0.64-3.82  | .319    |
|                     | 28-32            | 2.63       | 1.07-6.45  | .034    |
|                     | 33-37            | 1.87       | 0.62-5.71  | .270    |
|                     | 38-42            | 9.54       | 3.14-29.01 | <.001   |
|                     | >42              | 4.67       | 1.75-12.41 | .002    |
| Educational level   | None             | Ref        |            |         |
|                     | Primary          | 1.90       | 0.54-6.63  | .312    |
|                     | Secondary        | 0.72       | 0.19-2.68  | .626    |
|                     | Higher Secondary | 3.00       | 0.80-11.19 | .102    |
| Boil Drinking Water | No               | Ref        |            |         |
|                     | Yes              | 0.72       | 0.37-1.43  | .357    |
| Water Source        | Piped            | Ref        |            |         |
|                     | Spring           | 2.75       | 1.36-5.59  | .005    |
|                     | Open Water       | 8.35       | 3.11-22.42 | <.001   |
| Residence           | Rural            | Ref        |            |         |
|                     | Urban            | 1.32       | 0.69-2.53  | .396    |
| Smoking             | No               | Ref        |            |         |
|                     | Yes              | 6.47       | 2.41-17.41 | .001    |
| Alcohol Intake      | No               | Ref        |            |         |
|                     | Yes              | 0.70       | 0.26-1.90  | .494    |
| Anemic Status       | Non-Anemic       | Ref        |            |         |
|                     | Anemic           | 2.73       | 1.33-5.61  | .006    |

## DISCUSSION

*H. pylori* infection is ubiquitous by this bacteria and almost half of people in the globe are affected. Of these, people in the developing countries are the most infected, with Africa reporting the highest prevalence exceeding 70%.<sup>11</sup> In contrast, developed nations show lower rates, typically between 25% and 40%. The infection also rises with age: approximately half of those over 60 are infected, compared to just 10% among individuals aged 18 to 30.<sup>12</sup> In most parts of the world, people tend to acquire this bacterial infection during early childhood.<sup>13,14</sup> Given this, it is plausible that long-standing *H. pylori* infections in older adults may contribute to anemia by increasing the risk of gastrointestinal mucosal damage.

Out of total 285 dyspeptic patients *H. pylori* infection was present in 128 (44.9%). Our study is in line with

studies by Baingana et al with 45.2% *H. pylori* prevalence; and Yan Xu et al with 43.9% respectively.<sup>12,15</sup> Nekaka et al reported *H. pylori* prevalence at 27.3%, lower than our study.<sup>16</sup> In contrast Aje et al described *H. pylori* prevalence of 67.4%.<sup>17</sup> This difference in prevalence can be attributed to different geographic locations, study settings, design and variation in diagnostic techniques.

In our study 72 (25.3%) patients were anemic and 213 (74.7%) were non anemic and there was a statistically significant association between *H. pylori* infection and anemia. In numerical terms, anemic patients have slightly less than two times the risk of *H. pylori* infection (66.7%) as compared to non-anemic patients (37.5%)  $P < 0.001$ . From another perspective, in all *H. pylori* infected patients in our study, the prevalence of anemia was 48/128 (37.5%). On the other hand, in *H. pylori* uninfected patients the prevalence of anemia was 24/157 (15%). Our findings are consistent with those of Yan Xu et al., who reported that the prevalence of anemia 5.5% in *H. pylori*-infected subjects versus 5.2% in uninfected individuals (adjusted OR = 1.19; 95% CI: 1.03–1.39;  $P = 0.021$ ).<sup>15</sup> Similarly, Kibru et al. found that the prevalence of anemia among *H. pylori*-infected patients (30.9%) was significantly higher than in uninfected patients (22.5%)  $P < 0.001$ .<sup>18</sup>

Our findings are consistent with recent Pakistani data. Younus et al. reported anemia in 45% of *H. pylori* infected patients, supporting the positive association we observed.<sup>9</sup> In a recent Pakistani study by Shahzad et al., mean hemoglobin levels were significantly lower in *H. pylori*-positive individuals ( $9.8 \pm 3.1$  g/dL) compared to *H. pylori*-negative individuals ( $10.7 \pm 2.4$  g/dL) ( $P = 0.02$ ), although they also reported an association with male gender, which was not significant in our study.<sup>10</sup> These differences may reflect regional variations in socioeconomic and environmental exposures. However, Shak et al. and Santos et al. found no significant association between *H. pylori* and anemia.<sup>19,20</sup> This discrepancy may be explained by differences in study populations (rural Haiti and multi-country Latin America vs. urban Pakistani tertiary care setting), sample sizes, diagnostic methods (hemoglobin measured by finger stick, *H. pylori* checked by serology, Shak et al, hemoglobin assessed by venous blood/finger prick, *H. pylori* by 13C urea breath test, Santos et al), and adjustment for confounders such as water source and smoking, which were significant in our study but not accounted for in theirs.<sup>19,20</sup> In the study by Asimwee et al, the *H. pylori* infection, age, anemia and parasites in

stools were all positively related.<sup>3</sup> There is greater preponderance of *H. pylori* infection with age, and use of less purified water. Studies have shown variable results between smoking and *H. pylori*.<sup>21</sup> However, smoking definitely aggravates disease outcomes including risk of ulcers and cancer.

In our everyday clinical practice dyspepsia and anemia are commonly encountered. Based on findings of this study, it is recommended that clinicians should consider screening for *H. pylori* infection in dyspeptic patients presenting with anemia. Further investigation into modifiable risk factors such as water source and smoking may be warranted.

### LIMITATIONS OF THE STUDY

This cross-sectional study was conducted in one center. Multicenter validation studies with control group should be designed to discern the elements leading to anemia in dyspeptic patients with *H. pylori* infection.

### CONCLUSION

This study affirms that in dyspeptic patients, there was high prevalence of *H. pylori* infection and anemia; and both were strongly interrelated. It further infers that: age, smoking and source of water supply were also significantly associated with the infection. We recommend that dyspeptic patients should be checked for *H. pylori* and if infected have their hemoglobin levels tested. Efforts should be undertaken for access to clean

and safe water supply for population at large.

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### DISCLAIMER

The study results and inferences are for educational and academic purposes only. These are not a replacement for sound medical consult in an individual patient.

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#### Authors' contributions:

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Shahzad Ashraf: Conception of study / Designing / Planning, Analysis / Interpretation / Discussion, Critical Review

M. Fuad Ahmad Siddiqi: Critical Review, Facilitated for Reagents / Material Analysis

Ahmar Rashid: Analysis / Interpretation / Discussion

Abeera Maham Rana: Manuscript Writing

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# SCREEN TIME AND PHYSICAL ACTIVITY PATTERNS AMONG MEDICAL STUDENTS: A COMPARATIVE ANALYSIS OF PRIVATE AND PUBLIC INSTITUTIONS

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## ABSTRACT

**Objectives:** This study aimed to compare academic and recreational screen time, as well as physical activity levels, among medical students enrolled in public and private institutions in Pakistan. Furthermore, it explored the association between screen exposure and physical activity patterns within this population.

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

**Place and Duration of Study:** The study was carried out at two institutes, Liaquat National Medical College and Nishtar Medical University from 10<sup>th</sup> January 2025 till 30<sup>th</sup> April 2025.

**Patients and Methods:** A total of 374 MBBS students, 187 from each institution from first to final year were recruited using stratified random sampling. Data were collected through a structured questionnaire. Physical activity levels were assessed using the International Physical Activity Questionnaire (IPAQ). Statistical analyses were performed using SPSS version 27, with Binary Logistic regression employed to examine associations.

**Results:** This study showed the difference in screen time between private and public institution students is statistically significant based on the study's findings ( $p < 0.001$  for related screen time comparisons). Most (65%) exhibited low physical activity, with males, older ( $>20$  years), and married students more active; barriers were motivation (47.9%) and academics (35.6%). Academic screen time strongly reduced physical activity ( $p < 0.001$ ), recreational screen time moderately ( $OR = 0.385$ ,  $p = 0.002$ ). Recreational screen use impacted academic performance negatively for 59.9%, linked to burnout. Interventions are critical to curb screen time and promote activity, especially in private colleges.

**Conclusions:** Medical students, particularly those in private colleges exhibit excessive screen time and low physical activity levels (65%), posing significant health risks. Academic screen use was strongly linked to reduced physical activity, with key barriers including lack of motivation (47.9%) and academic pressure (35.6%). These findings highlight the urgent need for targeted interventions, such as institutional screen-time guidelines, motivational workshops, and accessible fitness programs, to foster healthier digital habits and active lifestyles.

**Keywords:** Medical, Physical Inactivity, Public Health, Screen Time, Sedentary Lifestyle, Students

## INTRODUCTION

Medical students experience significant academic pressure, requiring long hours of study, and often depend heavily on digital devices for learning, research, and

communication. This continuous exposure to screens can lead to increased sedentary behavior and reduced participation in physical activity.<sup>1</sup>

According to World Health Organization (WHO) physical inactivity is now identified as the fourth leading risk factor for global mortality. Physical inactivity levels are rising in many countries with major implications for the prevalence of non-communicable diseases (NCDs) and the general health of the population worldwide.<sup>2</sup> Conversely, screen time has dramatically increased, with research indicating that adolescents spend a significant portion of their day using digital devices.<sup>3</sup> This sedentary lifestyle is linked to a variety of health

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risks, including obesity, cardiovascular disease, type 2 diabetes, musculoskeletal disorders, and mental health issues such as anxiety and depression.<sup>4,5</sup>

Globally, medical students have reported unprecedented levels of screen time, often surpassing academic requirements. According to Liebig et al., daily screen exposure among medical students worldwide has significantly increased, particularly in private institutions where the integration of digital resources is more advanced.<sup>6</sup> Additionally, Deng et al. (GF) found that excessive screen time, combined with decreasing levels of physical activity, significantly affected students' overall well-being, adversely impacting their academic performance and mental health.<sup>7</sup>

In the context of Pakistan, recent studies highlight a concerning trend in screen time usage among medical students. According to Nisar et al., medical students in Pakistan spend an average of 7 to 9 hours daily on screens, which raises significant health concerns.<sup>8</sup> This issue is particularly prevalent in private medical institutions, where Rahman S et al. reported various adverse effects on students' physical and mental health due to excessive screen exposure.<sup>9</sup> Furthermore, a study conducted in Peshawar by Gul N et al. revealed a prevalence of 74.1% for Digital Eye Strain (DES) among medical students, highlighting the immediate physical effects of prolonged screen usage.<sup>10</sup>

While limited research has specifically focused on comparing screen time and physical activity levels between private and government medical students in Pakistan, Few studies offer valuable insights. Khidri FF et al. found that medical students in Sindh, Pakistan, typically engaged in 2 to 4 hours of screen time during regular academic periods, with students in private institutions reporting higher usage due to a greater reliance on digital resources.<sup>11</sup> Additionally, Roy et al. (2023) demonstrated that physical inactivity is an increasing concern among medical students, with those attending public institutions exhibiting relatively higher levels of physical activity, likely due to differences in campus infrastructure.<sup>12</sup> Nasir U et al. further highlighted that variations in screen time and lifestyle patterns among medical students are influenced by factors such as socioeconomic background, institutional resources, and academic schedules.<sup>13</sup> The increasing reliance on digital devices among medical students, driven by academic demands, has been linked to increased sedentary behavior and reduced physical activity, posing significant risks to their physical and mental well-being.

This study aimed to address the gap by examining the association between academic and recreational screen time and physical activity levels among private and government medical students in Pakistan.

## PARTICIPANTS AND METHODS

A cross-sectional study was conducted at Liaquat National Medical College and Nishtar Medical University from 10<sup>th</sup> January 2025 to 30<sup>th</sup> April 2025. Liaquat National Medical College (Karachi) and Nishtar Medical University (Multan) were chosen as representative private and public medical institutions, respectively, due to their contrasting digital resource availability, infrastructure, and student demographics. The study population consisted of individuals currently enrolled as first- to final-year medical students at these institutions. The inclusion criteria required participants to be within the specified age range  $21.48 \pm 1.36$  years, actively enrolled in the medical program, and to have provided informed consent to participate. Conversely, students with mental health conditions or physical disabilities, as well as those who declined to give consent, were excluded from the study.

The sample size was determined using a previously reported 41.8% physical activity level<sup>14</sup>, resulting in a total sample size of 374 participants, with a 95% confidence interval and a 5% margin of error.<sup>15</sup> The sample size was calculated using openEpi software.

A probability stratified random sampling technique was employed, selecting a total of 187 students from each institution. Each student was approached and provided with an explanation of the study. Written informed consent was obtained from every participant. Data were subsequently collected through interviews with the students using the study questionnaire. Each interview lasted approximately 15 minutes.

Approval of study was taken from Institutional Ethical Review Board (Ref. # 1503/NMU) dated 31<sup>st</sup> January, 2025.

The study questionnaire consisted of three sections; section-A for demographic information, section-B for screen time Academic (study-related) and recreational (social media, gaming, etc.) questions, and section-C for International Physical Activity Questionnaire (IPAQ). Screen time was measured in hours per day.

Section-A contained 9 questions about demographic profile of participants. Section-B contained screen time assessment (academic and recreational). Screen time

measured in hours per day. The questionnaire was piloted among 30 students to ensure clarity and reliability. Face validity was assessed through expert feedback, and internal consistency was measured using Cronbach's alpha ( $\alpha = 0.82$ ). Section-C contained International Physical Activity Questionnaire (IPAQ),<sup>16</sup> a validated tool that measures total physical activity in MET-minutes per week and the time spent sitting. It consists of seven open-ended questions that prompt individuals to recall their physical activity over the past seven days. The IPAQ has demonstrated high reliability, with a Cronbach's alpha of less than 0.80. Results were reported in categories (low activity levels, moderate activity levels or high activity levels) or as a continuous variable (MET minutes a week). MET minutes represent the amount of energy expended carrying out physical activity. Intensity levels are categorized based on metabolic equivalent tasks (METs): light (1.5-3.0 METs), moderate (3.0-6.0 METs), and vigorous (>6.0 METs).<sup>17</sup>

Data were entered and analyzed using SPSS version 27. Descriptive analyses, including frequencies and percentages, were conducted for categorical variables, while means and standard deviations were calculated for screen time and physical activity levels. Binary Logistic regression analysis was performed to examine associations between various categories of screen time and levels of physical activity. The significance level was set at 0.05.

## RESULTS

Table I summarizes the demographics of 374 participants, mostly females (52.9%) with an average age of 21.48 years; the majority were over 20 years old, single, and in their fourth or final academic year. Most reported adequate sleep, occasional fruit and vegetable intake, frequent fast food consumption, and minimal tobacco use.

The figure 1 illustrates that 121 participants (32.4%) used screens for academic purposes, while 326 (87.2%) engaged in recreational screen activities (e.g., social media, gaming), highlighting a significant preference for recreational over academic screen use ( $p < 0.001$ ).

In Table II Binary logistic regression analysis revealed significant associations between demographic/lifestyle factors and physical inactivity (low activity levels). Females (95% CI: 1.24-2.67,  $p = 0.002$ ) and younger students ( $\leq 20$  years 95% CI: 1.12-2.43,  $p = 0.011$ ) had higher odds of inactivity compared to males and older

students. Single students (95% CI: 1.05-2.12,  $p = 0.027$ ) and those in lower academic years (95% CI: 1.02-1.87,  $p = 0.037$ ) were also more likely to be inactive. Excessive academic screen time was strongly associated with physical inactivity (95% CI: 0.12-0.39,  $p < 0.001$ ), indicating that higher academic screen time significantly predicts lower physical activity. Recreational screen time showed a moderate association (95% CI: 0.21-0.71,  $p = 0.002$ ).

## DISCUSSION

This study demonstrates a significant association between elevated screen time and reduced physical activity among medical students in Pakistan, with private institution students reporting higher screen usage and lower physical activity levels (65% low activity) compared to public institution counterparts. A strong negative correlation was observed between academic screen time and physical activity, with recreational screen time showing a moderate effect. Key barriers to physical activity included lack of motivation (47.9%) and academic commitments (35.6%), while males (65.7%), older students (61.5%), and married individuals exhibited higher activity levels<sup>22,24</sup>. Additionally, 59.9% of students reported recreational screen time negatively impacting academic performance, consistent with its association with burnout and diminished well-being.<sup>1</sup>

These findings align with prior research, such as a Pakistani study during the COVID-19 lockdown noting increased screen time correlated with reduced physical activity in children<sup>18</sup>, and Stiglic et al. (2019), who reported similar trends among college students.<sup>19</sup> In another study done by Irshad K et al., also found that screen time of medical students has a significant correlation with burnout and has the potential to cause physical and mental health ailments.<sup>20</sup>

Studies on medical and dental students further corroborate the adverse effects of prolonged screen time on physical and mental health, potentially hindering academic success.<sup>21,22</sup> Gender and age disparities in physical activity are consistent with Karachi-based research, where males and older students were more active.<sup>23,14</sup> Sedentary behaviors linked to screen use, as observed in Lahore, reinforce the need for intervention.<sup>24</sup> However, some studies suggest educational screen time may not uniformly reduce physical activity, depending on motivation or context, contrasting with the significant barriers of academic pressure and disinterest identified

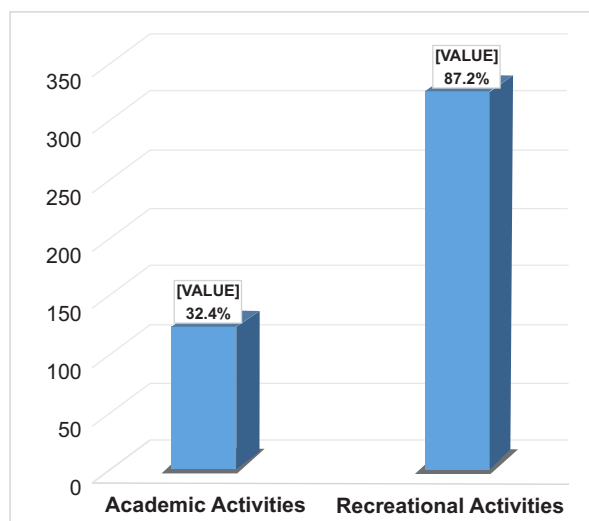
here.<sup>22</sup> Gender disparities may also vary in settings with equitable resource access, indicating contextual influences. These findings imply that excessive screen time, particularly in private institutions, poses risks to students' health and academic performance, necessitating targeted interventions like fitness programs and screen-time guidelines, especially for females and younger students.

This study's strength lies in its comparative analysis of screen time and physical activity between private and public medical institutions, utilizing a validated tool (IPAQ) and employing stratified random sampling to ensure reliable results. This study is limited by its cross-sectional design, which prevents the establishment of causality between screen time and physical activity patterns. Additionally, reliance on self-reported data may introduce recall bias potentially affecting the accuracy of the responses.

## CONCLUSION

The study found that medical students in Pakistan spend a significant amount of time on screens. excessive screen time related to academic work was strongly associated with reduced physical activity. Furthermore, students attending private institutions reported higher screen time and lower levels of physical activity compared to their counterparts in public institutions.

These findings underscore the urgent need for targeted interventions, such as institutional policies limiting non-essential academic screen time, integrating physical activity breaks into academic schedules, providing subsidized gym access, and implementing motivational workshops to address barriers.



**Fig 1: Proportion of Participants Engaging in Academic and Recreational Screen Time**

**Table I: Demographic characteristics of the study population (n=374)**

| Variables                                              | Frequency (%) |
|--------------------------------------------------------|---------------|
| <b>Gender</b>                                          |               |
| Male                                                   | 176(47.1)     |
| Female                                                 | 198(52.9)     |
| <b>Age(years)</b>                                      |               |
| mean± std. dev                                         | 21.48±1.36    |
| <b>Groups</b>                                          |               |
| ≤ 20 years                                             | 101(27)       |
| >20 years                                              | 273(73)       |
| <b>Study year</b>                                      |               |
| 1st year                                               | 51(13.6)      |
| 2nd year                                               | 55(14.7)      |
| 3rd year                                               | 46(12.3)      |
| 4th year                                               | 130(34.8)     |
| Final year                                             | 92(24.6)      |
| <b>Marital Status</b>                                  |               |
| Single                                                 | 225(60.2)     |
| Married                                                | 149(39.8)     |
| <b>Sleeping Hours</b>                                  |               |
| <6 hours                                               | 12(3.2)       |
| ≥ 6 hours                                              | 362(96.8)     |
| <b>Consumption of fruits/vegetables per day</b>        |               |
| Always                                                 | 23(6.1)       |
| Sometimes                                              | 335(89.6)     |
| Rarely                                                 | 16(4.3)       |
| <b>Consumption of fast-food/sugary snacks per week</b> |               |
| Always                                                 | 49(13.1)      |
| Sometimes                                              | 311(83.2)     |
| Rarely                                                 | 14(3.7)       |
| <b>Current smoker/ tobacco user</b>                    |               |
| Yes                                                    | 2(0.5)        |
| No                                                     | 372(99.5)     |

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**Disclaimer:** None

**Conflict of Interest:** None

**Ethical Statement:** Approval of study was taken from Institutional Ethical Review Board (Ref. # 1503/NMU).

**Source of funding:** None

**Table II: Association of demographic and lifestyle factors with physical activity levels among participants (n=364)**

|                                                        | Un-Adjusted              |         | Adjusted               |         |
|--------------------------------------------------------|--------------------------|---------|------------------------|---------|
|                                                        | Odds ratio (95% CI)      | p-value | Odds ratio (95% CI)    | p-value |
| <b>Gender</b>                                          |                          |         |                        |         |
| Male                                                   | 0.086(0.049-0.149)       | <0.001* | 0.328(0.131-0.819)     | 0.017*  |
| Female                                                 | REF                      |         | REF                    |         |
| <b>Age Group</b>                                       |                          |         |                        |         |
| ≤20 years                                              | 0.114(0.055-0.236)       | <0.001* | 0.179(0.026-1.248)     | 0.082   |
| >20 years                                              | REF                      |         | REF                    |         |
| <b>Study year</b>                                      |                          |         |                        |         |
| 1st year                                               | 0.008(0.002-0.028)       | <0.001* | 0.076(0.007-0.821)     | 0.034*  |
| 2nd year                                               | 0.012(0.004-0.036)       | <0.001* | 0.027(0.003-0.232)     | 0.001*  |
| 3rd year                                               | 0.218(0.083-0.568)       | 0.002*  | 0.137(0.026-0.710)     | 0.018*  |
| 4th year                                               | 0.007(0.003-0.019)       | <0.001* | 0.025(0.006-0.101)     | <0.001* |
| Final year                                             | REF (reference category) |         | REF                    |         |
| <b>Martial Status</b>                                  |                          |         |                        |         |
| Single                                                 | 106.255(25.673-439.762)  | <0.001* | 60.520(11.296-324.253) | <0.001* |
| Married                                                | REF (reference category) |         | REF                    |         |
| <b>Sleeping Hours</b>                                  |                          |         |                        |         |
| <6 hours                                               | 0.882(0.261-2.984)       | 0.840   |                        |         |
| ≥6 hours                                               | REF (reference category) |         |                        |         |
| <b>Consumption of fruits/vegetables per day</b>        |                          |         |                        |         |
| Rarely                                                 | REF (reference category) |         |                        |         |
| Sometimes                                              | 0.746(0.271-2.053)       | 0.570   |                        |         |
| Always                                                 | 0.357(0.088-1.447)       | 0.149   |                        |         |
| <b>Consumption of fast-food/sugary snacks per week</b> |                          |         |                        |         |
| Rarely                                                 | REF(reference category)  |         |                        |         |
| Sometimes                                              | 0.335(0.113-0.992)       | 0.048*  |                        |         |
| Often                                                  | 1.292(0.386-4.320)       | 0.678   |                        |         |
| <b>Excessive screen time-Academic activities</b>       |                          |         |                        |         |
| Yes                                                    | 13.419(7.978-22.572)     | <0.001* | 0.528(0.188-1.483)     | 0.226   |
| No                                                     | REF (reference category) |         | REF                    |         |
| <b>Excessive screen time-recreational activities</b>   |                          |         |                        |         |
| Yes                                                    | 0.385(0.208-0.713)       | 0.002*  | 1.134(0.351-3.663)     | 0.833   |
| No                                                     | REF(reference category)  |         |                        |         |

CI: confidence interval, REF: Reference category

Binary logistic regression was applied.

\*Significant at 0.05 level.

**Authors' Contributions:**

Nimra Akhtar: Conception of study/Designing/ Planning, Experimentation/Study Conduction, Analysis/ Interpretation/Discussion

Hamna Khan: Manuscript Writing, Critical Review, Analysis/ Interpretation/Discussion

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# ASSESSMENT OF OUTCOMES IN DONOR SITE CLOSURE OF ANTEROLATERAL THIGH FLAP WITH KEYSTONE FLAP

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## ABSTRACT

**Background:** After harvesting an anterolateral thigh (ALT) flap, closing the donor site too tightly can lead to problems or require skin grafting, which can impact both the structural and cosmetic results. The Keystone Perforator Island Flap (KPIF) is a reliable alternative to tension-free closure that preserves contour and reduces morbidity.

**Objective:** To look at the KPIF method for closing the donor site after harvesting a free ALT flap and see how safe, reliable, and attractive it is, as well as its results and problems.

**Methodology:** This study was conducted from 01 June 2024 to 30 November 2025 (18 months), at the Plastic Surgery Department of Fauji Foundation Hospital, Rawalpindi. This was a prospective descriptive cohort study. The study comprised consecutive patients undergoing donor-site closure for KPIF. In the first two weeks after surgery, the attributes such as demographic information, surgery details, and early postoperative problems were recorded. These problems included seroma, hematoma, epidermolysis, wound dehiscence, flap necrosis, and compartment syndrome. As part of a standard follow-up after three and six months of surgery, patients filled out structured questionnaires and underwent clinical examination. The examination comprised of checking for contour deformity, sensory symptoms like tingling or numbness, differences in thigh circumference compared to the other leg, and evaluating the quality of the scar using the Vancouver Scar Scale.

**Results:** Our study included 28 patients, with an average age of  $41 \pm 15$  years, an average BMI of  $20 \pm 1.2$  kg/m<sup>2</sup>, and 57.1% of them were women. In all cases, closure without any major complications was achieved. In 14.3% of cases, minor complications were seen and were managed conservatively. Measurements of thigh circumference showed no significant difference compared to the other limb, and most people said they had mild sensory problems. At three months, 85.7% rated the cosmetic results as good or excellent, and 42.9% of the patients as per the structured questionnaire, showed a contour deformity.

**Conclusion:** Closing the ALT donor site with KPIF is safe, effective, and looks good. It keeps the structure of the site intact and lowers the risk of problems.

**Keywords:** Morbidity, Perforator Flap, Plastic Surgery, Reconstruction, Treatment Outcomes

## INTRODUCTION

The anterolateral thigh (ALT) flap is a flexible and widely used choice in reconstructive surgery because its vascular anatomy is always the same, its soft tissue is flexible, and it can provide a large skin paddle.<sup>1</sup> You can

use it either as fasciocutaneous or a musculocutaneous flap, and it is often used to fix complex defects in the head and neck, trunk, and limbs. Changes to the design, such as the horseshoe shape, make it even more useful for restoring contours and covering large defects. However, optimizing the closure of the donor site is still important because it affects postoperative outcomes.<sup>2</sup> Despite the ALT flap's generally low donor-site morbidity, several complications have been documented. These involve protracted healing, wound dehiscence, contour irregularities, seroma development, hypertrophic scarring, and sensory disturbances such as lateral thigh paresthesia.

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Functional impairment resulting from quadriceps weakness or musculoskeletal dysfunction is infrequent that can affect postoperative quality of life; however, sensory alterations are considered the most prevalent donor-site complication.<sup>2,6</sup> Research indicates that the donor-site closure technique significantly influences postoperative outcomes, with primary closure typically associated with expedited healing and superior cosmetic results compared to skin grafting.<sup>8</sup>

With the given complications of wound dehiscence, healing difficulty, contour deformity, seroma, hypertrophic scars, and sensory changes, including lateral thigh numbness of 24% and musculoskeletal dysfunction of 4.8%, the morbidity of the donor site is thus a serious consideration.<sup>2</sup>

Small skin defects could be easily closed, however, the defects that are over 8 cm require a different method for reconstruction. While the use of local flap advances will increase the complexity of surgery, and this results in additional morbidity. In contrast, the traditional methods, including split-thickness skin grafting (when compared to adjacent native tissue) results in issues like colour differences, counter deformity, and relative mechanical weakness. This happens because they lack full dermal architecture of normal skin and are more prone to the secondary contraction, which compromises durability and contour at the donor site. Several alternative techniques, which involve local advancement flaps, V-Y advancement flaps, perforator-based propeller flaps, and anteromedial thigh flaps, have been suggested to address these constraints and enhance the aesthetic outcomes while reducing the donor-site morbidity.<sup>5</sup> Recent systematic reviews have also been suggested to use decision-making algorithms to assess the flap width in relation to thigh circumference and it helps to choose the best ways to close the donor site.<sup>4</sup>

One of the technique for ALT flap reconstruction of the donor site is Keystone Perforator Island Flap (KPIF) that is suggested by the Behan et al.<sup>7</sup> The KPIF is useful as it effectively redistributes the defect with robust vascularity by utilizing adjacent skin from preserved perforators. The benefits of this method are: (i) it reduces healing time, (ii) offers superior color and texture match, (iii) it allows primary closure without grafting, and (iv) it has a low morbidity rate. Although, most of the studies have small sample sizes (i.e., six or less patients), they resulted in good performances and high patient satisfaction.<sup>9</sup> Despite of their promising results, the literature that is currently available have significant

anomalies like they are retrospective studies, are inconsistent in reporting standardized donor-site outcomes, they are heterogeneous in patient selection, and are variable in choosing flap design. Also the objective assessment tools like Perfusion studies and validated scar scoring systems are rarely used in these studies. Furthermore, the current evidence's generalizability is limited by the dearth of the regional data, especially from South Asia.

The purpose of this study is to assess the safety, effectiveness, and structural and aesthetic results of keystone flap closure for ALT donor sites in Pakistani patients. To improve postoperative recovery, preserving the form, functional performance, and patient quality of life, this research aims to provide region-specific evidence. It supports the keystone flap as a dependable and functionally superior method for donor-site management by utilizing standardized assessment tools and a single-stage tension-free closure technique.

## METHODOLOGY

Between 01 June 2024 and 30 November 2025, consecutive patients who underwent donor-site closure with a keystone flap after free ALT flap harvest were enrolled in a prospective study carried out in the Plastic Surgery Department of Fauji Foundation Hospital, Rawalpindi. The Fauji Foundation Hospital's Ethical Review Committee granted ethical approval. On March 20, 2024, the approval was given with reference number 814/RC/FFH/RWP. We prospectively collected information on postoperative complications, operative details, and demographics of these patients.

## Inclusion and Exclusion Criteria

For this study, we enrolled adult patients of any gender presenting with ALT donor site defects exceeding 8 cm. We specifically excluded individuals under 18, as well as those with atypical defects resulting from chimeric or multiple perforator flaps. To ensure data integrity, we excluded cases with incomplete records or those lost to follow-up. Furthermore, we omitted patients with systemic conditions that hinder healing—such as uncontrolled diabetes, chronic kidney disease, or long-term steroid use—alongside any cases where the site was closed using alternative methods like skin grafting or local flaps. We identified participants through a consecutive convenience sampling protocol, ensuring that every patient receiving an anterolateral thigh (ALT) flap with KPIF donor site reconstruction during the study period was evaluated for eligibility. Our team recorded everything from demographic data to specific

surgical findings and recovery milestones using a standardized template. Only cases that aligned perfectly with our inclusion criteria made it into the final analysis.

### Sample Size and Consent

Between June 2024 and November 2025, we consecutively enrolled all patients undergoing ALT flap reconstruction. Out of this group, 28 individuals met the inclusion criteria. While this sample size might seem modest, it reflects our entire clinical volume for the 18-month period, driven by the specialized nature of the surgery and the specific requirement for Keystone donor site closure. We believe this prospective descriptive series provides a representative look at the feasibility, safety, and clinical outcomes of the reconstructive technique in this specific context. Every participant gave their informed consent.

### Surgical Technique

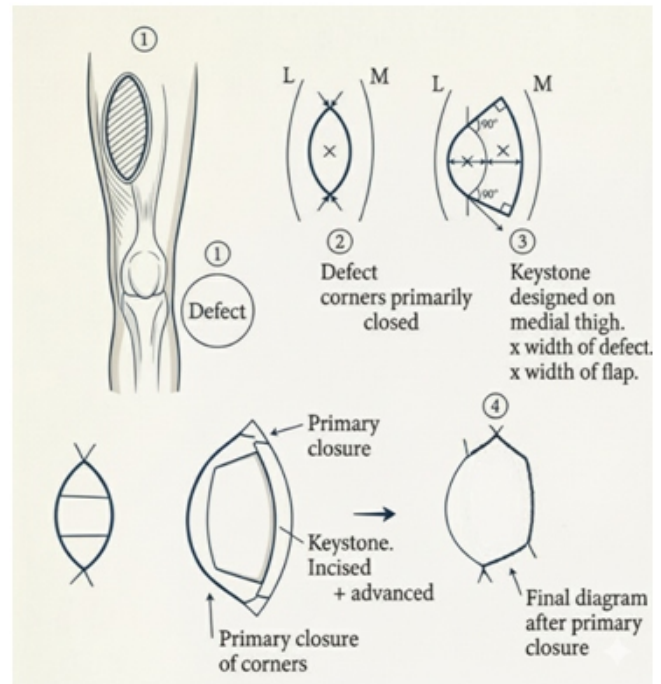
Before the procedure, we used a handheld Doppler to map out the cutaneous perforators in the anterolateral thigh. For every procedure, we utilized a two-team approach to keep the workflow moving efficiently. Once the ALT flap was elevated and the vascular pedicle was carefully isolated and split, the flap was transferred to the recipient site. While the primary reconstructive team managed the inset and microvascular anastomosis, a second surgical team worked simultaneously to reconstruct the donor-site defect.

Following flap harvest, the donor-site defect was evaluated and, if necessary, transformed into an elliptical shape. A sterile ruler was used to measure the defect's transverse width. Along the line of maximum skin laxity, a keystone perforator island flap had been designed next to the defect's medial edge. The keystone flap's width is almost identical to the donor-site defect's width. The two vertical limbs of the keystone flap were marked at an angle of 90 degrees perpendicular to the defect's medial margin.

Skin incisions were made down to the deep fascia along the flap's designated borders. To increase flap mobility and preserve vascular reliability, a Type IIA modification<sup>4</sup> of the keystone perforator island flap was used. To make it easier for the flap to advance, the deep fascia was split along its edges. To improve flap mobility while maintaining the integrity of the perforator blood supply, limited undermining beneath the fascia was carried out. The keystone flap's lateral limbs were then moved in the direction of the central defect, allowing tension to be redistributed throughout the surrounding tissue. This allowed for additional tissue advancement

and tension-free donor site closure. Layered wound closure was frequently preceded by the installation of closed-suction drains.

Donor-site closure using the keystone flap required an average operative time of approximately 45 minutes. However, because the donor-site reconstruction was performed concurrently with flap inset and microvascular anastomosis by the primary surgical team, the technique did not increase the overall operative time.



**Figure 1: Donor site defect, advancement, and outcome of the keystone flap procedure**

Closure was considered successful if the donor site was sealed with viable tissue, preserved thigh contour, and did not require split-thickness skin grafting or secondary revision procedures. Figure 1 is the general illustration of the procedure of keystone flap to the donor site used in the proposed architecture.

### Postoperative Assessment

To gauge the success of the procedure, we looked at a mix of clinical, structural, and aesthetic markers. From a clinical standpoint, the primary goal was a tension-free closure at the donor site. We tracked patient outcomes across two distinct phases. In the first two weeks, our focus remained on flap viability and wound healing, specifically monitoring for issues like hematoma, seroma, or partial necrosis. Later on, at the three and six-month marks, we evaluated more permanent results. These included assessing contour deformities, checking for sensory changes like numbness and measuring thigh

circumference relative to the unaffected limb. Scar quality was also formally graded using the Vancouver Scar Scale.

Patients completed structured questionnaires and a clinical examination as part of a standard follow-up at three and six months. Tingling, contour deformity, thigh circumference and scar quality were among the results. Both the operated and contralateral limbs had their thighs measured at a standardized level (15 cm proximal to the superior patellar border); a difference of more than 2 cm was considered a significant deformity.

The Vancouver Scar Scale (VSS) was used to score scar quality; total scores are classified as Excellent (0–3), Good (4–6), or Moderate (7–9). Clinical photos that were standardized were acquired. One plastic surgery fellow with at least three years of post-fellowship experience conducted all evaluations to minimize interobserver variability. For statistical analysis, medians were found for continuous data and frequencies and percentages were computed for patient characteristics and other categorical variables. The Statistical Package for the Social Sciences (SPSS version 23.0, Inc., Chicago, IL) was used for all analysis.



#### Patient 1

A 56-year-old female (BMI 23 kg/m<sup>2</sup>) known case of giant cell tumor of knee joint who underwent right sided ALT flap harvest. (A) The resulting donor-site defect measured approximately 17 x 11.6 cm. (B) The defect was reconstructed using a keystone perforator island flap, based on medial cutaneous perforators, allowing for tension-free primary closure. (C) six-month postoperative follow-up.



#### Patient 2

A 21-year-old female (BMI 19.4 kg/m<sup>2</sup>) with Post Burn scarring right hand underwent left ALT flap harvest. (A) The resulting donor-site defect measured approximately 15 x 9.5 cm. (B) The defect was reconstructed using a keystone perforator island flap, based on medial cutaneous perforators, allowing for tension-free primary closure. (C) three-month postoperative follow.



### Patient 3

A 58-year-old female patient with hypertension (BMI 19.4 kg/m<sup>2</sup>) who had a dorsal left foot defect following a car accident. (A) the resulting donorsite defect was about 16 by 11 cm in size. (B) Reconstruction based on medial cutaneous perforators using a keystone perforator island flap. (C). A six-month follow-up demonstrates stable healing and scar maturation.

**Figure 2: Pre-operative, Post-operative stages of three patients**

Microsoft Excel 2016 was used to create the tables and figures. The following figure 2 shows the pre-operative and post-operative recovery stages of three patients.

### RESULTS

This prospective study included 28 patients in total. The average body mass index (BMI) was 20.5 kg/m<sup>2</sup> ( $\pm 1.2$ ), and the average age was 41.1 years ( $\pm 15.8$ ). Males (42.9%, n=12) were slightly outnumbered by females (57.1%, n=16) in the gender distribution. In terms of comorbidities, over half of the patients (57.1%) had no

serious systemic illness and were in good medical health. With 28.6% of patients having hypertension and 14.3% having diabetes mellitus while hypertension was the most common comorbidity.

The average width and height of the anterolateral thigh flap donor site defects were 10.2 cm and 15.7 cm, respectively. Interestingly, female patients had slightly larger defects (mean 16.75  $\times$  10.75 cm) than male

**Table I: Patient Demographics**

| Demographics             | Mean $\pm$ SD     |
|--------------------------|-------------------|
| Age (years)              | 41.14 $\pm$ 15.83 |
| BMI (kg/m <sup>2</sup> ) | 20.5 $\pm$ 1.24   |
| <b>Gender</b>            |                   |
| Male n (%)               | 12 (42.9%)        |
| Female n (%)             | 14 (57.1)         |
| <b>Comorbidity</b>       |                   |
| None n (%)               | 16 (57.1%)        |
| Diabetes n (%)           | 4 (14.3%)         |
| Hypertension n (%)       | 8 (28.6%)         |

**Table II: Dimensions of Defects**

| Gender |                | Height (cm) | Width (cm) |
|--------|----------------|-------------|------------|
| Male   | Mean           | 14.333      | 9.5        |
|        | N              | 12          | 12         |
|        | Std. Deviation | 0.4924      | 1.1282     |
| Female | Mean           | 16.750      | 10.750     |
|        | N              | 16          | 16         |
|        | Std. Deviation | 0.8563      | 0.8563     |
| Total  | Mean           | 15.714      | 10.214     |
|        | N              | 28          | 28         |
|        | Std. Deviation | 1.4105      | 1.1501     |

patients (mean  $14.3 \times 9.5$  cm) when the data were stratified by gender. Even though it does not involve data with a statistical evaluation, this discrepancy is important as it displays anatomical variability that can influence the management of the donor site.

A successful closure was achieved with the keystone flap in closing the donor site in all 28 cases, thereby providing an overall success rate of 100% flap closure. Also, there was no case that had necrosis or compartment syndrome in this series. The absence of major complications is an important factor that indicates efficacy.

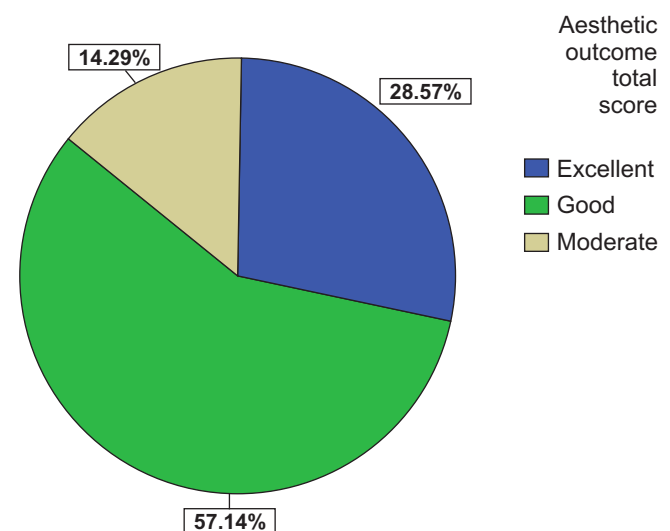
A small number of patients (14.3% of participants;  $n=4$ ) experienced minor complications. These included the development of seromas or hematomas, partial wound dehiscence, and epidermolysis. Notably, in each case, these complications were self-limiting or manageable with conservative care such as drainage, dressings, and wound care, and did not necessitate reoperation.

**Table III: Closure of Anterolateral Thigh Flap Donor Site through Keystone Flap**

| Outcomes                    | Frequency | % age  |
|-----------------------------|-----------|--------|
| <b>Hematoma/seroma</b>      |           |        |
| Yes                         | 04        | 14.3 % |
| No                          | 24        | 85.7 % |
| Total                       | 28        | 100 %  |
| <b>Partial dehiscence</b>   |           |        |
| Yes                         | 04        | 14.3 % |
| No                          | 24        | 85.7 % |
| Total                       | 28        | 100 %  |
| <b>Epidermolysis</b>        |           |        |
| Yes                         | 04        | 14.3 % |
| No                          | 24        | 85.7 % |
| Total                       | 28        | 100 %  |
| <b>Compartment syndrome</b> |           |        |
| Yes                         | 0         | 0 %    |
| No                          | 28        | 100 %  |
| <b>Flap necrosis</b>        |           |        |
| Yes                         | 0         | 0 %    |
| No                          | 28        | 100 %  |

A thorough evaluation at three months was done to assess the donor-site morbidity. Eight patients (28.6%) experienced major tingling sensation, that is indicative of slight sensory alterations at the donor site (Figure 3, whereas twenty-one patients (71.4%) experienced it to a mild extent. These findings suggest that although the symptom of sensory disturbance is not uncommon, the severity is likely to be minimal.

A total of twelve patients (42.9%) had a donor site bulge. Nevertheless, objective measurement did not show any measurable difference in the thigh dimensions in the operated limb and the opposite, unoperated limb. The tissue-advancement procedure provided a very good restoration of the contours without creating any appreciable asymmetry in the shape and dimensions. Not a single patient fulfilled the objective criteria for appreciable deformity, i.e.,  $> 2$  cm difference. At the cosmetic evaluation, a very high satisfaction rate at the donor site was obtained. "Excellent" results were observed in eight patients (28.6%), and "Good" results in sixteen patients (57.1%). "Moderate" results were found in only four patients (14.3%). These findings make it certain that the keystone flap procures a very good cosmetic result. The standardized photographs at the follow-up appointment, depicting well-formed scar and intact contour, validated the results.



**Figure 3: Aesthetic outcome total score**

The closing of the donor site was successful via the keystone flap without any major complications. Minor complications were not only insignificant and self-limiting, but they also didn't influence the result. Collectively, these data indicate that, despite a requirement for rather large skin flaps, the ALT donor site closing via the keystone flap is a safe and effective, aesthetically acceptable alternative.

## DISCUSSION

Due to this versatility, reliable vascular anatomy, and a very low incidence of donor site morbidity, the ALT flap is recognized as a central part of microsurgical reconstruction. In a low middle income country like Pakistan, the reconstruction procedure is required to

adapt to a series of constraints, including resource limitation and the requirement to find a balance in the restoration and the cosmetic aspect. However, it is hard to achieve ALT donor-site closure in such options. Although split-thickness skin grafting is popular due to its ease of use, it is linked to contour deformity, hypertrophic scarring, color mismatch, and donor-site morbidity that many patients find unsatisfactory. Primarily, the closure may not be achievable when the width of the flap is greater than 8-10 cm, split thickness skin grafting is preferred owing to its simplicity, although many patients remain disgruntled owing to deformity, hypertrophic scars, color match, or donor site morbidity. Our findings clarify that the keystone perforator flap (KPIF), providing tension-free closure, high success rates, minimal complications, and excellent aesthetic outcomes, could be an alternate to the ALT donor site reconstruction.

We have successfully reached the goal of 100% primary closure without serious complications of flap necrosis and compartment syndrome. The KPIF was first described by Behan<sup>4</sup>, who reported excellent perfusion, safety, and highly dependable closure in a variety of anatomical regions. Similar success rates have been reported in four studies that specifically evaluated ALT donor sites. In their series, Kumbla et al.<sup>10</sup> reported 100% donor-site closure, with only 16.7% encountering minor complications like seroma or partial dehiscence. We experienced six Minor complications, such as epidermolysis, partial dehiscence, and hematoma/seroma, in 14.3% of patients in our cohort and they resolved without surgery. These results are consistent with those of Turin et al.,<sup>11</sup> who showed that, in comparison to split-thickness skin grafting, keystone closure considerably lowers donor-site morbidity.

Collins and Ayeni's systematic review<sup>12</sup>, which summarized ALT donor-site morbidity across various closure techniques, found that wound complications occurred in approximately 5% of cases, seroma in approximately 2-3%, and paresthesia in up to 24% of cases. The higher mean skin paddle width (10.2 cm) in our patient population probably accounts for the slightly higher rates of minor wound-related events. Crucially, lack of significant complications in our study validates the keystone technique's dependability for repairing larger, higher-tension donor-site defects.

In our study, aesthetic results were one of the KPIF's most prominent benefits. Just 14.3% of patients described their outcome as "Moderate," whereas over 85% of patients rated their donor-site appearance as

"Good" or "Excellent." This is in line with research by Dobbs et al.<sup>13</sup>, who used both objective scar scales and patient-reported evaluations to show that keystone flaps had better scar quality and greater patient satisfaction than split-thickness grafts. Clinical photos showing linear scars, harmonious pigmentation, and preserved contour supported the Vancouver Scar Scale (VSS), which offered objective validation of aesthetic results. Grafted donor sites, on the other hand, often result in depressed, irregular scars with color mismatch, which can be upsetting, especially for younger patients or those who have visible donor sites.<sup>9</sup>

There are several ways to close the ALT donor site, and the width of the harvested flap and the properties of the surrounding tissue play a major role in the decision. For flaps narrower than 8 cm, primary closure is preferred but usually safe; beyond this, excessive tension raises the risk of wound breakdown. Split thickness skin grafting is still widely used, but it causes morbidity at a secondary donor site, hypertrophic scarring, and contour compromise. Propeller flaps and KPIF are two tissue-rearrangement techniques that are becoming more and more popular because they provide tension-free closure, maintain thigh contour, and eliminate the need for skin grafts. For intermediate-sized defects (8–12 cm width or 16–30% of thigh circumference), where primary closure is not practical but a graft would be less functional or aesthetically pleasing, modern decision-making algorithms<sup>9</sup> recommend keystone flaps.

In 42.9% of patients, we found donor-site bulging. The bulging was purely cosmetic and unrelated to functional impairment or patient dissatisfaction, even though this incidence is higher than that reported in some series. As in Type IIA keystone perforator island flaps (KPIF)<sup>7</sup>, which is used in larger defects where deep fascia along the flap is incised and defect is primarily closed without use of skin graft, bulging is frequently associated with fascial release, a technique we employed to improve flap mobility. Purnell et al.<sup>14</sup> and other authors have proposed that postoperative compression, quilting sutures, and careful fascial management can lower the risk of bulging. Although most of our patients were able to tolerate this change in contour, future cases may benefit from improved technique.

Our study's prospective design, standardized three-month follow-up, and use of validated assessment tools (all assessed by a single, qualified assessor to reduce interobserver variability) are among its strong points. A small sample size (n = 28), a brief follow-up period considering that scar maturation and sensory recovery

may take up to a year, and the lack of a comparative group, such as patients undergoing split-thickness graft closure, are some of the limitations. Larger, multicenter designs, longer follow-up periods, and randomized comparisons of closure techniques would be beneficial for future research.

The keystone perforator flap is a safe, dependable, and aesthetically pleasing method for ALT donor-site closure, according to the study's overall findings. The keystone flap offers a reliable and repeatable solution in resource-constrained environments where grafting results might not be ideal, and sophisticated techniques might not be feasible. With the achievement of full closure with little complication and high patient satisfaction, the KPIF provides a clinically valuable method of donor site closure which can be adopted with confidence by reconstructive surgeons working in similar environments.

## CONCLUSION

Keystone perforator flap closure allows for the safe, efficient, and aesthetically pleasing management of ALT donor sites. In our series, the approach resulted in dependable closure with low rates of complications, high patient satisfaction, and preserved structural outcomes. These findings support its routine use when

primary closure is not practical, especially in resource-constrained environments where avoiding skin grafts and secondary morbidity is essential.

**Conflict of interest:** None

**Disclaimer:** None

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## Authors' Contribution

Fatima Sohail: Conception of study / Designing / Planning, Experimentation / Study Conduction, Analysis / Interpretation / Discussion, Manuscript Writing, Critical Review, Facilitated for Reagents / Material Analysis

Ayesha Aslam: Conception of study / Designing / Planning, Experimentation / Study Conduction, Critical Review, Facilitated for Reagents / Material Analysis

Sameena Aman: Conception of study / Designing / Planning, Analysis / Interpretation / Discussion, Critical Review

Nousheen Saleem: Analysis / Interpretation / Discussion, Critical Review, Manuscript Writing

Hira Feroz Akbar: Manuscript Writing, Critical Review, Facilitated for Reagents / Material Analysis

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# EVALUATION OF KNOWLEDGE OF POSTGRADUATE TRAINEES IN TRANSFUSION MEDICINE: A CROSS-SECTIONAL SURVEY

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## ABSTRACT

**Objective:** The objective of study was to assess postgraduate trainees' knowledge of transfusion medicine.

**Study Design:** It was a descriptive, quantitative cross-sectional study

**Place and Duration of study:** The study was conducted at Fauji Foundation Hospital Rawalpindi in department of Hematology. Duration of study was from 15 Sep 2023 to 15 Nov 2023.

**Participants and Methods:** Total 177 postgraduate trainees of different departments of a Fauji Foundation Hospital, Rawalpindi, in different years of training were included in study. The sampling technique used was a Non probability Convenience sampling technique. Trainees were evaluated by a questionnaire. A data collection sheet that was peer-reviewed was used to score the final performance.

**Results:** Of 177 participants, 173 participants responded to the online questionnaire survey. Overall, 52.46% of participants across all specialties and training years correctly answered the questions. The mean score for the Medicine ( $M = .59$ ,  $SD = .15$ ) specialty group was statistically different from Medicine and Allied ( $M = .49$ ,  $SD = .16$ ,  $P = < .001$ ), Surgery and Allied ( $M = .50$ ,  $SD = .13$ ,  $P = .008$ ), and Surgery ( $M = .48$ ,  $SD = .12$ ,  $P = .032$ ).

**Conclusions:** Significant gaps in knowledge were observed in transfusion medicine. Medical colleges and training institutes might be more likely to contribute to transfusion medicine teaching if the study's findings could be replicated at other training facilities.

**Keywords:** Blood, Blood Component Transfusion, Blood transfusion, Transfusion Medicine

## INTRODUCTION

Knowledge of postgraduate trainees and treating physicians about blood products in context of their preparation, storage, indications, dosage calculation and administration, has a profound impact on patient care.<sup>1</sup> Due to resource limitation, less faculty, lack of proper curricula related to transfusion medicine there is lack of adequate knowledge in transfusion medicine and wrong transfusion practices which may jeopardize their safety. Decisions regarding transfusion are usually taken by residents and clinicians without adequate formal

training.<sup>2</sup> There is marked difference between clinical practice in context of blood components ordering and transfusion as compare to evidence-based knowledge.<sup>3</sup> Despite the critical nature of this field, there is a noticeable gap in research and discourse regarding the depth of knowledge among postgraduate trainees in Rawalpindi, Pakistan.<sup>4</sup> By highlighting this gap, we can improve the quality of our healthcare delivery and also contribute globally on transfusion medicine education.

The knowledge of transfusion medicine among postgraduate trainees is important for numerous reasons. Primarily, understanding the existing state of knowledge will shed light on important areas for improvement in the training curriculum. Secondly, it will help identify any existing misconceptions that may compromise patient safety.<sup>5</sup> Lastly, the findings may reveal the ways for targeted interventions and educational initiatives to foster the transfusion medicine expertise of postgraduate trainees, ultimately strengthening the healthcare system in Rawalpindi and beyond. There is scarcity in research highlighting the

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educational strategies and level of knowledge of post graduate students on blood transfusion practices in undergraduate and postgraduate medical curriculum in Pakistan. Lack of correct knowledge of transfusion medicine can be life threatening. Identifications of these gaps and bridging these gaps is the need of the hour.

### PARTICIPANTS & METHODS

The objective of the study was to evaluate the knowledge of transfusion medicine among Postgraduate trainees for effective use of blood bank resources, as well as to facilitate safe blood transfusion practices to the patients. Ethical approval was acquired from the ethical review committee of the respective institution (vide letter no. 725/RC/FFH/RWP dated 21-08-2023).

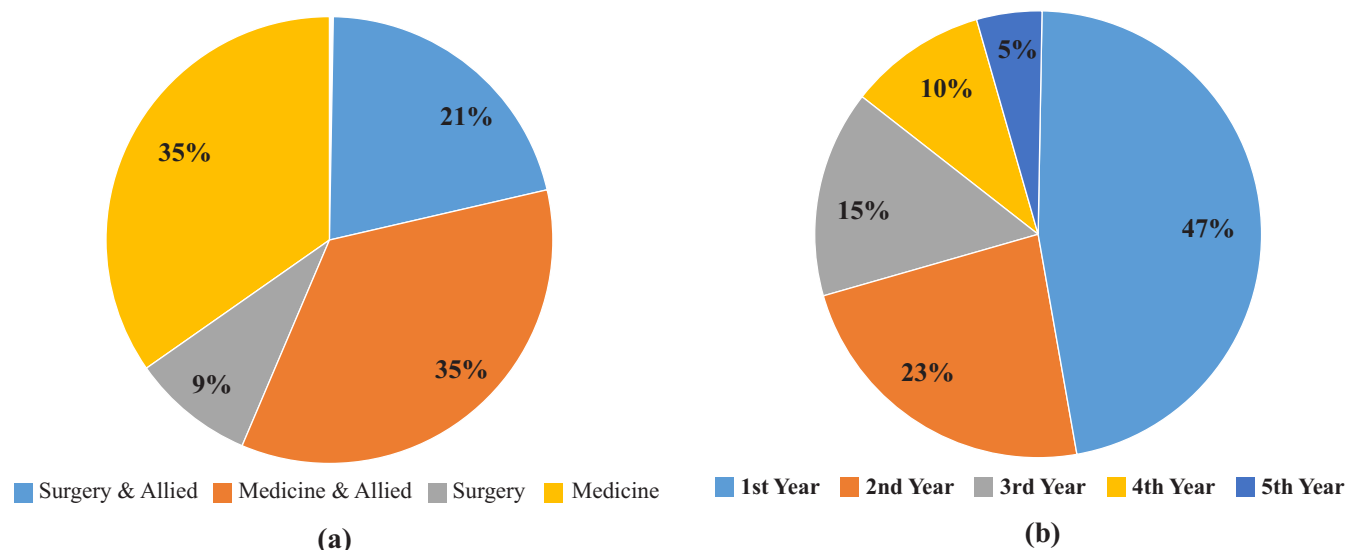
This study was descriptive cross-sectional research conducted within 3 months (15 Sep 2023 to 15 Nov 2023). The sampling technique used was a Non probability Convenience sampling technique. Participants from 22 specialties were included, which were then categorized into four primary specialties, including Medicine, Medicine and Allied, Surgery and Surgery and Allied. A total of 177 postgraduate trainees in different years of training from various departments participated in the study. Data collection was carried out using a self-developed, validated questionnaire (closed-ended), consisting of 25 items on 3 3-point Likert scale showing agree, disagree, and I don't know. These questions were formulated considering the main areas of transfusion medicine, such as basic knowledge about donor selection, demand and doses of blood components, administration of blood components,

interpretation of laboratory results, transfusion reactions and transfusion transmitted infections.

The demographic section included age, gender, specialty, and years of training. A pilot study of this questionnaire was performed by consulting on post-internship doctors working in the Department of Pathology and medicine at our institution. They agreed that the questions were relevant and understandable. Confidentiality and anonymity were assured. Informed consent was taken from all participants. After submission of the questionnaire, every participant was provided with the correct answers so they could update their knowledge. Data were analyzed using SPSS software, version 22 (SPSS, Inc).

### RESULTS

In total, 177 participants responded to the online questionnaire survey. Participants from 22 various specialties were then categorized into four primary specialties: Medicine, Medicine and Allied (Radiology, Pediatrics, Pulmonology, Cardiology, Hematology, Nephrology, Neurology, Oncology, Psychiatry, Dermatology, Emergency Medicine), Surgery and Surgery and Allied (Gynae and Obstetrics, Pediatric Surgery, Orthopedics, Urology, Cardiac Surgery, Anesthesia, Plastic Surgery, Ophthalmology, ENT ). Among various respondents, the highest percentage was found from Medicine and allied, followed by Medicine, Surgery and Allied and a smaller percentage from Surgery, Fig (1a). The training duration required for general specialties is four years, while subspecialties require five years of training. Therefore, the years of



**Figure 1: Distribution of Participants by Specialties (left side) and Year of Training (right side)**

training were classified ranging from 1 to 5, shown in Figure 1 (b).

The overall correct scores of postgraduate trainees from different specialties are presented in Table I. The findings were statistically assessed using analysis of variance (ANOVA), and the total correct score difference between these primary specialties was found to be statistically significant (Table II). Overall, 52.46% of participants across all specialties and training years correctly answered the questions. Participants from Medicine had the highest accuracy rate, reflecting a strong understanding of the material, while those from Surgery & Allied followed closely behind. While participants from Medicine and Surgery and Allied specialties showed slightly lower percentages of correct answers, respectively. Further post-hoc analysis was conducted to assess the significance of the difference between the four primary specialty groups using Tukey. The test indicated that the mean score for the Medicine (M =.59, SD =.15) specialty group was statistically different from Medicine and Allied (M =.49, SD =.16,  $P = <.001$ ), Surgery and Allied (M =.50, SD =.13,  $P = .008$ ), and Surgery (M =.48, SD =.12,  $P = .032$ ).

**Table I: Accuracy rate across primary specialties**

| Variable          | Surgery & Allied | Medicine & Allied | Surgery | Medicine | Overall |
|-------------------|------------------|-------------------|---------|----------|---------|
| Accuracy Rate (%) | 49.73            | 48.57             | 47.93   | 59.22    | 52.46   |
| Mean              | 0.50             | 0.49              | 0.48    | 0.59     | 0.52    |
| SD                | 0.13             | 0.16              | 0.12    | 0.13     | 0.15    |

Table II shows the percentage of correct scores for participants based on their training year. The "accuracy rate," as mentioned above, indicating the percentage of correctly answered questions, shows the highest accuracy rate among participants in the 2nd year of training, followed closely by the 1st year of training. Surprisingly, after the second year of training, as the training year's progress, the accuracy rates started gradually decreasing. But upon the statistical analysis conducted by employing ANOVA, no statistical differences were observed between the groups based on the number of years of training (Table III).

**Table II: Accuracy rate across years of training**

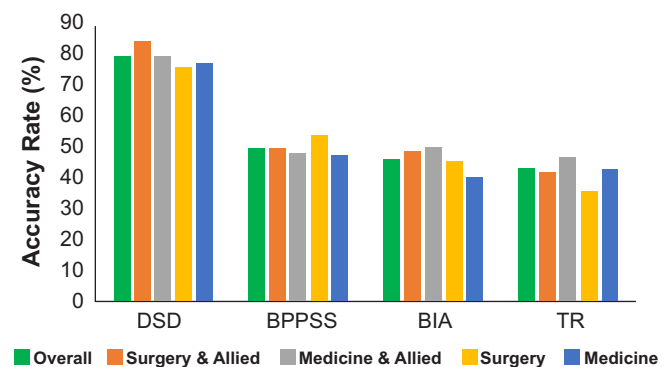
| Variable          | 1 <sup>st</sup> Year | 2 <sup>nd</sup> Year | 3 <sup>rd</sup> Year | 4 <sup>th</sup> Year | 5 <sup>th</sup> Year |
|-------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| Accuracy Rate (%) | 54.20                | 55.38                | 48.12                | 47.29                | 45.13                |
| Mean              | 0.54                 | 0.55                 | 0.48                 | 0.47                 | 0.45                 |
| SD                | 0.14                 | 0.14                 | 0.16                 | 0.16                 | 0.14                 |

Furthermore, based on the knowledge assessments, the 26 total questions were divided into four main

**Table III: ANOVA- Comparison of accuracy rates between years of Training**

| Source of variation | Sum of Squares | df     | Mean Square | F    | Sig.  |
|---------------------|----------------|--------|-------------|------|-------|
| Between Groups      | 0.20           | 4.00   | 0.05        | 2.29 | 0.062 |
| Within Groups       | 3.60           | 168.00 | 0.02        |      |       |

components of transfusion medicine. The first component included five questions related to assessing knowledge about donor selection and deferral criteria (DSD). The second component comprised nine questions related to assessing knowledge of blood product preparation, screening and storage (BPPSS). The third group included nine questions related to blood components indications and administration (BIA). The final group included three questions related to transfusion reaction (TR). The percentage of correct answers within each area of knowledge for both overall and each specialty is shown in the figure. The percentage of overall correct answers for Donor Selections and Deferrals (DSD) was the highest among all four areas of knowledge as well as the highest in each specialty. The overall correct answer for the area of transfusion knowledge titled Transfusion Reaction (TR) was the lowest at 42.97% (Surgery & Allied 41.44%; Medicine & Allied 46.45%; Surgery 35.56%; and Medicine 42.22%). (Figure 2).



**Figure 2: Accuracy Rate in Four Key Transfusion Areas across Four Primary Specialties**

## DISCUSSION

Transfusion medicine is an emergency mostly in acute lifesaving procedures. There is dire need of formal education and training of post graduate trainees and all medical staff for implementation of safe transfusion practices.<sup>6</sup>

According to the SHOT report, 2019, the major cause of

incorrect transfusion of blood component was due to wrong ordering of blood products which was found to be approximately 30.7%.<sup>7</sup>

According to results of our study, 56.4% of participants have given correct answers. In contrast to our study, interns have alarmingly poor knowledge about various aspects of blood transfusion services. According to study conducted by Gopal et al 41.5% residents out of total had inadequate knowledge about transfusion medicine.<sup>8</sup> In one study conducted by Hussel W there was marked deficiency of adequate knowledge related to use of blood warmers, exchange transfusion and massive transfusion protocols.<sup>9</sup>

Our study reflected the highest accuracy rate among participants in the 2nd year of training at 55.38%, followed closely by the 1st year with an accuracy rate of 54.20%. Surprisingly, after the second year of training, as the training year's progress, the accuracy rates gradually decrease, with a rate of 48.12% for participants in the third year, 47.29% for participants in the fourth year, and 45.13% for participants in the fifth year of their post-graduation training.

Knowledge of transfusion medicine in postgraduate trainees and clinicians was assessed by Poh Ky et al.<sup>10</sup> Total doctors assessed were 184, having a mean score of correct answers of 40.1% (SD 12.7%). The difference between our study and this study was that it included both clinicians and postgraduate trainees. Physicians from specialties including hematology, internal medicine, reflected notable higher scores (51%, 47.4%, and 46.4% respectively,  $p < 0.05$ ). This is following our study in which participants from Medicine stand out with the highest accuracy rate at 59.22%, indicating a commendable percentage of correctly answered questions. Participants from Surgery & Allied closely followed with an accuracy rate of 49.73%, while participants from Medicine and Surgery and Allied specialties showed slightly lower rates of accuracy at 48.57% and 47.93%, respectively. According to the results of our study, the overall correct answer for the area of transfusion knowledge titled Transfusion Reaction (TR) was the lowest. Similarly, in this study postgraduate trainees have been found to have deficient knowledge in areas of transfusion related acute lung injury (TRALI) and transfusion reactions.<sup>10</sup> In another study conducted by Vaena M et al in Brazil, showed the overall mean of correct answers to the questionnaire was 43.5%. An inadequacy of knowledge of transfusion medicine was found according to the results of this

study.<sup>11</sup>

In contrast to our study, maximum correct answers were related to the thresholds for transfusion of platelets, indication of different blood products (80%), and finally the diagnosis and management of transfusion reactions (87%).<sup>11</sup> However according to the results of our study best knowledge was observed in area of donor selection and deferral, blood products preparation screening and storage, blood indications and administration but poor knowledge in area of transfusion reactions.

Ngo A et al also observed that there is dire need of formal education programs in transfusion medicine.<sup>12</sup>

A cross-sectional study was conducted by Bouchrim AA on total fifty 1<sup>st</sup> year residents of first year medical and surgical specialty. According to the results major gaps identified in knowledge of transfusion medicine were in blood ordering, handling of blood products in wards, identification of responsibilities of residents in transfusion of blood products to the patients. Also they had inadequate knowledge about managing blood complications.<sup>13</sup> In a research conducted by VUK PT et al it was concluded that both Hemovigilance and transfusion medicine is not included in the educational curriculum of medical schools and at post graduate level which van tremendously effect the safe transfusion practice.<sup>14</sup> It has been suggested by Lin Y et al that Blood Transfusion Camps can improve postgraduate trainees knowledge and attitude towards transfusion medicine and can positively impact safe transfusion practices.<sup>15</sup>

## CONCLUSION

It is concluded that postgraduate trainees lack fundamental theoretical and practical understanding of transfusion medicine.

The knowledge gap identified by this study can be addressed by scheduling educational seminars, visits, frequent lectures, workshops for clinical postgraduate residents. The situation will be much improved by a range of educational measures, including one-on-one conversations, prospective audits and participation conferences, continuous medical education on hemovigilance, and the engagement of transfusion medicine physicians in clinical rounds. These steps will undoubtedly improve the relationship between our future clinician and transfusion medicine and, in the end, lead to better patient care.

## Limitations

One limitation of this study is the unequal distribution of

participants across training years, specialties, and gender, which may affect the generalizability of the findings. This imbalance resulted from the use of a non-probability convenience sampling technique and voluntary participation.

**Recommendations:** Future research should consider employing a probability-based sampling strategy with a more balanced representation across specialties and

demographic groups to enhance the robustness and external validity of the results.

#### Authors' Contribution

Madeeha Rehan: Conception of study / Designing / Planning

Nazia Nijat: Data Analysis, Statistical Analysis

Attika Khalid: Manuscript Writing, Critical Review

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## ISOLATION OF STREPTOCOCCUS PYOGENES FROM PLEURAL FLUID IN A CRITICALLY ILL PATIENT: A CASE REPORT WITH A RARE OCCURRENCE

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Uzma Zahid, Shahid Ahmad Abbasi

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### ABSTRACT

*Transudative or exudative pleural effusion has a diverse etiology including bacteria that differ depending upon hospital or community acquired infections. Most bacterial organisms isolated from pleural fluid include Gram positive bacteria including Staphylococcus aureus, Streptococcus pneumoniae and Streptococcus viridans followed by Gram negative bacteria. The Isolation of Streptococcus pyogenes (Group A Lancefield Group) from pleural fluid is unusual as this bacterium is responsible for causing skin and throat infections which range from asymptomatic cases to full blown symptomatic toxic shock syndrome. Patients with various comorbidities may have the worst prognosis and severe complications from asymptomatic or confirmed infections.*

*We report a case study of a patient with isolation of Streptococcus pyogenes from pleural fluid, This is a rare finding, but may happen owing to dysbiosis associated with systemic insufficiencies. To our understanding this is the first reported case in Pakistan of Streptococcus pyogenes isolation from pleural fluid.*

**Keywords:** Antibiotic resistance, Dysbiosis, Emm gene, Pleural effusion, Pleural fluid, Streptococcus pyogenes

### INTRODUCTION

Transudative or exudative pleural effusion, the accumulation of fluid is one of the sequelae of many systemic deficiencies e.g., congestive cardiac failure, chronic renal impairment, chronic liver disease, and malignancy. The key for good prognosis in such patients requires timely antibiotic intervention. This requires sound knowledge regarding microbiological isolation and identification from pleural fluid. Isolates may vary depending on hospital or community acquired infection.<sup>1</sup> A recent systemic review by European Respiratory Journal on most common bacterial isolates from pleural fluid reported *Staphylococcus aureus* to be the most common pathogen in pleural fluid globally followed by *Streptococcus pneumoniae* and *Streptococcus viridans* in community acquired infections. Beta hemolytic streptococci were reported as

the sixth most common clinical isolate.<sup>2</sup> *Streptococcus pyogenes* is a part of the normal flora of skin and upper respiratory tract. This bacterium, that makes up the local microbiome belongs to Group A of Lancefield grouping among beta hemolytic streptococci and is responsible for various acute skin and soft tissue infections e.g., cellulitis, pharyngitis, impetigo, and other life-threatening sequelae including scarlet fever, glomerulonephritis, pneumonia and toxic shock syndrome owing to its invasive nature, various exotoxins, and multiple mechanisms of drug resistance.<sup>3</sup> There are about 220 different isolates of *S. pyogenes* based on difference in genetic sequence of its M protein and therefore epidemiologically vast outbreaks of this bacterial infection have been reported in Asia and United Kingdom.

Pathogenesis of streptococcal infection involves a wide range of mechanisms, evading innate and adaptive immunity of the host resulting in invasive infections especially more so in immunocompromised individuals. These mechanisms include attachment and invasion of epithelial barrier and soft tissues via surface M protein, streptolysin O and S, breakdown of complement C5a via C5a peptidase, prevention of virulence recognition by host immune system, decreased neutrophil chemotaxis owing to streptolysin

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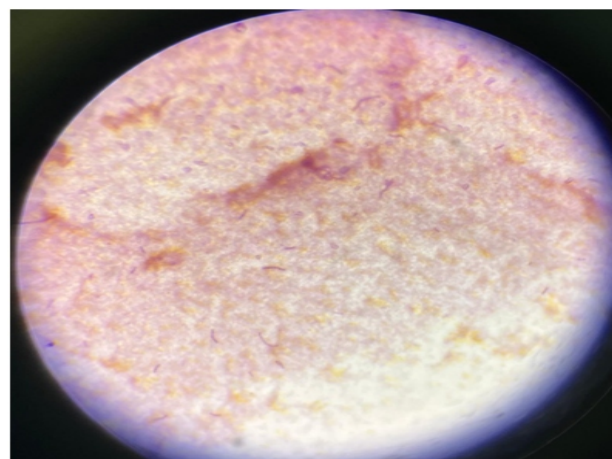
S, presence of enzymes that degrade IgG, and superantigens causing cytokine storm.<sup>4</sup> The degree of severity of disease caused by Group A Streptococci (GAS) is directly proportional to immunosuppression and it has been reported that bacteremia caused by streptococci is likely to have worse prognosis in immunocompromised patients resulting in toxic shock syndrome and morbidity.<sup>5</sup> Toxic shock syndrome and invasive streptococcal A infection causing dissemination of bacteria to pleural fluid with symptomatic pneumonia and empyema warrants bacterial isolation from pleural fluid (which is normally a sterile space) for definite diagnosis in elderly or in patients having an underlying systemic deficiency like diabetes or cardiovascular insufficiency.<sup>6</sup> Invasive infections are associated with presence of bacteria in sterile spaces we present a case of a 59-year-old patient, who reported with dyspnea and generalized edema with associated comorbid of diabetes and congestive cardiac failure.

## CASE REPORT

A 59-year-old patient with past history of diabetes and hypertension presented with aggravated symptoms of generalized body swelling, dyspnea, and orthopnea in emergency room of Fauji Foundation Hospital. She had a history of diabetes for 20 years, was hypertensive, and known case of congestive cardiac failure (CCF) and chronic kidney disease (CKD) in the last 1 year, with acute exacerbation of cardiac dysfunction. Severity of symptoms with ascites, eyelid swelling and pitting edema, had increased over the last one week. Associated complaints of fever, pallor, decreased alertness for the last 2 months were present, which had exacerbated for the last three days since admission. General physical examination revealed bilateral crepts and wheezing on chest auscultation, abdominal distention with shifting dullness, and bilateral pitting edema. The basic vitals had following picture; BP 100/70 mmHg, Pulse 115/min, SpO<sub>2</sub> 85%, respiratory rate 16/min, blood sugar level random 94mg/dl. Glasgow coma scale was recorded as E4 M6 V3 13/15. Chest X ray showed massive pleural effusion. The baseline laboratory results had following findings; complete blood picture showed hemoglobin count of 11.9 mg/dl (12-14mg/dl), white blood cell count  $5.21 \times 10^9/L$  ( $4-11 \times 10^9/L$ ), platelets  $181 \times 10^9/L$  ( $150-400 \times 10^9/L$ ), serum Urea 16.4 mg/dl (5-20mg/dl), creatinine 129 mg/dl (0.6-1.1mg/dl). Liver function tests showed bilirubin 9 (0.2-1.3mg/dl), ALT 23 U/L (4-36 U/L), ALP 157 U/L (44-147 IU/L), albumin 37g/L (34-54 g/L). Cardiac markers showed CK MB 30

(5-25 IU/L) and Troponin-T 0.17 (0 - 0.01 ng/mL). ECG showed T- wave inversion in leads 1 and 2 and aVR. Ejection fraction was reported at 20% (greater than 60%) on echocardiography, global hypokinesia, mild mitral regurgitation and severe left ventricular systolic dysfunction. D-dimers were less than 200. Lipid profile had following results; LDL 108mg/dL (100-129mg/dL), HDL 34.7mg/dL (35-80mg/dL) and serum triglycerides 79.2mg/dL (less than 150mg/dL). Prothrombin time (PT) was 13.5 seconds (11-13.5 seconds), activated partial thromboplastin time APTT was 31.9 seconds (30-40 seconds) and INR was recorded as 1.02 (less or equal to 1.1).

The patient was admitted to the hospital and conservative management was started with decreasing dyspnea with administration of oxygen, and nebulization with Ipratropium bromide 250mcg, Beclomethasone and Salbutamol 800/1600 mcg. Initially oral, prophylactic medicines for cardiac disease were continued and insulin was administered according to sliding scale with regular charting for blood sugar random (BSR). Basic lab tests were repeated and strict vital monitoring was advised. Injectable Ceftriaxone Sodium 2mg once daily was started as empirical antibiotic therapy. The condition of patient did not improve with renal function being deranged. High resolution computed tomography of the chest (HRCT) was advised and diagnostic and therapeutic pleural tap was done for routine examination, cytology, culture sensitivity on 3rd post admission day. The patient's condition continued worsening with not being able to maintain SpO<sub>2</sub> at room air. The pleural fluid routine examination showed protein level of 112 mg/dl (15-45mg/dl), microscopy revealed the presence of



**Figure I: Gram positive cocci arranged in chains as shown by arrow head.**

Gram-positive cocci arranged in chains as shown in figure I.

The specimen was inoculated on Blood, MacConkey and Chocolate agar and was incubated at 37 °C for 18-24 hours. After 18 hours the agar plates yielded  $\beta$  hemolytic growth on blood and chocolate agar. There was no growth on MacConkey agar plate.  $\beta$  hemolytic growth was Catalase negative. On further investigation, Lancefield grouping was done which showed agglutination with Group A anti sera. It confirmed the organism to be Group A Streptococcus (*Streptococcus pyogenes*). API -10 Strep (Analytical profile index--bioMerieux) was inoculated at 37 °C for 18-24 hrs. It was further confirmed on API to be *Streptococcus pyogenes*. Sensitivity for *Streptococcus pyogenes* was checked on Blood Agar Plate incubated at 37 °C for 18-24 hours which showed microorganism to be resistant to Ciprofloxacin (5  $\mu$ g), Ceftriaxone (30  $\mu$ g). The bacterial isolate was sensitive to Bacitracin (10  $\mu$ g), Doxycycline (30  $\mu$ g), Linezolid (30  $\mu$ g), Vancomycin (30  $\mu$ g), Penicillin (10  $\mu$ g) and Clindamycin (2  $\mu$ g). The patient was continued with IV Ceftriaxone 2g along with supportive parenteral therapy, supplemental oxygen, along with strict monitoring of vitals but unfortunately owing to multiple comorbidities the patient expired third post admission day.

## DISCUSSION

*Streptococcus pyogenes*, group A streptococci (GAS), a  $\beta$  hemolytic Gram-positive bacterium is one of the leading cause of invasive infections worldwide with yearly incidence of 6/100,000 cases. The high degree of virulence related to different serotypes owing to variance in emm gene corresponds to increased disease severity.<sup>7</sup> An epidemiological study on incidence, clinical, and microbiological features of streptococcal infections in Brussels and Hungary has reported that isolation of bacteria from pleural fluid is a rare findings (1% and 3% isolated from pleural fluid) in both probable and confirmed cases of invasive GAS corroborating an unusual finding similar to our case study where bacteria was isolated from pleural fluid.<sup>7,8</sup> Diabetes, cardiovascular disease, and renal insufficiency are one of many risk factors for streptococcal adherence, colonization and infection in adults as reported by a study in USA. All these comorbidities affirmative in our case study.<sup>9</sup>

Regarding antibiotic susceptibility of streptococci, this clinical isolate was sensitive to Penicillin and Chloramphenicol similar to a cohort analysis in Norway

except that this study reports bacteria to be resistant to Tetracycline, Clindamycin, and Erythromycin differing from our antibiotic sensitivity tests.<sup>10</sup> This may reflect the evolutionary change of microorganism due to its diverse serotype distributed across different geographical location. The isolated bacteria in our hospital setup were susceptible to clindamycin but there has been reports of emerging increase in resistance to this antibiotic and macrolides in large studies in US which may be a cause for concern regarding antibiotic prescription and administration in streptococcal infections.<sup>11</sup> Analysis of antibiotic sensitivity to *Streptococcus pyogenes* in one study from Pakistan has also shown conferred resistance to this bacterium which differs from our report but is sensitive to Ceftriaxone which was prescribed in this patient although sensitivity tests indicated otherwise.<sup>12</sup> Such variation in sensitivity to one antibiotic has been documented in Egypt where the isolates from one hospital is 100% resistant to Ceftriaxone whereas another study showed 50% resistance to this antibiotic.<sup>13</sup> Critically ill patients with multiple risk factors are likely to have a dysbiosis owing to interplay of lung and oral microflora within the body, its interaction with outside environment including shifting between different nursing setups, invasive treatment measures such as intubation, face masks and therefore ability of microflora to cause disease escalation similar to our case study where unusual isolation of *Streptococcus pyogenes* from pleural fluid was a rare finding therefore it is necessary to take precautionary and prophylactic measures in such medical scenarios where appropriate and timely antibiotic regimes could save lives.<sup>14</sup> Moreover, emerging resistance trends of  $\beta$  hemolytic streptococci requires a collaborative approach between critical care providers, microbiologists, infection control specialists and diagnostic labs to implement antibiotic stewardship policy as required according to local antibiogram which will help curb rising infection outbreaks and will contribute to benefit population in the long run.<sup>15</sup>

## Authors' Contribution

Saima Ishtiaq: Conception of study / Designing / Planning, Experimentation / Study Conduction, Analysis / Interpretation / Discussion, Manuscript Writing

Amna Waheed: Analysis / Interpretation / Discussion, Manuscript Writing

Muhammad Moaaz Ali: Facilitated for Reagents / Material Analysis

Uzma Zahid: Facilitated for Reagents / Material Analysis  
Hareem Fatima Niazi: Facilitated for Reagents / Material Analysis

Shahid Ahmad Abbasi: Conception of study / Designing / Planning, Critical Review

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