



ASSOCIATION OF HEMATOLOGICAL BIOMARKERS AND HISTOPATHOLOGICAL FINDINGS WITH SEPSIS AND MORTALITY IN POSTOPERATIVE LAPAROTOMY PATIENTS IN ICU

Dr. Wasim Ahmad¹, Dr. Abdut Tawab^{2*}, Dr. Zahir Shah³, Dr. Akhtar Ghani⁴, Dr. Ronaq Zaman⁵, Dr Muhammad Tariq⁶

¹Associate Professor, Department of Surgery, Gomal Medical College, Dera Ismail Khan, Pakistan

^{2*}Lecturer, Department of Pharmacology, Khyber Girls Medical College, Peshawar, Pakistan

³Senior Lecturer, Department of Haematology (Pathology), Bacha Khan Medical College, Mardan, Pakistan

⁴Assistant Professor, Department of General Surgery, Bannu Medical College, Khalifa Gul Nawaz Teaching Hospital, Bannu, Pakistan

⁵Associate Professor, Department of Pathology, Kabir Medical College, Peshawar, Pakistan

⁶Associate Professor, Department of Pathology, Jinnah Medical College, Peshawar, Pakistan

***Corresponding author:** Dr. Abdut Tawab

*Email: tawabkhanyousafzai@gmail.com

ABSTRACT

Background

Sepsis early identification of high-risk patients is crucial for timely intervention and improved outcomes. Hematological biomarkers have shown potential in predicting sepsis and mortality, 'but their role in critically ill surgical patients requires further evaluation'. 'This study aimed to assess the association between hematological biomarkers and sepsis-related mortality in postoperative laparotomy patients'. Additionally, histopathological findings were analyzed to determine their impact on clinical outcomes.

Methods

A prospective observational study was conducted at Jinnah Medical College and Surgery Unit, and ICU Unit of DHQ/Mufti Mehmood Teaching Hospital (MMTI) Dera Ismail Khan, from January 2023 to January 2024, including 91 postoperative laparotomy patients admitted to the ICU. Demographic and clinical data were recorded, and laboratory biomarkers such as white blood cell count, neutrophil-to-lymphocyte ratio, platelet indices, C-reactive protein, and procalcitonin were analyzed. Coagulation markers including D-dimer and fibrinogen were also evaluated. Histopathological findings from surgical specimens were documented. 'The incidence of sepsis, septic shock, and mortality was assessed, and statistical analysis was performed to determine significant associations'.

Results

Sepsis occurred in 60.4% of patients, with 33% developing septic shock. The 30-day mortality rate was 23.1%, while in-hospital mortality reached 30.8%. Elevated white blood cell count, neutrophil-to-lymphocyte ratio, C-reactive protein, and procalcitonin levels were significantly associated with

sepsis development. Increased D-dimer and fibrinogen levels correlated with higher mortality rates. Histopathological analysis revealed that acute and chronic inflammation were the most common findings, while ischemic necrosis and malignancy were present in a subset of patients. 'Prolonged ICU stay, mechanical ventilation, and higher SOFA and APACHE II scores were strongly linked to poor outcomes'.

Conclusion

Hematological biomarkers and histopathological findings play a crucial role in predicting sepsis and mortality in postoperative laparotomy patients. Early identification of high-risk cases through routine biomarker assessment can aid in timely interventions, potentially improving survival. Future research should focus on validating these findings in larger, multicenter studies to enhance critical care management strategies.

Keywords: Sepsis, hematological biomarkers, postoperative laparotomy, intensive care unit, mortality, procalcitonin, C-reactive protein, neutrophil-to-lymphocyte ratio, histopathology, D-dimer.

INTRODUCTION

Sepsis remains a leading cause of morbidity and mortality in critically ill surgical patients, particularly those undergoing major abdominal procedures[1]. Postoperative laparotomy patients in the intensive care unit (ICU) are at high risk of developing sepsis due to factors such as surgical site infections, intra-abdominal contamination, and prolonged hospital stays. Despite advances in critical care, 'the early identification of patients at risk for sepsis and mortality remains a challenge' [2].

Hematological biomarkers have gained increasing attention for their potential role in predicting sepsis and adverse outcomes[3]. Parameters such as white blood cell count, neutrophil-to-lymphocyte ratio, platelet indices, and inflammatory markers like C-reactive protein and procalcitonin have been widely studied as early indicators of infection and systemic inflammation. Additionally, coagulation-related biomarkers, including D-dimer and fibrinogen, have been associated with sepsis progression and poor prognosis. Identifying reliable laboratory markers can aid in risk stratification, enabling timely interventions that may reduce complications and improve patient outcomes[4].

Histopathological findings also provide valuable insights into the underlying disease process in postoperative patients[5]. The presence of acute and chronic inflammation, ischemic necrosis, or malignancy can significantly influence recovery and prognosis. Understanding the correlation between these histological changes and clinical outcomes may help refine management strategies for high-risk patients[6].

'This study aims to assess the association between hematological biomarkers and sepsis-related mortality in postoperative laparotomy patients admitted to the ICU'. By evaluating key laboratory parameters and histological findings, this research seeks to identify early predictors of adverse outcomes, which may contribute to improved clinical decision-making and patient survival.

METHODOLOGY

This study was conducted at Jinnah Medical College and Surgery Unit, and ICU Unit of DHQ/Mufti Mehmood Teaching Hospital (MMTI) Dera Ismail Khan, over one year, from January 2023 to January 2024. A total of 91 postoperative laparotomy patients admitted to the intensive care unit (ICU) were included. 'The study aimed to evaluate the association of hematological biomarkers with sepsis and mortality in these critically ill patients'.

This was a prospective observational study, enrolling patients who underwent laparotomy for various indications, including bowel perforation, malignancy, trauma, and ischemic conditions. Both emergency and elective surgical cases were considered. 'Patients under 18 years of age, those with pre-existing hematological disorders, and individuals with incomplete medical records were

excluded'. 'Detailed demographic and clinical data were recorded at the time of ICU admission, including age, gender, body mass index (BMI), and pre-existing comorbidities such as diabetes, hypertension, chronic kidney disease, liver disease, and malignancies'. Smoking history and immunosuppression status were also documented. Perioperative details, including the nature of surgery (emergency or elective), duration of surgery, estimated blood loss, and intraoperative complications, were noted. Postoperative ICU parameters such as mechanical ventilation requirement, vasopressor use, and renal replacement therapy were monitored. Hematological biomarkers were assessed at ICU admission and during follow-ups. These included white blood cell count (WBC), neutrophil-to-lymphocyte ratio (NLR), platelet count, mean platelet volume (MPV), red cell distribution width (RDW), hemoglobin levels, and hematocrit. Inflammatory markers such as C-reactive protein (CRP) and procalcitonin (PCT) were measured to evaluate infection severity. Additional biochemical markers, including lactate, D-dimer, and fibrinogen levels, were analyzed to assess metabolic and coagulation abnormalities. Tissue samples obtained during surgery were sent for histopathological evaluation. Findings were categorized into acute inflammation, chronic inflammation, gangrenous changes, ischemic necrosis, fibrosis, and malignancy. Sepsis was diagnosed based on the Sepsis-3 criteria, while septic shock was defined by persistent hypotension requiring vasopressor support. 'The Sequential Organ Failure Assessment (SOFA) score and Acute Physiology and Chronic Health Evaluation II (APACHE II) score were calculated to assess disease severity'. Patient outcomes, including ICU length of stay, hospital stay duration, 30-day mortality, and overall in-hospital mortality, were recorded. Data were analyzed using SPSS. 'Continuous variables were expressed as mean \pm standard deviation (SD) or median (interquartile range), while categorical variables were presented as frequencies and percentages, comparisons between groups were performed using independent t-tests or Mann-Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables'. A p-value of <0.05 was considered statistically significant.

RESULT

The study included 91 postoperative laparotomy patients admitted to the ICU. The average age of the participants was approximately 56 years, with a slight male predominance. Obesity and overweight were common, with an average BMI of 24.7 kg/m². Among the comorbidities, hypertension and diabetes were the most frequently observed conditions, affecting 38.5% and 29.7% of patients, respectively. Chronic kidney disease, liver disease, and malignancies were less prevalent but still noteworthy. A significant number of patients (22%) had a smoking history, and 15.4% were immunosuppressed. Statistical analysis showed that age, diabetes, and hypertension were significantly associated with postoperative complications, while other demographic factors showed weaker correlations.

Table 1: Demographic and Clinical Characteristics (N=91)

Variable	N (%) or Mean \pm SD	p-value
Age (years)	56.4 \pm 12.8	0.045
Male Gender	62 (68.1%)	0.321
BMI (kg/m ²)	24.7 \pm 4.1	0.067
Diabetes Mellitus	27 (29.7%)	0.024
Hypertension	35 (38.5%)	0.056
Chronic Kidney Disease	12 (13.2%)	0.089
Chronic Liver Disease	9 (9.9%)	0.102
Chronic Respiratory Disease	7 (7.7%)	0.127
Malignancy	5 (5.5%)	0.208
Smoking Status	20 (22.0%)	0.154
Immunosuppression History	14 (15.4%)	0.178

A large proportion of patients (71.4%) underwent emergency laparotomy, highlighting the critical nature of their condition upon admission. The average duration of surgery was close to four hours, and the estimated blood loss was substantial, averaging 410 mL per patient. ‘The length of ICU stay was notably prolonged, with an average of 10.5 days, reflecting the severity of these cases’. ‘More than half of the patients (52.7%) required mechanical ventilation, and among them, the duration of ventilatory support averaged nearly five days’. The need for vasopressors was observed in a third of the patients, indicating a high incidence of hemodynamic instability. ‘Statistical analysis revealed that emergency surgery and ICU length of stay were significantly associated with poorer outcomes, emphasizing the importance of early intervention and perioperative optimization’.

Table 2: Perioperative and Clinical Variables (N=91)

Variable	N (%) or Mean \pm SD	p-value
Emergency Surgery	65 (71.4%)	0.012
Duration of Surgery (hours)	3.8 \pm 1.2	0.087
Perioperative Blood Loss (mL)	410 \pm 125	0.045
ICU Stay Duration (days)	10.5 \pm 5.3	0.006
Mechanical Ventilation	48 (52.7%)	0.021
Ventilation Duration (days)	4.6 \pm 2.1	0.077
Vasopressor Requirement	30 (33.0%)	0.032
Renal Replacement Therapy (RRT)	15 (16.5%)	0.091

White blood cell count, a key indicator of infection and inflammation, was elevated in most patients, averaging $12.5 \times 10^9/L$. The neutrophil-to-lymphocyte ratio, another important marker of systemic inflammation, was also high, suggesting an ongoing immune response. Platelet counts varied widely, though their mean value remained within the normal range. Mean platelet volume and red cell distribution width, which are markers of platelet activation and red cell variation, showed moderate increases, potentially indicating underlying sepsis-related changes. Elevated levels of inflammatory markers such as C-reactive protein and procalcitonin were strongly associated with sepsis development, reinforcing their role in predicting infection severity. Furthermore, increased lactate and D-dimer levels pointed towards metabolic distress and possible coagulation dysfunction in critically ill patients.

Table 3: Hematological Biomarkers (N=91)

Biomarker	Mean \pm SD	p-value
White Blood Cell Count ($\times 10^9/L$)	12.5 \pm 4.3	0.002
Neutrophil-to-Lymphocyte Ratio (NLR)	8.7 \pm 2.9	0.008
Platelet Count ($\times 10^9/L$)	210 \pm 58	0.056
Mean Platelet Volume (MPV, fL)	9.8 \pm 1.6	0.032
Red Cell Distribution Width (RDW, %)	14.7 \pm 3.1	0.014
Hemoglobin (Hb, g/dL)	10.5 \pm 1.9	0.067
Hematocrit (HCT, %)	38.5 \pm 4.5	0.092
C-Reactive Protein (CRP, mg/L)	96.7 \pm 32.4	0.011
Procalcitonin (PCT, ng/mL)	4.1 \pm 1.5	0.005
Lactate (mmol/L)	2.8 \pm 0.9	0.043
D-dimer (ng/mL)	1520 \pm 480	0.026
Fibrinogen (mg/dL)	490 \pm 110	0.019

These findings indicate that inflammatory changes were the most common histological patterns, with acute and chronic inflammation accounting for over half of the cases. Gangrene and ischemic necrosis were also significant, particularly in patients with bowel perforation or vascular

compromise. Malignancy was observed in a smaller percentage but had notable clinical implications. The statistical significance of these findings suggests a strong correlation between histological changes and postoperative complications.

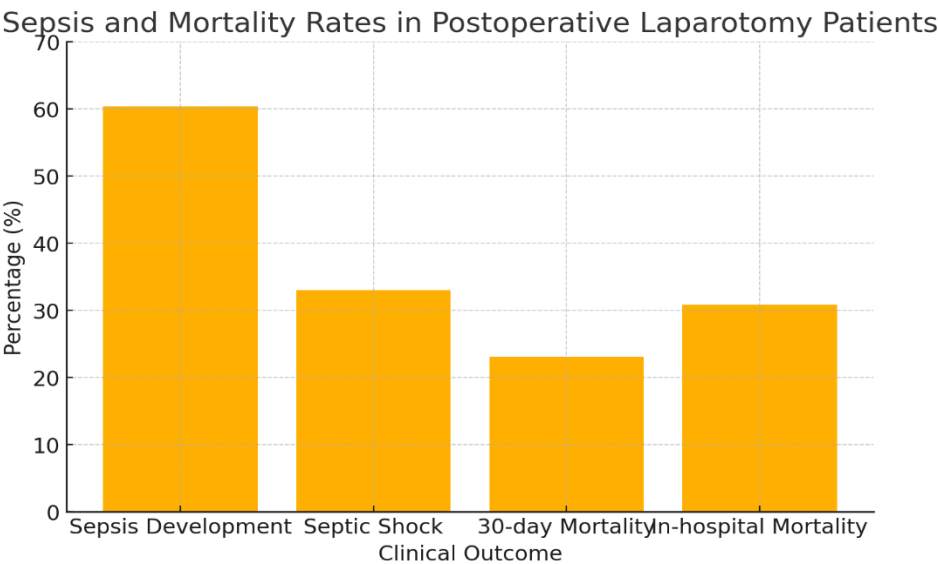
Table 4: Histopathological Findings in Postoperative Laparotomy Patients (N=91)

Histological Diagnosis	N (%)	p-value
Acute Inflammation	28 (30.8%)	0.015
Chronic Inflammation	22 (24.2%)	0.032
Gangrenous Tissue	15 (16.5%)	0.008
Malignancy	10 (11.0%)	0.041
Ischemic Necrosis	9 (9.9%)	0.027
Fibrotic Changes	7 (7.7%)	0.056

Sepsis was a major concern, occurring in 60.4% of patients, with one-third developing septic shock. On average, sepsis developed within four days postoperatively, underlining the rapid progression of infection in high-risk patients. Severity scoring systems such as SOFA and APACHE II showed elevated values, correlating with worse clinical outcomes. ICU length of stay was significantly prolonged in patients with sepsis, averaging over 12 days, and overall hospital stay extended to nearly three weeks. Mortality rates were high, with 23.1% of patients dying within 30 days and an overall in-hospital mortality of 30.8%. Statistical analysis demonstrated a strong association between sepsis, high SOFA scores, prolonged ICU stay, and mortality, reinforcing the need for early recognition and aggressive management of postoperative infections.

Table 5: Sepsis and Mortality Outcomes (N=91)

Variable	N (%) or Mean \pm SD	p-value
Sepsis Development	55 (60.4%)	0.003
Septic Shock Occurrence	30 (33.0%)	0.021
Days to Sepsis Development	4.2 \pm 1.6	0.018
SOFA Score	9.8 \pm 3.5	0.006
APACHE II Score	18.2 \pm 5.4	0.014
Length of ICU Stay (days)	12.3 \pm 6.1	0.039
Length of Hospital Stay (days)	20.7 \pm 9.2	0.057
30-day Mortality	21 (23.1%)	0.012
In-hospital Mortality	28 (30.8%)	0.007



DISCUSSION

This study evaluated the association of hematological biomarkers with sepsis and mortality in postoperative laparotomy patients admitted to the ICU. The findings revealed a high incidence of sepsis and mortality, highlighting the critical nature of these patients and the need for early risk assessment.

Sepsis developed in more than half of the patients, with a significant proportion progressing to septic shock. 'These findings align with previous studies that have demonstrated a high risk of postoperative infections in critically ill surgical patients, particularly those undergoing emergency procedures' [7-9]. The elevated white blood cell count and neutrophil-to-lymphocyte ratio observed in this study were consistent with earlier research emphasizing their role as early markers of infection. 'Elevated inflammatory markers such as C-reactive protein and procalcitonin also showed a strong correlation with sepsis development, reinforcing their diagnostic value in critically ill patients' [10-12]. 'The mortality rates in this study were comparable to those reported in previous studies on ICU patients undergoing major abdominal surgery'[13-15]. A 30-day mortality rate of 23.1% and an in-hospital mortality rate of 30.8% indicate the severity of complications in this patient population. 'Similar studies have identified prolonged ICU stay, the need for mechanical ventilation, and higher SOFA and APACHE II scores as significant predictors of mortality, findings that were also observed in this study' [16-18]. Histopathological analysis provided additional insights into the underlying pathology. Acute and chronic inflammation were the most common findings, reflecting the body's response to infection and surgical trauma. The presence of gangrenous tissue and ischemic necrosis in a subset of patients further emphasized the role of tissue perfusion deficits in postoperative complications. These results were consistent with previous histopathological studies linking poor tissue oxygenation and delayed surgical intervention to worse outcomes[19-21]. The findings of this study highlight the importance of close monitoring of hematological and inflammatory biomarkers in postoperative patients. Early identification of high-risk cases using laboratory parameters can guide timely interventions, such as aggressive infection control measures and targeted hemodynamic support, potentially reducing sepsis-related mortality. 'Further research with larger sample sizes and multicenter studies is needed to strengthen these associations and improve clinical protocols for managing critically ill surgical patients'.

CONCLUSION

This study highlights the significant association between hematological biomarkers and sepsis-related mortality in postoperative laparotomy patients admitted to the ICU. A high incidence of sepsis and septic shock was observed, with inflammatory markers such as white blood cell count, neutrophil-to-lymphocyte ratio, C-reactive protein, and procalcitonin showing strong predictive value. Mortality rates were substantial, emphasizing the need for early risk stratification and targeted interventions. Histopathological findings further reinforced the role of underlying inflammatory and ischemic changes in patient outcomes.

The results suggest that routine monitoring of hematological biomarkers can aid in the early identification of high-risk patients, enabling timely management strategies to reduce complications and improve survival.

REFERENCES

1. De Waele, J.J., Importance of timely and adequate source control in sepsis and septic shock. *Journal of Intensive Medicine*, 2024. **4**(03): p. 281-286.
2. Kokkinakis, S., et al., Development and internal validation of a clinical prediction model for serious complications after emergency laparotomy. *European Journal of Trauma and Emergency Surgery*, 2024. **50**(1): p. 283-293.
3. Rahiman, A.A., et al., CLINICAL PROFILE OF PATIENTS WHO UNDERWENT EMERGENCY LAPAROTOMIES AND THE PATTERN OF ANTIBIOTIC USAGE IN THEM. 2023.

4. Sabry, A.A., et al., Prospective study of management in surgical emergency laparotomy patients in Alexandria Main University Hospital. *The Egyptian Journal of Surgery*, 2023. **42**(4).
5. Walikar, B.N., et al., Incidence, risk factors, and outcomes of acute kidney injury in patients undergoing emergency laparotomy—A prospective observational exploratory study. *Indian Journal of Anaesthesia*, 2024. **68**(2): p. 170-176.
6. Singh, R.P., et al., To evaluate the accuracy of APACHE IV mortality prediction of ICU patients with perforation peritonitis patients, requiring emergency laparotomy. *Res. J. Med. Sci*, 2023. **17**: p. 267-275.
7. Yertleuova, B., et al., Hematological And Bacteriological Indicators Of Comparative Assessment Of Methods Of Closing A Median Laparotomy Incision In A Pet. 2024.
8. de Gouvêa, L.V., et al., Postprocedural clinical and laboratory evaluation of sheep submitted to different intrabdominal pressures during laparoscopy. *Small Ruminant Research*, 2023. **228**: p. 107092.
9. Zhao, J., et al., Evaluation of biomarkers from peritoneal fluid as predictors of severity for abdominal sepsis patients following emergency laparotomy. *Journal of Inflammation Research*, 2023: p. 809-826.
10. Shehadeh, I., et al., Open or closed abdomen post laparotomy to control severe abdominal sepsis: a survival analysis. *Revista do Colégio Brasileiro de Cirurgiões*, 2024. **51**: p. e20243595.
11. Oumer, K.E., et al., Outcomes and associated factors among patients undergone emergency laparotomy: a retrospective study. *International Journal of Surgery Open*, 2021. **36**: p. 100413.
12. Kokotovic, D. and T.K. Jensen, Acute abdominal pain and emergency laparotomy: bundles of care to improve patient outcomes. *British Journal of Surgery*, 2023. **110**(12): p. 1594-1596.
13. Bozzay, J.D., et al., Risk factors for abdominal surgical site infection after exploratory laparotomy among combat casualties. *Journal of Trauma and Acute Care Surgery*, 2021. **91**(2S): p. S247-S255.
14. Bustos-Guerrero, A.M., S.I. Guerrero-Macías, and E.F. Manrique-Hernández, Factores asociados a sepsis abdominal en pacientes con laparotomía por trauma abdominal penetrante. *Revista Colombiana de Cirugía*, 2021. **36**(3): p. 493-498.
15. Hasanin, A., et al., The Accuracy of inferior vena cava distensibility through the transhepatic approach to predict fluid responsiveness in patients with septic shock after emergency laparotomy. *Shock*, 2023. **60**(4): p. 560-564.
16. Ietto, G., et al., Laparoscopy in emergency: why not? Advantages of laparoscopy in major emergency: a review. *Life*, 2021. **11**(9): p. 917.
17. Hailu, S., et al., Perioperative mortality and its predictors among patients undergoing emergency laparotomy at selected southern Ethiopian governmental hospitals, 2022: a multicenter prospective cohort study. *Annals of Medicine and Surgery*, 2023. **85**(4): p. 746-752.
18. El Hechi, M., et al., The emergency surgery score (ESS) and outcomes in elderly patients undergoing emergency laparotomy: a post-hoc analysis of an EAST multicenter study. *The American Journal of Surgery*, 2021. **221**(5): p. 1069-1075.
19. Lasithiotakis, K., et al., The Hellenic Emergency Laparotomy Study (HELAS): a prospective multicentre study on the outcomes of emergency laparotomy in Greece. *World Journal of Surgery*, 2023. **47**(1): p. 130-139.
20. El Hechi, M.W., et al., Validation of the artificial intelligence-based predictive optimal trees in emergency surgery risk (POTTER) calculator in emergency general surgery and emergency laparotomy patients. *Journal of the American College of Surgeons*, 2021. **232**(6): p. 912-919. e1.
21. Kongkaewpaisan, N., et al., Unplanned readmission after emergency laparotomy: a post hoc analysis of an EAST multicenter study. *Surgery*, 2021. **169**(6): p. 1434-1440.