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# Role of Total Leukocyte Count and Platelet Count as Combined Predictors of Early Mortality in Patients with Sepsis: A Prospective Observational Study

**Original Article (ID: 460)**

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## ABSTRACT

**Background:** Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Simple laboratory markers may be useful for early risk stratification where rapid access to complex prognostic tools is limited. Total leukocyte count (TLC) and platelet count are inexpensive, routinely available components of the complete blood count and may reflect inflammatory and hematologic responses to sepsis.

**Objective:** To evaluate the association and discriminatory performance of admission TLC and platelet count, individually and as a joint TLC-platelet classification, for 7-day mortality among adults with sepsis and leukocytosis.

**Methods:** This prospective observational cohort study enrolled 136 adults with Sepsis-3-defined sepsis admitted to the medical wards and medical ICU of Jinnah Postgraduate Medical Centre from March to May 2026 using consecutive sampling. For the joint classification, patients with leukocytosis were categorized as high TLC with normal platelet count or high TLC with thrombocytopenia. The primary outcome was all-cause mortality within 7 days of sepsis onset; deaths within 48 hours were recorded as an early temporal component of this endpoint. Continuous variables were compared using the independent-samples t-test or Mann-Whitney U test as appropriate, categorical variables using chi-square or Fisher's exact test, and discrimination using receiver operating characteristic (ROC) analysis with bootstrap 95% confidence intervals.

**Results:** Fifty-seven of 136 patients (41.9%) died within 7 days. Admission platelet count was lower in non-survivors than survivors (median 144.0 vs 186.5 $\times 10^3/\mu L$; p=0.044), but discrimination was weak (AUC 0.60, 95% CI 0.50-0.70). Admission TLC did not differ significantly between non-survivors and survivors (median 19.3 vs 16.5 $\times 10^9/L$; p=0.073) and showed similarly weak discrimination (AUC 0.59, 95% CI 0.49-0.68). Seven-day mortality was 38.2% in the high-TLC/normal-platelet group and 45.6% in the high-TLC/thrombocytopenia group (Fisher's exact p=0.49). SOFA score was higher in non-survivors (median 7 vs 5; p<0.001).

**Conclusion:** Among sepsis patients with leukocytosis, lower admission platelet count was associated with 7-day mortality, but neither platelet count nor TLC alone provided adequate discrimination for bedside risk stratification. The joint TLC-platelet classification also did not significantly distinguish survivors from non-survivors. These routinely available indices may complement, but should not replace, established clinical severity assessment.

**Keywords:** Sepsis; thrombocytopenia; leukocytosis; platelet count; total leukocyte count; early mortality; SOFA score; risk stratification

## INTRODUCTION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. The Sepsis-3 framework operationalizes organ dysfunction as an acute increase of at least 2 points in the Sequential Organ Failure Assessment (SOFA) score.[1,14] Global estimates continue to demonstrate a substantial burden of sepsis, although the magnitude varies according to case definitions and analytic methods. Contemporary global analyses and earlier Global Burden of Disease estimates consistently identify sepsis as a major contributor to morbidity and mortality worldwide.[3,10] In Pakistan and other resource-constrained health systems, delayed recognition, limited critical-care capacity, and variability in access to advanced diagnostics can further complicate early risk assessment.[6] Routine complete blood count parameters provide rapid information on inflammatory and hematologic responses. Platelets participate in hemostasis, endothelial interactions, immune signaling, and microvascular thrombosis; thrombocytopenia during sepsis may result from consumption, immune-mediated destruction, altered production, sequestration, and disseminated intravascular coagulation.[4,5] Recent studies have reported associations between low platelet count, dynamic platelet decline, and adverse sepsis outcomes.[2,7,9,15] However, the prognostic performance of a single admission platelet count varies across populations and outcome definitions.

TLC is another readily available marker of host response. Leukocytosis commonly accompanies acute infection, whereas leukopenia may reflect severe dysregulation or marrow/peripheral consumption. In a large Sepsis-3 cohort, leukopenia was associated with higher mortality than leukocytosis, although part of this relationship was attenuated after accounting for the platelet component of SOFA.[11] Contemporary work has also explored composite blood-count indices, including platelet-related and neutrophil-related ratios, to improve prognostic information beyond a single cell count.[12] Despite these observations, prospective local evidence on the combined bedside interpretation of TLC and platelet count remains limited. Because both parameters are inexpensive and universally available in routine clinical practice, a simple joint classification may be particularly relevant in settings where more complex biomarker panels are impractical. This study therefore evaluated the individual and joint association of admission TLC and platelet count with 7-day mortality in adults with sepsis and leukocytosis, and assessed the discriminatory performance of the two continuous laboratory measures for early mortality.

## MATERIALS AND METHODS

This prospective observational cohort study was conducted over three months, from March 2026 to May 2026, in the medical wards and medical intensive care unit (MICU) of Jinnah Postgraduate Medical Centre (JPMC). Consecutive sampling was used so that eligible patients presenting during the study period could be enrolled without selective recruitment. Adults aged 18 years or older of either sex with community-acquired sepsis or sepsis developing during hospitalization were eligible. Sepsis was defined according to Sepsis-3 as suspected or confirmed infection accompanied by an acute increase in SOFA score of at least 2 points.[1,14] Baseline SOFA was considered zero in patients without known pre-existing organ dysfunction; for hospital-acquired sepsis, the most recent stable clinical status before onset of infection was used as the clinical baseline. Patients with hematological malignancy, chronic liver disease with hypersplenism, ongoing chemotherapy or immunosuppressive therapy, known primary platelet disorders, or blood transfusion within the preceding 72 hours were excluded because these conditions could materially alter TLC or platelet count independently of the septic process. For community-acquired sepsis, the admission blood count was used; for hospital-acquired sepsis, the blood count obtained at the time sepsis was diagnosed was used. TLC and platelet count reported by the hospital laboratory were recorded as the index measurements. For analytic classification, leukocytosis (high TLC) was defined as TLC $>11.0 \times 10^9$/L, consistent with a commonly used adult upper reference limit. Thrombocytopenia was defined as platelet count $<150 \times 10^3/\mu L$, while platelet count $\geq 150 \times 10^3/\mu L$ was classified as normal.[4,2]

The term combined predictor in this study refers to a joint bedside classification rather than a multivariable prediction score. Participants were categorized into two predefined groups: Group 1, high TLC with normal platelet count; and Group 2, high TLC with thrombocytopenia. All 136 enrolled patients were represented in one of these two groups. The principal investigator collected demographic and clinical information on a structured proforma, including age, sex, admission location, selected comorbidities, source of infection, admission TLC, platelet count, SOFA score, and survival status. The primary outcome was all-cause mortality within 7 days of sepsis onset. Deaths occurring within 48 hours were recorded separately for temporal description but were included in the 7-day mortality endpoint. Outcome status at 7 days was established for all 136 participants. Data were analyzed using Python with pandas, SciPy, and scikit-learn. Age was summarized as mean ± standard deviation, whereas TLC, platelet count, and SOFA score were summarized as median and interquartile range (IQR) because their distributions were treated as non-normal for group comparisons. Age was compared using the independent-samples t-test; TLC, platelet count, and SOFA score were compared using the Mann-Whitney U test. Categorical variables were summarized as frequencies and percentages and compared using the chi-square test or Fisher's exact test, as appropriate. ROC analysis was used to evaluate discrimination of admission TLC and platelet count for 7-day mortality. Areas under the curve (AUCs) were reported with 95% confidence intervals estimated by 2,000 bootstrap resamples. The Youden index was used to identify data-derived cut-offs, and corresponding sensitivity and specificity were reported. Because no formal paired statistical comparison of the two AUCs was performed, numerical differences between AUCs were not interpreted as evidence that one marker was superior. All tests were two-sided and $p<0.05$ was considered statistically significant. The analyses were intended to evaluate unadjusted association and discrimination; no claim of independent prediction was made.

 

The study was conducted following institutional approval at Jinnah Postgraduate Medical Centre. Informed consent was obtained from the patient or an attendant, confidentiality was maintained, and participants retained the right to withdraw from the study process.

## RESULTS

A total of 136 patients with sepsis and leukocytosis were enrolled. Mean age was 39.8 ± 18.4 years, and the cohort included 69 males (50.7%) and 67 females (49.3%). Sixty-one patients (44.9%) were managed in the medical ICU and 75 (55.1%) in a medical ward/HDU. The most frequently identified infection sources were respiratory (28.7%), central nervous system (22.8%), bloodstream (10.3%), and urinary tract (7.4%); 17 patients (12.5%) had multiple concurrent sites. At least one of the reported comorbidities (diabetes mellitus, hypertension, or chronic kidney disease) was present in 55 patients (40.4%). Median SOFA score was 6 (IQR 4-8), median TLC was 18.1 ×10⁹/L (IQR 14.6-23.8), and median platelet count was 156 ×10³/µL (IQR 103-269).

Table 1. Baseline characteristics of the study cohort (N=136).

| Characteristic | Value |
|---|---|
| Age, years, mean ± SD | 39.8 ± 18.4 |
| Male sex, n (%) | 69 (50.7%) |
| Female sex, n (%) | 67 (49.3%) |
| Medical ICU admission, n (%) | 61 (44.9%) |
| Medical ward/HDU, n (%) | 75 (55.1%) |
| Diabetes mellitus, n (%) | 39 (28.7%) |
| Hypertension, n (%) | 37 (27.2%) |
| Chronic kidney disease, n (%) | 4 (2.9%) |
| Respiratory source, n (%) | 39 (28.7%) |
| CNS source, n (%) | 31 (22.8%) |
| Bloodstream source, n (%) | 14 (10.3%) |
| SOFA score, median (IQR) | 6 (4-8) |
| Admission TLC, ×10⁹/L, median (IQR) | 18.1 (14.6-23.8) |
| Admission platelet count, ×10³/µL, median (IQR) | 156 (103-269) |

Fifty-seven of 136 patients (41.9%) died within 7 days of sepsis onset and 79 (58.1%) survived beyond 7 days. The 57 deaths comprised 29 deaths within 48 hours and 28 additional deaths between 48 hours and 7 days. Mean age did not differ significantly between non-survivors and survivors (40.8 ± 18.3 vs 39.2 ± 18.5 years; p=0.620). Sex, diabetes, hypertension, and ICU versus ward admission were also not significantly associated with 7-day mortality (all p>0.05). Median SOFA score was higher in non-survivors than survivors (7 [IQR 5-9] vs 5 [IQR 3-7]; p<0.001).

Admission platelet count was significantly lower in patients who died within 7 days than in survivors (median 144.0 ×10³/µL [IQR 86.0-235.0] vs 186.5 ×10³/µL [IQR 112.8-296.3]; p=0.044). Admission TLC was numerically higher in non-survivors but the difference did not reach statistical significance (19.3 ×10⁹/L [IQR 15.6-24.7] vs 16.5 ×10⁹/L [IQR 13.2-22.6]; p=0.073).

Table 2. Comparison of survivors and non-survivors at 7 days.

| Parameter | Survivors (n=79) | Non-survivors (n=57) | p-value |
|---|---|---|---|
| TLC, ×10⁹/L, median (IQR) | 16.5 (13.2-22.6) | 19.3 (15.6-24.7) | 0.073 |
| Platelet count, ×10³/µL, median (IQR) | 186.5 (112.8-296.3) | 144.0 (86.0-235.0) | 0.044* |
| SOFA score, median (IQR) | 5 (3-7) | 7 (5-9) | <0.001* |
| Age, years, mean ± SD | 39.2 ± 18.5 | 40.8 ± 18.3 | 0.620 |

**Statistically significant at p<0.05. TLC, platelet count, and SOFA score: Mann-Whitney U test; age: independent-samples t-test.*

The joint classification contained 68 patients in each group. Seven-day mortality was 38.2% (26/68) in Group 1 (high TLC with normal platelet count) and 45.6% (31/68) in Group 2 (high TLC with thrombocytopenia). The difference was not statistically significant (Fisher's exact OR 1.35, 95% CI 0.66-2.79; p=0.49).

Table 3. Seven-day mortality according to the joint TLC-platelet classification.

| Joint classification | Total, n | Deaths, n (%) | Survivors, n (%) |
|---|---|---|---|
| High TLC + normal platelet count | 68 | 26 (38.2%) | 42 (61.8%) |
| High TLC + thrombocytopenia | 68 | 31 (45.6%) | 37 (54.4%) |

*Fisher's exact OR 1.35 (95% CI 0.66-2.79), p=0.49.*

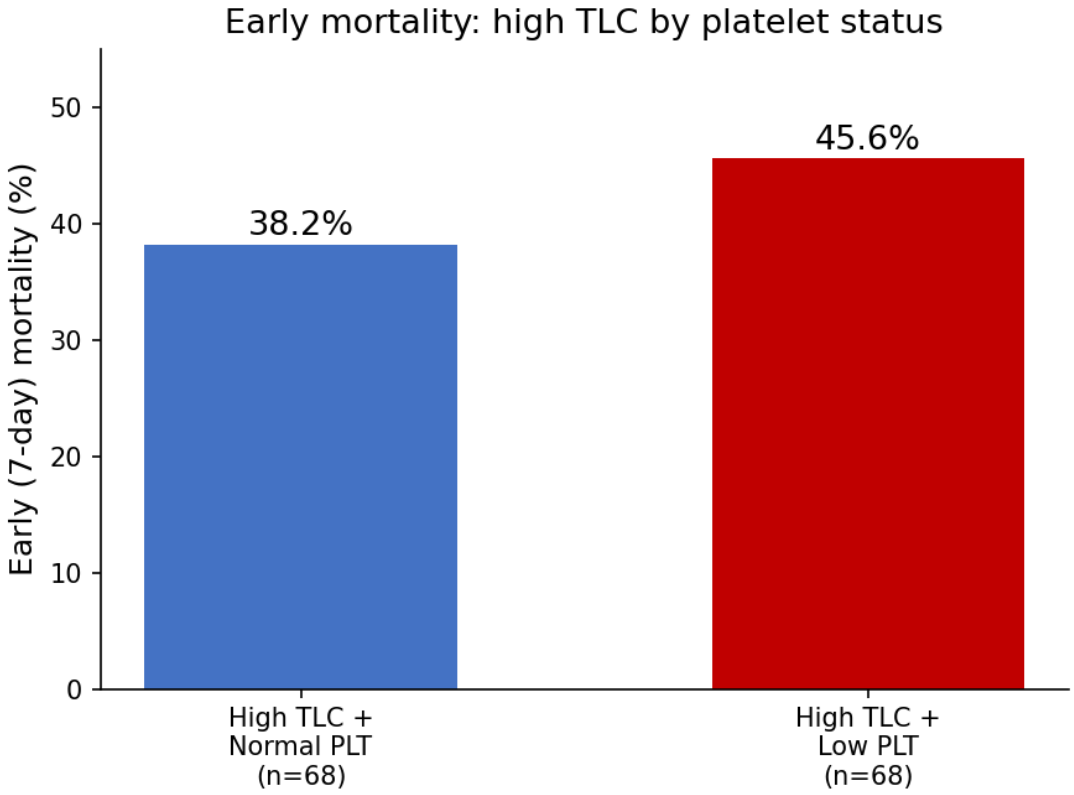


*Figure 1. Seven-day mortality among patients with high TLC according to platelet status (Group 1: normal platelet count; Group 2: thrombocytopenia).*

Admission platelet count showed weak discrimination for 7-day mortality, with an AUC of 0.60 (95% CI 0.50-0.70). The Youden-index cut-off was ≤270 $\times 10^3/\mu L$, with sensitivity 89.5% and specificity 32.9%. Admission TLC also showed weak discrimination, with an AUC of 0.59 (95% CI 0.49-0.68); the corresponding cut-off was ≥17.2 $\times 10^9/L$, with sensitivity 71.4% and specificity 51.3%. These AUCs are close to chance-level discrimination and were not formally compared with one another.

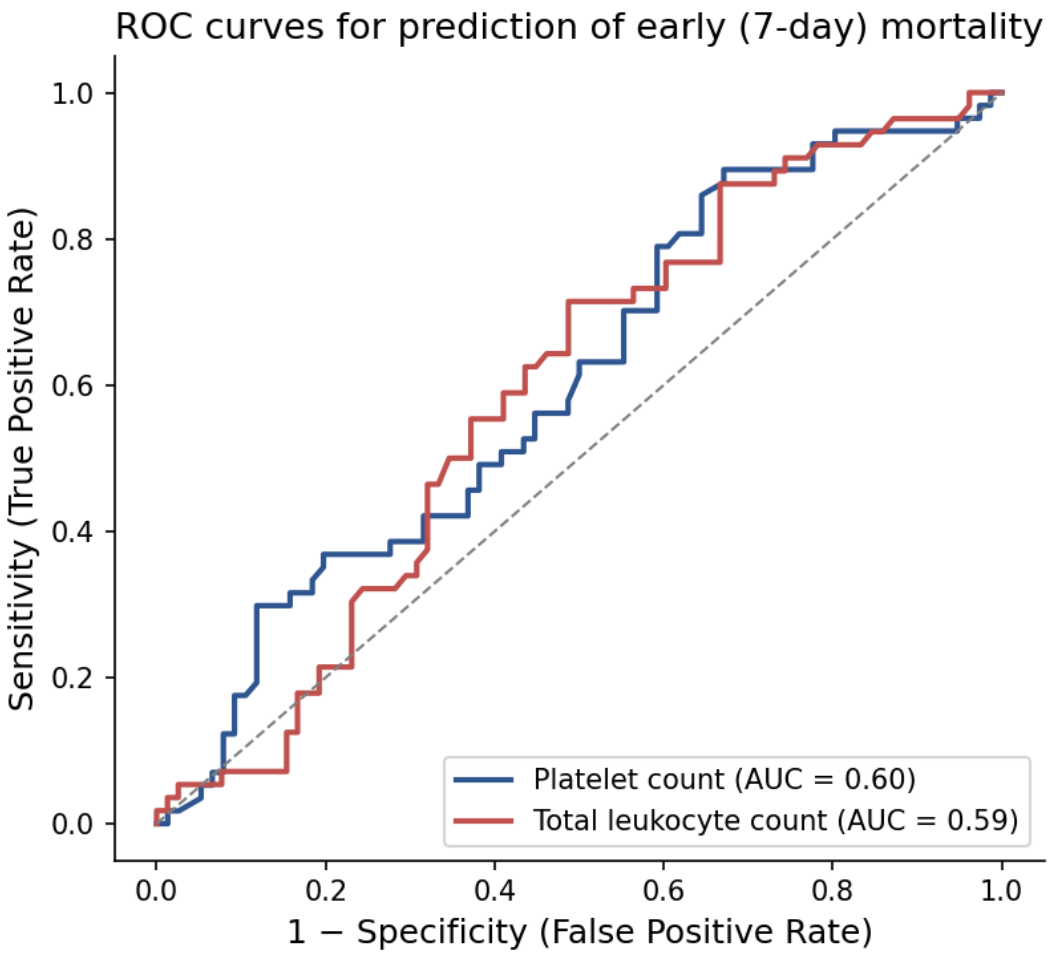


*Figure 2. Receiver operating characteristic curves for admission platelet count and total leukocyte count as predictors of 7-day mortality.*

Table 4. ROC performance of admission platelet count and TLC for 7-day mortality.

| Parameter | AUC (95% CI) | Optimal cut-off | Sensitivity | Specificity |
|---|---|---|---|---|
| Platelet count | 0.60 (0.50-0.70) | ≤270 ×10³/μL | 89.5% | 32.9% |
| Total leukocyte count | 0.59 (0.49-0.68) | ≥17.2 ×10⁹/L | 71.4% | 51.3% |

## DISCUSSION

In this prospective cohort of 136 adults with sepsis and leukocytosis, admission platelet count was lower in patients who died within 7 days, whereas admission TLC did not differ significantly between survivors and non-survivors. Despite the statistically significant difference in platelet medians, its AUC was only 0.60, indicating weak discrimination. The joint high-TLC/platelet-status classification also did not significantly separate survivors from non-survivors. These findings suggest that a single admission complete-blood-count parameter may provide limited prognostic information when used in isolation. The direction of the platelet association is biologically plausible. Sepsis can produce platelet consumption through endothelial activation and microvascular thrombosis, immune-mediated clearance, altered platelet production, and coagulopathic processes.[4,5] Contemporary studies have similarly linked thrombocytopenia or platelet decline with adverse outcomes. Schupp et al. reported that thrombocytopenia and a decline in platelet count during sepsis were associated with 30-day mortality, while Hua et al. found lower admission platelets in non-survivors and an AUC of 0.763 for mortality prediction.[2,7] A large MIMIC-IV analysis also demonstrated a nonlinear association between platelet count and 28-day mortality, particularly at lower platelet levels.[9] The weaker discrimination in the present study may reflect the shorter 7-day endpoint, smaller sample size, different case mix, restriction to patients with leukocytosis, and use of a single admission measurement rather than serial platelet trajectories.

 

TLC showed no statistically significant association with 7-day mortality in this cohort and had an AUC of 0.59. This finding is compatible with the concept that leukocyte count alone is an imprecise marker of sepsis severity. Belok et al. found that leukopenia, rather than leukocytosis, was associated with higher mortality among ICU patients with suspected infection, and that the association was attenuated after adjustment for the platelet component of SOFA.[11] Because the current cohort was restricted to leukocytotic patients, it could not evaluate prognostic differences across leukopenia, normal leukocyte count, and leukocytosis. This restriction is important when interpreting the apparent lack of TLC discrimination. Recent work increasingly emphasizes combinations of routine hematologic indices rather than isolated cell counts. For example, composite neutrophil-lymphocyte and neutrophil-platelet measures have shown prognostic associations in sepsis populations.[12] Platelet-related functional and activation markers have also been explored as potential indicators of disease severity.[15] The present study used a deliberately simpler joint classification based only on TLC and platelet status. Although easy to implement, this binary classification did not significantly improve separation of early outcomes and should not be treated as a validated prediction score.

SOFA score was significantly higher among non-survivors, supporting the expected relationship between organ dysfunction burden and mortality. However, the present analysis did not calculate a SOFA AUC or formally compare SOFA with the laboratory markers, so the results should not be interpreted as a head-to-head predictive superiority analysis. Established severity assessment remains clinically important, and routine blood-count indices are best considered complementary rather than substitutive markers.[13,14,16] From a clinical perspective, the main value of TLC and platelet count is their immediacy, low cost, and universal availability. A low platelet count at presentation may appropriately prompt closer clinical attention, but the weak AUC and low specificity of the data-derived platelet threshold in this cohort do not support using a fixed cut-off as a stand-alone bedside rule. Future prospective work should evaluate serial changes in platelet count and leukocyte indices, incorporate major clinical confounders, and test whether adding routine hematologic variables to established severity scores improves calibration and discrimination.

This study has several limitations. It was conducted at a single tertiary-care centre over a three-month recruitment period, which limits external generalizability. The sample size was modest, reducing precision for subgroup and discrimination analyses. All participants had leukocytosis and were therefore not representative of the full spectrum of leukocyte responses in sepsis, particularly leukopenia and normal TLC. Only admission TLC and platelet count were evaluated, so potentially informative serial trends were not assessed. The analyses were unadjusted and therefore cannot establish that platelet count or TLC independently predicts mortality after accounting for illness severity, comorbidities, infection source, or treatment-related factors. Finally, the data-derived ROC cut-offs were obtained in the same cohort in which performance was assessed and require external validation before clinical use.

## CONCLUSION

Among adults with sepsis and leukocytosis, non-survivors had lower admission platelet counts than survivors, but platelet count alone showed only weak discrimination for 7-day mortality. Admission TLC was not significantly associated with mortality and also demonstrated weak discrimination. A simple joint classification of high TLC with normal versus low platelet count did not significantly distinguish 7-day outcomes. These routinely available laboratory indices may contribute to early clinical assessment, but they should not be used as stand-alone prognostic tools or fixed bedside mortality thresholds without validation in larger, adjusted, and externally validated cohorts.

## REFERENCES

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287.

2. Schupp T, Weidner K, Rusnak J, Jawhar S, Forner J, Dulatahu F, et al. Diagnostic and prognostic role of platelets in patients with sepsis and septic shock. Platelets. 2023;34(1):2131753. doi:10.1080/09537104.2022.2131753.

3. GBD 2021 Global Sepsis Collaborators. Global, regional, and national sepsis incidence and mortality, 1990-2021: a systematic analysis. Lancet Glob Health. 2025;13(12):e2013-e2026. doi:10.1016/S2214-109X(25)00356-0.

4. Jonsson AB, Rygård SL, Hildebrandt T, Perner A, Møller MH, Russell L. Thrombocytopenia in intensive care unit patients: a scoping review. Acta Anaesthesiol Scand. 2021;65(1):2-14. doi:10.1111/aas.13699.

5. Gonzalez DA, Kumar R, Asif S, Bali A, Dang AK. Sepsis and thrombocytopenia: a nowadays problem. Cureus. 2022;14(6):e25421. doi:10.7759/cureus.25421.

6. Raza HA, Hashmi AP, Khakwani MM, Ali MH, Jamil B. Review of sepsis in Pakistan: how far have we come? IJID Reg. 2024;10:108-113. doi:10.1016/j.ijregi.2023.12.002.

7. Hua Y, Wang R, Yang J, Ou X. Platelet count predicts mortality in patients with sepsis: a retrospective observational study. Medicine (Baltimore). 2023;102(38):e35335. doi:10.1097/MD.0000000000035335.

 

8. Comitangelo A, Vozza A, Ditaranto G, et al. Early prediction of in-hospital mortality in patients with acute infections: development of the Acute Severity Infection Score (ASIs). Infect Dis Ther. 2025;14:2053-2070. doi:10.1007/s40121-025-01200-8.

9. Wang D, Wang S, Wu H, Gao J, Huang K, Xu D, Ru H. Association between platelet levels and 28-day mortality in patients with sepsis: a retrospective analysis of a large clinical database MIMIC-IV. Front Med (Lausanne). 2022;9:833996. doi:10.3389/fmed.2022.833996.

10. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200-211. doi:10.1016/S0140-6736(19)32989-7.

11. Belok SH, Bosch NA, Klings ES, Walkey AJ. Evaluation of leukopenia during sepsis as a marker of sepsis-defining organ dysfunction. PLoS One. 2021;16(6):e0252206. doi:10.1371/journal.pone.0252206.

12. Zhang Y, Peng W, Zheng X. The prognostic value of the combined neutrophil-to-lymphocyte ratio (NLR) and neutrophil-to-platelet ratio (NPR) in sepsis. Sci Rep. 2024;14(1):15075. doi:10.1038/s41598-024-64469-8.

13. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med. 1996;22(7):707-710. doi:10.1007/BF01709751.

14. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288.

15. Zhang C, Shang X, Yuan Y, Li Y. Platelet-related parameters as potential biomarkers for the prognosis of sepsis. Exp Ther Med. 2023;25(3):133. doi:10.3892/etm.2023.11832.

16. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y.

## AUTHOR CONTRIBUTION

| Author | Contribution |
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| Dr Hiba Khairat Rizvi | Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision |
| Saba Mehkari | Methodology, Investigation, Data Curation, Writing - Review & Editing |
| Dr Rija Shadab Rizvi | Investigation, Data Curation, Formal Analysis, Software |
| Dr Zeeshan Ali | Software, Validation, Writing - Original Draft |

 