



Association of platelet-to-lymphocyte ratio with sepsis based on MIMIC-IV database

Povezanost odnosa trombocita i limfocita sa sepsom na osnovu baze podataka MIMIC-IV

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Abstract

Background/Aim. Sepsis is a potentially lethal condition that ranks among the most severe medical disorders globally and results in elevated mortality rates. The aim of this study was to examine the correlation between sepsis outcomes in patients and the platelet-to-lymphocyte ratio (PLR), including mortality and duration of intensive care unit (ICU) stay from admission, while considering relevant demographic and clinical factors. **Methods.** In this retrospective study, the Medical Information Mart for Intensive Care (MIMIC)-IV dataset information was used. Sepsis patients were de-identified, and their PLR values were calculated upon admission. Multivariate logistic regression models were used to assess the relationship between PLR and mortality, adjusting for confounding variables such as age, gender, comorbidities, and vital signs. Additionally, the association between PLR and the length of the ICU stay was analyzed using linear regression models. **Results.** This study included 4,624 sepsis patients. Higher PLR values were significantly correlated with decreased survival probabilities in the unadjusted model [Model 1 – odds ratio (OR): 0.890, 95% confidence interval (CI): 0.810–0.970, $p < 0.001$]. This association remained significant after adjusting for demographic factors (Model 2 – OR: 0.920, 95% CI: 0.850–0.995, $p < 0.001$),

comorbidities and biochemical parameters (Model 3 – OR: 0.880, 95% CI: 0.800–0.960, $p = 0.0273$), and vital signs (Model 4 – OR: 0.860, 95% CI: 0.780–0.940, $p = 0.0301$). Furthermore, our analyses revealed a trend towards prolonged ICU stay with higher PLR values, although the association did not reach statistical significance. Survivors were younger (median age 63.37 vs. 70.84 years) and had lower Charlson Comorbidity Index (CCI) scores (median CCI 4.00 vs. 6.00, $p < 0.001$) compared to non-survivors. **Conclusion.** The outcomes indicate that higher PLR levels correlate with greater fatality rates in sepsis patients, underscoring its potential as a predictive biomarker. The observed trend towards prolonged ICU stay with higher PLR warrants further investigation. Model 4, which includes demographic factors, comorbidities, biochemical parameters, and vital signs, demonstrated the strongest association between PLR and mortality, suggesting it may be the most clinically useful model for predicting sepsis outcomes. Incorporating PLR into risk assessment and therapeutic decision-making frameworks may enhance sepsis treatment and improve patient outcomes.

Key words:
biomarkers; blood platelets; intensive care unit; lymphocytes; mortality; sepsis.

Apstrakt

Uvod/Cilj. Sepsa je potencijalno smrtonosno stanje koje se ubraja među najteže zdravstvene poremećaje širom sveta i rezultira povišenom stopom smrtnosti. Cilj rada bio je da se ispita korelacija između ishoda sepse kod bolesnika i odnosa trombocita i limfocita (TLO), uključujući mortalitet i dužinu boravka u jedinici intenzivne nege (JIN), uzimajući u obzir relevantne demografske i kliničke faktore. **Metode.** U ovoj retrospektivnoj studiji, korišćene su informacije iz

baze podataka *Medical Information Mart for Intensive Care* (MIMIC)-IV. Bolesnici sa sepsom bili su anonimni, a njihove TLO vrednosti izračunate su po prijemu. Za procenu odnosa između TLO i mortaliteta korišćeni su modeli multivarijantne logističke regresije, uz prilagođavanje za varijable koje mogu da utiču na rezultat kao što su starost, pol, komorbiditeti i vitalni znaci. Pored toga, analizirana je povezanost između TLO i dužine boravka na JIN korišćenjem modela linearne regresije. **Rezultati.** Ova studija obuhvatila je 4 624 bolesnika sa

sepsom. Više vrednosti TLO značajno su korelisale sa smanjenom verovatnoćom preživljavanja u modelu bez prilagođavanja [Model 1 – *odds ratio* (OR): 0,890, 95% *confidence interval* (CI): 0,810–0,970, $p < 0,001$]. Ova povezanost ostala je značajna nakon prilagođavanja za demografske faktore (Model 2 – OR: 0,920, 95% CI: 0,850–0,995, $p < 0,001$), komorbiditete i biohemijske parametre (Model 3 – OR: 0,880, 95% CI: 0,800–0,960, $p = 0,0273$) i vitalne znake (Model 4 – OR: 0,860, 95% CI: 0,780–0,940, $p = 0,0301$). Štaviše, naše analize su pokazale trend ka produženom boravku u JIN kod viših vrednosti TLO, iako ta povezanost nije dostigla statističku značajnost. Preživeli su bili mlađi (medijana starosti 63,37 vs. 70,84 godine) i imali su niže *Charlson Comorbidity Index* (CCI) rezultate (medijana CCI 4,00 vs. 6,00, $p < 0,001$) u poređenju sa onima koji nisu preživeli. **Zaključak.**

Rezultati ukazuju da viši nivoi TLO korelišu sa većim stopama smrtnosti kod bolesnika sa sepsom, što naglašava potencijal TLO kao prediktivnog biomarkera. Uočeni trend ka produženom boravku u JIN kod viših vrednosti TLO zahteva dalja istraživanja. Model 4, koji uključuje demografske faktore, komorbiditete, biohemijske parametre i vitalne znake, pokazao je najjaču vezu između TLO i mortaliteta, što sugerise da bi mogao biti klinički najkorisniji model za predviđanje ishoda sepe. Uključivanje TLO u okvire za procenu rizika i donošenje odluka u vezi sa terapijom može poboljšati lečenje sepe i ishode stanja bolesnika.

Ključne reči:
biomarkeri; trombociti; intenzivna nega, odeljenja; limfociti; mortalitet; sepsa.

Introduction

Sepsis is characterized by a dysregulated host reaction to infection, representing a potentially lethal condition that ranks among the most severe medical disorders globally and results in elevated mortality rates among patients in intensive care units (ICUs) ^{1, 2}. Despite various biomarkers having been identified to influence the development and prognosis of sepsis, there is still a need to discover useful biomarkers to improve patient survival ³.

The platelet-to-lymphocyte ratio (PLR) is a widely accessible haematological metric linked to diverse inflammatory and immunological responses. In certain diseases, such as cardiovascular diseases and cancer, PLR has been considered an important prognostic indicator. PLR has been reported to have potential predictive value in sepsis, but current studies are limited, and most have small sample sizes ^{4, 5}. A recent systematic review and meta-analysis by Wang et al. ⁶ found that PLR levels were significantly higher in sepsis non-survivors than in survivors, indicating its potential as a prognostic marker. Additionally, Zheng et al. ⁷ reported that both low and high PLR levels are associated with higher in-hospital mortality, and specifically, the early decrease in PLR after admission correlates with increased mortality in sepsis patients. Existing research has analyzed the predictive value of PLR in sepsis using the Medical Information Mart for Intensive Care (MIMIC) – III database ⁸, but systematic studies utilizing larger databases (e.g., MIMIC-IV) are scarce. Given the wealth of clinical data provided by the MIMIC-IV database, including patients' laboratory test results and clinical courses, it presents a unique opportunity to further investigate the role of PLR in predicting mortality in sepsis.

The aim of this study was to conduct an in-depth analysis of the application of PLR in sepsis patients using the MIMIC-IV database, analyzing the relationship between PLR and mortality rates in sepsis patients, as well as to explore the associations between PLR and other clinical parameters to evaluate its potential as an effective biomarker for sepsis severity and prognosis.

Methods

Data sources

The MIMIC-IV database was utilized for this retrospective study. MIMIC-IV is an extensive repository encompassing detailed patient data from the ICU of premier tertiary care facilities in Boston, Massachusetts, the United States, spanning from 2008 to 2019 ⁹. This database contains extensive patient data, including vital signs, care plan documents, severity evaluations, diagnoses, therapeutic interventions, and laboratory findings. All patient information in the dataset has been de-identified to safeguard privacy. The dataset's ethical usage was approved by the review boards at Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology, which exempted this study from the requirement for written consent due to the de-identified content of the data.

For accessing the database, the research team completed the Collaborative Institutional Training Initiative course, achieving certification (ID: 60447838) and passing relevant examinations concerning "conflict of interest" and "data or specimen study only". This study was meticulously executed using STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) standards, thereby ensuring both methodological rigor and adherence to ethical guidelines. This structured approach underscores the commitment to ethical standards and scientific integrity in the handling and analysis of patient data. The MIMIC dataset is the primary source of the data used in this study, which has been previously approved for research use.

The study was approved by the Ethics Committee of Zhejiang Xinan International Hospital (approval No. 345/PLR/2022, from April 13, 2022).

Study population and definitions

Sepsis was defined according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), which identified individuals with a Sequential Organ

Failure Assessment (SOFA) score of ≥ 2 and suspected infections¹⁰. Exclusions for the study were as follows: patients under the age of 18, those with a SOFA score less than 2 upon ICU admission, or those with ICU stays shorter than 48 hrs. Initial ICU-acquired infections were defined according to the Centers for Disease Control and Prevention (CDC) standards¹¹ as any new infection occurring 48 hrs after ICU admission, evidenced by positive microbial culture and the initiation of a new antibiotic regimen¹².

Data collection

Only sepsis patients who satisfied the inclusion criteria and were admitted to the ICU for the first time were examined to prevent duplication. Extracted patient baseline parameters included age, gender, weight, duration of hospital and ICU stays, and death. Baseline ICU scoring standards collected at admission included SOFA, Acute Physiology Score III (APS III), and Charlson Comorbidity Index (CCI). Comorbidities at admission included shock, cardiovascular disease, surgical status, cancer, kidney diseases, and liver dysfunction. Intervention events covered pharmacological treatments (vasopressors, corticosteroids, heparin), blood transfusion, renal replacement therapy, mechanical ventilation, central venous catheters, and urinary catheters. Laboratory data were gathered at the time of ICU admission. The database's microbiological examination findings provided proof of illnesses acquired in the ICU.

Statistical analysis

Missing values were imputed using the random forest method to ensure data consistency and interpretability. Continuous factors were provided as median [interquartile range (IQR)]. Intergroup comparisons employed appropriate statistical methods, including the *t*-test, Wilcoxon rank-sum test, analysis of variance, or Kruskal-Wallis test. Linear correlations were evaluated between PLR and the duration of ICU stay. Extended model approaches were used for covariate ad-

justments as follows: Model 1 was a simple predictive model for survival rate based on PLR; Model 2 incorporated demographic indicators such as age, gender, and race; Model 3 added comorbidities and biochemical test results after 24 hrs of ICU admission; Model 4 integrated parameters of vital signs including heart rate, mean blood pressure, respiration rate, peripheral capillary oxygen saturation (SpO₂), and temperature. The goodness-of-fit tests were performed for all logistic regression models. In a two-tailed test, a *p*-value < 0.05 was determined statistically noteworthy. Utilizing R software, statistical analyses were conducted.

Results

This research involved a group of 4,624 patients who fulfilled the inclusion criteria. The demographic and clinical characteristics upon admission are delineated in Table 1. Of the total 4,624 patients, the survivor group comprised 1,819 patients, while the non-survivor group consisted of 2,805 patients. Within the entire cohort, male patients in the survivor group accounted for 22.34% (1,033/4,624) of the total sample, whereas male patients in the non-survivor group represented 34.08% (1,576/4,624). The proportion of males within the survivor group was 56.79% (1,033/1,819), and the proportion of males within the non-survivor group was 56.19% (1,576/2,805). The individuals who survived had an average age of 63.37 years (IQR: 52.37–74.35), significantly younger compared to those who did not survive, whose average age was 70.84 years (IQR: 64.02–80.87) ($p < 0.001$). Regarding comorbidities, patients who survived had a lower median CCI of 4.00 (IQR: 2.00–6.00) than those who did not, with a median of 6.00 (IQR: 4.00–8.00). At the time of ICU admission, the white blood cell count was notably higher in the survivor group with a median of 9.10 (IQR: 6.55–14.40) compared to 8.80 (IQR: 6.30–13.10) in the non-survivor group. Additionally, the median platelet count was comparable between the two groups, with 208.00 (IQR: 148.00–283.00) in the survivor group and 209.00 (IQR: 144.00–284.00) in the non-survivor group.

Table 1

Demographic and clinical characteristics of patients upon admission

Parameters	Survivors (n = 1,819)	Non-survivors (n = 2,805)	SMD	<i>p</i>
Demographics				
gender, male	1,033 (22.34)	1,576 (34.08)	-0.012	0.693
age, years	63.37 (52.37–74.35)	70.84 (64.02–80.87)	0.487	< 0.001
weight, kg	81.60 (67.80–98.00)	76.90 (64.00–93.20)	0.186	< 0.001
Comorbidities				
CCI	4.00 (2.00–6.00)	6.00 (4.00–8.00)	0.721	< 0.001
Laboratory results at admission				
WBCs, $\times 10^9$ (4.0–10.0)	9.10 (6.55–14.40)	8.80 (6.30–13.10)	0.042	0.002
platelets, $\times 10^9$ (150–400)	208.00 (148.00–283.00)	209.00 (144.00–284.00)	0.005	0.769
glucose, mg/dL (78–110)	205.08 (164.00–286.17)	207.00 (163.30–283.15)	0.007	0.884
Vital parameters at admission				
heart rate, bpm (60–100)	97.17 (90.47–104.13)	97.52 (89.68–104.14)	0.074	0.225
MBP, mmHg (70–105)	75.58 (72.47–79.23)	75.31 (71.84–78.99)	0.098	0.008
respiration rate, breaths/min (12–20)	21.00 (19.08–23.00)	21.02 (19.00–23.00)	0.001	0.683
SpO ₂ , % (95–100)	96.16 (95.00–97.04)	96.06 (95.00–97.04)	0.033	0.257
temperature, °C (36.0–37.5)	36.98 (36.74–37.18)	36.90 (36.65–37.13)	0.214	< 0.001

Table 1 (continued)

Parameters	Survivors (n = 1,819)	Non-survivors (n = 2,805)	SMD	<i>p</i>
Score				
SOFA	4.00 (3.00–5.00)	4.00 (3.00–6.00)	0.164	< 0.001
APSI	50.00 (39.00–63.00)	62.00 (48.00–79.00)	0.594	< 0.001
Hematological indices				
hemoglobin, g/dL (male: 13.5–17.5, female: 12.0–16.0)	12.30 (10.50–13.70)	11.80 (10.20–13.30)	0.182	< 0.001
MCV, fL (80–100)	91.00 (87.00–95.00)	92.00 (88.00–98.00)	0.191	< 0.001
RBC, $\times 10^{12}/L$ (male: 4.5–6.0, female: 4.5–5.5)	4.07 (3.54–4.56)	3.91 (3.35–4.40)	0.224	< 0.001
RDW, % (11.5–14.5)	14.20 (13.30–15.50)	14.70 (13.70–16.50)	0.313	< 0.001
Predictors				
lymphocyte, % (20–40)	19.64 (7.10–28.65)	21.50 (9.30–28.93)	0.103	< 0.001
NLR (1–3)	0.28 (0.09–0.45)	0.32 (0.12–0.46)	0.008	< 0.001
PLR (50–300)	124.78 (105.73–219.58)	129.68 (107.47–238.07)	0.089	0.012
LAR	1.12 (0.82–1.45)	1.19 (0.90–1.63)	0.225	< 0.001
Outcomes				
LOS ICU, days	3.18 (1.90–6.71)	3.56 (1.92–7.37)	0.043	0.041

SMD – standardized mean difference; CCI – Charlson Comorbidity Index; WBCs – white blood cells; bpm – beats per minute; MBP – mean blood pressure; SpO₂ – peripheral capillary oxygen saturation; SOFA – Sequential Organ Failure Assessment; APSI – Acute Physiology and Chronic Health Evaluation III; MCV – mean Corpuscular volume; RBC – red blood cells; RDW – red cell distribution width; NLR – neutrophil-to-lymphocyte ratio; PLR – platelet-to-lymphocyte ratio; LAR – lymphocyte-to-adrenal ratio; LOS ICU – Length of Stay in Intensive Care Unit.

Values in brackets in the first column indicate the reference range for each respective parameter. Group values are expressed as numbers (percentages) or median (interquartile range).

Vital parameters at admission also exhibited some differences. The median heart rate for survivors was 97.17 beats per minute (bpm) (IQR: 90.47–104.13) as opposed to 97.52 bpm (IQR: 89.68–104.14) for non-survivors. The median SOFA score at admission, a critical measure of organ failure, was equal in both groups, 4.00 (IQR: 3.00–5.00). Similarly, there was no significant difference in the APSI, with a median of 50.00 (IQR: 39.00–63.00) for the survivor group and 62.00 (IQR: 48.00–79.00) for the non-survivor group. In terms of blood count, hemoglobin levels were slightly elevated in the survivor group, with a median of 12.30 g/dL (IQR: 10.50–13.70), compared to the non-survivor group, which had a median of 11.80 g/dL (IQR: 10.20–13.30). The mean corpuscular volume was marginally lower in the surviving patients, with a median value of 91.00 fL (IQR: 87.00–95.00) vs. 92.00 fL (IQR: 88.00–98.00) in those who died. The analysis of predictors such as lymphocyte percentage showed a median of 19.64% (IQR: 17.10–26.85) for survivors compared to 21.50% (IQR: 9.30–28.93) for non-survivors. Inflammatory markers like the neutrophil-to-lymphocyte ratio (NLR) and PLR were also considered, showing that survivors had a median NLR of 0.28 (IQR: 0.09–0.45) and PLR of 124.78 (IQR: 105.73–219.58).

Ultimately, the duration of ICU stay was reduced for survivors, averaging 3.18 days (IQR: 1.90–6.71) compared to 3.56 days (IQR: 1.92–7.37) for non-survivors. This comprehensive data analysis underscores the complex nature of sepsis outcomes and highlights the importance of specific clinical and laboratory factors in predicting patient survival.

In evaluating the association between the PLR and the duration of ICU stay, our analyses reveal a trend that

warrants attention. Figure 1 suggests a distribution where higher PLR values correlate with a prolonged length of stay in the ICU, as indicated by the concentration of data points and the trend line. This scatterplot visually demonstrates the potential utility of PLR as a predictor for ICU length of stay, with higher PLR values indicating a longer anticipated duration of stay in the ICU.

The logistic regression models further substantiate the influence of PLR on patient survival (Table 2). Model 1, which includes the PLR as the sole predictor, yields an odds ratio (OR) of 0.890 [95% confidence interval (CI): 0.810–0.970, $p < 0.001$], indicating that elevated PLR levels are modestly correlated with a decrease in the odds of survival. Model 2, controlling for demographic characteristics such as age, gender, and race, demonstrates a marginally elevated OR of 0.920 (95% CI: 0.850–0.995, $p < 0.001$). Model 3 incorporates comorbidities and biochemical test results recorded 24 hrs after ICU admission, producing an OR of 0.880 (95% CI: 0.800–0.960, $p = 0.0273$). Comprehensive Model 4, which adds vital signs parameters to the previous model, demonstrates an OR of 0.860 (95% CI: 0.780–0.940, $p = 0.0301$). This indicates that when vital signs are considered alongside PLR, a higher PLR is significantly associated with decreased survival odds. Model 4 shows the strongest association between PLR and mortality (lowest OR value) and therefore appears to be the most clinically useful model for predicting sepsis outcomes. These results highlight the potential of PLR as a prognostic indicator in ICU patients with sepsis, warranting further investigation into its role as a biomarker for clinical outcomes.

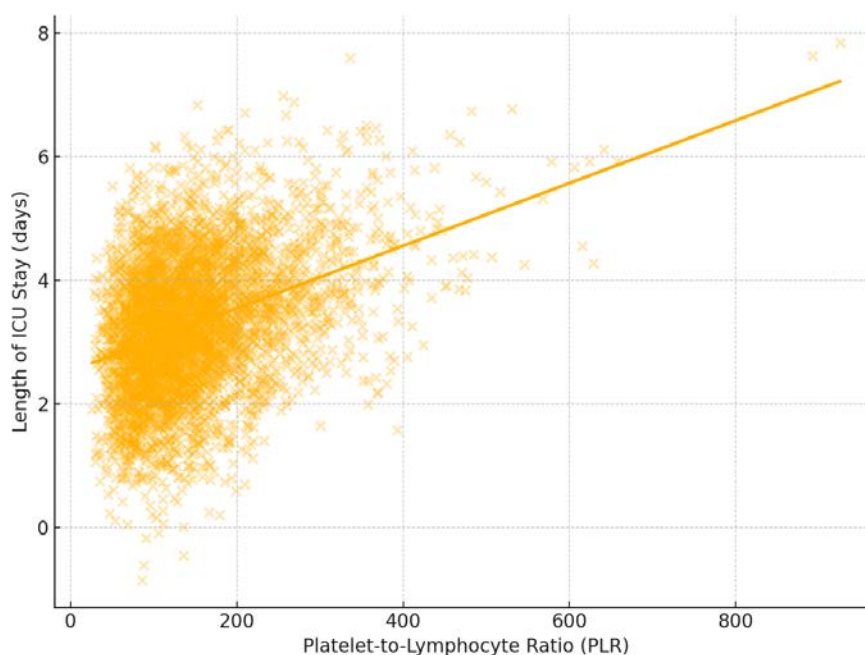


Fig. 1 – The relationship between PLR and length of ICU stay.

PLR – platelet-to-lymphocyte ratio; ICU – intensive care unit.

Note: this scatterplot depicts the correlation between PLR values at ICU admission and the duration of ICU stay in 4,624 sepsis patients from the Medical Information Mart for Intensive Care (MIMIC)-IV database. A trend line has been added to highlight the positive correlation observed – higher PLR levels are associated with a tendency toward longer ICU stays. Although the association did not reach statistical significance in the regression model, this pattern suggests PLR may offer prognostic utility in predicting ICU resource use.

Table 2

The results of logistic regression between the PLR and the survival outcome

Model	PLR survival outcome [OR (95% CI)]	<i>p</i> -value
1	0.890 (0.810–0.970)	< 0.001
2	0.920 (0.850–0.995)	< 0.001
3	0.880 (0.800–0.960)	0.0273
4	0.860 (0.780–0.940)	0.0301

PLR – platelet-to-lymphocyte ratio;
OR – odds ratio; CI – confidence interval.

Note: results of multiple logistic regression models analyzing the association between the PLR and survival outcome. Model 1 is the unadjusted model with PLR as the sole predictor. Model 2 adjusts for demographic factors including age, gender, and race. Model 3 further adjusts for comorbidities and biochemical test results recorded after 24 hrs of intensive care unit admission. Model 4 additionally incorporates vital signs parameters, including heart rate, mean blood pressure, respiration rate, peripheral capillary oxygen saturation, and temperature. ORs along with 95% CIs and *p*-values are reported for each model. A *p*-value < 0.05 is considered statistically significant, representing a significant association between PLR and survival outcome after adjusting for the included covariates in that particular model.

Discussion

This study revealed that PLR is a key biomarker for the prognosis of patients with sepsis. This study examined the demographic and clinical features of septic patients upon admission, along with the impact of PLR on individual survival and duration of stay in the ICU. Several previous stud-

ies have examined the diagnostic and prognostic value of PLR in sepsis ⁴⁻⁸. A recent systematic review and meta-analysis by Wang et al. ⁶ analyzed 16 studies with 2,403 septic patients and found that PLR levels were significantly higher in non-survivors than in survivors. Furthermore, Zheng et al. ⁷ reported a U-shaped relationship between baseline PLR and in-hospital mortality, indicating that both low

and high PLR values are associated with poorer outcomes. Our findings align with these previous studies and provide additional evidence from a larger dataset using the newer MIMIC-IV database.

The observed differences in demographic and clinical parameters between surviving and non-surviving patients underline the multifactorial nature of sepsis outcomes. Notably, survivors tended to be slightly younger and had lower CCI scores upon admission. While these findings align with previous literature, the significance lies in the confirmation of these trends within our cohort^{7,13}. Socioeconomic and clinical risk factors, such as race, education, hospital type, and delirium duration, are linked to worse long-term cognitive impairment after an ICU stay, particularly CCI¹³. CCI has been reported to synergize with age to affect patient survival⁷.

Our analyses revealed intriguing insights into the predictive value of PLR in sepsis prognosis. Higher PLR values were associated with decreased odds of survival, even after adjusting for demographic variables, comorbidities, and vital signs. Previous studies have also demonstrated that higher PLR levels upon admission in patients with various conditions correlate with increased morbidity and mortality^{3,14}. For instance, Zheng et al.⁷ found a significant difference in PLR change over time between survivors and non-survivors in sepsis patients. Similarly, studies examining PLR in patients diagnosed with coronavirus disease 2019 have shown that higher levels correlate with disease severity and poorer outcomes⁶.

Nevertheless, due to the poor quality of this evidence, more research on the PLR threshold is required¹⁵. These findings corroborate previous studies suggesting PLR as a potential biomarker for adverse outcomes in sepsis patients⁶. Further research is necessary to clarify the processes behind this connection and to assess the applicability of PLR in treatment. The association between PLR and duration of ICU stay also merits attention. While our analyses indicated a trend towards a prolonged ICU stay with higher PLR values, the clinical implications of this observation warrant further investigation. The lack of statistical significance does not necessarily indicate no effect, but rather reflects the limitations of our current dataset and analytical approach. Future studies with larger sample sizes and possibly different analytical methods might reveal a statistically significant relationship.

Understanding the relationship between PLR and ICU outcomes could inform risk stratification and resource allocation strategies in sepsis management¹⁶. This research enhances the existing knowledge on prognostic indicators and therapeutic approaches in sepsis. By examining multiple

models with varying degrees of adjustment for confounding factors, we have demonstrated that Model 4, which includes demographic variables, comorbidities, biochemical test results, and vital signs, provides the best assessment of PLR's relationship with mortality. This comprehensive model could be valuable for clinical decision-making, offering a more precise prediction of patient outcomes than simpler models or PLR alone.

Variables influencing patient outcomes were carefully analyzed by combining demographic, clinical, and laboratory data. Identifying PLR as a potential prognostic predictor underscores the significance of examining inflammatory markers in determining the treatment of sepsis and the probability of recurrence. Nevertheless, our study is not without limitations. Our findings may not be as broadly applicable as they may be due to the retrospective nature of our research and our reliance on a single-center dataset. Additionally, while we adjusted for various confounding factors in our analysis, including demographic variables, comorbidities, biochemical markers, and vital signs, the presence of unmeasured confounders cannot be entirely excluded. Future studies incorporating larger, multi-center datasets and prospective designs are required to corroborate our results and elucidate the PLR clinical implications in sepsis management.

Conclusion

This study provides valuable insights into the relationship between PLR and sepsis outcomes, contributing to the growing body of literature on prognostic markers and treatment strategies in sepsis. Our findings suggest that PLR could be a valuable tool in risk stratification and prognostic evaluation for sepsis patients. Furthermore, our analysis of four different models indicates that comprehensive consideration of demographic factors, comorbidities, biochemical parameters, and vital signs alongside PLR (Model 4) provides the most robust approach for predicting mortality in sepsis patients.

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Angus DC, van der Poll T. Severe sepsis and septic shock. *N Engl J Med* 2013; 369(9): 840–51. Erratum in: *N Engl J Med* 2013; 369(21): 2069.
2. Gaieski DF, Edwards JM, Kallan MJ, Carr BG. Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med* 2013; 41(5): 1167–74.
3. Póvoa P, Coelho L, Dal-Pizzol F, Ferrer R, Huttner A, Conway Morris A, et al. How to use biomarkers of infection or sepsis at the bedside: guide to clinicians. *Intensive Care Med* 2023; 49(2): 142–53.
4. Kriplani A, Pandit S, Chawla A, de la Rosette JJMCH, Laguna P, Jayadeva Reddy S, et al. Neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and lymphocyte-monocyte ratio (LMR) in predicting systemic inflammatory response syndrome (SIRS) and sepsis after percutaneous nephrolithotomy (PNL). *Urolithiasis* 2022; 50(3): 341–8.

5. *Biyyikli E, Kayipmaz AE, Kavalci C.* Effect of platelet-lymphocyte ratio and lactate levels obtained on mortality with sepsis and septic shock. *Am J Emerg Med* 2018; 36(4): 647–50.
6. *Wang G, Mivefroshan A, Yaghoobpoor S, Khanzadeh S, Siri G, Rahmani F,* et al. Prognostic Value of Platelet to Lymphocyte Ratio in Sepsis: A Systematic Review and Meta-analysis. *Biomed Res Int* 2022; 2022: 9056363.
7. *Zheng R, Shi YY, Pan JY, Qian SZ.* Decrease in the Platelet-to-Lymphocyte Ratio in Days after Admission for Sepsis Correlates with In-Hospital Mortality. *Shock* 2023; 59(4): 553–9.
8. *Shen Y, Huang X, Zhang W.* Platelet-to-lymphocyte ratio as a prognostic predictor of mortality for sepsis: interaction effect with disease severity-a retrospective study. *BMJ Open* 2019; 9(1): e022896.
9. *Pollard TJ, Johnson AEW, Raffa JD, Celi LA, Mark RG, Badawi O.* The eICU Collaborative Research Database, a freely available multi-center database for critical care research. *Sci Data* 2018; 5: 180178.
10. *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): 801–10.
11. *Van Vught LA, Wiewel MA, Hoogendijk AJ, Frencken JF, Scicluna BP, Klouwenberg PMC,* et al. The host response in patients with sepsis developing intensive care unit-acquired secondary infections. *Am J Respir Crit Care Med* 2017; 196(4): 458–70.
12. *Johnson AEW, Aboab J, Raffa JD, Pollard TJ, Deliberato RO, Celi LA,* et al. A Comparative Analysis of Sepsis Identification Methods in an Electronic Database. *Crit Care Med* 2018; 46(4): 494–9.
13. *Haddad DN, Mart MF, Wang L, Lindsell CJ, Raman R, Nordness MF,* et al. Socioeconomic Factors and Intensive Care Unit-Related Cognitive Impairment. *Ann Surg* 2020; 272(4): 596–602.
14. *Sarkar S, Kannan S, Khanna P, Singh AK.* Role of platelet-to-lymphocyte count ratio (PLR), as a prognostic indicator in COVID-19: A systematic review and meta-analysis. *J Med Virol* 2022; 94(1): 211–21.
15. *Simadibrata DM, Pandhita BAW, Ananta ME, Tango T.* Platelet-to-lymphocyte ratio, a novel biomarker to predict the severity of COVID-19 patients: A systematic review and meta-analysis. *J Intensive Care Soc* 2022; 23(1): 20–6.
16. *Muşat F, Păduraru DN, Bolocan A, Pălcău CA, Copăceanu AM, Ion D,* et al. Machine Learning Models in Sepsis Outcome Prediction for ICU Patients: Integrating Routine Laboratory Tests-A Systematic Review. *Biomedicines* 2024; 12(12): 2892.

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