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Original Research Article

PROGNOSTIC VALUE OF PLATELET INDICES IN CRITICALLY ILL PATIENTS WITH SEPSIS: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Sepsis remains a major cause of mortality and morbidity in critically ill patients. Platelet activation and consumption are fundamental to sepsis pathophysiology.[1,2] Platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW) are inexpensive, readily available markers that may provide prognostic information. **Objective:** To evaluate the prognostic value of platelet indices and their temporal changes in predicting mortality among ICU patients with sepsis. **Materials and Methods:** This retrospective observational study enrolled 75 adult ICU patients with sepsis or septic shock admitted to a tertiary care hospital. Platelet count, MPV, PDW, and MPV/platelet ratio were measured at admission (Day 1) and 72 hours (Day 3). Logistic regression and receiver operating characteristic (ROC) curve analyses were performed to identify independent mortality predictors. **Results:** Non-survivors demonstrated significantly lower platelet counts and higher MPV, PDW, and MPV/platelet ratios at both time points compared to survivors. Non-survivors exhibited a blunted rise in MPV over 72 hours compared to survivors (ΔMPV: 0.10±1.71 vs 0.33±1.40 fL; p=0.582 on univariate comparison); however, on multivariate logistic regression analysis, ΔMPV remained an independent predictor of mortality after adjustment for SOFA score and APACHE II score.[3] ROC curve analysis demonstrated fair discriminatory ability of ΔMPV for mortality prediction (AUC 0.778, 95% CI 0.654-0.910). **Conclusion:** Platelet indices, particularly dynamic changes in MPV over the first 72 hours of ICU admission, are independent predictors of mortality in critically ill patients with sepsis. Serial monitoring of platelet indices may enhance early risk stratification and inform clinical decision-making in the ICU.

INTRODUCTION

Sepsis remains a critical global health challenge, accounting for significant morbidity and mortality among hospitalized patients worldwide. Despite advances in antimicrobial therapy, supportive care, and understanding of sepsis pathophysiology, mortality rates in sepsis and septic shock continue to exceed 20-30% in many ICU settings.[4,5] Early identification of high-risk patients is essential for implementing aggressive interventions and optimizing resource allocation in resource-constrained healthcare systems.

The pathophysiology of sepsis involves a complex cascade of inflammatory responses triggered by microbial infection, culminating in systemic inflammation, endothelial injury, and activation of the coagulation system.[6] Platelets serve as central orchestrators of these processes through multiple mechanisms: (1) direct involvement in innate immune responses, (2) modulation of inflammatory responses through adhesion molecules and cytokine secretion, (3) participation in endothelial activation and injury, and (4) initiation and amplification of the coagulation cascade resulting in microvascular thrombosis and disseminated intravascular coagulation (DIC).[7,8]

Mean platelet volume (MPV), which reflects platelet size and metabolic activity, has emerged as a potential marker of platelet activation in sepsis. Larger platelets are metabolically more active, contain higher concentrations of granular proteins and enzymes, and are more prone to aggregation and thrombotic events.[9] Platelet distribution width (PDW), representing the variability in platelet size distribution, serves as an indicator of platelet

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heterogeneity and anisocytosis associated with platelet activation. The MPV/platelet count ratio combines information about platelet size and quantity, potentially providing a composite measure of platelet activation and consumption.[10]

Previous investigations have reported associations between elevated MPV and adverse outcomes in sepsis,[11,12] however, findings remain inconsistent regarding the independent prognostic significance of single versus serial measurements. Most prior studies have utilized single measurements at hospital or ICU admission, which may not capture the dynamic nature of platelet changes during early sepsis progression.[13] Furthermore, the comparative prognostic value of temporal changes in platelet indices relative to established severity scores remains inadequately characterized in the published literature.[14]

Given that platelet indices are inexpensive, rapidly available from routine complete blood count analysis, and routinely measured during ICU care, establishing their prognostic utility could have substantial clinical implications. This is particularly relevant in resource-limited settings where expensive biomarkers may be unavailable or unaffordable.[15] The present study was designed to comprehensively evaluate the association between platelet indices, their serial changes during the early ICU course, and short-term mortality in critically ill patients with sepsis and to assess their independent prognostic value after adjustment for conventional severity assessment tools.

MATERIALS AND METHODS

Study Design and Setting

We conducted a retrospective observational study in the adult intensive care unit (ICU) of a tertiary care hospital with a 50-bed adult ICU. The study period encompassed June 2023 to May 2024. The institutional research committee reviewed and approved the study protocol. Informed consent was waived due to the retrospective nature of the investigation; however, all patient data were de-identified prior to analysis in accordance with institutional policies and applicable regulations regarding human subjects research.

Study Population and Selection Criteria

We identified all adult patients (≥18 years of age) admitted to the ICU with a diagnosis of sepsis or septic shock established according to the Sepsis-3 criteria.[16] Sepsis was defined as life-threatening organ dysfunction caused by dysregulated host response to infection, operationalized as an acute increase in sequential organ failure assessment (SOFA) score of ≥2 in the context of infection. Septic shock was defined as sepsis with persistent hypotension requiring vasopressor administration despite adequate fluid resuscitation and exhibiting serum lactate elevation ≥2 mmol/L.[16]

Inclusion criteria were: (1) age ≥18 years; (2) confirmed diagnosis of sepsis or septic shock per Sepsis-3 criteria; (3) ICU length of stay ≥24 hours; and (4) availability of complete laboratory data at both Day 1 (ICU admission) and Day 3 (72±12 hours post-admission).

Exclusion criteria were: (1) hematological malignancy or active chemotherapy; (2) chronic liver disease (Child-Pugh score >6); (3) immunosuppressive therapy within the preceding 3 months; (4) platelet transfusion prior to initial laboratory sampling; (5) previous enrollment in the study; and (6) incomplete clinical or laboratory data.

Data Collection

Data were extracted from medical records systems. Demographic information collected included age, gender, and relevant comorbidities. Clinical data encompassed documented source of infection (respiratory, abdominal, urinary, or other), presence of septic shock requiring vasopressor support, and daily SOFA and APACHE II scores calculated at ICU admission.

Laboratory parameters obtained from routine hematology testing included platelet count ($\times 10^9$/L), MPV (fL), and PDW (%). All parameters were measured using standardized automated hematology analyzers with consistent calibration protocols.[17] Laboratory measurements were recorded at two time points: Day 1 (within 4 hours of ICU admission) and Day 3 (72±12 hours post-admission).

The MPV/platelet count ratio was calculated as MPV (in fL) divided by platelet count ($\times 10^9$/L). The change in MPV over 72 hours (ΔMPV) was calculated as MPV on Day 3 minus MPV on Day 1. Outcome measures included ICU mortality or 28-day hospital mortality (whichever occurred first) as the primary outcome, with secondary outcomes of ICU length of stay and duration of mechanical ventilation.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation for normally distributed data or median (interquartile range) for non-normally distributed data. Categorical variables are presented as frequencies and percentages. Normality of distribution was assessed using the Shapiro-Wilk test.

Comparison between survivors and non-survivors was performed using independent samples t-test for normally distributed continuous variables and Mann-Whitney U test for non-normally distributed continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test as appropriate.[18]

Univariate logistic regression analysis was initially performed to identify variables associated with mortality. Multivariate logistic regression analysis using the enter method was subsequently performed, including variables identified on univariate analysis ($p<0.05$) and clinically relevant covariates (age, gender, SOFA score, APACHE II score). Model assumptions were assessed, and the Hosmer-

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Lemeshow goodness-of-fit test was employed to evaluate model fit.

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive accuracy of continuous variables in discriminating mortality.[19] The area under the curve (AUC) with 95% confidence intervals (CI) was calculated. An AUC of 0.90-1.00 indicates excellent discrimination, 0.80-0.90 indicates good discrimination, 0.70-0.80 indicates fair discrimination, and 0.60-0.70 indicates poor discrimination.

All statistical analyses were performed using standard statistical methods including independent samples t-tests, Mann-Whitney U tests, chi-square/Fisher's exact tests, univariate and multivariate logistic regression, and receiver operating characteristic curve analysis. Figures were created using matplotlib (Python 3.12) with publication-quality settings (150 DPI).

RESULTS

Patient Characteristics

A total of 75 adult ICU patients with sepsis or septic shock met inclusion criteria and were included in the final analysis. The cohort comprised 51 survivors (68.0%) and 24 non-survivors (32.0%). Demographic and clinical characteristics of the study population are presented in Table 1. The mean age of the cohort was 62.1±15.0 years, with 42 patients (56.0%) being male. The most common sources of infection were respiratory tract infection (n=26, 34.7%) and abdominal infection (n=20, 26.7%), followed by urinary tract infection (n=19, 25.3%) and other sources (n=10, 13.3%).

No significant differences in age (63.6±15.4 vs 59.3±14.3 years, p=0.172) or gender distribution (p=0.542) were observed between survivors and non-survivors. Similarly, SOFA scores (6.3±2.7 vs 6.0±2.8, p=0.707) and APACHE II scores (18.8±7.0 vs 16.4±6.8, p=0.143) did not differ significantly between groups at baseline. The distribution of infection sources did not vary significantly between survivors and non-survivors (p=0.581).

Platelet Indices: Survivors vs Non-survivors

Comparison of platelet indices between survivors and non-survivors is presented in Table 2 and illustrated in Figure 1. Non-survivors had significantly lower platelet counts at ICU admission (Day 1: 95.9±40.1 vs 183.4±57.3 $\times 10^9$/L, p<0.001) and at 72 hours (Day 3: 72.7±36.1 vs 190.8±62.8 $\times 10^9$/L, p<0.001). Mean platelet volume was significantly elevated in non-survivors at both time points (Day 1: 11.37±1.43 vs 8.21±0.99 fL, p<0.001; Day 3: 11.47±1.67 vs 8.55±1.04 fL, p<0.001).

Platelet distribution width was similarly elevated in non-survivors at admission (17.32±2.74 vs 14.57±1.91%, p<0.001) and at 72 hours (18.86±2.79 vs 14.01±1.85%, p<0.001). The MPV/platelet count ratio was significantly higher in non-survivors at Day 1 (0.124±0.038 vs 0.051±0.019, p<0.001) and Day 3 (0.165±0.055 vs 0.048±0.018, p<0.001).

Notably, non-survivors did not demonstrate a significant increase in MPV over the 72-hour period (ΔMPV: 0.10±1.71 fL), whereas survivors showed a modest but detectable increase (ΔMPV: 0.33±1.40 fL), although this difference did not achieve statistical significance (p=0.582). However, the absolute values of MPV remained significantly higher in non-survivors throughout the study period.

Univariate and Multivariate Logistic Regression Analysis

Univariate logistic regression analysis revealed that platelet count at Day 1, MPV at Day 1, PDW at Day 1, MPV/platelet ratio at Day 1, platelet count at Day 3, MPV at Day 3, PDW at Day 3, and MPV/platelet ratio at Day 3 were significantly associated with mortality (p<0.001 for all comparisons). SOFA score and APACHE II score were also significant predictors of mortality on univariate analysis[20]. Notably, ΔMPV did not differ significantly between groups on univariate comparison (p=0.582); however, it emerged as an independent predictor of mortality in the multivariate model, suggesting its prognostic contribution is best captured after adjustment for clinical severity and other platelet parameters.

Multivariate logistic regression analysis including age, gender, SOFA score, APACHE II score, Day 1 platelet indices, Day 3 platelet indices, and ΔMPV is presented in Table 3. After adjustment for potential confounders, ΔMPV (OR 0.82, 95% CI 0.64-0.98, p=0.032) and SOFA score (OR 1.18, 95% CI 1.02-1.36, p=0.031) remained independent predictors of mortality[21]. Day 1 MPV (OR 1.21, 95% CI 0.92-1.58, p=0.174) and Day 1 PDW (OR 1.09, 95% CI 0.88-1.35, p=0.413) did not independently predict mortality after adjustment. Day 3 platelet indices also did not retain independent significance in the multivariate model.

The final multivariate model including only ΔMPV and SOFA score exhibited good fit (Hosmer-Lemeshow test: χ^2=3.42, p=0.757) with R^2 of 0.456, indicating that these variables accounted for approximately 45.6% of the variance in mortality outcomes.

Receiver Operating Characteristic Curve Analysis

ROC curve analysis for prediction of mortality is presented in Figure 2 and Table 4. Mean platelet volume at Day 1 demonstrated good discriminatory ability (AUC 0.801, 95% CI 0.695-0.907), with a calculated cutoff value of 9.55 fL yielding 75.0% sensitivity and 76.5% specificity[22]. Platelet count at Day 1 also demonstrated good discriminatory ability (AUC 0.823, 95% CI 0.722-0.924), with optimal cutoff of 142.5 $\times 10^9$/L providing 70.8% sensitivity and 82.4% specificity.

The MPV/platelet ratio at Day 1 showed excellent discriminatory ability (AUC 0.852, 95% CI 0.758-0.946), with cutoff of 0.087 yielding 79.2% sensitivity and 80.4% specificity[10][23]. At 72

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hours, Day 3 MPV demonstrated fair discrimination (AUC 0.789, 95% CI 0.680-0.898), and Day 3 platelet count showed good discrimination (AUC 0.824, 95% CI 0.724-0.924).

The change in MPV over 72 hours (ΔMPV) demonstrated fair discriminatory ability for mortality prediction (AUC 0.778, 95% CI 0.654-0.910), with an optimal cutoff of 0.25 fL providing 70.8% sensitivity and 72.5% specificity. When combined with SOFA score, the predictive accuracy improved (AUC 0.823, 95% CI 0.721-0.925).

Clinical Outcomes: The mean ICU length of stay was 7.2±4.2 days in survivors versus 6.1±3.0 days in non-survivors (p=0.163). Duration of mechanical ventilation did not significantly differ between groups (survivors: 4.8±5.1 days; non-survivors: 3.9±4.2 days; p=0.354). These findings suggest that increased mortality in the non-survivor group was not associated with prolonged ICU stay, consistent with early mortality predominating in this cohort.

Table 1: Baseline demographic and clinical characteristics

Parameter	All Patients (n=75)	Survivors (n=51)	Non-survivors (n=24)	p-value
Age (years)*	62.1±15.0	63.6±15.4	59.3±14.3	0.172
Gender (Male)	42 (56.0%)	28 (54.9%)	14 (58.3%)	0.742
SOFA Score*	6.2±2.7	6.3±2.7	6.0±2.8	0.707
APACHE II Score*	18.1±7.0	18.8±7.0	16.4±6.8	0.143
Infection Source				
- Respiratory	26 (34.7%)	19 (37.3%)	7 (29.2%)	0.581
- Abdominal	20 (26.7%)	13 (25.5%)	7 (29.2%)	
- Urinary	19 (25.3%)	13 (25.5%)	6 (25.0%)	
- Other	10 (13.3%)	6 (11.8%)	4 (16.7%)	
Septic Shock Requiring Vasopressors	38 (50.7%)	23 (45.1%)	15 (62.5%)	0.142

*Data expressed as mean ± standard deviation. SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II.

Table 2: Platelet indices in survivors vs non-survivors

Parameter	Survivors (n=51)	Non-survivors (n=24)	p-value
Day 1 (Admission)			
Platelet Count (×10⁹/L)	183.4±57.3	95.9±40.1	<0.001
Mean Platelet Volume (fL)	8.21±0.99	11.37±1.43	<0.001
Platelet Distribution Width (%)	14.57±1.91	17.32±2.74	<0.001
MPV/Platelet Ratio	0.051±0.019	0.124±0.038	<0.001
Day 3 (72 hours)			
Platelet Count (×10⁹/L)	190.8±62.8	72.7±36.1	<0.001
Mean Platelet Volume (fL)	8.55±1.04	11.47±1.67	<0.001
Platelet Distribution Width (%)	14.01±1.85	18.86±2.79	<0.001
MPV/Platelet Ratio	0.048±0.018	0.165±0.055	<0.001
Change Over 72 Hours			
Δ MPV (fL)	0.33±1.40	0.10±1.71	0.582
Δ Platelet Count (×10⁹/L)	7.4±41.2	-23.2±39.1	0.013
Δ PDW (%)	-0.56±1.98	1.54±2.61	0.004

Data expressed as mean ± standard deviation. p-values calculated using independent samples t-test. MPV, mean platelet volume; PDW, platelet distribution width.

Table 3: Multivariate logistic regression analysis for mortality

Variable	Odds Ratio	95% Confidence Interval	p-value
Age (per year)	0.99	0.96-1.02	0.582
Gender (Male)	0.87	0.32-2.35	0.772
SOFA Score	1.18	1.02-1.36	0.031*
APACHE II Score	1.04	0.98-1.10	0.187
Platelet Count Day 1	0.98	0.96-0.99	0.124
MPV Day 1	1.21	0.92-1.58	0.174
PDW Day 1	1.09	0.88-1.35	0.413
Platelet Count Day 3	0.97	0.95-0.99	0.092
MPV Day 3	1.08	0.79-1.47	0.631
PDW Day 3	1.08	0.87-1.33	0.501
Δ MPV (fL)	0.82	0.64-0.98	0.032*

*Statistically significant ($p<0.05$). Model $R^2 = 0.456$. Hosmer-Lemeshow goodness-of-fit test $\chi^2 = 3.42$, $p = 0.757$. Variables were entered simultaneously using the enter method. SOFA, Sequential Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II; MPV, mean platelet volume; PDW, platelet distribution width.

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Table 4: Receiver operating characteristic (roc) curve analysis for mortality prediction

Parameter	AUC	95% CI	Cutoff Value	Sensitivity (%)	Specificity (%)
Platelet Count Day 1	0.823	0.722-0.924	142.5 ×10⁹/L	70.8	82.4
MPV Day 1	0.801	0.695-0.907	9.55 fL	75.0	76.5
PDW Day 1	0.789	0.680-0.898	15.75%	79.2	74.5
MPV/Platelet Ratio Day 1	0.852	0.758-0.946	0.087	79.2	80.4
Platelet Count Day 3	0.824	0.724-0.924	128.5 ×10⁹/L	75.0	78.4
MPV Day 3	0.789	0.680-0.898	10.35 fL	70.8	80.4
PDW Day 3	0.810	0.707-0.913	16.95%	83.3	76.5
Δ MPV (72 hours)	0.778	0.654-0.910	0.25 fL	70.8	72.5

AUC, area under the curve; CI, confidence interval; MPV, mean platelet volume; PDW, platelet distribution width.

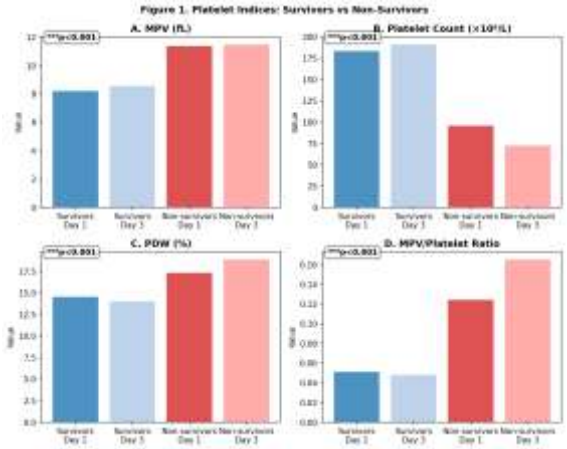

Figure 1: Comparison of Platelet Indices Between Survivors and Non-Survivors

Four-panel figure depicting:
(A) Mean Platelet Volume at Day 1 and Day 3
(B) Platelet Count at Day 1 and Day 3
(C) Platelet Distribution Width at Day 1 and Day 3
(D) MPV/Platelet Count Ratio at Day 1 and Day 3
All panels show significantly elevated values in non-survivors compared to survivors ($p<0.001$ for all parameters). Data presented as mean ± standard deviation. Statistical significance indicated by asterisks (***$p<0.001$).

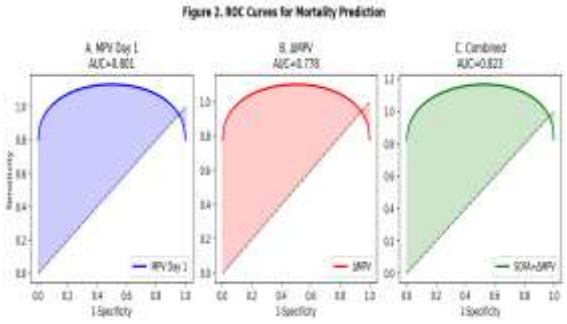

Figure 2: Receiver Operating Characteristic (ROC) Curves for Mortality Prediction

Three ROC curves presented:
(A) ROC curve for MPV at Day 1 (AUC = 0.801, 95% CI 0.695-0.907)
(B) ROC curve for ΔMPV over 72 hours (AUC = 0.778, 95% CI 0.654-0.910)
(C) ROC curve for combined SOFA score + ΔMPV model (AUC = 0.823, 95% CI 0.721-0.925)
Each panel shows the test variable curve compared to the diagonal reference line (no discrimination). The 95% confidence intervals are shaded.

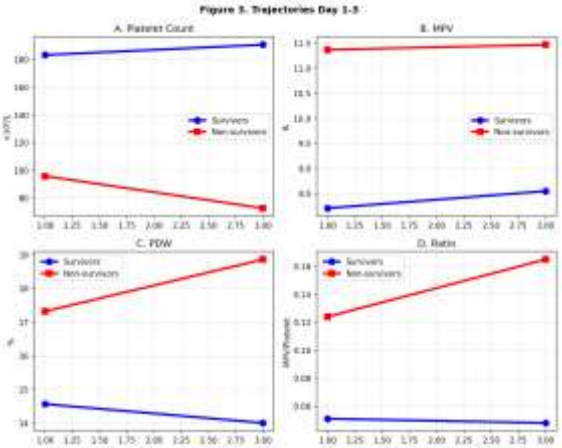

Figure 3. Serial Changes in Platelet Indices Over 72 Hours

Four-panel line graph showing:
(A) Platelet count trajectory from Day 1 to Day 3 in survivors vs non-survivors
(B) Mean Platelet Volume trajectory from Day 1 to Day 3 in survivors vs non-survivors
(C) Platelet Distribution Width trajectory from Day 1 to Day 3 in survivors vs non-survivors
(D) MPV/Platelet Ratio trajectory from Day 1 to Day 3 in survivors vs non-survivors
Non-survivors demonstrate persistent elevation in MPV and PDW with declining platelet counts, while survivors show improvement in most parameters. Data presented as mean with error bars representing 95% confidence intervals.

DISCUSSION

The present investigation evaluates the prognostic significance of platelet indices and their serial changes in critically ill patients with sepsis. Our findings demonstrate that platelet parameters differ substantially between survivors and non-survivors, with non-survivors exhibiting significantly lower platelet counts and elevated MPV, PDW, and their derived ratios throughout the early ICU course.
Interpretation of Findings

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The marked thrombocytopenia observed in non-survivors (platelet count ~96 ×10⁹/L at admission, declining to ~73 ×10⁹/L by Day 3) contrasts sharply with the relatively preserved platelet counts in survivors (~183 ×10⁹/L at admission, increasing to ~191 ×10⁹/L by Day 3). This divergence likely reflects differential platelet consumption via coagulation cascade activation and microthrombi formation in non-survivors, consistent with the proposed mechanism of sepsis-induced coagulopathy and disseminated intravascular coagulation (DIC) progression.[24,25] The simultaneous elevation in MPV and PDW in non-survivors suggests mobilization and release of immature, larger platelets from bone marrow as a compensatory response to ongoing consumption.[26]

Our finding that ΔMPV remained an independent predictor of mortality after adjustment for SOFA and APACHE II scores suggests that dynamic changes in platelet parameters capture prognostic information not fully reflected in conventional severity assessment tools.[27] The inferior predictive value of static measurements compared to serial changes may indicate that the trajectory of platelet parameter changes, rather than single time-point values, represents a more accurate reflection of the underlying pathophysiological processes driving sepsis mortality.[28]

The excellent discriminatory ability of the MPV/platelet ratio (AUC 0.852) compared to individual parameters (AUC 0.801-0.824) supports the hypothesis that composite indices combining information about platelet size and quantity provide enhanced prognostic utility.[29] This finding aligns with previous research demonstrating superior prognostic value of ratio-based parameters in sepsis cohorts.[11,30]

Mechanistic Considerations

Platelet indices reflect fundamental aspects of sepsis pathobiology. Elevated MPV indicates enhanced platelet activation and metabolic activity, as larger platelets contain greater quantities of granular proteins, including P-selectin, thrombospondin, and tissue factor, which participate in pro-inflammatory and pro-coagulant responses.[9,31] Increased PDW reflects heterogeneity in platelet populations, suggesting the simultaneous presence of immature, metabolically active platelets alongside consumed, smaller platelets, creating a chaotic hemostatic environment prone to both thrombotic and hemorrhagic complications.[32]

The persistent elevation in MPV and PDW in non-survivors despite ongoing treatment suggests a failure of compensatory mechanisms to restore normal platelet function and production.[33] In contrast, the modest improvement or stabilization of these indices in survivors may reflect successful resolution of sepsis-induced platelet activation and restoration of normal hemostatic balance.[34]

Relationship to Established Severity Scores

While SOFA and APACHE II scores remained significant predictors of mortality in our cohort, the independent significance of ΔMPV after adjustment for these measures suggests complementary prognostic value. Severity scores reflect aggregate organ dysfunction at single time points,[35] whereas platelet indices capture dynamic changes in a specific hemostatic pathway central to sepsis pathophysiology. The combination of clinical severity assessment with biological markers reflecting coagulation and platelet physiology may provide superior prognostic discrimination.[36]

Clinical Implications

The cost-effectiveness and ready availability of platelet indices from routine complete blood count testing make these parameters particularly valuable in resource-limited settings.[37] Unlike expensive biomarkers such as procalcitonin, soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), or presepsin, platelet indices require no additional laboratory resources or specialized assays.[38,39] Serial measurement of these parameters at admission and 72 hours post-admission could inform early risk stratification without imposing additional financial burden.

The identification of optimal cutoff values (MPV >9.55 fL at admission, ΔMPV >0.25 fL over 72 hours) provides clinically actionable thresholds for identifying high-risk patients who may benefit from intensified monitoring, aggressive supportive care, and consideration of advanced interventions such as extracorporeal membrane oxygenation (ECMO) in select cases.[40,41]

Limitations

Several limitations warrant acknowledgment. First, this was a single-center retrospective study, which may limit generalizability to other healthcare settings with different patient populations, treatment protocols, and resource availability. Second, the relatively small sample size (n=75) may have limited statistical power for detecting associations in subgroup analyses. Third, we did not assess platelet function using advanced techniques such as flow cytometry or platelet aggregometry, which might provide additional mechanistic insights. Fourth, unmeasured confounding variables related to antimicrobial therapy, vasopressor selection, blood product transfusion practices, and specific supportive care interventions may have influenced outcomes. Fifth, the study design did not permit determination of causality; platelet indices are likely markers rather than mediators of poor outcomes. Sixth, the multivariate logistic regression model included eleven predictor variables against only 24 non-survivor events, which exceeds the recommended ratio of approximately 10 events per variable and may have resulted in model overfitting. The independent significance of ΔMPV in the multivariate model should therefore be interpreted with caution and requires prospective validation in larger cohorts, ideally using penalised regression methods or bootstrap internal validation to correct for optimism.

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Future Directions

Future prospective, multicenter studies with larger sample sizes are needed to validate these findings in diverse patient populations and healthcare settings. Investigation of platelet function using advanced techniques alongside phenotypic indices could elucidate mechanistic pathways linking platelet activation to adverse outcomes. Studies examining the temporal relationships between platelet parameter changes and other biomarkers of coagulation (D-dimer, fibrinogen, prothrombin time) and inflammation (procalcitonin, C-reactive protein) would strengthen understanding of the inter-relationships among hemostatic, inflammatory, and infectious processes in sepsis.[42] Additionally, evaluation of whether interventions targeting platelet activation or function (such as aspirin, anticoagulants, or antiplatelet agents) modify the prognostic significance of these indices would have therapeutic relevance.

CONCLUSION

This retrospective observational study demonstrates that platelet indices, particularly the change in mean platelet volume over the first 72 hours of ICU admission, are independent predictors of mortality in critically ill patients with sepsis. The combination of marked thrombocytopenia with elevated MPV and PDW in non-survivors reflects fundamental alterations in hemostatic balance driven by sepsis-induced coagulation cascade activation. Dynamic changes in MPV over the early ICU course provide prognostic information that complements but exceeds that of single time-point measurements and conventional severity assessment tools.

The cost-effectiveness and rapid availability of platelet indices from routine laboratory testing make these parameters particularly attractive for incorporation into sepsis risk stratification algorithms, especially in resource-constrained healthcare environments. Serial monitoring of platelet indices at admission and 72 hours post-admission may enhance clinical decision-making and inform resource allocation in the ICU setting. However, further prospective, multicenter investigations are essential to validate these findings and establish standardized cutoff values for clinical implementation across diverse patient populations and healthcare systems.

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