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RED CELL DISTRIBUTION WIDTH, MEAN PLATELET VOLUME, AND NEUTROPHIL-LYMPHOCYTE RATIO AS PREDICTORS OF MORTALITY IN SEPSIS

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ABSTRACT

Background: Early identification of high-risk patients with sepsis remains a clinical challenge, especially in resource-constrained settings. Hematological indices such as Red Cell Distribution Width (RDW), Mean Platelet Volume (MPV), and Neutrophil-to-Lymphocyte Ratio (NLR), routinely available from complete blood counts, have emerged as potential prognostic biomarkers. This study aimed to evaluate the prognostic significance of RDW, MPV, and NLR in predicting severity and in-hospital mortality among sepsis patients admitted to a tertiary care center.

Materials and Methods: A prospective observational study was conducted in the intensive care unit of a tertiary care teaching hospital over 12 months. A total of 112 adult patients diagnosed with sepsis, as per Sepsis-3 criteria, were enrolled. Baseline demographic data, comorbidities, infection source, and clinical outcomes were recorded. Hematological parameters (RDW, MPV, NLR), SOFA, and APACHE II scores were compared between survivors and non-survivors. Correlation analyses and multivariate logistic regression were performed. Predictive performance was assessed using Receiver Operating Characteristic (ROC) curves.

Results: The in-hospital mortality rate was 33.9% (n=38). Non-survivors were significantly older and had higher rates of diabetes and chronic kidney disease. RDW, MPV, and NLR were significantly elevated in non-survivors (RDW: 15.3% vs. 13.8%, $p<0.001$; MPV: 10.5 fL vs. 9.4 fL, $p<0.001$; NLR: 11.8 vs. 6.5, $p<0.001$). All three indices positively correlated with SOFA and APACHE II scores. NLR demonstrated the strongest correlation (SOFA: $r=0.588$, $p<0.001$). ROC analysis showed good discriminative ability: AUC for NLR was 0.846, RDW 0.812, and MPV 0.795. In multivariate analysis, RDW >14.5%, MPV >9.8 fL, and NLR >9.0 were independent predictors of mortality with adjusted odds ratios of 2.94, 2.57, and 3.83, respectively ($p<0.05$ for all).

Conclusion: RDW, MPV, and particularly NLR are independent predictors of mortality in sepsis and correlate strongly with disease severity. Given their availability from routine blood counts, these markers offer valuable, cost-effective tools for early risk stratification in sepsis, especially in low-resource settings.

Keywords: Sepsis, Red Cell Distribution Width, Mean Platelet Volume, Neutrophil Lymphocyte Ratio, Mortality.

INTRODUCTION

Sepsis is a complex clinical syndrome characterized by life-threatening organ dysfunction resulting from a dysregulated host response to infection. Globally, sepsis contributes to approximately 11 million deaths annually, accounting for nearly 20% of all deaths worldwide.[1] In India, hospital-based studies report

sepsis-related mortality ranging from 25% to 55%, particularly among patients admitted to tertiary care intensive care units (ICUs).[2] Early identification and timely risk stratification remain critical for improving outcomes, especially in resource-constrained healthcare settings.[2]

While established scoring systems such as the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) are widely used for assessing disease severity and prognosis in sepsis, they require multiple laboratory and clinical variables, limiting their utility in emergency settings and peripheral hospitals.[1] As a result, interest has grown in utilizing inexpensive, widely available hematological parameters derived from the complete blood count (CBC) test to predict severity and mortality in sepsis.[1]

Red Cell Distribution Width (RDW), a measure of the heterogeneity in red blood cell size (anisocytosis), has emerged as a significant marker of systemic inflammation. Elevated RDW values have been associated with increased oxidative stress, inflammation-mediated bone marrow dysfunction, and poor outcomes in septic patients.[3] It was found that an RDW >14.5% was independently associated with increased 28-day mortality in patients with severe sepsis and septic shock.[4]

Mean Platelet Volume (MPV) reflects the average size of circulating platelets and serves as an indirect marker of platelet activation. Larger platelets are metabolically more active and prothrombotic, contributing to microvascular thrombosis observed in sepsis-induced organ dysfunction.[5] Elevated MPV levels have been associated with increased mortality in critically ill patients, including those with sepsis and septic shock.[6]

Neutrophil-to-Lymphocyte Ratio (NLR) is a composite marker that reflects both innate immune activation (neutrophilia) and adaptive immune suppression (lymphopenia)—two key features in the immunopathology of sepsis. High NLR values have been significantly associated with worse prognosis in septic patients, with studies reporting NLR >10 to be predictive of ICU mortality and prolonged hospitalization.[7,8]

Despite increasing recognition of these parameters, the combined prognostic utility of RDW, MPV, and NLR has not been comprehensively evaluated in the Indian clinical setting. Most existing studies have been conducted in Western populations, with limited applicability to Indian ICUs where etiological, demographic, and healthcare delivery differences may influence outcomes.

Therefore, this study was done to analyse the prognostic significance of RDW, MPV, and NLR in adult patients diagnosed with sepsis in a tertiary care hospital. Specifically, the study aimed to evaluate the association of these parameters with in-hospital mortality and clinical severity, thereby assessing their potential role as cost-effective, accessible tools for early risk stratification and management of sepsis in Indian healthcare settings.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted at the Department of Pathology in collaboration with the Department of General Medicine a tertiary care teaching hospital located in North India. The study was carried out over a period of 12 months, from July 2024 to July 2025, and aimed to evaluate the prognostic role of select hematological indices in patients diagnosed with sepsis.

Study Population: The study included adult patients aged 18 years and above who were admitted to the ICU with a diagnosis of sepsis, based on the Sepsis-3 criteria, which defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection, with an acute increase in the Sequential Organ Failure Assessment (SOFA) score of ≥2 points.[9,10] All eligible patients presenting during the study period were recruited consecutively to avoid selection bias.

Patients were excluded if they had pre-existing hematologic malignancies (such as leukemia or lymphoma), chronic liver disease with hypersplenism, recent blood transfusions within the past seven days, current immunosuppressive or chemotherapy use, known autoimmune diseases, or were pregnant. These exclusions were necessary to eliminate confounding factors that could independently alter RDW, MPV, or NLR values.

Sample Size Estimation: The sample size was calculated based on study by Mandal et al., with in-hospital mortality rate of 30% among sepsis patients, with a 95% confidence level and a margin of error of 10%.[2] Using the formula for estimating a single proportion, the minimum required sample size was 81 patients. To enhance statistical power and accommodate potential data loss, a total of 112 patients were enrolled during the study period.

Data Collection and Clinical Assessment: After obtaining informed consent, data were recorded using a structured case record form. Demographic information (age, gender), clinical parameters (heart rate, respiratory rate, blood pressure, oxygen saturation), and underlying comorbidities (diabetes, hypertension, chronic kidney disease, etc.) were documented. The likely source of infection (e.g., respiratory, urinary, abdominal) was identified based on clinical, radiological, and microbiological findings.

Severity of illness was assessed within 24 hours of admission using both the SOFA score and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, calculated by ICU physicians trained in critical care documentation.[11,12]

Laboratory Analysis: Venous blood samples were collected within the first six hours of ICU admission and before the administration of vasopressors or blood products. Complete blood counts (CBC) were analyzed using an automated hematology analyzer

that underwent daily quality control calibration. From the CBC report, the following indices were obtained: Red Cell Distribution Width (RDW) – reported as a percentage (%), Mean Platelet Volume (MPV) – measured in femtolitres (fL), and Absolute Neutrophil Count (ANC) and Absolute Lymphocyte Count (ALC) – used to calculate the Neutrophil-to-Lymphocyte Ratio (NLR). All tests were performed in the central clinical laboratory following standard operating procedures and quality control protocols.

Outcome Measures: The primary outcome of the study was in-hospital mortality, defined as death occurring during the index hospital admission. Secondary outcomes included the need for invasive mechanical ventilation, vasopressor support, and the duration of ICU stay (in days). Each patient was followed prospectively from the time of ICU admission until discharge or death.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Kolmogorov–Smirnov test. Normally distributed data were summarized as mean ± standard deviation (SD), while non-normally distributed data were presented as median with interquartile range (IQR). Categorical variables were presented as frequencies and percentages.

Comparisons between survivors and non-survivors were performed using the independent samples t-test for normally distributed variables and the Mann–Whitney U test for skewed data. The Chi-square test or Fisher's exact test was used for comparing categorical variables. Receiver Operating Characteristic (ROC) curves were constructed to evaluate the predictive ability of RDW, MPV, and NLR for in-hospital mortality, and the Area Under the Curve (AUC) was calculated. The optimal cut-off points for each marker were determined using Youden's Index. Multivariate logistic regression analysis was conducted to adjust for potential confounders including age, gender, and SOFA score. A p-value <0.05 was considered statistically significant.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants or their legally authorized representatives prior to enrollment. All data were anonymized, and patient confidentiality was maintained in accordance with the Declaration of Helsinki (2013 revision) and applicable national ethical guidelines.

RESULTS

A total of 112 patients diagnosed with sepsis were included in the study, with an overall in-hospital mortality rate of 33.9% (n=38). The remaining 66.1% (n=74) of patients survived to discharge. The mean age of the study population was 54.8 ± 16.3 years, with non-survivors being significantly older than survivors (62.9 ± 14.8 vs. 50.7 ± 15.4 years, p=0.001). While gender distribution was comparable between the two groups (p=0.873), comorbidities such as diabetes mellitus (65.8% vs. 41.9%, p=0.019) and chronic kidney disease (34.2% vs. 12.2%, p=0.004) were significantly more prevalent among non-survivors. Respiratory infections were more commonly associated with mortality (55.3% vs. 32.4%, p=0.023). The need for mechanical ventilation (86.8% vs. 35.1%, p<0.001) and vasopressor support (100% vs. 39.2%, p<0.001) were markedly higher in non-survivors. Interestingly, survivors had a longer median ICU stay (8 vs. 5 days, p=0.009), possibly reflecting successful recovery after prolonged management [Table 1].

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (n = 112).

Variable	Total (n=112)	Survivors (n=74)	Non-survivors (n=38)	p-value
	Frequency (%)/mean ± SD/median (IQR)			
Age (years)	54.8 ± 16.3	50.7 ± 15.4	62.9 ± 14.8	0.001
Gender				
Male	68 (60.7%)	44 (59.5%)	24 (63.2%)	0.873
Female	44 (39.3%)	30 (40.5%)	14 (36.8%)	
Diabetes Mellitus	56 (50.0%)	31 (41.9%)	25 (65.8%)	0.019
Hypertension	48 (42.9%)	27 (36.5%)	21 (55.3%)	0.059
Chronic Kidney Disease	22 (19.6%)	9 (12.2%)	13 (34.2%)	0.004
Source of Infection				
Respiratory	45 (40.2%)	24 (32.4%)	21 (55.3%)	0.023
Urinary Tract	28 (25.0%)	20 (27.0%)	8 (21.1%)	0.408
Abdominal	17 (15.2%)	13 (17.6%)	4 (10.5%)	0.218
Others/Unknown	22 (19.6%)	17 (23.0%)	5 (13.2%)	0.129
Mechanical Ventilation	59 (52.7%)	26 (35.1%)	33 (86.8%)	<0.001
Vasopressor Support	67 (59.8%)	29 (39.2%)	38 (100%)	<0.001
ICU Stay (days)	7 (4–11)	8 (5–12)	5 (3–9)	0.009

Non-survivors had significantly elevated Red Cell Distribution Width (RDW) (15.3% vs. 13.8%, p<0.001) and Mean Platelet Volume (MPV) (10.5 fL vs. 9.4 fL, p<0.001). The Neutrophil-to-Lymphocyte Ratio (NLR) was also markedly higher in non-survivors, with a median value of 11.8 compared to 6.5 in survivors (p<0.001). This was primarily driven by elevated neutrophil counts and lymphopenia in those who succumbed. These findings indicate that elevated RDW, MPV, and NLR are significantly associated with poor outcomes in sepsis [Table 2].

Table 2: Hematological Indices in Survivors vs Non-Survivors.

Parameter	Survivors (n=74)	Non-survivors (n=38)	p-value
	mean ± SD/median (IQR)		
RDW (%)	13.8 ± 1.2	15.3 ± 1.5	<0.001
MPV (fL)	9.4 ± 1.0	10.5 ± 1.3	<0.001
Neutrophil Count (×10⁹/L)	10.8 ± 3.6	13.4 ± 4.2	0.001
Lymphocyte Count (×10⁹/L)	1.8 ± 0.7	1.2 ± 0.5	<0.001
NLR	6.5 (4.2–9.8)	11.8 (8.5–17.2)	<0.001

Non-survivors had significantly higher SOFA scores (10.4 ± 3.1 vs. 6.8 ± 2.5, p<0.001) and APACHE II scores (24.2 ± 5.3 vs. 17.6 ± 4.8, p<0.001) than survivors, reinforcing the prognostic utility of these established scoring systems. The need for life-sustaining therapies was also significantly greater among non-survivors, including mechanical ventilation (86.8% vs. 35.1%, p<0.001) and vasopressor use (100% vs. 39.2%, p<0.001) [Table 3].

Table 3: Severity Scores and Outcomes among Survivors and Non-Survivors.

Parameter	Survivors (n=74)	Non-survivors (n=38)	p-value
	Frequency (%)/mean ± SD/median (IQR)		
SOFA Score	6.8 ± 2.5	10.4 ± 3.1	<0.001
APACHE II Score	17.6 ± 4.8	24.2 ± 5.3	<0.001
ICU Stay (days)	8 (5–12)	5 (3–9)	0.009
Mechanical Ventilation	26 (35.1%)	33 (86.8%)	<0.001
Vasopressor Use	29 (39.2%)	38 (100%)	<0.001

All three indices—RDW, MPV, and NLR—showed statistically significant positive correlations with both SOFA and APACHE II scores (p<0.001). Among these, NLR demonstrated the strongest correlation with SOFA (r=0.588) and APACHE II (r=0.552), suggesting a robust association between elevated NLR and increased illness severity [Table 4].

Table 4: Correlation of Hematological Markers with SOFA and APACHE II Scores.

Marker	r (SOFA)*	p-value	r (APACHE II)*	p-value
RDW	0.446	<0.001	0.411	<0.001
MPV	0.403	<0.001	0.329	<0.001
NLR	0.588	<0.001	0.552	<0.001

*Spearman correlation coefficient (r)

NLR had the highest Area Under the Curve (AUC) at 0.846 (95% CI: 0.782–0.922), with a sensitivity of 81.6% and specificity of 81.1% at a cut-off of >9.0. RDW and MPV also demonstrated good predictive ability, with AUCs of 0.812 and 0.795 respectively. These findings indicate that all three parameters, particularly NLR, have substantial discriminative power in predicting sepsis mortality [Table 5].

Table 5: ROC Curve Analysis of RDW, MPV, and NLR for Predicting In-Hospital Mortality.

Parameter	AUC (95% CI)	Cut-off Value*	Sensitivity (%)	Specificity (%)	p-value
RDW (%)	0.812 (0.731–0.895)	>14.5	76.3	75.7	<0.001
MPV (fL)	0.795 (0.703–0.878)	>9.8	73.7	73.0	<0.001
NLR	0.846 (0.782–0.922)	>9.0	81.6	81.1	<0.001

*Cut-offs from Youden's Index.

An RDW >14.5% was associated with nearly threefold increased odds of mortality (AOR: 2.94, p=0.016), while MPV >9.8 fL (AOR: 2.57, p=0.028) and NLR >9.0 (AOR: 3.83, p=0.002) were also found to be independent predictors. Additionally, increasing SOFA (AOR: 1.29 per point, p<0.001) and APACHE II scores (AOR: 1.14 per point, p=0.006) remained strong predictors of mortality. Age >60 years showed a trend toward significance (p=0.061) but was not independently associated with mortality in the final model [Table 6].

Table 6: Multivariate Logistic Regression Analysis for Predictors of In-Hospital Mortality.

Variable	Adjusted Odds Ratio (95% CI)*	p-value
RDW >14.5%	2.942 (1.222–7.083)	0.016
MPV >9.8 fL	2.573 (1.113–5.928)	0.028
NLR >9.0	3.827 (1.633–8.957)	0.002
SOFA Score (per unit)	1.292 (1.131–1.489)	<0.001
APACHE II (per unit)	1.141 (1.046–1.265)	0.006
Age >60 years	2.188 (0.970–4.927)	0.061

*Multivariate logistic regression adjusted for age, sex, comorbidities.

DISCUSSION

In this prospective study of 112 sepsis patients admitted to a tertiary care intensive care unit, we evaluated the prognostic utility of three easily accessible hematological parameters: Red Cell Distribution Width (RDW), Mean Platelet Volume (MPV), and Neutrophil-to-Lymphocyte Ratio (NLR). The overall in-hospital mortality rate in our cohort was 33.9%, aligning with Indian and global estimates of sepsis mortality ranging between 25% and 45% depending on the setting and severity of illness.[13,14]

Our findings demonstrated that non-survivors were significantly older than survivors (62.9 ± 14.8 vs. 50.7 ± 15.4 years; p = 0.001), with a higher prevalence of diabetes mellitus (65.8% vs. 41.9%; p = 0.019) and chronic kidney disease (34.2% vs. 12.2%; p = 0.004). These comorbidities have previously been identified as independent risk factors for mortality in sepsis, as reported in multicentric studies by Shankar-Hari et al., and Kang et al., both of which emphasized the additive impact of pre-existing organ dysfunction on sepsis outcomes.[15,16] Respiratory infections were also more frequently implicated among non-survivors (55.3% vs. 32.4%; p = 0.023), a trend consistent with studies by Kao et al. and Li et al., which demonstrated higher mortality in pneumonia-related sepsis, likely due to acute respiratory failure and delayed diagnosis.[17,18]

The hematological indices under evaluation—RDW, MPV, and NLR—showed significant differences between survivors and non-survivors, suggesting their value as prognostic markers. Elevated RDW, observed in non-survivors (15.3 ± 1.5%) compared to survivors (13.8 ± 1.2%; p < 0.001), reflects anisocytosis and underlying oxidative stress, inflammation, and bone marrow dysfunction in critically ill patients.[19] These findings corroborate previous studies by Jandial et al., and Wu et al., which reported RDW as a strong independent predictor of 30-day mortality in sepsis patients, particularly when RDW exceeded 14.5%.[19,20] Our multivariate analysis further confirmed this association, with RDW >14.5% yielding an adjusted odds ratio (AOR) of 2.94 (95% CI: 1.22–7.08; p = 0.016), supporting its inclusion in early sepsis risk stratification.[20]

Mean Platelet Volume (MPV), a marker of platelet activation and turnover, was also significantly higher in non-survivors (10.5 ± 1.3 fL) than in survivors (9.4 ± 1.0 fL; p < 0.001). This finding is consistent with studies by Vardon-Bounes et al., and van Vught et al., who reported elevated MPV as a reflection of consumptive coagulopathy and inflammatory endothelial injury associated with worse sepsis outcomes.[21,22] The pathophysiological basis lies in the fact that activated platelets are larger, metabolically more active, and contribute to microvascular thrombosis and organ dysfunction—hallmarks of severe sepsis. Our analysis revealed MPV >9.8 fL to be an independent predictor of mortality (AOR: 2.57; 95% CI: 1.11–5.93; p = 0.028), reinforcing its clinical significance.[22]

The Neutrophil-to-Lymphocyte Ratio (NLR) emerged as the strongest predictor among the three markers. Median NLR was markedly elevated in non-survivors (11.8 [IQR: 8.5–17.2]) compared to survivors (6.5 [4.2–9.8]; p < 0.001). Elevated NLR reflects an exaggerated innate immune response (neutrophilia) and impaired adaptive immunity (lymphopenia), both critical drivers of sepsis-related immunopathology. Several studies, including those by Spoto et al., Li et al., and Liu et al., have demonstrated the prognostic accuracy of NLR in predicting mortality in sepsis and septic shock.[23-25] In our study, NLR >9.0 showed excellent discriminative ability for mortality with an AUC of 0.846 (95% CI: 0.782–0.922), 81.6% sensitivity, and 81.1% specificity. Moreover, it remained an independent predictor in multivariate regression (AOR: 3.83; 95% CI: 1.63–8.95; p = 0.002). Given its high predictive value and cost-effectiveness, NLR could serve as a bedside screening tool in triaging high-risk sepsis patients, especially in resource-constrained settings.[25]

The correlation analysis revealed statistically significant positive correlations between all three markers and the SOFA and APACHE II scores, which are established predictors of sepsis severity and mortality. NLR demonstrated the strongest correlation with SOFA (r = 0.588) and APACHE II (r = 0.552; p < 0.001), reinforcing its role as a reliable proxy for illness severity.[26] Similar correlations were noted by Chung et al., and Drăgoescu et al., who suggested incorporating NLR and MPV into early warning scores to improve prognostic accuracy.[26,27]

Our ROC curve analysis demonstrated good overall performance for all three markers, with RDW (AUC = 0.812), MPV (AUC = 0.795), and NLR (AUC = 0.846) showing strong discriminative power. These findings are comparable to a study by Lin et al., where NLR >10 was associated with high sensitivity and specificity for 28-day sepsis mortality.[28] The utility of these markers is particularly noteworthy considering their availability from routine complete blood counts (CBCs), which are inexpensive and universally accessible—even in peripheral and district hospitals across India.[29]

While SOFA and APACHE II scores continue to be valuable for prognosis, their calculation requires detailed physiological and laboratory parameters. In contrast, hematological indices like RDW, MPV, and NLR offer rapid, low-cost, and widely reproducible alternatives or adjuncts to existing scoring systems. Notably, the inclusion of these indices could enhance early risk stratification, enable timely escalation of care, and improve clinical outcomes.[30]

Limitations: Our study has several strengths, including prospective design, adjustment for known confounders, and robust statistical analysis. However, certain limitations must be acknowledged. First, being a single-center study limits the

generalizability of findings. Second, serial measurements of RDW, MPV, and NLR were not performed, which could have provided insights into their dynamic trends during clinical progression or recovery. Third, other biomarkers such as procalcitonin, CRP, or IL-6 were not evaluated in parallel due to resource constraints. Future multicentric studies incorporating these markers and assessing serial trends may better define their additive value in sepsis management algorithms.

CONCLUSION

In conclusion, our study demonstrates that elevated RDW, MPV, and especially NLR are significantly associated with sepsis severity and in-hospital mortality. These hematological indices, derived from routine CBCs, are cost-effective, readily available, and independently predictive of poor outcomes. Their integration into early warning systems and triage protocols may substantially improve sepsis care, particularly in resource-limited settings like India.

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