Section: General Medicine

Original Research Article

ASSOCIATION OF RED CELL DISTRIBUTION WIDTH-TO-PLATELET RATIO (RPR) AND MORTALITY IN SEPSIS PATIENTS AND COMPARING ITS PREDICTABILITY WITH APACHE IV SCORING SYSTEM

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ABSTRACT

Background: Sepsis is a life-threatening condition with significant mortality in intensive care settings that requires effective prognostic tools to guide management. The RPR and APACHE IV scoring systems are potential predictors of outcomes in patients with sepsis. This study aimed to assess the relationship between RPR and mortality in patients with sepsis and compare its predictive value with that of the APACHE IV scoring system. **Materials and Methods:** This hospital-based cross-sectional study included 84 patients from Sri Manakula Vinayagar Medical College and Hospital over six months. Data on RPR, APACHE IV scores, demographics, ICU duration, and in-hospital mortality were obtained. **Result:** The mean age of sepsis patients was 61.7 ± 13.2 years, with 66.6% aged 51–75 years. Males comprised 63% of cases. Overall survival was 75%, with females (87%) having a higher survival rate than males (68%, p = 0.05). Mortality increased with rising RPR levels, from 11% (low RPR) to 47.1% (high RPR, p = 0.04). Similarly, higher APACHE IV scores were associated with increased mortality, from 2.5% (low risk) to 83.3% (very high risk, p = 0.00). Regression analysis confirmed significant associations between RPR (B = 1.57, p = 0.04) and APACHE IV score (B = 5.33, p = 0.00) with mortality, highlighting the predictive strength of APACHE IV over RPR. **Conclusion:** APACHE IV outperformed RPR as a predictor of mortality in sepsis, although RPR is a simple and cost-effective marker. These findings suggest a complementary role for RPR alongside APACHE IV in prognostic assessments.

INTRODUCTION

Sepsis is a life-threatening condition due to a dysregulated host immune response to infection that leads to organ dysfunction. It is one of the leading causes of death in intensive care units and emergency departments.[1] Severity and outcome of sepsis can be assessed using various biomarkers, including single- and multiple-parameter markers such as lactic acid, chloride, neutrophil-to-albumin ratio, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratio.[2] Furthermore, several scoring systems such as Acute Physiology Score III, Sequential Organ Failure Assessment, and Simplified Acute Physiology Score II are widely applied.[2] However, single-parameter biomarkers are typically subject to drug effects, malignancies, and immune disorders and thus lack good predictive accuracy.[3] Similarly, most multiparameter biomarkers are not practically useful due to their low sensitivity and specificity.[4]

Red cell distribution width (RDW) indicates the range of RBC size. Clinically significant elevation of RDW occurs in several conditions, such as AKI, critical trauma, and acute respiratory distress syndrome.[5] Research has shown that RDW is highly correlated with the prognosis of these conditions. Platelets, which are derived from megakaryocytes in the bone marrow, play a vital role in haemostasis. Evidence has shown that septic patients who have low platelet counts on admission have worse illness and higher mortality than patients with normal platelet counts.[6] Additionally, thrombocytopenia is an independent risk factor for adverse sepsis outcomes.[7] Both RDW and platelet variation are

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central elements in the pathophysiology of sepsis, so they are related, not mutually exclusive.

A CBC is the most common and cheapest laboratory test for hospitals. RDW, as a parameter of CBC, quantifies RBC volume heterogeneity and is used to classify anaemia. Elevated RDW is recognised as an inflammatory marker and indicates unfavourable outcomes in a number of diseases.[8] Impairment of haematopoiesis is frequent in sepsis, where systemic infection and inflammation lead to increased peripheral erythrocyte destruction and reduced bioavailability of iron, both of which are causally associated with sepsis-related anaemia.[9,10] The Acute Physiology and Chronic Health Evaluation IV system is a strong tool that considers physiological monitoring, laboratory variables, and chronic health factors to ascertain the severity of illness. It also accounts for demographic factors such as age, sex, and admission type. The APACHE IV model enhances predictive effectiveness by accounting for alterations in medical practice.[11]

Aim

This study aimed to evaluate the relationship between the red cell distribution width-to-platelet ratio (RPR) and mortality in patients with sepsis, while also comparing its predictive value against the APACHE IV scoring system.

MATERIALS AND METHODS

This hospital-based cross-sectional study included 84 patients from the Department of General Medicine at Sri Manakula Vinayagar Medical College and Hospital, Puducherry, over six months from January 2024 to June 2024. The study protocol was approved by the Internal Human Ethics Committee (EC Code No: 135/2024). Written informed consent was obtained from all patients before their enrolment.

Inclusion and exclusion criteria

Patients aged ≥18 years who met the sepsis-3 criteria were included. Patients with an ICU stay of < 24 h, pregnant patients, and those readmitted to the ICU within one week were excluded.

Methods

Data collection involved patients who met the Sepsis-3 criteria for assessing outcome parameters, including ICU stay duration and in-hospital mortality. The RDW, platelet ratio, and APACHE IV score were determined for each patient. The correlation between the scoring system and the mortality rate was analysed.

Statistical analysis

Data was input into EpiInfo software (version 7.2) and analyzed using SPSS software (version 28). Categorical variables are presented as frequencies and percentages, while continuous variables are expressed as mean±SD. Independent sample t-tests were performed to compare continuous variables.

RESULTS

The mean age of the patients with sepsis was 61.7 ± 13.2 years. The majority of patients were aged 51–75 years (66.6%), followed by 25–50 years (22.6%), and >75 years (10.8%). In terms of sex, 53 (63%) were men and 31 (37%) were women [Table 1].

Table 1: Demographic and outcome characteristics

		N (%)
Age (years)	25–50	19 (22.6%)
	51–75	56 (66.6%)
	>75	9 (10.8%)
Gender	Male	53 (63%)
	Female	31 (37%)
Mortality	Survived	63 (75%)
	Died	21 (25%)

The highest percentage was observed in the 25–50 age group (79%), followed by >75 years (77.8%) and 51–75 years (73.2%), with no significant association (p = 0.86). Females (87%) showed a higher survival rate than males (68%), with a borderline significant association (p = 0.05). Survival rates decreased with increasing RPR levels, from 89% (low) to 79.3% (moderate) and 52.9% (high), with high RPR associated with greater mortality (47.1%) and borderline significance (p = 0.04). Similarly, survival rates decreased as APACHE IV risk increased, from 97.5% (low risk) to 81% (moderate risk), 45.5% (high risk), and 16.7% (very high risk), with mortality significantly higher in the very high-risk group (83.3%, p = 0.00) [Table 2].

Table 2: Association of age, gender, RPR, and APACHE IV score with mortality

		Mortality N (%)		P-value
		Survived	Died	
Age in years	25-50	15 (79%)	4 (21%)	0.86
	51-75	41 (73.2%)	15 (26.8%)	
	>75	7 (77.8%)	2 (22.2%)	
Gender	Male	36 (68%)	17 (32%)	0.05
	Female	27 (87%)	4 (13%)	
RPR	Low (<0.003)	8 (89%)	1 (11%)	0.04
	Moderate (0.003-0.01)	46 (79.3%)	12 (20.7%)	
	High (>0.01)	9 (52.9%)	8 (47.1%)	

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APACHE IV	Low risk (<10%)	39 (97.5%)	1 (2.5%)	0.00
	Moderate risk (10-25%)	17 (81%)	4 (19%)	
	High risk (25-50%)	5 (45.5%)	6 (54.5%)	
	Very high risk (>50%)	2 (16.7%)	10 (83.3%)	

Regression analysis showed that RPR (B=1.57, p=0.04) was significantly associated with outcomes, whereas the APACHE IV score (B=5.33, p=0.00) demonstrated a strong significant association [Table 3].

Table 3: Regression analysis of RPR and APACHE IV Score with mortality outcomes

	B coefficient	P-value
RPR	1.57	0.04
APACHE IV score	5.33	0.00

DISCUSSION

Our study found a mean age of 61.7 ± 13.2 years among patients with sepsis, with the majority (66.6%) aged 51–75 years, followed by 22.6% aged 25–50 years and 10.8% aged >75 years. Males comprised 63% of the study population, and the overall mortality rate was 25%. These demographic characteristics align with those of several prior studies. For example, Varma et al. reported a mean age of 51.32 ± 16.98 years in a study of 200 patients with sepsis, with 57.5% males, though their 30-day mortality rate was higher at 57%. The higher mortality may reflect differences in disease severity or healthcare settings, as their mean APACHE II score (22.49 ± 5.72) suggests a sicker population compared to ours.12 Similarly, Li et al. included 9743 sepsis patients with a male predominance.[13]

Our finding of a 25% overall mortality rate is lower than that of some studies, such as Ren et al., who reported higher 28-day mortality rates in pulmonary sepsis (versus abdominal sepsis),[14] and Zhou et al., where mortality reached 85.8% in the high RPR group. This discrepancy could be attributed to differences in patient populations, sepsis aetiology, or the timing of interventions.[1] Notably, our study observed a higher survival rate in females (87%) than in males (68%, p = 0.05). This borderline significant sex difference warrants further exploration, potentially reflecting physiological or immunological differences in the response to sepsis.

We observed a clear gradient in mortality with increasing RPR levels: low RPR (<0.003) was associated with 11% mortality, moderate RPR (0.003–0.01) with 20.7%, and high RPR (>0.01) with 47.1% (p = 0.04). Regression analysis confirmed a borderline significant association (B = 1.57, p = 0.04), suggesting that RPR is a potential biomarker for risk stratification. This finding is consistent with those of several previous studies. Ge et al. found RPR independently correlated with 28-day mortality (HR = 1.04 per 0.1 increase, p < 0.001), with worse survival in the high-RPR group (≥0.134).8 Similarly, Zhou et al. reported a strong association between elevated RPR and 28-day mortality (HR = 1.896, p < 0.001) in a propensity-matched analysis of the MIMIC-IV database.[1] Li et al. also noted a positive correlation between RPR and mortality rates in critically ill patients experiencing acute myocardial infarction (HR = 1.63, p = 0.0357), covering RPR's relevance beyond sepsis.[15]

However, our findings contrast with those of Varma et al., where RDW (a component of RPR) showed a hierarchical association with 30-day mortality but was not an independent predictor when adjusted for APACHE II, serum albumin, and other factors.12 This discrepancy from our use of RPR (RDW-to-platelet ratio) rather than RDW alone suggests that the inclusion of platelet count enhances prognostic utility. Lorente et al. further supports the prognostic role of RDW, finding higher levels in non-survivors across multiple time points, correlating with disease severity (SOFA score) and inflammation markers (TNF-α).[16] Our study extends this by demonstrating RPR's specific association with mortality, supporting its potential as a composite biomarker.

Our research identified a significant link between APACHE IV scores and mortality, with survival decreasing across risk categories: 97.5% at low risk (<10%), 81% at moderate risk (10–25%), 45.5% at high risk (25–50%), and 16.7% at very high risk (>50%) (p = 0.00). Regression analysis confirmed the predictive strength (B = 5.33, p = 0.00). This is consistent with previous research. Liu et al. reported that an APACHE II score ≥15, combined with plasma suPAR, independently predicted unfavourable outcomes in sepsis.[17] While, Kalaiselvan et al. found APACHE IV outperformed APACHE II in discriminative power (AUC 0.82 vs. 0.75), though both had poor calibration.[18] Li et al. also noted that RDW's association with mortality persisted regardless of APACHE IV scores, suggesting complementary roles.[13]

Ren et al. further support APACHE II's utility, identifying it as an independent predictor of 28-day mortality in both pulmonary and abdominal sepsis, though pulmonary sepsis showed higher mortality overall.[14] Zangmo et al. validated APACHE IV's role in predicting ICU length of stay (LOS). However, they emphasised its poor correlation with actual LOS (R^2 = 0.02, p < 0.001), suggesting limitations.[19] Our study found that APACHE IV outperforms RPR in predictive strength, aligning with these studies and emphasising its robustness as a severity-of-illness scoring system, although its application may be context-specific.

In our study, both RPR and APACHE IV were associated with mortality, but APACHE IV

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demonstrated a greater predictive power. This contrasts with studies by Ge et al. and Zhou et al., where RPR's prognostic value of RPR was emphasised, potentially reflecting differences in study design (e.g. retrospective vs. prospective) or patient heterogeneity.[1,8] Our findings suggest that while RPR is a simple, cost-effective biomarker derived from routine blood counts, APACHE IV's comprehensive assessment of physiological parameters offers superior discrimination. The borderline significance of RPR ($p = 0.04$) versus the strong significance of APACHE IV ($p = 0.00$) underscores this disparity.

Compared with RDW-focused studies, Li et al. and Lorente et al. reported that RPR's inclusion of platelet count may capture additional pathophysiological aspects of sepsis, such as thrombocytopenia or microcirculatory dysfunction, enhancing its utility over RDW alone. However, its weaker association compared to APACHE IV suggests that it may serve best as an adjunct rather than a standalone predictor.[13,16] The sex difference in survival (females 87% vs. males 68%) is a novel observation not widely reported in prior studies, meriting further investigation into sex-specific sepsis outcomes.

CONCLUSION

The APACHE IV system demonstrates superior predictive accuracy, reflecting its comprehensive integration of physiological and clinical parameters, whereas RPR provides a practical, readily available biomarker derived from routine blood counts. The observed sex disparity in survival emphasises the need for further investigation into potential sex-specific differences in sepsis outcomes. Although the RPR captures critical aspects of sepsis pathophysiology, its utility is maximised when used in conjunction with more robust tools, such as APACHE IV. These results support an integrated approach to risk stratification in clinical practice, combining the accessibility of RPR with the detailed precision of APACHE IV to optimise sepsis management and improve patient outcomes.

REFERENCES

1. Zhou Y, Zhong L, Chen W, Liang F, Liao Y, Zhong Y. Enhanced red blood cell distribution width to platelet ratio is a predictor of mortality in patients with sepsis: a propensity score matching analysis based on the MIMIC-IV database. BMJ Open 2022;12: e062245. https://doi.org/10.1136/bmjopen-2022-062245.
2. 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: e022896. https://doi.org/10.1136/bmjopen-2018-022896.
3. Jia L, Cui S, Yang J, Jia Q, Hao L, Jia R, et al. Red blood cell distribution width predicts long-term mortality in critically ill patients with acute kidney injury: a retrospective database study. Sci Rep 2020; 10:4563. https://doi.org/10.1038/s41598-020-61516-y.
4. Liu J, Huang X, Yue S, Wang J, Ye E, Huang J, et al. Association of red cell distribution width-to-platelet ratio and mortality in patients with sepsis. Mediators Inflamm 2022; 2022:4915887. https://doi.org/10.1155/2022/4915887.
5. Wang B, Gong Y, Ying B, Cheng B. Relation between red cell distribution width and mortality in critically ill patients with acute respiratory distress syndrome. Biomed Res Int 2019; 2019:1942078. https://doi.org/10.1155/2019/1942078.
6. Burunsuzoğlu B, Saltürk C, Karakurt Z, Öngel EA, Takır HB, Kargın F, et al. Thrombocytopenia: A risk factor of mortality for patients with sepsis in the intensive care unit. Turk Thorac J 2016; 17:7–14. https://doi.org/10.5578/ttj.17.1.002.
7. Claushuis TAM, van Vught LA, Scicluna BP, Wiewel MA, Klein Klouwenberg PMC, Hoogendijk AJ, et al. Thrombocytopenia is associated with a dysregulated host response in critically ill sepsis patients. Blood 2016; 127:3062–72. https://doi.org/10.1182/blood-2015-11-680744.
8. Ge S, Lin S, Zhang L, Zeng M. The association of red blood cell distribution width to platelet count ratio and 28-day mortality of patients with sepsis: A retrospective cohort study. Ther Clin Risk Manag 2020; 16:999–1006. https://doi.org/10.2147/TCRM.S268523.
9. Bateman R, Sharpe M, Singer M, Ellis C. The effect of sepsis on the erythrocyte. Int J Mol Sci 2017; 18:1932. https://doi.org/10.3390/ijms18091932.
10. Ekregbesi P, Shankar-Hari M, Bottomley C, Riley EM, Mooney JP. Relationship between Anaemia, Haemolysis, Inflammation and Haem Oxygenase-1 at Admission with Sepsis: a pilot study. Sci Rep 2018;8. https://doi.org/10.1038/s41598-018-29558-5.
11. Friedman G, Silva E, Vincent JL. Has the mortality of septic shock changed with time? Crit Care Med 1998; 26:2078–86. https://doi.org/10.1097/00003246-199812000-00045.
12. Varma S, Varma N, Jandial A, Kumar S. Elevated red cell distribution width as a prognostic marker in severe sepsis: A prospective observational study. Indian J Crit Care Med 2017; 21:552–62. https://doi.org/10.4103/ijccm.ijccm_208_17.
13. Li Y, She Y, Fu L, Zhou R, Xiang W, Luo L. Association between red cell distribution width and hospital mortality in patients with sepsis. J Int Med Res 2021; 49:3000605211004221. https://doi.org/10.1177/03000605211004221.
14. Ren E, Xiao H, Li J, Yu H, Liu B, Wang G, et al. Clinical characteristics and predictors of mortality differ between pulmonary and abdominal sepsis. Shock 2023; 60:42–50. https://doi.org/10.1097/SHK.0000000000002151.
15. Tong L, Liu Y-Q, Shen JH, B O M, Zhou Q, Duan X-J, et al. Relationship between the red cell distribution width-to-platelet ratio and in-hospital mortality among critically ill patients with acute myocardial infarction: a retrospective analysis of the MIMIC-IV database. BMJ Open 2022;12: e062384. https://doi.org/10.1136/bmjopen-2022-062384.
16. Lorente L, Martín MM, Abreu-González P, Solé-Violán J, Ferreres J, Labarta L, et al. Red blood cell distribution width during the first week is associated with severity and mortality in septic patients. PLoS One 2014;9: e105436. https://doi.org/10.1371/journal.pone.0105436.
17. Liu X, Shen Y, Li Z, Fei A, Wang H, Ge Q, et al. Prognostic significance of APACHE II score and plasma suPAR in Chinese patients with sepsis: a prospective observational study. BMC Anesthesiol 2016; 16:46. https://doi.org/10.1186/s12871-016-0212-3.
18. Varghese YE, Kalaiselvan MS, Renuka MK, Arunkumar AS. Comparison of acute physiology and chronic health evaluation II (APACHE II) and acute physiology and chronic health evaluation IV (APACHE IV) severity of illness scoring systems, in a multidisciplinary ICU. J Anaesthesiol Clin Pharmacol 2017; 33:248–53. https://doi.org/10.4103/0970-9185.209741.
19. Zangmo K, Khwannimit B. Validating the APACHE IV score in predicting length of stay in the intensive care unit among patients with sepsis. Sci Rep 2023; 13:5899. https://doi.org/10.1038/s41598-023-33173-4.

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