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ORIGINAL ARTICLE

Red Cell Distribution Width to Albumin Ratio (RAR) versus Red Cell Distribution Width to Platelet Ratio (RPR) as Predictors of 28-Day Mortality in Sepsis Patients

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Abstract

Background: Sepsis is a leading cause of mortality in the Intensive Care Unit (ICU). Early identification of high-risk patients requires simple and accessible prognostic biomarkers. The Red Cell Distribution Width to Albumin Ratio (RAR) and Red Cell Distribution Width to Platelet Ratio (RPR) have been proposed as potential biomarkers.

Methods: This prospective cohort study was conducted in the ICU of Dr. Hasan Sadikin General Hospital, Bandung, from July to September 2025, involving 71 subjects who met the Sepsis-3 criteria. RAR and RPR values were calculated from blood tests within the first 24 hours of ICU admission. The primary outcome was 28-day mortality. Statistical analysis used the Receiver Operating Characteristic (ROC) curve to determine the cut-off value, sensitivity, specificity, and Area Under the Curve (AUC). The AUC comparison between RAR and RPR was analyzed using the DeLong test.

Results: A total of 41 patients (57.7%) experienced 28-day mortality. The optimal cut-off value for RAR was 5.7404 (Sensitivity 85.4%; Specificity 73.3%) with an AUC of 89.3% (95% CI: 79.8–95.4%). The optimal cut-off value for RPR was 0.0627 (Sensitivity 75.6%; Specificity 76.7%) with an AUC of 74.7% (95% CI: 63.0–84.3%). RAR had a significantly better discriminatory value than RPR (p=0.026).

Discussion: The RAR value is a better predictor of 28-day mortality than the RPR value in septic patients treated in the ICU.

Conclusion: RAR can be considered a simple and effective prognostic tool for the early risk stratification of septic patients.

Keywords: ICU; mortality; red cell distribution width to albumin ratio ; red cell distribution width to platelet ratio; sepsis

Introduction

Sepsis remains a major global health challenge and continues to be one of the leading causes of death in critically ill patients. It is characterized by a life-threatening organ dysfunction that arises from an abnormal and uncontrolled host response to infection, often progressing rapidly to septic shock or multiple organ failure if not treated promptly.[1] Even with significant advances in intensive care medicine, sepsis continues to account for substantial morbidity and mortality worldwide. Reports suggest that death rates among septic patients in the intensive care unit (ICU) may reach between 30% and 60%, depending on disease severity

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and associated comorbidities.[2,3] Such figures highlight the urgent need for reliable, practical, and easily obtainable prognostic markers that can assist clinicians in recognizing high- risk patients early and tailoring management accordingly.

Prognostic assessment in sepsis often relies on clinical scoring systems such as the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II). While these tools are valuable, their complexity and reliance on numerous physiological and laboratory variables can make them cumbersome, particularly in emergency or resource-limited settings.[4,5]

This limitation has encouraged growing interest in identifying simpler, cost-effective biomarkers that can still provide meaningful prognostic information. Among these, the Red Cell Distribution Width (RDW) has attracted considerable attention. Higher RDW values have been linked to systemic inflammation, oxidative stress, and poor clinical outcomes in patients with sepsis and other critical illnesses.[6,7] Similarly, serum albumin and platelet count are long-recognized indicators of inflammation and disease severity, both of which have been shown to correlate with prognosis in septic patients.[8,9]

In recent years, novel indices that combine these laboratory markers, such as the Red Cell Distribution Width-to-Albumin Ratio (RAR) and Red Cell Distribution Width-to-Platelet Ratio (RPR), have been proposed to improve predictive accuracy. These ratios offer a more integrated view of patients' inflammatory and nutritional status while maintaining simplicity and accessibility.[10-12]

Several studies have demonstrated that both RAR and RPR may serve as useful prognostic markers in various critical illnesses, including sepsis. However, comparative evidence evaluating their predictive performance in ICU patients remains limited, particularly within the Indonesian healthcare context.

The present study was conducted to compare the RAR and RPR as predictors of 28-day mortality among septic patients admitted to the Intensive Care Unit of Dr. Hasan Sadikin General Hospital, Bandung. By identifying which index provides better prognostic accuracy, this study aims to provide practical evidence supporting early risk stratification and improving outcome prediction for patients with sepsis in critical care settings.

Subjects and Methods

This study employed a prospective cohort design and was carried out in the Intensive Care Unit (ICU) of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. The research took place over three months, from July to September 2025. The ICU serves as a tertiary referral center for critically ill patients from across West Java Province, offering a comprehensive, multidisciplinary approach to intensive care management.

The study population included adult patients diagnosed with sepsis according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). All patients aged 18 years or older who were admitted to the ICU during the study period and fulfilled the diagnostic criteria were screened for eligibility.

Patients were included if they had complete hematological and biochemical test results obtained within the first 24 hours of ICU admission, and if the patient or their legal guardian provided informed consent. Exclusion criteria included pre-existing hematologic disorders, liver failure, end-stage renal failure, active malignancy or incomplete medical records. Each subject was monitored for 28 days following ICU admission, or until death, whichever occurred first.

The minimum sample size was calculated a priori to compare the areas under the receiver operating characteristic (ROC) curves of two prognostic indices. Using the method described by Hanley and McNeil for comparing two AUCs, and assuming an expected AUC of 0.80 for RAR, a null hypothesis AUC of 0.65 (minimal acceptable discrimination), a two-sided type I error (α) of 0.05, and a statistical power (1-β) of 80%, a minimum of 64 subjects was required. To account for potential data incompleteness or exclusions, we enrolled 71 subjects meeting all inclusion criteria.

Eligible patients were selected using consecutive sampling during the study period. Because this was an observational cohort study, no randomization or intervention was applied. Participants were classified into survivor and non-survivor groups based on their outcomes 28 days after ICU admission. Blood samples for routine laboratory examination were collected within the first 24 hours of ICU admission. To ensure accuracy and minimize measurement bias, all analyses were conducted in the hospital's central laboratory using standardized equipment and protocols.

Hematological parameters, including RDW and platelet count, were measured with an automated hematology analyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan). Serum albumin levels were determined using the bromocresol green method on a biochemistry analyzer (Cobas 6000, Roche Diagnostics, Mannheim, Germany). Similarly, to prevent assessment bias in the primary outcome, 28-day mortality was verified by two independent researchers through a review of electronic medical records.

RAR was calculated by dividing RDW (%) by the serum albumin concentration (g/dL), while RPR was obtained by dividing RDW (%) by the platelet count ($\times 10^9$/L). The primary outcome of interest was 28-day mortality. Additional data, including demographic characteristics and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, were recorded from medical charts.

Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA) and MedCalc version 22.014 (MedCalc Software Ltd., Ostend, Belgium). Continuous data were presented as means with standard deviations or medians with interquartile ranges, as appropriate. Categorical variables were summarized as frequencies and percentages. ROC curve analysis was used to identify the optimalcut-off values, sensitivity, specificity, and area under the curve (AUC) for both RAR and RPR in predicting 28-day mortality. The comparison of AUCs between RAR and RPR was performed using the DeLong test, a nonparametric test for comparing correlated ROC curves. Statistical significance was set at a two-tailed p-value of less than 0.05. Given the sample size of this preliminary cohort study, a multivariable regression analysis to provide confounder-adjusted estimates (e.g., adjusted odds ratios) was not performed. The primary analysis, therefore, focuses on comparing the unadjusted discriminatory performance of RAR and RPR using ROC curve analysis.

Ethical approval was granted by the Health Research Ethics Committee of the Dr. Hasan Sadikin General Hospital, Bandung (Approval No. 743/UN6.KEP/EC/2025). Written informed consent was obtained from each participant or their legal representative before inclusion. All patient data were treated confidentially and anonymized before analysis to maintain privacy and compliance with ethical research standards.

All patients received standard sepsis management according to the 2021 Surviving Sepsis Campaign (SSC) guidelines, including timely fluid resuscitation, vasopressor therapy, empiric antibiotics, and organ support, such as mechanical ventilation, when clinically indicated. No experimental or off-protocol treatments were administered during the study period.

Results

Between July and September 2025, 86 sepsis patients admitted to the ICU were screened. Of these, 71 met the inclusion criteria and were enrolled in the final analysis. Fifteen patients were excluded for the following reasons: pre-existing hematologic disorders (n=2), liver failure (n=2), end-stage renal failure (n=5), active malignancy (n=5), and incomplete medical records (n=1). All enrolled subjects were followed for 28 days or until death, with no loss to follow-up and no missing data for the

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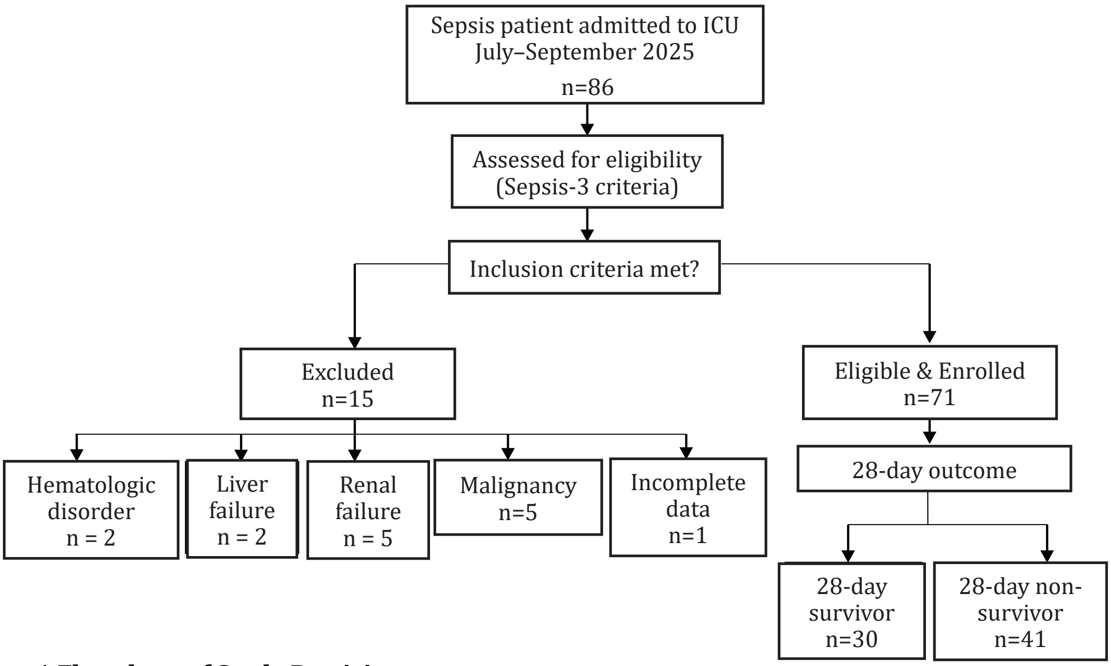

Figure 1 Flowchart of Study Participants

primary variables (RDW, albumin, platelets) or the primary outcome. At the end of the follow-up period, 30 patients (42.3%) had survived, and 41 patients (57.7%) had died.

The demographic and clinical characteristics of the study population are summarized in Table 1. The mean age of the participants was 56.58±16.3 years, and slightly more than half were male (54.9%).

The most common comorbidity was hypertension (18.3%), followed by diabetes mellitus (14.1%), stroke (7%), heart disease (4.2%) and COPD (2.8%). The median body mass index was 22.6 (IQR 14.5–31.1), while the mean APACHE II score was 15.96 ± 7.902, indicating a generally severe illness burden among the cohort.

When comparing the two outcome groups (Table 2), non-survivors had significantly higher RAR, RPR, and APACHE II scores ($p < 0.05$). The mean RAR among non-survivors was 8.36±3.347 (IQR 4.79–22.97), compared with 5.18±0.901 (IQR 3.25–7.2) in survivors (p=0.0001). Similarly, RPR was significantly higher in non-survivors, with a mean value of 0.15±0.111 (IQR 0.02–1.06) versus 0.06±0.049 (IQR 0.03–0.027) among survivors (p=0.0001). These findings indicate that patients who did not survive tended to have more pronounced hematologic abnormalities related to inflammation and coagulation during the early phase of sepsis and a higher APACHE II score.

Analysis of potential confounding variables listed in Table 3 did not demonstrate a statistically significant association with 28- day mortality (all p>0.05). The mean age between non-survivors (57.24±16.32 years) and survivors (55.67±16.50 years) was comparable (p=0.553), suggesting that age was not a significant determinant of outcome in this study population. Similarly, gender distribution did not differ significantly between groups (p=0.089). Furthermore, an analysis of common comorbidities revealed no significant statistical relationships with mortality. This includes hypertension (p=0.354), diabetes mellitus (p=0.502), a history of stroke or heart disease, and Chronic Obstructive Pulmonary Disease (COPD, p=1.000). Although numerical

Table 1 Baseline Characteristics of Patients with Sepsis Admitted to The ICU

Variable	n=71
Age (years)	
Mean±Std	56.58±16.300
Median	59.00
Range (min-max)	25.00–84.00
Gender	
Male	39 (54.9%)
Female	32 (45.1%)
RAR	
Mean±Std	7.02±3.040
Median	5.99
Range (min-max)	3.25–22.97
RPR	
Mean±Std	0.11±0.108
Median	0.07
Range (min-max)	0.02–1.06
APACHE II Score	
Mean±Std	15.96±7.902
Median	16.00
Range (min-max)	6.00–41.00
Comorbidities	
Diabetes melitus	10 (14.1%)
Hypertension	13 (18.3%)
Cardiac disease	3 (4.2%)
Stroke	5 (7.0%)
COPD	2 (2.8%)
Body Mass Index (BMI)	
Mean±Std	22.69±3.660
Median	22.60
Range (min-max)	14.50–31.10
Nutritional status	
Undernourished	13 (18.3%)
Normal	40 (56.3%)
Overweight	12 (16.9%)
Obese	6 (8.5%)
Albumin administration	
Yes	0 (0.0%)
No	71 (100.0%)

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Table 1 (Continue)

Variable	n=71
Blood product transfusion	
Yes	11 (15.5%)
No	60 (84.5%)
Vasopressor usage	
Yes	27 (38.0%)
No	44 (62.0%)
Septic shock	
Yes	27 (38.0%)
No	44 (62.0%)
Mortality	
Yes	41 (57.7%)
No	30 (42.3%)

Note: Categorical data are presented as counts/frequencies and percentages, while numerical data are presented as mean, median, standard deviation, and range

trends, such as a higher prevalence of hypertension and diabetes in the non-survivor group, were observed, these differences did not reach statistical significance. Other factors, including nutritional status/Body Mass Index (BMI) (p=0.348) and a history of blood transfusion before ICU admission (p=0.335), also showed no significant association with patient outcomes.

The ability of both indices to predict 28- day mortality was further evaluated using Receiver Operating Characteristic (ROC) curveanalysis (Table 4). The area under the curve (AUC) for RAR was 89.3% (95% CI: 79.8%–95.4%), reflecting excellent discriminative performance. The optimal cut-off point for RAR was 5.7404, which provided a sensitivity of 85.4% and a specificity of 73.3% for predicting mortality. Similarly, RPR showed a strong predictive capacity, with an AUC of 74.7% (95% CI: 63%–84.3%).

The best cut-off value for RPR was 0.0627, giving a sensitivity of 75.6% and a specificity of 76.7%. The APACHE II score also demonstrated good discriminative performance as a prognostic benchmark, with an AUC of 83.2% (95% CI: 72.5%–91.0%). Its optimal cut-off was 14, yielding a sensitivity of 80.5% and a specificity of 73.3%.

When RAR and RPR ROC curves were compared using the DeLong test (Table 5), the AUC difference was significant

Table 2 Comparison of Mean RAR, RPR and APACHE II Score between Survivors and Non-Survivors.

Outcome	RAR	RPR	APACHE II score
Survivors (n = 30)	5.18 ± 0.901 (3.25–7.2)	0.06 ± 0.049 (0.03–0.27)	10.97 ± 5.203 (6.00–22.00)
Non-survivors (n = 41)	8.36 ± 3.347 (4.79–22.97)	0.15 ± 0.111 (0.02–1.06)	19.61 ± 7.569 (10.00–41.00)
P value	0.0001**	0.0001**	0.0001**

Note: Values are presented as mean ± standard deviation or median (interquartile range); *p < 0.05 indicates statistical significance; **indicate p < 0.01 (highly statistically significant difference); Statistical tests: Independent t-test or Mann–Whitney U test, as appropriate

Table 3 Analysis of Potential Confounding Variables

Variable	Non-survivors (n=41)	Survivors (n=30)	p-value
Age (years)			0.553
Mean±Std	57.24 ± 16.321	55.67 ± 16.504	
Median	60.00	55.00	
Range (min-max)	25.00–83.00	26.00–84.00	
Gender			0.089
Male	19 (46.3%)	20 (66.7%)	
Female	22 (53.7%)	10 (33.3%)	
Comorbidities			
Diabetes melitus	7 (17.1%)	3 (10.0%)	0.502
Hypertension	9 (22.0%)	4 (13.3%)	0.354
Cardiac disease	3 (7.3%)	0 (0.0%)	0.258
Stroke	3 (7.3%)	0 (0.0%)	1.000
COPD	1 (2.4%)	1 (3.3%)	1.000
Body Mass Index (BMI)			0.348
Mean±Std	22.34 ± 3.679	23.17±3.640	
Median	22.40	22.65	
Range (min-max)	14.50–31.10	14.60–31.10	
Nutritional status			0.250
Undernourished	9 (22.0%)	4 (13.3%)	
Normal	23 (56.1%)	17 (56.7%)	
Overweight	7 (17.1%)	5 (16.7%)	
Obese	2 (4.9%)	4 (13.3%)	
Blood product transfusion			0.335
Yes	8 (19.5%)	3 (10.0%)	
No	33 (80.5%)	27 (90.0%)	

Note: values are presented as mean ± standard deviation or median (interquartile range); *p < 0.05 indicates statistical significance; **indicate p < 0.01 (highly statistically significant difference); Statistical tests: Independent t-test or Mann–Whitney U test, as appropriate

(p=0.024), suggesting that RAR had a higher discriminatory value than RPR in predicting mortality among septic ICU patients. When RAR and APACHE II ROC curves were compared using the DeLong test, there was no significant difference between their AUC values (p=0.287).

Discussion

This study clearly demonstrates that RAR is a statistically superior prognostic marker comparedto RPR in predicting 28-day mortality among septic patients in the ICU. The ROC curve analysis provided compelling evidence for this conclusion. While both ratios showed strong predictive capacity, RAR exhibited excellent discriminative performance with a significantly higher AUC of 89.3% compared to 74.7% for RPR. Most importantly, the DeLong test confirmed that this difference in AUC values was statistically significant (p=0.024). This finding robustly indicates that RAR has a meaningfully better ability to distinguish between survivors and non-survivors than

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Table 4 ROC Curve Analysis for RAR, RPR and APACHE II in Predicting 28–Day Mortality

Parameter	AUC (95% CI)	Cut-off Value	Sensitivity (%)	Specificity (%)	p-value
RAR	89.3% (79.8%–95.4%)	5.7404	85.4	73.3	0.0001**
RPR	74.7% (63%–84.3%)	0.0627	75.6	76.7	0.0001**
APACHE II	83.2% (72.5%–91.0%)	14	80.5	73.3	0.0001**

Note: AUC = Area Under the Curve; CI = Confidence Interval; RAR = Red Cell Distribution Width-to-Albumin Ratio; RPR = Red Cell Distribution Width-to-Platelet Ratio;*p<0.05 considered significant; **p<0.01 considered highly significant

Table 5 DeLong Test Analysis for RAR, RPR and APACHE II in Predicting 28-Day Mortality

Comparison (DeLong test)	Differencce AUC	Z	P value
RAR vs RPR	0.1460 (0.0172–0.276)	2.221	0.026*
RAR vs APACHE II	0.0614 (-0.0517–0.174)	1.064	0.287

Note: AUC = Area Under the Curve; CI = Confidence Interval; RAR = Red Cell Distribution Width-to-Albumin Ratio; RPR = Red Cell Distribution Width to Platelet Ratio; *p<0.05 considered significant; **p<0.01 considered highly significant; Statistical analyses were performed using the DeLong test to compare ROC curves

RPR. Furthermore, at its optimal cut-off, RAR provided a more favorable diagnostic profile with higher sensitivity (85.4% vs 75.6%), making it a more effective tool for ruling out mortality risk.

The observed elevation of RAR and RPR among non-survivors reflects the underlying pathophysiology of sepsis, which involves widespread inflammation, oxidative stress, and immune dysregulation. RDW, a marker of erythrocyte size variability, increases in response to systemic inflammation and impaired erythropoiesis.[6,7] In sepsis, proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) can disrupt red blood cell maturation and reduce erythrocyte survival, leading to anisocytosis and elevated RDW values.[13] Several studies have shown that higher RDW is independently associated with adverse outcomes in critically ill and septic patients. [6,7,14]

Serum albumin, on the other hand, is a negative acute-phase reactant that decreases during systemic inflammation due to capillary leakage, reduced hepatic synthesis, and increased catabolism.8 Hypoalbuminemia in sepsis reflects both the inflammatory burden and the degree of organ dysfunction. A low albumin level is also associated with impaired colloid osmotic pressure, leading to tissue oedema, altered drug pharmacokinetics, and worse clinical outcomes.[15] The RAR, therefore, combines the prognostic relevance of RDW and albumin into a single ratio that simultaneously represents inflammatory activation and nutritional or hepatic function. In this study, RAR demonstrated excellent discriminative ability consistent with previous reports suggesting that RAR may be a strong mortality predictor in septic and critically ill populations.[11,12]

Similarly, the RPR reflects the balance between inflammation-induced erythrocyte alterations and thrombocytopenia, both of which are hallmarks of sepsis-related coagulopathy. Platelet consumption and destruction is common during sepsis due to disseminated intravascular coagulation (DIC) and immune-mediated platelet activation. Lower platelet counts have been consistently associated with poor outcomes in sepsis and septic shock.[9,17]

When combined with RDW, RPR provides a broader view of hematologic and inflammatory responses. In this study, RPR demonstrated good predictive value for mortality, in line with previous studies reporting that higher

RPR values are significantly associated with an increased risk of mortality in patients with systemic inflammatory conditions.[10]

Despite both ratios providing simple, accessible prognostic information derived from routine blood tests, RAR demonstrated superior performance and should be considered the biomarker of choice for early mortality risk assessment in sepsis. Its application is particularly valuable in resource-limited ICUs where complex scoring systems may be impractical.

A pivotal finding of this study is that the discriminative ability of RAR for 28-day mortality was statistically equivalent to that of the APACHE II score (p=0.287, DeLong test), an established but more complex prognostic tool. While APACHE II integrates numerous clinical and laboratory variables, RAR is derived from only two routine and inexpensive blood parameters. This suggests that RAR could serve as a practical and efficient alternative for initial mortality risk stratification in sepsis, especially in emergency or resource-constrained settings where rapid assessment is crucial. The significantly superior performance of RAR compared to RPR (p = 0.026) further solidifies its position as the hematologic ratio of choice.

From a physiological perspective, these results reinforce the understanding that sepsis-related inflammation simultaneously affects multiple hematologic pathways, disrupting erythrocyte morphology, platelet function, and plasma protein synthesis. Biomarkers such as RAR and RPR capture these interactions more comprehensively than single laboratory parameters alone, offering a more integrated reflection of the patient's clinical condition. Their prognostic value also suggests potential utility in guiding therapeutic interventions and monitoring treatment response, although this warrants further investigation.

This study's findings are consistent with previous literature, demonstrating that composite hematologic ratios derived from routine laboratory data can be reliable predictors of sepsis outcomes.[10–12] However, differences in predictive strength across studies may be attributed to variations in population characteristics, sample sizes, and the timing of laboratory measurements. Earlier studies reported slightly lower predictive accuracies for albumin and platelet-based ratios, possibly due to differences in disease severity or institutional treatment protocols.[8,16]

Despite its strengths, this study has several limitations that must be acknowledged. First, it was conducted in a single tertiary-care center with a relatively small sample size, which may limit the generalizability of the results. Second, and relatedly, our sample size precluded performing a multivariable regression analysis to adjust for potential confounders such as APACHE II score, age, or the presence of septic shock. The sample size calculation was based on detecting a significant AUC for RAR. While this provides adequate power for the primary evaluation of RAR, a larger sample might be needed for more complex multivariate comparisons or to confirm the observed difference between RAR and RPR with higher precision. Third, dynamic changes in RAR and RPR over time were not assessed; serial measurements might provide additional prognostic value beyond a single baseline measurement. Fourth, while the study controlled for several key variables, other potential confounding factors such as detailed nutritional status, underlying chronic inflammatory conditions, and transfusion history could still have influenced the findings. Future studies with larger multicenter cohorts should incorporate multivariable models and serial biomarker monitoring to further validate the prognostic value of RAR and to determine whether its changes during treatment could serve as early indicators of therapy response or clinical deterioration.

Conclusion

RAR demonstrated a statistically superior prognostic performance compared to RPR in predicting 28-day mortality among septic patients in the ICU. The higher sensitivity of RAR is particularly crucial in the critical

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care setting, as it implies a better ability to correctly identify patients at the highest risk of mortality, potentially allowing for earlier and more aggressive interventions.

These findings firmly establish RAR, a parameter derived from simple and inexpensive routine blood tests, as the more accurate and reliable prognostic tool for the early risk stratification of sepsis in the ICU. Its implementation can significantly aid clinicians, especially in resource-limited settings, in identifying high-risk patients promptly, thereby facilitating timely interventions and optimizing resource allocation.

AI Use Disclosure

Artificial intelligence (AI) tools (e.g., ChatGPT, OpenAI, San Francisco, CA, USA) were used to assist in language editing, grammar correction, and structuring the manuscript during the preparation of this article. The authors have carefully reviewed and verified all content, and they take full responsibility for the accuracy, integrity, and originality of the final manuscript. The use of AI does not replace the responsibility of the authors. Any AI contribution must be properly acknowledged, and failure to disclose may result in rejection.

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