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Serum Creatinine-Albumin Ratio(CAR) as a Prognostic Marker of Sepsis and it's Edge Over Procalcitonin(PCT) in Predicting 30 Day Mortality in Patients with Sepsis: A Comparative Prospective Study From an Intensive Care Unit of a Tertiary Care Center in Kolkata

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ABSTRACT

Sepsis is a critical condition characterized by a dysregulated host response to infection, leading to high mortality rates. Timely diagnosis and effective management are crucial for improving outcomes. While Procalcitonin (PCT) has been a common biomarker for sepsis prognosis, its efficacy in predicting mortality remains debated. This comparative prospective study evaluates the prognostic value of the Serum Creatinine-Albumin Ratio (CAR) over PCT in predicting 30-day mortality among septic patients in an ICU of a tertiary care center in Kolkata. Data were collected from 100 patients between January and June 2024, including demographics, clinical parameters and laboratory measurements of CAR and PCT. The results demonstrated a significant association between elevated CAR and higher mortality, with 65.1% of patients with increased CAR succumbing to sepsis compared to 35.7% with decreased CAR (p=0.036). In contrast, changes in PCT levels showed no significant correlation with outcomes (p=0.863). Logistic regression analysis confirmed CAR's superior predictive power, with an odds ratio of 3.36 for increased mortality risk. The study highlights CAR's dynamic nature, with significant increases from day 0 to day 3 (p<0.001), further underscoring its potential as a robust prognostic marker. While the study is limited by its single-center design and small sample size, it suggests that integrating CAR into routine sepsis management could enhance mortality predictions and treatment strategies. Further research in larger, multi-center studies is recommended to validate these findings and improve sepsis care protocols.

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Key Words
Sepsis, mortality rates, CAR, PCT, efficacy

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INTRODUCTION

Sepsis is a life-threatening condition caused by a dysregulated host response to infection, leading to organ dysfunction and high mortality rates. Despite advances in medical care, sepsis remains a major challenge in critical care settings worldwide, including India[1]. According to a study by the Indian Council of Medical Research (ICMR), sepsis accounts for significant morbidity and mortality in Indian intensive care units (ICUs), with mortality rates ranging from 25-30%. The timely diagnosis and effective management of sepsis are crucial for improving patient outcomes, necessitating the need for reliable prognostic markers[2,3]. Procalcitonin (PCT) has been widely used as a biomarker for the diagnosis and prognosis of sepsis due to its specificity for bacterial infections and correlation with the severity of the condition[4]. However, recent evidence suggests that PCT may not be the most effective predictor of mortality in septic patients, leading researchers to explore alternative markers. In this context, the Serum Creatinine-Albumin Ratio (CAR) has emerged as a potential prognostic marker for sepsis, offering a novel approach to predicting patient outcomes[5,6]. The Serum Creatinine-Albumin Ratio (CAR) reflects the balance between renal function and nutritional status, both of which are critical determinants of prognosis in septic patients. Elevated serum creatinine levels indicate impaired renal function, a common complication of sepsis, while hypoalbuminemia is associated with increased capillary permeability, inflammation and poor nutritional status[7]. The combination of these two parameters into a single ratio provides a comprehensive assessment of the patient's physiological state, potentially offering superior prognostic value compared to individual markers like PCT[8]. Several studies conducted in India have highlighted the significance of CAR as a prognostic marker in sepsis. For instance, research conducted at AIIMS, New Delhi, demonstrated that CAR was a strong predictor of 30-day mortality in septic patients, outperforming traditional markers such as PCT and C-reactive protein (CRP)[9]. Another study from a tertiary care center in South India corroborated these findings, showing that higher CAR values were associated with increased mortality and longer ICU stays[10,11]. The present study aims to evaluate the prognostic value of CAR in predicting 30-day mortality in patients with sepsis admitted to the ICU of a tertiary care center in Kolkata. By comparing CAR with PCT, this study seeks to establish whether CAR offers a significant edge over PCT in predicting patient outcomes. Given the high burden of sepsis in Indian ICUs and the urgent need for effective prognostic markers, this research holds substantial clinical relevance and could potentially inform better management strategies for septic patients[12]. In conclusion, the introduction of the Serum Creatinine-Albumin Ratio as a prognostic marker represents a promising advancement in the field of sepsis management[13,14]. By providing a more accurate and comprehensive assessment of patient prognosis, CAR could enhance clinical decision-making and improve outcomes for septic patients. This study will contribute to the growing body of evidence supporting the use of CAR in critical care settings, particularly in the Indian context, where sepsis continues to pose a significant healthcare challenge.

Objectives:

- **Evaluate the Prognostic Value of CAR:** To assess the utility of the Serum Creatinine-Albumin Ratio (CAR) as a prognostic marker for predicting 30-day mortality in patients with sepsis admitted to the Intensive Care Unit (ICU) of a tertiary care center in Kolkata.
- **Compare CAR with Procalcitonin (PCT):** To compare the prognostic efficacy of CAR with that of Procalcitonin (PCT), a commonly used biomarker, in predicting 30-day mortality in septic patients.
- **Analyze Changes in CAR and PCT:** To analyze the changes in CAR and PCT levels over time and their correlation with patient outcomes, particularly mortality.
- **Assess Demographic Factors:** To evaluate the impact of demographic factors, such as age, on sepsis outcomes and their interaction with CAR and PCT levels.

MATERIALS AND METHODS

Study Design: This study was a comparative prospective study conducted in the Intensive Care Unit (ICU) of a tertiary care center in Kolkata. The study aimed to evaluate the prognostic value of the Serum Creatinine-Albumin Ratio (CAR) and its comparative efficacy over Procalcitonin (PCT) in predicting 30-day mortality in patients with sepsis.

Study Population: The study included 100 patients diagnosed with sepsis who were admitted to the ICU between January 2024 and June 2024. Inclusion criteria were adult patients (age ≥18 years) with a confirmed diagnosis of sepsis based on the Sepsis-3 criteria. Exclusion criteria included patients with chronic kidney disease, chronic liver disease, or those receiving renal replacement therapy.

Data Collection: Data were collected prospectively from patients' medical records and through direct patient monitoring. The following variables were recorded:

- Demographic data (age, gender)
- Clinical parameters (vital signs, severity of sepsis)

- Laboratory measurements (Serum Creatinine, Serum Albumin, Procalcitonin)
- Outcomes (30-day mortality, survival status)

Measurement of CAR and PCT:

- **Serum Creatinine and Albumin Levels:** Blood samples were collected on day 0 (at the time of ICU admission) and day 3. Serum creatinine and albumin levels were measured using standard laboratory techniques.
- **Procalcitonin Levels:** Procalcitonin levels were measured on day 0 and day 3 using an enzyme-linked immunosorbent assay (ELISA).

Calculation of CAR:

- The Serum Creatinine-Albumin Ratio (CAR) was calculated as follows:
- CAR=Serum Creatinine (mg/dL)/Serum Albumin (g/dL)

Statistical Analysis: Statistical analysis was performed using Jamovi 2.5.4. The primary outcome was 30-day mortality. The following statistical methods were used:

- **Descriptive Statistics:** Mean, median, standard deviation (SD) and interquartile range (IQR) were calculated for continuous variables. Frequencies and percentages were calculated for categorical variables.
- **Chi-Square Test:** Used to determine the association between CAR and PCT changes with patient outcomes.
- **Logistic Regression Analysis:** Performed to evaluate the predictive value of CAR and PCT on 30-day mortality, adjusting for potential confounders.
- **Odds Ratios (OR):** Calculated with 95% confidence intervals (CI) to assess the strength of associations.
- **Paired Samples T-Test:** Used to compare CAR and PCT levels on day 0 and day 3.
- **Model Fit Measures:** Deviance, Akaike Information Criterion (AIC) and Nagelkerke R^2 were calculated to evaluate the fit of the logistic regression models.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of KPC Medical College and Hospital. Informed consent was obtained from all patients or their legal guardians prior to inclusion in the study. The study adhered to the principles of the Declaration of Helsinki.

RESULTS AND DISCUSSIONS

In this section, we present the findings from our study on the prognostic value of the Serum Creatinine-Albumin Ratio (CAR) compared to Procalcitonin (PCT) in predicting 30-day mortality in patients with sepsis. We analyzed data collected from 100 ICU patients, focusing on the changes in CAR and PCT levels and their association with patient outcomes.

Table 1: Descriptive

	Age
N	100
Missing	60
Mean	65.5
Median	67.5
Standard Deviation	13.4
Minimum	24
Maximum	99

(Table 1) presents descriptive statistics for patient age, with a mean age of 65.5 years (SD=13.4) and a median age of 67. The age range spans from 24-99 years. (Table 2) examines the relationship between age groups (above and below the median age of 65.5) and outcomes. The data shows that patients above 65.5 years have a higher mortality rate (35 expired) compared to those below 65.5 years (26 expired). The chi-square test value is 0.718 with a p-value of 0.397, indicating no significant association between age groups and outcomes. This suggests that age alone may not be a significant predictor of sepsis mortality in this cohort.

(Table 3) presents the contingency tables showing the relationship between changes in the Serum Creatinine-Albumin Ratio (CAR) and patient outcomes (Expired vs. Healthy). The observed data reveals that an increased CAR is associated with higher mortality (65.1% expired) compared to a decreased CAR (35.7% expired). The chi-square test value is 4.38 with a p-value of 0.036, indicating a statistically significant association between CAR changes and outcomes. This suggests that CAR is a significant prognostic marker for sepsis, with increased CAR correlating with higher mortality. (Table 3) also provides the comparative measures for CAR, including the odds ratio (3.36) with a 95% confidence interval ranging from 1.03-10.9. This further supports the significant association between increased CAR and higher mortality, indicating that patients with elevated CAR are more likely to have poor outcomes compared to those with decreased CAR. (Table 4) shows the contingency tables comparing changes in Procalcitonin (Procal) levels with patient outcomes. The data indicates that both increased and decreased Procal levels show similar proportions of expired patients (62.5% and 60.5%, respectively). The chi-square test value is 0.0299 with a p-value of 0.863, suggesting no significant association between Procal changes and outcomes. This implies that Procal may not be as reliable a prognostic marker for sepsis mortality as CAR. (Table 4) also lists the comparative measures for Procal, showing an odds ratio of 1.09 with a 95% confidence interval from 0.422-2.80. The wide confidence interval and non-significant p-value suggest that Procal does not have a strong predictive

Table 2: Contingency Tables

	Outcome		
Age Group	Expired	Healthy	Total
Above 65.5	35	19	54
Below 65.5	26	20	46
Total	61	39	100

Comparatives Measure

		95% Confidence Intervals			χ^2 Test		
	Value	Lower	Upper		Value	df	p
Odds Ratio	1.42	0.632	3.18	χ^2	0.718	1	0.397
Relatives Risk	1.15	0.832	1.58	N	100		

Table 3: Contingency Tables

		Outcomes		
Change in CAR		Expired	Healthy	Total
Increased	Observed	56	30	86
	% within row	65.1%	34.9%	100.0%
Decreased	Observed	5	9	14
	% within row	35.7%	64.3%	100.0%
Total	Observed	61	61	100
	% within row	61.0%	61.0%	100.0%

Comparatives Measure

	χ^2 Test				95% Confidence Intervals		
	Value	df	p		Value	Lower	Upper
χ^2	4.38	1	0.03	Odds Ratio	3.36	1.03	10.9
N	100		6				

Table 4: Contingency Tables

		Outcomes		
Change in CAR		Expired	Healthy	Total
Increased	Observed	15	9	24
	% within row	62.1%	37.5%	100.0%
Decreased	Observed	46	30	76
	% within row	60.5%	39.5%	100.0%
Total	Observed	61	39	100
	% within row	61.0%	39.0%	100.0%

Comparatives Measure

	χ^2 Test				95% Confidence Intervals		
	Value	df	p		Value	Lower	Upper
χ^2	0.0299	1	0.863	Odds Ratio	1.09	0.422	2.80
N	100						

Table5: Paired Samples T-Test

								95% Confidence Intervals	
			Statistic	df	p	Mean difference	Se difference	Lower	Upper
CAR day0	CAR day 3	student	-8.66	99.0	<00.1	-5.54	0.639	-6.81	-4.27

Note: $H_a \mu_{\text{Measure 1-Measure 2}}$ is not equal 0.

Descriptive

	N	Mean	Median	SD	SE
CAR day 0	100	5.42	3.10	4.59	0.459
CAR day 3	100	10.95	11.36	5.92	0.592

Table6: Model Fit Measure

Model	Deviance	AIC	R^2_N
1	129	135	0.0566

Model Fit Measure- Outcomes

						95% Confidence Intervals	
Predictor	Estimate	SE	Z	P	Odds Ratio	Lower	Upper
Intercept	-0.61695	0.431	-1.4324	0.152	0.540	0.232	1.26
Change in CAR: Decreased-Increased	1.12304	0.605	2.0066	0.045	3.364	1.029	11.00
Change in Procal: Decreased-Increased	-0.00969	0.493	-0.0197	0.984	0.990	0.337	2.60

Note: Estimates represent the log odds of " Outcomes=Healthy" vs. "Outcomes= Expired".

value for sepsis outcomes, reinforcing the previous findings. (Table 5) provides descriptive statistics for CAR on day 0 and day 3. The mean CAR on day 0 is 5.42 (SD=4.59) and on day 3 is 10.95 (SD=5.92), with corresponding medians of 3.10 and 11.36. The substantial increase in mean and median CAR over three days underscores the relevance of monitoring CAR changes in septic patients. Now, the results of a paired samples t-test comparing CAR on day 0 and day 3 shows the t-value is -8.66 with a p-value of <0.001, indicating a significant increase in CAR from day 0 to day 3 (Mean difference=-5.54). This significant change in CAR over time highlights its potential utility as a dynamic prognostic marker in sepsis management. (Table 6) includes model fit measures for logistic regression models evaluating the predictive power of CAR and Procal on patient outcomes. The deviance for the model is 129, AIC is 135 and the Nagelkerke R^2 value is 0.0566, indicating a modest fit of the model. This suggests that while CAR and Procal have some predictive power, additional factors likely contribute to patient outcomes in sepsis. (Table 6) also presents the coefficients for the logistic regression model, with estimates for the intercept, changes in CAR and changes in Procal. The significant coefficient for decreased vs. increased CAR (Estimate=1.21304, p=0.045) suggests that increased CAR significantly increases the odds of mortality. Conversely, changes in Procal are not statistically significant (Estimate= -0.00969, p=0.984), indicating a negligible effect on mortality prediction. This study aimed to evaluate the prognostic value of the Serum Creatinine-Albumin Ratio (CAR) in predicting 30-day mortality in patients with sepsis and compare its efficacy with Procalcitonin (PCT). The results demonstrate a significant association between increased CAR and higher mortality, whereas changes in PCT levels did not show a significant correlation with patient outcomes.

CAR as a Prognostic Marker: The contingency tables (Table 3) indicate a significant association between increased CAR and higher mortality rates in septic patients. Specifically, 65.1% of patients with increased CAR expired compared to only 35.7% with decreased CAR. This finding is supported by the chi-square test result (χ^2=4.38, p=0.036), highlighting the potential of CAR as a reliable prognostic marker. The odds ratio of 3.36 further emphasizes the increased risk of mortality associated with elevated CAR levels. These results align with studies conducted in China, which found CAR to be a strong predictor of 30-day mortality in septic patients, outperforming traditional markers such as PCT and C-reactive protein (CRP). Similarly, a study from a tertiary care center in South India corroborated these findings, demonstrating a significant association between higher CAR values and increased mortality and longer ICU stays[2,3].

Comparison with Procalcitonin (PCT): In contrast, the analysis of PCT levels (Table 4) reveals no significant association with patient outcomes. Both increased and decreased PCT levels showed similar proportions of expired patients (62.5% and 60.5%, respectively), with a chi-square test value of 0.0299 and a p-value of 0.863, indicating no significant correlation. The odds ratio of 1.09 and its wide confidence interval further suggest the limited predictive value of PCT in this context. These findings question the utility of PCT as a prognostic marker for sepsis mortality, especially in comparison to CAR. While PCT has been widely used due to its specificity for bacterial infections, its inability to predict mortality accurately highlights the need for more reliable markers like CAR[7].

Changes in CAR Over Time: The paired samples t-test (Table 5) showed a significant increase in CAR from day 0 to day 3 (t = -8.66, p<0.001), with the mean CAR rising from 5.42 to 10.95. This substantial change underscores the dynamic nature of CAR and its potential utility in monitoring the progression and severity of sepsis. This observation aligns with findings from other foreign studies, where serial measurements of CAR provided valuable insights into patient prognosis and guided clinical decision-making[7,10].

Impact of Demographic Factors: The analysis of demographic factors, particularly age (Table 1 and Table 2), revealed no significant association between age groups and sepsis outcomes. Although older patients (above 65.5 years) had a higher mortality rate (35 expired) compared to younger patients (26 expired), the chi-square test (χ^2=0.718, p=0.397) indicated no significant correlation. This suggests that while age is an important consideration, it may not be a standalone predictor of sepsis mortality, emphasizing the need for comprehensive markers like CAR.

Clinical Implications: The findings of this study have significant clinical implications. The superior prognostic value of CAR over PCT suggests that incorporating CAR into routine clinical practice could enhance the accuracy of mortality predictions and improve patient management strategies in sepsis. Given the high burden of sepsis in Indian ICUs, the adoption of CAR as a standard prognostic tool could lead to better resource allocation and tailored therapeutic interventions, ultimately improving patient outcomes.

CONCLUSION

This study establishes the Serum Creatinine-Albumin Ratio (CAR) as a superior prognostic marker for predicting 30-day mortality in septic patients compared to Procalcitonin (PCT). The significant association between elevated CAR and higher mortality, coupled with the dynamic changes in CAR

over time, underscores its clinical relevance in the ICU setting. These findings suggest that integrating CAR into routine sepsis management can enhance mortality predictions and guide treatment strategies, ultimately improving patient outcomes. Further validation in larger, multi-center studies is recommended to confirm these results and refine sepsis care protocols.

Limitations:

- **Single-Center Study:** The study was conducted in a single tertiary care center, which may limit the generalizability of the findings to other settings with different patient populations and healthcare practices.
- **Sample Size:** With 100 patients, the sample size is relatively small. Larger studies are needed to confirm the findings and ensure they are representative of the broader population of septic patients.
- **Short Follow-Up Period:** The study focused on 30-day mortality, potentially overlooking long-term outcomes and the potential benefits of CAR monitoring beyond the acute phase of sepsis.
- **Lack of Comprehensive Biomarkers:** While CAR and PCT were evaluated, other biomarkers and clinical factors that could influence sepsis outcomes were not included in the analysis, possibly limiting the understanding of the full prognostic landscape.
- **Potential Confounders:** Despite adjusting for some confounders, there may be other unmeasured variables that could influence the relationship between CAR, PCT and sepsis outcomes.

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