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Presepsin as a Diagnostic and Prognostic Indicator in Sepsis: An Observational Study

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ABSTRACT

Background and Objectives: Sepsis management remains challenging despite considerable progress in intensive care, primarily because of its high rates of illness and death. Timely and accurate identification of sepsis is a persistent problem in clinical settings, prompting interest in a wide range of physiological parameters and laboratory biomarkers. Among newer candidates, Presepsin has attracted considerable attention owing to its favorable sensitivity and reasonable specificity for sepsis detection. Nevertheless, evidence regarding its utility in directing antimicrobial management is still emerging. This investigation was therefore undertaken to determine the diagnostic and prognostic value of Presepsin when evaluated alongside C-reactive protein (CRP) and Procalcitonin (PCT) in hospitalized sepsis patients.

Materials and Methods: A single-center, prospective, hospital-based, non-interventional observational study was carried out. Eligible participants were adults aged above 18 years who presented with a diagnosis of sepsis or septic shock fulfilling the Sepsis-3 classification criteria. Venous blood was drawn at baseline (day 0) and again on day 5. Levels of CRP, PCT, and Presepsin, along with the Sequential Organ Failure Assessment (SOFA) score, were obtained and compared.

Results: A total of 176 adult patients meeting the eligibility requirements were recruited. The cohort comprised 129 males (73.30%) and 47 females (26.70%), with a mean age of 58 ± 14.36 years. By day 5 of hospitalization, patients who subsequently died showed markedly elevated levels of all measured parameters compared to survivors: CRP (168.62 vs. 54; $p<0.001$), Procalcitonin (4.207 vs. 1.11; $p<0.001$), Presepsin (3.75 vs. 1.76; $p=0.003$), and SOFA score (6 vs. 1; $p<0.001$).

Conclusions: Serial monitoring of serum Presepsin holds promise as a complementary biomarker to guide outcome prediction in sepsis. Its trajectory over time may assist clinicians in identifying patients at risk of mortality.

Keywords: *Presepsin, biomarker, sepsis, ICU, Procalcitonin, CRP, SOFA, prognostic marker.*

INTRODUCTION

Sepsis is a multifaceted, life-threatening condition arising from a dysregulated host response to infection, resulting in widespread pathophysiological, biochemical, and organ-level dysfunction [1]. Although critical care medicine has evolved substantially over recent decades, timely recognition of sepsis remains one of the greatest clinical hurdles, given the variability in its presentation and the associated burden of morbidity and death [1]. Earlier diagnostic frameworks relied on the systemic inflammatory response syndrome (SIRS) criteria, which proved insufficiently specific. An international expert panel subsequently introduced revised diagnostic standards—collectively referred to as Sepsis-3—substituting SIRS with the SOFA score, which more accurately captures the extent of organ dysfunction accompanying sepsis [2].

Presepsin—formally known as soluble CD14 subtype (sCD14-ST)—has emerged as a potentially valuable indicator for both diagnosing and monitoring sepsis [3]. It is generated when membrane-bound CD14 undergoes proteolytic cleavage, releasing a truncated soluble fragment into the bloodstream [4]. CD14 itself acts as a co-receptor within the Toll-like receptor (TLR) signaling network, participating in the host immune recognition of both gram-positive and gram-negative organisms. In the case of gram-negative bacteria, lipopolysaccharide (LPS) binds to LPS-binding protein (LBP), and this complex interacts with CD14 to activate TLR-mediated pathways [4,5]. The downstream consequence of this signaling cascade is the activation of immune cells and liberation of pro-inflammatory cytokines, initiating the hallmark systemic inflammatory response of sepsis.

CD14 exists in a membrane-anchored configuration (mCD14) as well as a freely circulating soluble form (sCD14). The soluble variant is released into plasma either by direct cellular secretion or by proteolytic shedding from the cell surface in response to immune activation [5]. As Presepsin is a direct product of this CD14-mediated innate immune activation, it functions as a measurable indicator of the degree to which the innate immune response has been triggered by microbial invasion.

MATERIALS AND METHODS

The Department of General Medicine and the Department of Critical Care Medicine at Pradyumna Bal Memorial Hospital, Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar, Odisha, a tertiary-level teaching facility, were the sites of this prospective, non-interventional, observational study. Enrollment of patients was scheduled to start in March 2023 and run until March 2025. The Institutional Ethics Committee (IEC) approved the study protocol before it was started.

Criteria for Inclusion and Exclusion: Adults 18 years of age or older who were admitted with clinical signs of septic shock or sepsis, as determined by the Sepsis-3 diagnostic criteria, were included. The study excluded patients undergoing immunosuppressive medications, those with established malignant disease, and those with terminal diseases where survival was not anticipated to last more than 24 hours due to causes unrelated to infection.

Sample Size Calculation: The estimated minimum sample size needed was found to be 176 participants based on previously published data showing a specificity of roughly 92% for Presepsin in diagnosing sepsis, taking into account a statistical power of 80%, a significance threshold of 5%, and a 95% confidence interval.

Data Collection: At enrollment, baseline demographic information (age, sex), presenting symptoms and clinical history, and physiological parameters (vital signs) were documented. Blood samples were obtained at two time points: on the day of admission (day 0) and on the fifth day of hospital stay (day 5). The following laboratory analyses were performed:

- C-reactive protein (CRP) — quantified by immunoturbidimetric method.
- Procalcitonin (PCT) — determined by quantitative electrochemiluminescence immunoassay (e.g., VIDAS® B.R.A.H.M.S PCT).
- Presepsin (sCD14-ST) — estimated using chemiluminescent enzyme immunoassay (e.g., PATHFAST® Presepsin Assay).
- Sequential Organ Failure Assessment (SOFA) score — computed from clinical and laboratory parameters.

Statistical Analysis: Depending on anticipated cell frequencies, chi-square or Fisher's exact tests were used to compare categorical data between groups. When comparing continuous variables, the Wilcoxon signed-rank test or the Student's t-test were used. To choose cut-off values and calculate sensitivity, specificity, and overall diagnostic accuracy, receiver operating characteristic (ROC) curve analysis was utilized.

RESULTS

During the trial period, 176 adult sepsis patients who met the inclusion criteria were included. The mean age was 58 ± 14.36 years, with ages ranging from 18 to 84. There were 47 female patients (26.70%) and 129 male patients (73.30%) in the cohort. After receiving antibiotic medication, 151 (85.8%) of all enrolled participants made a clinical recovery, whilst 25 (14.2%) did not survive.

Table 1: Longitudinal trends in sepsis biomarkers from baseline to Day 5

(Wilcoxon signed-rank test applied)

Parameter	At Admission Median	At Admission IQR	Day 5 Median	Day 5 IQR	P-Value
CRP	168.62	189.74	54	99.35	<0.001
PROCALCITONIN	4.207	21.31	1.11	8.09	<0.001
PRESEPSIN	3.75	4.63	1.76	2.89	<0.001
SOFA	6	3	1	1	<0.001

All metrics showed statistically significant decreases by day 5 as compared to baseline levels at day 0, according to the Wilcoxon signed-rank test. In particular, PCT reduced from 4.207 to 1.11 ($p<0.001$), Presepsin decreased from 3.75 to 1.76 ($p<0.001$), SOFA score went from 6 to 1 ($p<0.001$), and CRP decreased from a median of 168.62 to 54 ($p<0.001$).

Table 2: Diagnostic performance of CRP, Procalcitonin, and Presepsin as prognostic biomarkers for sepsis mortality

Parameter	CRP	PROCALCITONIN	PRESEPSIN
Cut-off value	294.7 mg/ml	15.05 ng/ml	6.4 ng/ml
AUC	0.506	0.611	0.577
Sensitivity	53.2%	45.23%	73.50%
Specificity	97.23%	89.56%	92.83%
PPV	88.93%	49.67%	94.71%
NPV	87.62%	87.22%	64.32%
Accuracy	89.30%	81.20%	84.80%

Each biomarker's prognostic usefulness was assessed using ROC curve analysis. Sensitivity was 53.2%, specificity was 97.23%, and overall accuracy was 89.30% (AUC = 0.506) at the ideal cut-off of 294.7 mg/ml for CRP. Sensitivity was 45.23%, specificity was 89.56%, and accuracy was 81.20% for PCT at a threshold of 15.05 ng/ml (AUC = 0.611). Among the three biomarkers, presepsin showed the highest sensitivity (73.50%), specificity (92.83%), and accuracy (84.80%) at a cut-off of 6.4 ng/ml (AUC = 0.577, $p<0.001$).

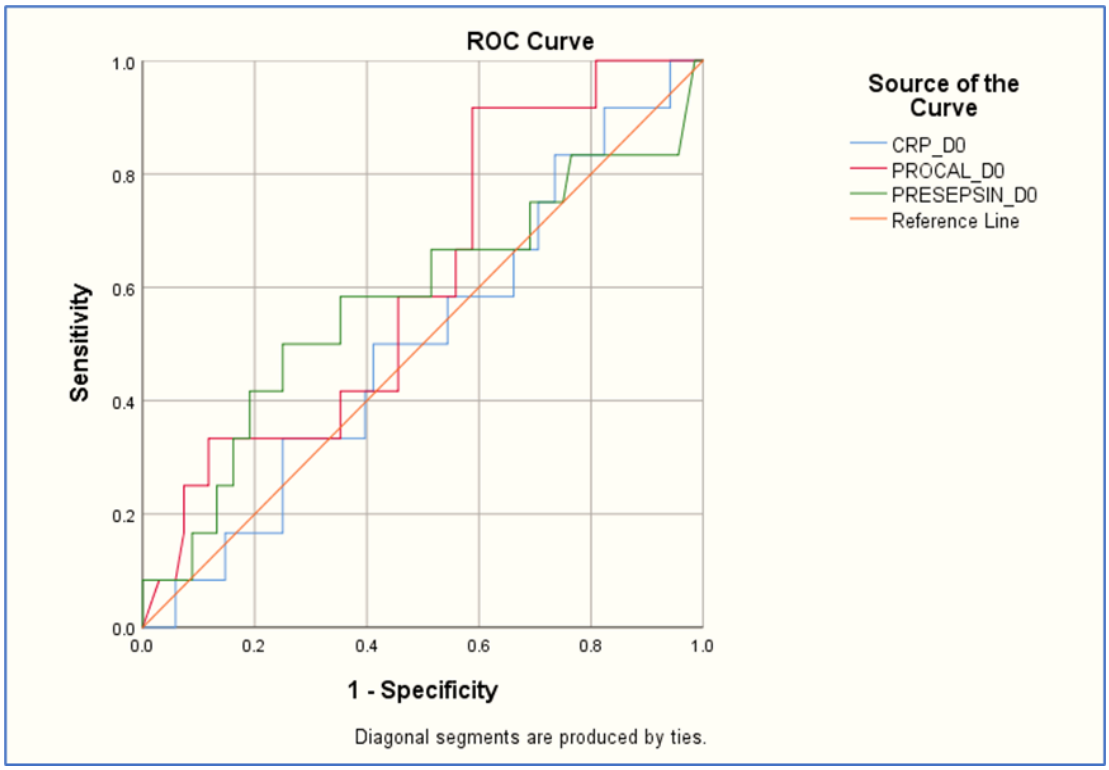


Figure 1: ROC curves for CRP, PCT, and Presepsin as mortality predictors in sepsis

Presepsin exhibited the most favorable prognostic profile in this dataset, combining the highest sensitivity and positive predictive value along with acceptable specificity, despite a modest AUC. CRP demonstrated excellent specificity but was limited in its sensitivity, making it most useful for ruling in high-risk cases rather than early identification. PCT, while contributing meaningfully to a multimarker panel, had the most limited stand-alone prognostic utility.

Table 3: Biomarker levels stratified by clinical outcome (death vs. recovery) at admission and Day 5 (Mann-Whitney U test applied)

Time Point	Parameter	Death Median	Death IQR	Recovery Median	Recovery IQR	P-Value
At Admission	CRP	168.62	189.64	155.3	189.74	0.978

	PROCALCITONIN	35.186	96.11	3.0615	17.947	0.182
	PRESEPSIN	4.345	7.79	3.75	4.615	0.271
	SOFA	8.5	1	5	2	<0.001
Day 5	CRP	121.1	110.36	45.2	72.85	<0.001
	PROCALCITONIN	7.705	10.97	1.02	7.026	<0.001
	PRESEPSIN	2.64	2.57	1.315	2.495	0.003
	SOFA	9	9	1	1	<0.001

At initial presentation (day 0), none of the inflammatory biomarkers—CRP (168.62 vs. 155.3; p=0.978), PCT (35.186 vs. 3.06; p=0.182), or Presepsin (4.34 vs. 3.75; p=0.271)—showed statistically significant differences between patients who later died and those who recovered. However, SOFA score at baseline was already significantly higher among those who ultimately died (8.5 vs. 5; p<0.001), suggesting that early organ dysfunction, rather than biomarker elevation alone, was predictive of fatal outcomes.

By day 5, all parameters had diverged significantly. CRP (121.1 vs. 45.2; p<0.001), PCT (7.705 vs. 1.02; p<0.001), Presepsin (2.64 vs. 1.315; p=0.003), and SOFA score (9 vs. 1; p<0.001) were each significantly higher in patients who died compared to those who recovered, underscoring the value of serial measurements in outcome prediction.

CRP levels by outcome — Day 0 and Day 5 (median values: Day 0: 168.2 vs. 155.3; Day 5: 121.1 vs. 45.2 in death vs. recovery)

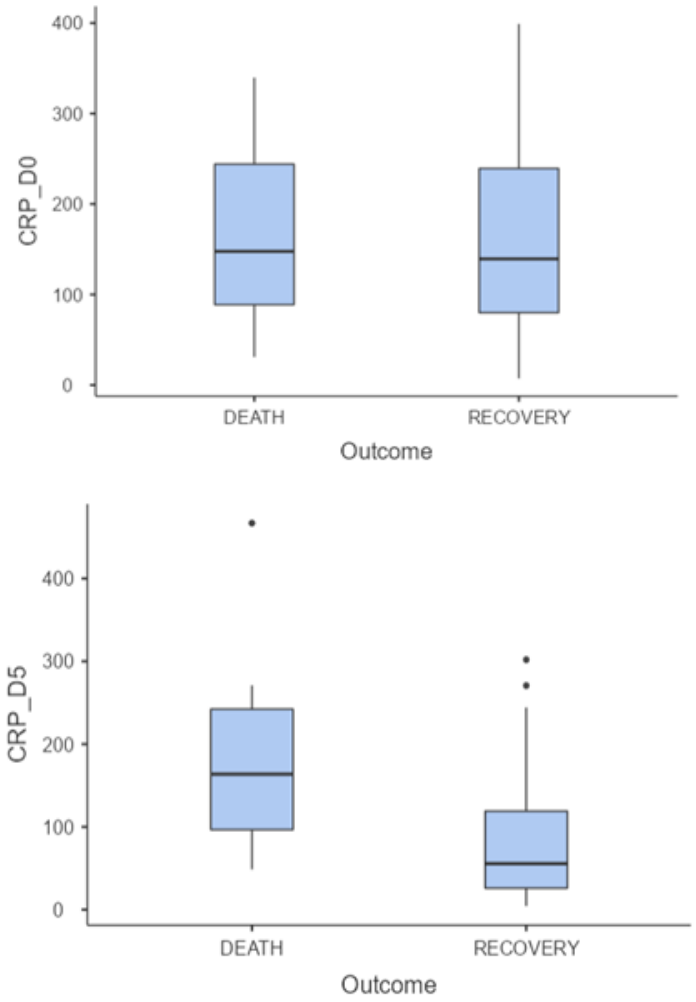
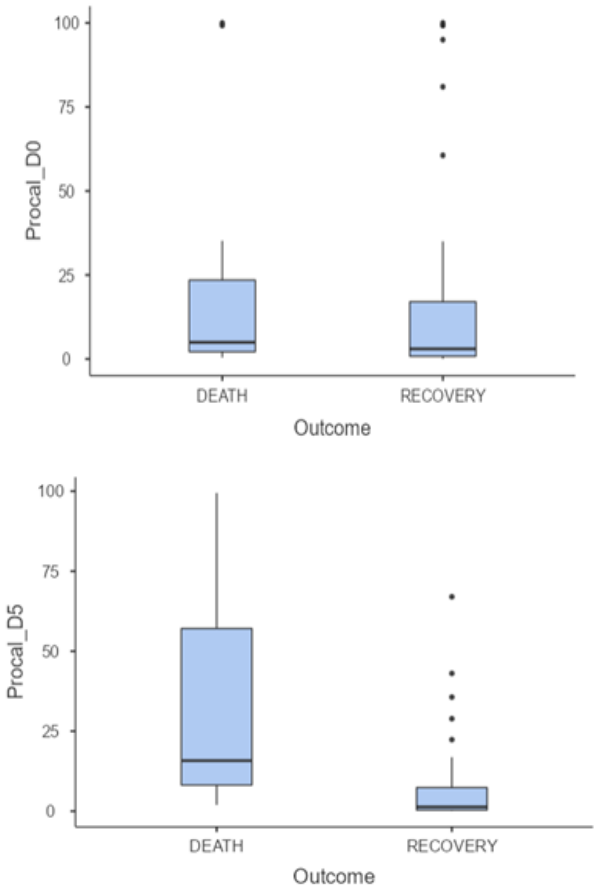
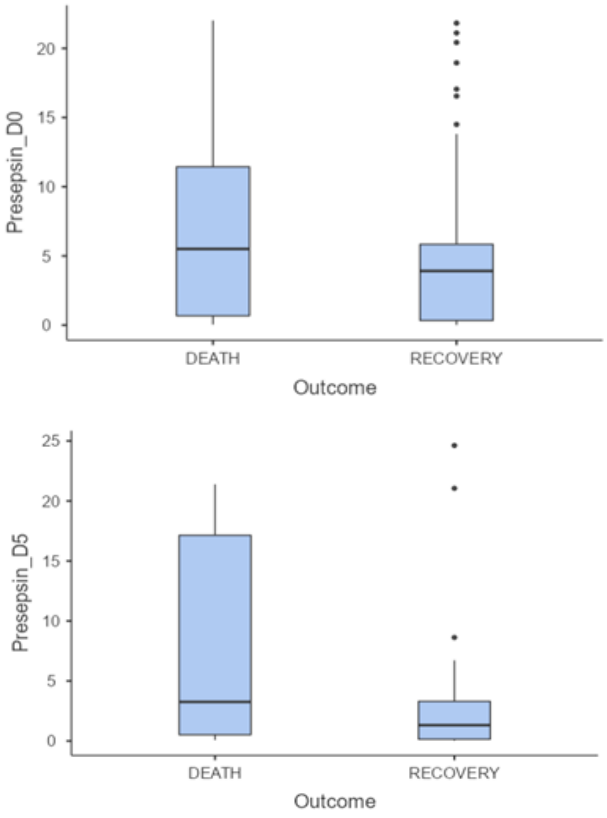


Figure 2: Box-and-whisker plots comparing biomarker levels by outcome on Day 0 and Day 5

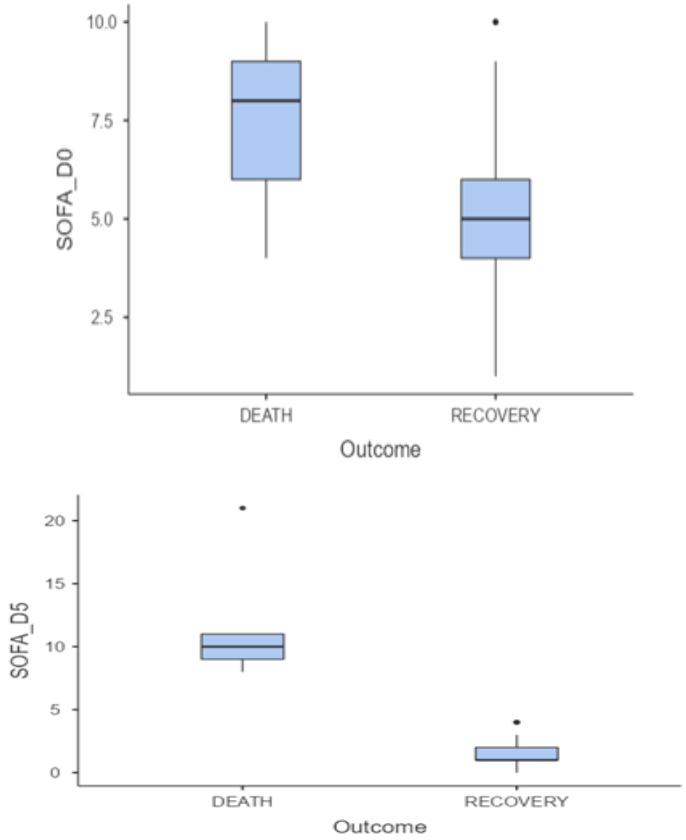
Procalcitonin levels by outcome — Day 0 and Day 5 (median values: Day 0: 35.18 vs. 3.06; Day 5: 7.70 vs. 1.02 in death vs. recovery)



Presepsin levels by outcome — Day 0 and Day 5 (median values: Day 0: 4.34 vs. 3.75; Day 5: 2.64 vs. 1.31 in death vs. recovery)



SOFA score by outcome — Day 0 and Day 5 (median values: Day 0: 8.5 vs. 5; Day 5: 9 vs. 1 in death vs. recovery)



DISCUSSION

Multiple biomarkers have been proposed for monitoring disease trajectory and treatment response in sepsis. Among conventional laboratory tests, white blood cell (WBC) count is one of the most frequently ordered in clinical practice; however, its diagnostic utility is hampered by poor specificity, and sole reliance on this parameter is insufficient to confirm or exclude sepsis. Consequently, more refined indicators such as PCT and CRP have gained widespread clinical adoption. According to the 2021 international Surviving Sepsis Campaign guidelines, PCT is preferred over other biomarkers for evaluating prognosis, though its contribution to early diagnosis remains debatable [6]. Certain published reports suggest PCT outperforms CRP and WBC in predicting clinical outcomes [7], while others, relying on AUC-based evaluations, have questioned its predictive reliability [8]. Cytokines have also demonstrated strong associations with the severity of the septic response [9]. Presepsin, first characterized in 2004, has since been explored both as a diagnostic indicator and an outcome predictor in sepsis [10]. Notably, elevated Presepsin concentrations have been observed in non-infectious conditions—including coronary artery disease, hepatic cirrhosis, cardiac failure, and hyperglycemia—which may limit its specificity in certain patient populations [11].

In our cohort, 25 of 176 patients died, yielding a case fatality rate of 14.20%. Published epidemiological data indicate that mortality among ICU-admitted sepsis patients varies substantially by region, with pooled ICU and in-hospital mortality rates of approximately 25.8% and 35.3%, respectively, and geographic variation ranging from roughly 12–19% in Oceania to 40–47% in Africa [12].

In our study, Presepsin demonstrated a meaningful correlation with in-hospital mortality and showed promise as a prognostic tool. At an optimal cut-off of 6.4 ng/ml, sensitivity reached 73.50%, specificity was 92.83%, and overall accuracy was 84.80% (AUC = 0.577, $p<0.001$).

Abdelshafey et al. reported considerably higher prognostic accuracy for Presepsin in predicting ICU mortality (AUC = 0.920; sensitivity 100.0%; specificity 66.67%; cut-off 640 pg/mL) [13]. Endo et al. demonstrated Presepsin's capacity to distinguish bacterial from non-bacterial infections at a threshold of 600 pg/mL, yielding an AUC of 0.908, sensitivity of 87.8%, and specificity of 81.4% [14]. Initial Presepsin concentrations were significantly lower in survivors than in non-survivors (standardized mean difference 0.92; 95% CI: 0.62–1.22 in a random-effects model), according to a pooled meta-analysis by Yang et al. [15]. This finding held true for subgroups defined by sepsis severity and study location. Presepsin levels above 1,176 pg/mL were also found by Koh et al. to be an independent predictor of in-hospital mortality (OR 3.352; 95% CI: 1.707–6.585; $p<0.001$) [16]. A Presepsin threshold of 1,898.5 pg/mL produced 75.0% sensitivity and 87.5% specificity for sepsis-related death (AUC = 0.764), according to Baik et al. [17].

Across these published reports and in our own findings, day 5 biomarker levels were significantly divergent between survivors and non-survivors—validating the clinical importance of serial biomarker assessment rather than one-time measurement. Among the three biomarkers studied, Presepsin at day 5 was the only one to reach statistical significance for differentiating the two outcome groups (p=0.003), emphasizing its particular utility at this time point.

Regarding CRP, Zhu et al. reported that CRP demonstrated an AUC of 0.593 for sepsis prognosis (sensitivity 84.1%; specificity 37.4%; p=0.027), and PCT showed an AUC of 0.702 (sensitivity 72.7%; specificity 67.0%; p<0.001) [18]. Roy et al. concluded that combined use of PCT and Presepsin improved screening sensitivity for sepsis in the ICU setting [19]. Our study found that at a CRP threshold of 294.7 mg/ml, sensitivity was 53.2% and specificity 97.23% (accuracy 89.23%); at a PCT cut-off of 15.05 ng/ml, sensitivity was 45.23%, specificity 89.56%, and accuracy 81.20%.

Jain et al. reported that PCT is a better predictor of short-term mortality than CRP, with levels <7 ng/ml associated with improved survival. Suberviola et al. found that increasing PCT levels indicated poorer outcomes, while ≥70% PCT clearance predicted favorable prognosis. Qu et al. showed comparable predictive accuracy for ICU mortality with PCT (AUC 0.696) and CRP (AUC 0.684) [20-22].

CONCLUSION

Sepsis and septic shock account for a major proportion of fatalities in critically ill patients globally. Among the available biomarkers—including PCT, Presepsin, and CRP—each contributes distinct diagnostic and prognostic information. Serial Presepsin measurement, particularly by day 5 of hospitalization, appears to offer meaningful prognostic value for predicting sepsis-associated mortality. The AUC observed in our study was comparatively modest relative to some prior publications; this discrepancy may be attributable to differences in sample size, patient demographics, or the heterogeneity of underlying conditions across study populations. Further multi-center trials with larger cohorts are warranted to establish standardized cut-off values and define the optimal clinical role of Presepsin in routine sepsis management.

Institutional Ethics Approval: KIIT/KIMS/IEC/1181/2023
Consent for publication was obtained from patients' attendants/legal guardians.

Author Contributions:
1) Prof. CBK Mohanty — Study conception and design
2) Dr. Srilakshmi Devraj — Data acquisition
3) Dr. Rabi Narayan Rout — Data analysis and interpretation
4) Dr. B R P Rao — Statistical analysis
5) Dr. Nihar Ranjan Mohanty — Manuscript preparation and writing

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Conflict of Interest: Nil
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