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Original Research Article

# Comparative Utility of Presepsin and C-Reactive Protein in the Clinical Management of Sepsis: A Prospective Observational Study

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**Abstract**

**Background:** Rapid recognition and risk stratification of sepsis remain challenging in the intensive care unit (ICU). C-reactive protein (CRP) is inexpensive and widely available but lacks specificity, whereas presepsin, a soluble CD14 subtype released during activation of innate immune pathways, has been proposed as an earlier and potentially more specific biomarker of bacterial sepsis. We compared the clinical utility of presepsin and CRP in the management of adults with sepsis admitted to a medical ICU.

**Methods:** In this prospective observational model, 70 adult patients with clinically suspected sepsis admitted to the Medical ICU of Agartala Government Medical College were included. Presepsin and CRP were measured at ICU admission (0 hour), and their association with sepsis severity, microbiological confirmation, organ dysfunction and 07-day outcome was assessed. Receiver operating characteristic (ROC) analysis was used to compare discriminatory performance. The numerical findings in this draft are simulated and must be replaced with actual study data before publication.

**Results:** Among the patients, 48 patients had sepsis and 22 had non-infectious systemic inflammation. Median presepsin and CRP concentrations were higher among patients with sepsis. Presepsin demonstrated an area under the ROC curve (AUC) of 0.86 for discrimination of sepsis compared with 0.74 for CRP. A presepsin threshold of 720 pg/mL yielded sensitivity of 83.3% and specificity of 77.3%, whereas a CRP threshold of 96 mg/L yielded sensitivity of 79.2% and specificity of 63.6%. Presepsin also showed stronger correlation with Sequential Organ Failure Assessment (SOFA) score. However, isolated baseline biomarker measurement showed only modest prognostic discrimination for 07-day mortality.

**Conclusion:** In this study, presepsin demonstrated better diagnostic discrimination than CRP and may provide additional information regarding sepsis severity. Nevertheless, biomarkers should complement, rather than replace, clinical assessment, microbiological investigation and serial evaluation.

**Keywords:** Sepsis; presepsin; C-reactive protein; biomarker; intensive care unit; SOFA score.

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## Introduction

Sepsis is a life-threatening syndrome caused by a dysregulated host response to infection and remains a major cause of morbidity and mortality among critically ill adults. Early recognition and timely treatment are essential, yet the clinical diagnosis is frequently complicated by overlap between infection and non-infectious systemic inflammation. Biomarkers are therefore widely used as adjuncts to clinical assessment, although no single biomarker can independently establish or exclude sepsis. CRP is among the most commonly available inflammatory markers. It is inexpensive and familiar to clinicians, but it is an acute-phase reactant that may rise in a broad range of infectious and non-infectious conditions. Its kinetics may also limit its utility for very early diagnosis, and recent systematic evidence has highlighted considerable heterogeneity and limited specificity in adult sepsis [1]. Presepsin, also known as soluble CD14 subtype (sCD14-ST), is generated during activation of monocytes and macrophages in response to microbial components. It has attracted interest as a biomarker for bacterial infection and sepsis because of its potential relationship with innate immune activation. Meta-analytic evidence suggests that presepsin has useful diagnostic performance,

although thresholds vary substantially across studies and heterogeneity remains high. In an earlier comparative meta-analysis, presepsin demonstrated pooled sensitivity of approximately 84% and specificity of approximately 76% for sepsis, with diagnostic accuracy broadly comparable with other commonly used biomarkers. [2]

More recent evidence has reinforced the potential of presepsin while also emphasising uncertainty. A 2025 network meta-analysis ranked several biomarkers and clinical scores for detection of sepsis and found that presepsin had useful diagnostic performance, although the certainty of evidence was limited and heterogeneity between studies was important [3]. Similarly, a recent meta-analysis suggested moderate prognostic accuracy of presepsin for mortality, but with substantial threshold and geographical variation. [4]

For clinicians working in an ICU, the clinically relevant question is not simply which biomarker has the higher concentration. A useful test should contribute to decisions regarding the likelihood of infection, urgency of investigation, severity assessment and serial response to treatment. The relative value of an advanced biomarker such as presepsin must also be considered in relation to the low cost and wide availability of CRP, particularly in resource-constrained healthcare settings [5].

There is limited prospective comparative evidence from northeastern India. The present study was therefore designed to compare the utility of presepsin and CRP among adults with suspected sepsis admitted to the Medicine ICU of Agartala Government Medical College (AGMC). The primary objective was to compare their diagnostic performance for sepsis. Secondary objectives were to examine their relationship with organ dysfunction, microbiological confirmation and short-term clinical outcome.

## Materials and Methods

**Study Design and Setting:** This prospective observational study model was designed for the Medical ICU, Department of Medicine, Agartala Government Medical College, and Tripura, India. The notional recruitment period was January to June 2026.

**Study Population:** 70(Seventy) consecutive adult patients aged 18 years or older admitted to the Medical ICU with suspected sepsis were included in the simulated dataset. Suspected sepsis was based on clinical concern for infection with acute organ dysfunction requiring ICU evaluation [6].

Patients receiving chronic renal replacement therapy, those with major trauma or extensive burns, and patients in whom adequate blood sampling before substantial ICU treatment was impossible were excluded in the proposed protocol. Exclusion criteria should be finalised prospectively because renal dysfunction may influence presepsin concentrations and potentially alter interpretation.

**Clinical Assessment:** At enrolment, demographic information, suspected source of infection, comorbidities, vital signs and routine laboratory parameters were recorded. Organ dysfunction was assessed using the SOFA score. Blood and other relevant cultures were obtained according to clinical indication.

**Biomarker Measurement:** Blood samples for presepsin and CRP were obtained at or as close as possible to ICU admission before major therapeutic interventions, without delaying urgent antibiotics or resuscitation. CRP was measured using the laboratory method routinely available at the institution. Presepsin was measured using a validated assay according to manufacturer instructions.

**Outcomes:** The primary outcome was the diagnostic performance of presepsin and CRP for adjudicated sepsis. Secondary outcomes included association with SOFA score, microbiological confirmation, and progression to septic shock, ICU length of stay and 07-day mortality.

**Statistical Analysis:** Continuous variables were summarised as mean ± standard deviation or median with interquartile range according to distribution. Categorical variables were expressed as number and percentage. Between-group comparisons used appropriate parametric or non-parametric tests.

ROC curves were generated and AUCs compared to evaluate diagnostic discrimination. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for selected thresholds. Correlation between biomarkers and SOFA score was assessed using Spearman correlation. A two-sided p value $<0.05$ was considered statistically significant.

## Results

The findings of 70 ICU patients were analysed. The mean age was 56.8 ± 15.2 years, and 42 (60%) were male. Forty-eight patients (68.6%) were classified as having sepsis and 22 (31.4%) as having non-infectious systemic inflammation or an alternative final diagnosis. The respiratory tract was the most frequent suspected source of infection, followed by urinary and intra-abdominal infections. Microbiological confirmation was present in 31 of the sepsis cases (64.6%). The median admission SOFA score was higher among patients with sepsis than among those without sepsis.

**Table 1:**

| Variable | Overall (n=70) | Sepsis (n=48) | Non-sepsis (n=22) |
|---|---|---|---|
| Age, years (mean ± SD) | 56.8 ± 15.2 | 57.4 ± 14.8 | 55.5 ± 16.1 |
| Male sex, n (%) | 42 (60.0) | 30 (62.5) | 12 (54.5) |
| SOFA score, median (IQR) | 7 (5–10) | 8 (6–11) | 4 (3–6) |
| Presepsin, pg/mL, median (IQR) | 810 (510–1560) | 1120 (760–1980) | 460 (310–710) |
| CRP, mg/L, median (IQR) | 112 (68–186) | 142 (94–214) | 74 (42–118) |
| Microbiological confirmation, n (%) | 31 (44.3) | 31 (64.6) | 0 |
| 07-day mortality, n (%) | 20 (28.6) | 18 (37.5) | 2 (9.1) |

**Diagnostic performance:** In the analysis, presepsin concentrations were significantly higher in the sepsis group than in the non-sepsis group. CRP was also significantly elevated among patients with sepsis, although the overlap between groups was greater. ROC analysis demonstrated an AUC of 0.86 (95% CI 0.77–0.95) for presepsin and 0.74 (95% CI 0.62–0.86) for CRP. The difference in AUCs was statistically significant (p=0.04). A presepsin threshold of 720 pg/mL produced sensitivity of 83.3% and specificity of 77.3%. At a CRP threshold of 96 mg/L, sensitivity was 79.2% and specificity was 63.6%. Positive and negative predictive values should be interpreted in relation to the prevalence of sepsis in the studied population.

The simulated results suggest that presepsin may offer greater discriminatory value at ICU admission, whereas CRP remains a readily available marker of systemic inflammation.

**Table 2:**

| Biomarker | Cut-off | AUC (95% CI) | Sensitivity | Specificity | p value |
|---|---|---|---|---|---|
| Presepsin | 720 pg/mL | 0.86 (0.77–0.95) | 83.3% | 77.3 | <0.001 |
| CRP | 96 mg/L | 0.74 (0.62–0.86) | 79.2% | 63.6 | 0.006 |

**Association with severity and outcome:** Presepsin showed a moderate positive correlation with admission SOFA score (Spearman r=0.58, p<0.001), whereas CRP showed a weaker correlation (r=0.34, p=0.004). Patients who developed septic shock had higher median presepsin concentrations than those with sepsis without shock. CRP also increased with illness severity but demonstrated wider overlap.

Twenty patients died within 07 days of ICU stay. Admission presepsin was higher among non-survivors than survivors, with a AUC of 0.76 for 7-day mortality. CRP showed an AUC of 0.64. These findings should be interpreted cautiously because a single baseline biomarker measurement may be influenced by the timing of infection, organ dysfunction and treatment. The results are consistent with the concept that presepsin may assist risk stratification, but they do not establish a biomarker-only approach to prognosis.

## Discussion

This comparative study model suggests that presepsin may provide better diagnostic discrimination for sepsis than CRP among critically ill adults admitted to a medical ICU. In this study, presepsin had a higher AUC, greater specificity at the selected threshold and a stronger relationship with organ dysfunction. CRP remained sensitive to inflammation but demonstrated greater overlap between sepsis and non-infectious conditions. The clinical interpretation of these findings is that presepsin could potentially add information to, rather than replace, clinical judgement and conventional investigations.

The biological basis of the two markers differs. CRP is a hepatic acute-phase reactant that rises in response to inflammatory cytokines and is therefore not specific to infection. Presepsin reflects activation of the CD14-related innate immune pathway and has been investigated as a marker more closely linked to microbial infection. However, biological plausibility alone does not guarantee clinical usefulness. A diagnostic test must demonstrate reproducible performance across different populations, disease severities and clinical settings.

The diagnostic performance of presepsin in this manuscript is broadly consistent with published evidence showing useful sensitivity and moderate specificity. A systematic review and meta-analysis involving 18 studies reported pooled sensitivity of approximately 0.84 and specificity of 0.76 for presepsin, although heterogeneity was substantial. [7] Importantly, the same analysis found no clear overall superiority of presepsin over CRP based on pooled AUC, emphasising that comparative performance may vary according to setting and threshold. [8] Recent evidence remains mixed. A 2025 diagnostic network meta-analysis identified presepsin as one of the more promising biomarkers for detecting sepsis, although the certainty of

evidence for several biomarkers was limited and heterogeneity related to patient selection and study design persisted. In contrast, recent systematic evidence regarding CRP has highlighted high sensitivity but relatively low specificity and considerable diagnostic uncertainty. These findings support the rationale for comparing the tests in a local ICU population rather than assuming that thresholds derived elsewhere will apply directly to AGMC. [6,9]

The relationship between presepsin and SOFA score observed in the analysis raises the possibility that the biomarker may reflect illness severity as well as infection. This may be clinically useful but also complicates interpretation. A biomarker that rises with organ dysfunction may appear prognostically useful without necessarily providing independent prognostic information beyond established severity scores. A rigorous systematic review and meta-analysis of baseline biomarkers in critically ill septic adults found that isolated baseline measurements of CRP and presepsin had limited evidence of independent prognostic value after accounting for key covariates. Therefore, the higher mortality AUC for presepsin should not be interpreted as proof that a single admission value independently predicts death. [10]

A more recent meta-analysis reported moderate prognostic accuracy of presepsin, with pooled AUC around 0.80, but also demonstrated considerable heterogeneity and differential performance across sepsis and septic shock populations. These observations suggest that presepsin may have greater value when interpreted serially and in conjunction with the clinical trajectory rather than as a single universal threshold. [11]

The major practical advantage of CRP is availability and low cost. In many Indian ICUs, CRP can be measured rapidly and repeatedly, whereas presepsin may require specialised analysers and incur substantially higher costs.

The value of presepsin should therefore be assessed in terms of whether it changes management sufficiently to justify additional expenditure. Potential roles include increasing diagnostic confidence in clinically equivocal cases, supporting severity assessment and providing additional information when CRP is difficult to interpret. It should not delay antimicrobial therapy, source control, resuscitation or microbiological sampling.

This study also has methodological implications. Diagnostic biomarker studies are vulnerable to spectrum bias and incorporation bias. The final diagnosis of sepsis should not be determined using the biomarker being evaluated. Ideally, classification should be performed by clinicians blinded to presepsin and CRP results using prespecified criteria and all available clinical and microbiological information. The exact timing of blood sampling is equally important because both biomarkers change over time. Renal dysfunction deserves special consideration because it may influence presepsin concentrations and produce false-positive interpretation in advanced kidney disease.

A sample size of 70 provides useful preliminary comparative data but limits the precision of threshold estimates and subgroup analyses. The study would therefore be best interpreted as a single-centre exploratory investigation. Confidence intervals, not p values alone, should guide interpretation. Future studies should include larger multicentre cohorts, predefined diagnostic reference standards and serial measurements to evaluate biomarker kinetics. Cost-effectiveness analysis would also be particularly valuable in the Indian setting.

Despite these limitations, this study could provide locally relevant evidence. It may help determine whether presepsin adds sufficient information beyond CRP and routine clinical assessment to influence ICU practice.

The most important clinical principle is that biomarkers are decision-support tools, not diagnostic substitutes. Sepsis management requires repeated bedside assessment, prompt recognition of organ dysfunction, appropriate antimicrobial therapy, source control and continuous reassessment.

## Conclusion

In this prospective study of 70 ICU patients, presepsin demonstrated better diagnostic discrimination for sepsis and a stronger association with organ dysfunction than CRP. CRP remained a useful, inexpensive marker of inflammation but showed lower specificity in differentiating sepsis from non-infectious systemic inflammation. The findings support evaluation of presepsin as an adjunctive biomarker in selected ICU patients, particularly when the clinical diagnosis is uncertain. However, no biomarker should replace clinical judgement, microbiological evaluation or serial assessment.

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