

Evaluation of Serum Procalcitonin and C-Reactive Protein as Biochemical Markers of Severity in Sepsis

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Abstract

Introduction: Sepsis is a life-threatening condition associated with dysregulated host response to infection and progressive organ dysfunction. Early assessment of disease severity is essential for appropriate management. Serum procalcitonin (PCT) and C-reactive protein (CRP) are commonly used inflammatory biomarkers, but their relative usefulness in assessing sepsis severity remains uncertain.

Aims: To evaluate serum procalcitonin and C-reactive protein as biochemical markers of severity in patients with sepsis and to assess their association with SOFA score.

Materials and Methods: A prospective observational study was conducted among 120 adult patients with sepsis at the Department of Biochemistry, Santiniketan Medical College and Hospital. Serum PCT and CRP levels were measured and correlated with clinical severity assessed using the SOFA score. Patients were categorized into mild, moderate and severe sepsis groups.

Result: The mean age of participants was 58.9 ± 16.1 years, and 61.7% were males. The mean PCT, CRP and SOFA scores were 8.62 ± 10.48 ng/mL, 144.2 ± 77.6 mg/L and 7.24 ± 3.38 , respectively. PCT increased significantly from 2.76 ± 2.28 ng/mL in mild cases to 17.48 ± 13.14 ng/mL in severe cases ($p < 0.001$). CRP increased from 92.8 ± 46.6 mg/L to 204.8 ± 81.6 mg/L ($p < 0.001$). PCT showed a stronger correlation with SOFA ($r = 0.674$) than CRP ($r = 0.508$), both $p < 0.001$. The AUC was 0.858 for PCT and 0.751 for CRP.

Conclusion: Both PCT and CRP were significantly associated with sepsis severity. PCT demonstrated stronger correlation with SOFA and better discriminatory performance than CRP, suggesting greater potential as an adjunctive biomarker for severity assessment.

Keywords: Sepsis; Procalcitonin; C-reactive protein; SOFA score; Biomarkers; Disease severity.

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Introduction

Sepsis is a major global health problem and remains an important cause of morbidity and mortality among critically ill patients. It is characterized by life-threatening organ dysfunction resulting from a dysregulated host response to infection. The clinical presentation of sepsis is highly variable, ranging from uncomplicated infection to severe organ dysfunction and septic shock. Early recognition and appropriate assessment of disease severity are therefore essential for timely treatment and improvement of patient outcomes.[1] The current international definition of sepsis emphasizes the development of life-threatening organ dysfunction

due to a dysregulated host response to infection, with the Sequential Organ Failure Assessment (SOFA) score being an important tool for evaluating organ dysfunction and disease severity.[1,2] The pathophysiology of sepsis involves a complex interaction between infectious microorganisms and the host immune response. Activation of inflammatory pathways results in the release of cytokines, endothelial dysfunction, abnormalities in coagulation, altered microcirculation and impaired tissue perfusion. Persistent inflammatory and immunological disturbances may subsequently lead to cellular injury, tissue hypoxia and progressive

dysfunction of multiple organs.[1] Although clinical scoring systems such as SOFA and Acute Physiology and Chronic Health Evaluation II (APACHE II) are widely used for assessing disease severity and prognosis, they require the evaluation of multiple clinical and laboratory parameters. Therefore, considerable interest has developed in the identification of biochemical biomarkers that may provide additional information regarding infection, systemic inflammation and severity of illness.[3]

Procalcitonin (PCT) is one of the most extensively studied biochemical biomarkers in bacterial infection and sepsis. Under normal physiological conditions, procalcitonin is present in the circulation at very low concentrations. During systemic bacterial infection, its production is stimulated in several tissues in response to microbial products and inflammatory mediators, resulting in increased circulating PCT concentrations.[4] Procalcitonin may increase relatively early during systemic bacterial infection and its concentration has been reported to vary according to the extent and severity of the inflammatory response. These characteristics have led to extensive investigation of PCT as a biomarker for diagnosis, severity assessment and prognosis in patients with sepsis. [5]

Several studies and systematic reviews have evaluated the diagnostic usefulness of PCT in sepsis. Evidence suggests that PCT has moderate accuracy in differentiating sepsis from non-infectious systemic inflammatory conditions.[6] Comparative evidence has also demonstrated that PCT may have better diagnostic performance than C-reactive protein (CRP) for identifying sepsis.[7] However, increased PCT concentrations are not exclusively associated with bacterial infection. Elevated levels may also occur in conditions such as major trauma, surgery, severe burns and other systemic inflammatory states. Consequently, PCT should not be interpreted as an isolated diagnostic test and should be considered together with clinical findings, microbiological investigations and other laboratory parameters.[4,6]

C-reactive protein is another widely used biochemical marker of systemic inflammation. It is an acute-phase protein synthesized mainly by the liver in response to inflammatory cytokines, particularly interleukin-6. CRP concentrations increase during infection and systemic inflammation and the test is routinely available in most clinical laboratories. Its relatively low cost, simple measurement and widespread availability make it a useful marker in patients with suspected infection and sepsis.[3] However, CRP is a non-specific inflammatory marker and may be elevated in bacterial and viral infections, autoimmune disorders, trauma, malignancy and postoperative inflammatory conditions. Furthermore, the increase in CRP

generally occurs more slowly than the rise in PCT following the onset of systemic infection.[5,7]

The potential relationship between serum PCT, CRP and the severity of sepsis is of particular clinical interest. Higher PCT concentrations have been reported in patients with more severe forms of sepsis, including severe sepsis and septic shock.[9] Several investigations have also examined the relationship between PCT, CRP and established severity scoring systems such as SOFA and APACHE II. These studies indicate that biochemical biomarkers may provide additional information regarding the degree of systemic inflammation and organ dysfunction, although their performance may vary according to the characteristics of the studied population and clinical setting.[10] Despite extensive research, the usefulness of PCT and CRP specifically as markers of sepsis severity remains an important area of investigation. Neither biomarker can replace comprehensive clinical assessment or established severity scoring systems. Nevertheless, their measurement may provide supplementary information for early risk stratification when interpreted alongside clinical examination, organ-function parameters, microbiological findings and established severity scores.[3,6,7] A comparative assessment of PCT and CRP may therefore help determine whether these readily measurable biochemical markers can assist in identifying patients with greater disease severity and potentially higher risk of adverse outcomes. Therefore, the present study is planned to evaluate serum procalcitonin and C-reactive protein as biochemical markers of severity in patients with sepsis. The study will also assess the association of serum procalcitonin and C-reactive protein levels with established clinical and laboratory indicators of disease severity.

Materials and Methods

Study design: Prospective observational study.

Place of study: Department of Biochemistry, Santiniketan Medical College and Hospital

Period of study: 18 months.

Study Population: The study population will comprise adult patients diagnosed with sepsis attending or admitted to Santiniketan Medical College and Hospital during the study period and fulfilling the predefined inclusion and exclusion criteria. The biochemical parameters serum procalcitonin and C-reactive protein (CRP) will be assessed in these patients to evaluate their association with the severity of sepsis.

Sample size: 120 patients.

Inclusion Criteria

1. Adult patients aged ≥ 18 years.

2. Patients diagnosed with sepsis according to the predefined clinical criteria.
3. Patients admitted to or attending Santiniketan Medical College and Hospital during the study period.
4. Patients who provide written informed consent to participate in the study.
5. Patients for whom serum procalcitonin and C-reactive protein (CRP) can be measured.

Exclusion Criteria

1. Patients aged <18 years.
2. Patients who do not fulfill the predefined criteria for sepsis.
3. Patients with chronic inflammatory or autoimmune diseases that may significantly affect CRP or procalcitonin levels.
4. Patients with recent major surgery, severe trauma, extensive burns, or active malignancy.
5. Patients who refuse or withdraw informed consent or have incomplete clinical/laboratory data required for the study.

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result and Interpretation

Table 1: Baseline Characteristics of Study Participants (N=120)

Variable	n (%) / Mean $\pm$ SD
Age (years)	58.9 $\pm$ 16.1
Male	74 (61.7)
Female	46 (38.3)
Diabetes mellitus	39 (32.5)
Hypertension	44 (36.7)
CKD	22 (18.3)

Table 2: Clinical and Biochemical Parameters

Parameter	Mean $\pm$ SD
Heart rate (beats/min)	109.2 $\pm$ 18.6
SBP (mmHg)	102.8 $\pm$ 21.4
TLC (/ μ L)	14,760 $\pm$ 6,180
Lactate (mmol/L)	3.22 $\pm$ 1.84
Procalcitonin (ng/mL)	8.62 $\pm$ 10.48
CRP (mg/L)	144.2 $\pm$ 77.6
SOFA score	7.24 $\pm$ 3.38

Table 3: Distribution According to Severity of Sepsis

Severity	n (%)
Mild	38 (31.7)
Moderate	52 (43.3)
Severe	30 (25.0)
<u>Total</u>	<u>120 (100.0)</u>

Table 4: Procalcitonin and CRP According to Sepsis Severity

Biomarker	Mild	Moderate	Severe	p-value
Procalcitonin (ng/mL)	2.76 $\pm$ 2.28	7.24 $\pm$ 6.62	17.48 $\pm$ 13.14	<0.001
CRP (mg/L)	92.8 $\pm$ 46.6	146.2 $\pm$ 61.8	204.8 $\pm$ 81.6	<0.001

Table 5: Correlation of Biomarkers with SOFA Score

Biomarker	r	p-value
Procalcitonin	0.674	<0.001
CRP	0.508	<0.001

Table 6: ROC Analysis for Severe Sepsis

Parameter	Procalcitonin	CRP
AUC	0.858	0.751
Cut-off	>8.5 ng/mL	>160 mg/L
Sensitivity (%)	83.3	73.3
Specificity (%)	80	68.9
p-value	<0.001	<0.001

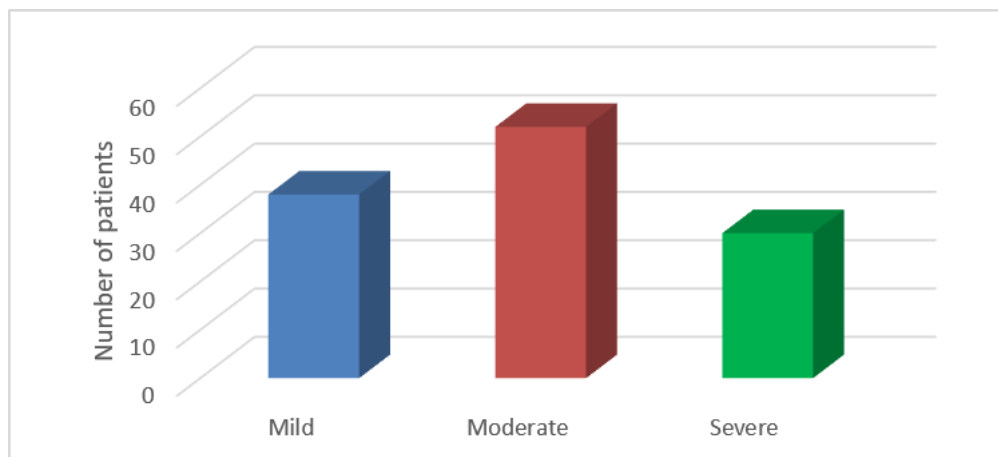
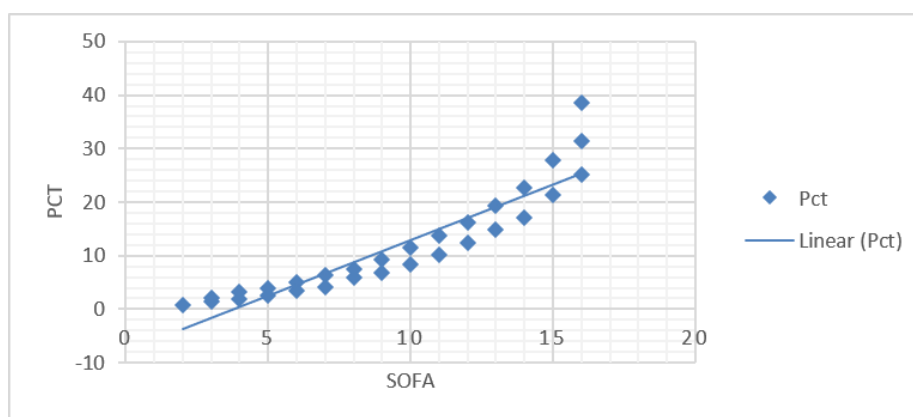
**Figure 1: Distribution According to Severity of Sepsis****Figure 2: Correlation of Biomarkers with SOFA Score**

Table 1 shows the baseline characteristics of the study participants. The mean age of the patients was 58.9 ± 16.1 years. Among the 120 participants, 74 (61.7%) were males and 46 (38.3%) were females. Diabetes mellitus was present in 39 (32.5%) patients, while 44 (36.7%) had hypertension and 22 (18.3%) had chronic kidney disease.

Table 2 presents the clinical and biochemical characteristics of the study population. The mean heart rate was 109.2 ± 18.6 beats/min, while the mean systolic blood pressure was 102.8 ± 21.4 mmHg. The mean total leukocyte count was $14,760 \pm 6,180/\mu\text{L}$ and mean serum lactate was 3.22 ± 1.84 mmol/L. The mean serum procalcitonin level was 8.62 ± 10.48 ng/mL, whereas the mean CRP level was 144.2 ± 77.6 mg/L. The mean SOFA score was 7.24 ± 3.38 .

Table 3 shows the distribution of patients according to severity of sepsis. Among the 120 patients, 38

(31.7%) had mild sepsis, 52 (43.3%) had moderate severity, and 30 (25.0%) had severe sepsis.

Table 4 demonstrates the comparison of serum procalcitonin and CRP levels across different severity groups. Mean procalcitonin increased progressively from 2.76 ± 2.28 ng/mL in mild cases to 7.24 ± 6.62 ng/mL in moderate cases and 17.48 ± 13.14 ng/mL in severe cases ($p < 0.001$). Similarly, mean CRP increased from 92.8 ± 46.6 mg/L in mild cases to 146.2 ± 61.8 mg/L in moderate cases and 204.8 ± 81.6 mg/L in severe cases ($p < 0.001$).

Table 5 presents the correlation between biochemical biomarkers and SOFA score. Serum procalcitonin demonstrated a strong positive correlation with SOFA score ($r = 0.674$, $p < 0.001$). CRP also showed a moderate positive correlation with SOFA score ($r = 0.508$, $p < 0.001$). Thus, higher levels of both biomarkers were significantly associated with greater severity of organ

dysfunction, with procalcitonin showing the stronger correlation.

Table 6 presents the ROC analysis for identification of severe sepsis. Procalcitonin demonstrated an AUC of 0.858, with an optimal cut-off of >8.5 ng/mL, sensitivity of 83.3% and specificity of 80.0% ($p < 0.001$). CRP demonstrated an AUC of 0.751, with an optimal cut-off of >160 mg/L, sensitivity of 73.3% and specificity of 68.9% ($p < 0.001$).

Discussion

The present study evaluated serum procalcitonin (PCT) and C-reactive protein (CRP) as biochemical markers of severity among 120 patients with sepsis. The mean age was 58.9 ± 16.1 years, with males comprising 61.7% of the study population. The mean serum PCT, CRP and SOFA scores were 8.62 ± 10.48 ng/mL, 144.2 ± 77.6 mg/L and 7.24 ± 3.38 , respectively. PCT increased significantly with increasing severity of sepsis, from 2.76 ± 2.28 ng/mL in mild cases to 7.24 ± 6.62 ng/mL in moderate cases and 17.48 ± 13.14 ng/mL in severe cases ($p < 0.001$). This finding is consistent with previous studies showing that PCT concentrations increase with increasing severity of infection and organ dysfunction.[11]

CRP also showed a significant increase with increasing severity of sepsis in the present study. Mean CRP increased from 92.8 ± 46.6 mg/L in mild cases to 146.2 ± 61.8 mg/L in moderate cases and 204.8 ± 81.6 mg/L in severe cases ($p < 0.001$). Similar findings have been reported in previous investigations, in which both PCT and CRP were elevated in patients with systemic inflammatory response syndrome, sepsis and organ dysfunction.[12] However, the association between CRP and severity has generally been weaker than that observed with PCT. Differences in the kinetics of the two biomarkers may partly explain this finding, as PCT tends to increase more rapidly during systemic bacterial infection, whereas CRP has a relatively slower response.[12] In the present study, PCT demonstrated a strong positive correlation with SOFA score ($r = 0.674$, $p < 0.001$), whereas CRP demonstrated a moderate positive correlation ($r = 0.508$, $p < 0.001$). Thus, higher concentrations of both biomarkers were associated with greater organ dysfunction, although the relationship was stronger for PCT. Previous studies have similarly demonstrated stronger associations between PCT and established severity scores such as SOFA and APACHE II compared with CRP.[13] A comparative study among critically ill patients also reported better performance of PCT than CRP in assessing the severity of sepsis, supporting the findings of the present study.[14] ROC analysis further demonstrated that PCT had better discriminatory performance than CRP for identifying severe sepsis. PCT showed an AUC of

0.858, with an optimal cut-off of >8.5 ng/mL, sensitivity of 83.3% and specificity of 80.0%. In comparison, CRP showed an AUC of 0.751, sensitivity of 73.3% and specificity of 68.9% at a cut-off of >160 mg/L.

These findings are broadly consistent with studies reporting superior diagnostic or severity-discriminating performance of PCT compared with CRP.[15] However, some investigations have reported that neither PCT nor CRP alone provides adequate prognostic discrimination in severe sepsis or septic shock, indicating that biomarker results should be interpreted in combination with clinical assessment and established severity scores.[16]

Conclusion

The present study demonstrated that serum procalcitonin and C-reactive protein were significantly associated with the severity of sepsis. Both biomarkers showed progressively higher levels with increasing severity of disease and demonstrated significant positive correlations with SOFA score. Procalcitonin showed a stronger correlation with SOFA score ($r = 0.674$) compared with CRP ($r = 0.508$). ROC analysis also demonstrated better discriminatory performance of procalcitonin, with an AUC of 0.858, compared with 0.751 for CRP.

These findings suggest that procalcitonin may be a more useful biochemical marker than CRP for assessing severity among patients with sepsis. However, both biomarkers should be interpreted alongside clinical findings, organ-function parameters and established severity scoring systems rather than being used as standalone indicators for clinical decision-making.

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