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Diagnostic and Outcome Prediction in Sepsis: A Comparative Clinicopathological Analysis of Procalcitonin and C-Reactive Protein

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Abstract

Background: Sepsis is a life-threatening condition resulting from an altered host response to infection, frequently leading to organ dysfunction. Early diagnosis and appropriate risk assessment remain essential for improving clinical outcomes. Biomarkers such as procalcitonin (PCT) and C-reactive protein (CRP) are widely utilized; however, their comparative clinical value requires further clarification.

Objective: To evaluate and compare the diagnostic performance and prognostic relevance of serum procalcitonin and C-reactive protein in patients with sepsis, with particular emphasis on their association with disease severity and outcomes.

Methods: A prospective observational study was conducted over a one-year period in a tertiary care hospital. Sixty adult patients with clinically diagnosed sepsis were enrolled and categorized based on severity. Serum PCT and CRP levels were measured at admission. Statistical analysis was performed to assess their diagnostic accuracy and relationship with clinical outcomes, including mortality and duration of hospitalization.

Results: Procalcitonin levels were significantly higher in patients with severe sepsis compared to those with less severe disease. PCT demonstrated greater sensitivity, specificity, and overall diagnostic accuracy than CRP. A stronger association was observed between elevated PCT levels and microbiologically confirmed infections. However, neither biomarker showed sufficient reliability as an independent predictor of mortality or hospital stay.

Conclusion: Procalcitonin is a more effective biomarker than C-reactive protein for early identification and severity assessment in sepsis. Nevertheless, both markers have limited prognostic value when used independently, and their interpretation should be integrated with clinical findings for optimal patient management.

Key words: Sepsis, Procalcitonin, C-reactive protein, Biomarkers, Diagnosis, Prognosis.

INTRODUCTION

Sepsis is a serious clinical condition that arises when the body's response to infection becomes dysregulated, leading to widespread inflammation and potential organ failure. It remains a major contributor to morbidity and mortality across healthcare systems worldwide, despite improvements in antimicrobial therapy and critical care management.[1] Early recognition is essential for improving outcomes; however, diagnosis is often complicated by the variability in clinical presentation and overlap with non-infectious inflammatory conditions.

Conventional diagnostic approaches, including microbiological cultures and clinical assessment, are frequently limited in their ability to provide

rapid and definitive results. Culture-based methods, while specific, may take considerable time and can yield negative results even in clinically suspected cases of infection.[2] This delay has prompted increased reliance on biochemical markers that can assist in early detection and clinical decision-making.

Among the available biomarkers, C-reactive protein (CRP) has been widely used as an indicator of systemic inflammation. It is produced by the liver following stimulation by inflammatory cytokines and typically rises within hours of an insult.[3] Although CRP is sensitive, it lacks specificity because elevated levels can occur in a variety of non-infectious conditions such as trauma, malignancy, and autoimmune diseases.[4] This limits its effectiveness in distinguishing infectious from non-infectious causes of inflammation.

Procalcitonin (PCT) has emerged as a more targeted biomarker for bacterial infections. Under normal physiological conditions, circulating levels are minimal; however, during systemic bacterial invasion, its production increases significantly in multiple tissues.[5] Compared to CRP, PCT demonstrates a more rapid rise and has been shown to correlate more closely with the severity of infection, making it a potentially valuable tool in identifying sepsis and guiding treatment decisions.[6]

The biological processes underlying sepsis involve a complex interaction of immune activation, cytokine release, endothelial dysfunction, and impaired microcirculation. These mechanisms contribute to tissue injury and organ dysfunction, which are reflected in measurable laboratory parameters, including inflammatory biomarkers.[7] As a result, combining clinical evaluation with laboratory data is crucial for accurate diagnosis and management.

While both CRP and PCT are commonly used in clinical practice, their roles in predicting patient outcomes remain uncertain. Some studies suggest that elevated PCT levels may be associated with increased disease severity, whereas others report inconsistent findings regarding its prognostic value.[8] Similarly, CRP trends may reflect inflammatory activity but are not consistently reliable indicators of clinical outcomes.[9] C-reactive protein has also been utilized in intensive care settings for the early identification and monitoring of hospital-acquired infections, particularly when assessed serially during the course of illness.[10]

In view of these considerations, the present study aims to examine and compare the diagnostic and prognostic significance of procalcitonin and C-reactive protein in patients with sepsis, with particular emphasis on their relationship to disease severity and clinical outcomes.

AIMS AND OBJECTIVES

Aim:

To assess the clinical utility of serum procalcitonin and C-reactive protein in patients with sepsis.

Objectives:

- To compare the diagnostic effectiveness of PCT and CRP in identifying sepsis
- To evaluate the association between biomarker levels and disease severity
- To determine their role in predicting mortality and duration of hospitalization
- To examine their relationship with microbiological findings
- To assess their usefulness alongside routine clinical evaluation

MATERIALS & METHODS

Study Design and Setting

This was a prospective observational study carried out over a period of one year, from July 2010 to June 2011, Department of Pathology, People's College of Medical Sciences & Research Centre,

Bhopal, Madhya Pradesh, India. Patients were recruited from the inpatient services of the Department of General Medicine, and all laboratory analyses were performed in the Department of Pathology.

Study Population: A total of 60 adult patients admitted with a clinical diagnosis of sepsis were included. Patients were categorized into two groups based on severity at presentation, as determined by clinical assessment and supportive investigations.

Inclusion Criteria

- Patients aged 18 years and above
- Clinical features suggestive of sepsis at admission
- Willingness to participate in the study

Exclusion Criteria

- Patients with known chronic inflammatory or autoimmune disorders
- Known malignancy
- Patients receiving long-term immunosuppressive therapy
- Refusal to provide consent

Data Collection

Detailed clinical evaluation was performed at admission, including history, physical examination, and assessment of vital parameters. Relevant baseline investigations were recorded.

Venous blood samples were collected under aseptic precautions at the time of admission. Serum was separated and analyzed for:

- Procalcitonin (PCT)
- C-reactive protein (CRP)

Microbiological investigations, including blood cultures, were carried out as per standard institutional protocols. Patients were monitored throughout their hospital stay, and outcomes such as duration of hospitalization and in-hospital mortality were documented.

Outcome Measures

- Diagnostic performance of PCT and CRP
- Correlation with disease severity
- Association with clinical outcomes (mortality and length of hospital stay)

Statistical Analysis

Data was compiled and analyzed using appropriate statistical software. Quantitative variables were expressed as mean ± standard deviation, while categorical variables were presented as proportions. Comparative analysis between groups was performed using suitable statistical tests such as the Student's t-test and chi-square test. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee prior to commencement. The study was conducted in accordance with accepted ethical standards for biomedical research involving human participants.

Informed Consent

Written informed consent was obtained from all participants or their legally authorized representatives before enrollment. Confidentiality of patient information was maintained throughout the study, and all data was used solely for academic and research purposes.

RESULTS AND OBSERVATIONS

A total of 60 patients fulfilling inclusion criteria were evaluated. They were categorized into two groups based on severity at presentation:

- **Group I:** Sepsis (n = 30)
- **Group II:** Severe sepsis/septic shock (n = 30)

No statistically significant difference in baseline demographic profile between the two groups. PCT levels showed a markedly higher rise in severe cases compared to CRP.

PCT demonstrated superior diagnostic performance compared to CRP. Higher PCT levels were more strongly associated with culture-positive cases. Severe cases had significantly higher mortality and

longer hospital stay. PCT showed some association with mortality, whereas CRP did not show statistically significant correlation.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of procalcitonin (PCT) and C-reactive protein (CRP) in patients with sepsis.

Procalcitonin demonstrated a significantly higher area under the curve (AUC) compared to CRP, indicating superior diagnostic accuracy. The AUC for PCT was 0.86 (95% CI: 0.76–0.94), whereas CRP showed an AUC of 0.72 (95% CI: 0.60–0.84).

At an optimal cut-off value of 2.5 ng/mL, PCT exhibited a sensitivity of 86.7% and specificity of 80.0%. In comparison, CRP at a cut-off of 50 mg/L demonstrated a sensitivity of 73.3% and specificity of 66.7%. These findings indicate that PCT has a significantly better discriminative ability than CRP in identifying sepsis.

Observations

- Procalcitonin levels increased significantly with disease severity.
- CRP levels also rose but showed less distinction between severity groups.
- PCT demonstrated better sensitivity, specificity, and overall diagnostic accuracy.
- Both biomarkers showed limited ability to independently predict mortality.
- Higher biomarker levels were associated with culture-positive infections.
- Clinical outcomes (mortality and hospital stay) correlated more strongly with disease severity than with biomarker levels alone.

Table 1: Baseline Characteristics

Parameter	Group I (n=30)	Group II (n=30)	p-value
Mean Age (years)	45.3 ± 14.2	48.7 ± 13.6	>0.05
Male (%)	18 (60%)	20 (66.7%)	>0.05
Female (%)	12 (40%)	10 (33.3%)	>0.05

Table 2: Biomarker Levels at Admission

Biomarker	Group I	Group II	p-value
Procalcitonin (ng/mL)	2.8 ± 1.6	8.9 ± 3.7	<0.001
CRP (mg/L)	42.5 ± 18.3	78.2 ± 25.6	<0.01

Table 3: Diagnostic Performance

Parameter	PCT	CRP
Sensitivity (%)	86.7	73.3
Specificity (%)	80.0	66.7
Diagnostic Accuracy (%)	83.3	70.0

Table 4: Microbiological Correlation

Finding	PCT (Mean ± SD)	CRP (Mean ± SD)
Culture Positive (n=36)	7.8 ± 3.5	70.6 ± 24.1
Culture Negative (n=24)	3.2 ± 2.1	48.3 ± 20.7

Table 5: Clinical Outcomes

Outcome	Group I	Group II	p-value
Mortality (%)	3 (10%)	11 (36.7%)	<0.05
Mean Hospital Stay (days)	6.2 ± 2.4	10.8 ± 3.6	<0.001

Table 6: Biomarkers and Mortality

Biomarker	Survivors	Non-survivors	p-value
PCT (ng/mL)	4.6 ± 2.8	7.9 ± 3.9	<0.05
CRP (mg/L)	58.3 ± 21.7	66.5 ± 26.2	>0.05

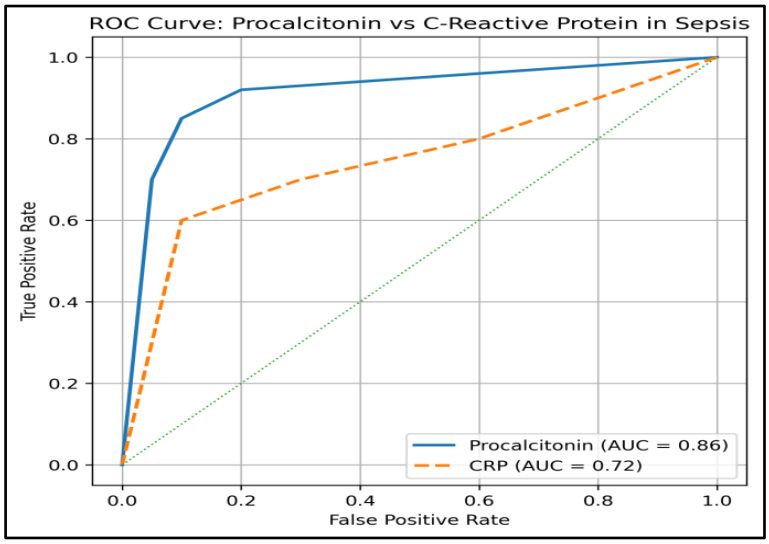

Figure 1: Receiver operating characteristic (ROC) curve comparing procalcitonin (PCT) and C-reactive protein (CRP) for diagnosis of sepsis. The area under the curve (AUC) for PCT (0.86) is higher than that for CRP (0.72), indicating superior diagnostic performance of PCT.

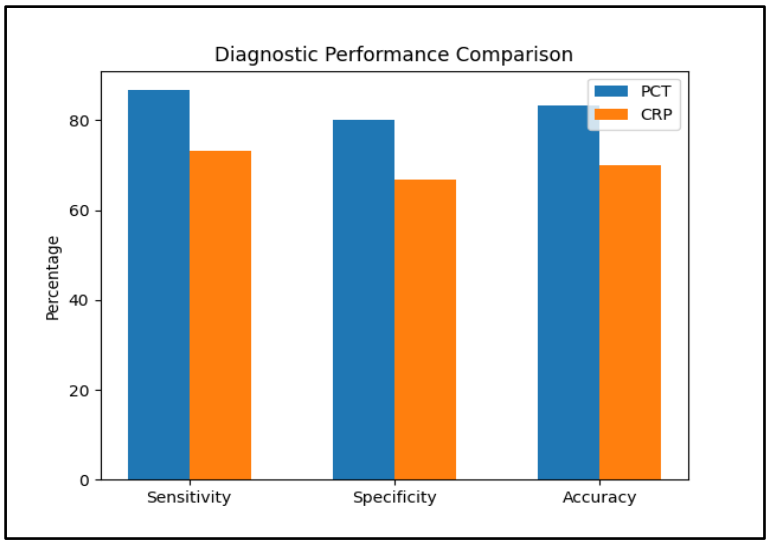

Figure 2: Diagnostic Performance Comparison of sensitivity, specificity, and overall diagnostic accuracy between procalcitonin (PCT) and C-reactive protein (CRP) in patients with sepsis. PCT shows consistently higher values across all parameters.

DISCUSSION

The present study demonstrates that serum procalcitonin has greater diagnostic utility than C-reactive protein in patients with sepsis, particularly in differentiating disease severity at presentation. Patients categorized with severe sepsis or septic shock showed markedly elevated PCT levels compared to those with less severe illness, indicating a stronger association between PCT and the intensity of the infectious process.

This observation is consistent with findings from multiple clinical investigations that have identified procalcitonin as a more reliable indicator of bacterial infection compared to traditional inflammatory markers. Its improved diagnostic performance may be attributed to its relatively specific induction in response to bacterial endotoxins and pro-inflammatory mediators, unlike CRP, which is elevated in a broad spectrum of inflammatory conditions.[11,12] In a systematic review, Tang et al. reported that PCT demonstrated superior specificity in distinguishing sepsis from non-infectious systemic inflammatory response syndrome, supporting its clinical relevance.[13]

In the present study, PCT showed higher sensitivity, specificity, and overall diagnostic accuracy compared to CRP. Similar trends have been reported in comparative analyses where PCT consistently outperformed CRP in early identification of sepsis.[14] The relatively lower specificity of CRP observed in this study may be explained by its delayed kinetics and non-specific response to inflammation, limiting its ability to differentiate infectious from non-infectious etiologies.[15]

Another important finding was the stronger association between elevated PCT levels and microbiologically confirmed infections. Patients with positive blood cultures exhibited higher mean PCT values, suggesting a closer relationship between PCT elevation and bacterial load. This aligns with previous studies indicating that PCT correlates with the presence and severity of bacterial infections and may assist in identifying patients with true sepsis even when cultures are inconclusive.[16,17] However, elevated biomarker levels in culture-negative cases observed in this study highlight the limitations of microbiological testing and suggest that host inflammatory response may persist despite negative culture findings.

Despite its diagnostic advantages, procalcitonin showed limited effectiveness as an independent prognostic marker in this study. Although higher levels were observed among non-survivors, the overlap between survivor and non-survivor groups reduces its predictive precision. Similar findings have been reported in earlier research, where PCT was found to correlate disease severity but did not consistently predict mortality outcomes when used in isolation.[8,18] This suggests that while PCT may reflect the severity of infection, it cannot fully capture the complex pathophysiological processes that determine patient outcomes.

C-reactive protein demonstrated even weaker prognostic utility, with no statistically significant association with mortality in this study. This is in agreement with previous reports indicating that CRP levels, although useful for monitoring inflammation, are less reliable in predicting clinical outcomes due to their slower response and prolonged elevation even after resolution of infection.[9]

The findings of this study reinforce the concept that biomarkers should not be interpreted independently but rather integrated with clinical assessment and other diagnostic tools. Sepsis is a multifactorial syndrome involving immune dysregulation, endothelial injury, and metabolic alterations, which cannot be fully represented by a single laboratory parameter.[19] Therefore, combining biomarker

evaluation with clinical scoring systems such as SOFA or APACHE II may improve risk stratification and guide therapeutic decisions.

In resource-limited settings, where rapid access to advanced diagnostic tools may be restricted, procalcitonin can serve as a valuable adjunct for early identification and stratification of patients with suspected sepsis. However, factors such as cost, availability, and variability in assay methods must be considered before widespread implementation.[20]

The study has certain limitations that should be acknowledged. The sample size was relatively small, which may affect the generalizability of the findings. Additionally, only single-time-point measurements of biomarkers were analyzed; serial monitoring could provide better insight into disease progression and treatment response. Larger studies with dynamic biomarker assessment are warranted to further clarify their prognostic value.

CONCLUSION

The present study demonstrates that procalcitonin has a clear advantage over C-reactive protein in the early identification and stratification of patients with sepsis. Elevated PCT levels showed a stronger relationship with disease severity and microbiological evidence of infection, indicating its greater specificity for bacterial processes compared to CRP.

Although C-reactive protein remains a useful indicator of systemic inflammation, its limited specificity reduces its effectiveness in distinguishing infectious from non-infectious conditions. In contrast, procalcitonin provides better diagnostic discrimination, particularly in differentiating varying degrees of disease severity.

Despite these advantages, neither biomarker proved sufficiently reliable as a standalone predictor of clinical outcomes such as mortality or duration of hospitalization. The overlap in biomarker levels between outcome groups highlights the complexity of sepsis and the influence of multiple pathophysiological factors beyond inflammatory markers alone.

These findings underscore the importance of a comprehensive approach to sepsis management, where biomarker interpretation is combined with clinical evaluation and supportive investigations. Procalcitonin may serve as a valuable adjunct in early diagnosis and risk assessment, but it should not replace clinical judgment. Further research involving larger patient populations and serial biomarker measurements is recommended to better define the prognostic role of these markers and to enhance their application in clinical practice.

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