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Procalcitonin versus C-Reactive Protein: Evaluating Their Role in Sepsis Severity and Prognosis

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Abstract

Background: Sepsis remains a major contributor to morbidity and mortality worldwide, particularly in hospitalized and critically ill patients. Early recognition of disease severity and accurate prediction of outcomes are essential for timely intervention and improved survival. Biomarkers play an important role in this process, with procalcitonin (PCT) and C-reactive protein (CRP) being among the most commonly utilized indicators of systemic inflammation. However, differences in their biological behavior may influence their effectiveness in clinical practice.

Objective: To compare the effectiveness of procalcitonin and C-reactive protein as biomarkers in assessing severity and predicting outcomes in patients with sepsis.

Methods: This prospective clinico-microbiological study was conducted over a period of one year at a tertiary care teaching hospital and included 90 adult patients diagnosed with sepsis. Serum levels of procalcitonin and C-reactive protein were measured at the time of admission. These values were analyzed in relation to disease severity, microbiological findings, and clinical outcomes, including recovery, complications, and mortality.

Results: Both biomarkers demonstrated a progressive increase with worsening severity of sepsis. However, procalcitonin showed a more marked rise, with mean levels increasing from 1.8 ng/mL in patients with sepsis to 12.2 ng/mL in those with septic shock. Patients with adverse outcomes exhibited significantly higher procalcitonin levels (13.5 ng/mL) compared to those who recovered (3.2 ng/mL). Receiver operating characteristic analysis indicated superior predictive performance of procalcitonin (AUC 0.89) compared to C-reactive protein (AUC 0.76).

Conclusion: These findings indicate that procalcitonin provides better correlation with disease severity and clinical outcomes than C-reactive protein. Its use as part of routine evaluation may facilitate early risk stratification and support more effective clinical decision-making in the management of sepsis.

Key words: Procalcitonin, C-reactive protein, Sepsis, Biomarkers, Disease Severity, Clinical Outcomes, Microbiology.

INTRODUCTION

Sepsis is a complex clinical condition resulting from an abnormal host response to infection, often leading to organ dysfunction and significant mortality.[1,2] Despite advances in antimicrobial therapy, intensive care management, and supportive interventions, sepsis continues to pose a substantial burden on healthcare systems worldwide.[3,4] One of the major challenges in managing this condition lies in the early identification of patients at risk of progression to severe disease or adverse outcomes. Timely recognition is essential, as delays in diagnosis and treatment are associated with increased morbidity and mortality.[5,6] The clinical presentation of sepsis can vary widely, ranging from subtle systemic

symptoms to overt organ failure. Common features such as fever, tachycardia, hypotension, and altered mental status are frequently encountered but are not specific to sepsis. In many cases, these signs may develop late in the disease course, limiting their usefulness in early risk assessment.[7,8] Furthermore, overlapping features with other inflammatory conditions can complicate clinical evaluation. As a result, reliance on clinical parameters alone may not provide sufficient accuracy in determining disease severity or predicting outcomes.

To overcome these limitations, attention has increasingly shifted toward the use of biochemical markers that reflect the underlying inflammatory response. Among these, C-reactive protein has been widely used due to its availability and sensitivity.[9,10] It is produced by the liver in response to inflammatory cytokines and serves as a general indicator of systemic inflammation.[11] However, CRP lacks specificity for infection and may be elevated in a variety of non-infectious conditions, including trauma, surgery, and chronic inflammatory disorders. Additionally, its delayed rise following the onset of infection reduces its utility in early diagnosis[12,13] and immediate clinical decision-making.

Procalcitonin has emerged as an alternative biomarker with greater specificity for bacterial infections. Under normal physiological conditions, circulating levels of procalcitonin are minimal. During systemic infection, however, its production increases significantly across multiple tissues in response to inflammatory mediators and bacterial endotoxins.[14,15] One of the key advantages of procalcitonin is its rapid increase following the onset of infection, often within a few hours. This early response, combined with its closer association with bacterial etiology, makes it a potentially valuable marker for both diagnosis and prognostication.[16,17] From a microbiological perspective, the identification of causative pathogens remains central to the management of sepsis. Blood cultures and other microbiological investigations provide definitive evidence of infection and guide targeted antimicrobial therapy. However, these methods require time and may not always yield positive results, particularly in patients who have received prior antibiotics. In such situations, biomarkers can offer supportive information that assists clinicians in initiating empirical therapy and assessing disease progression while awaiting culture results.

In clinical practice, the ability to assess disease severity and predict outcomes is crucial for determining the level of care required. Patients at higher risk of complications or mortality may benefit from early admission to intensive care units, closer monitoring, and more aggressive therapeutic interventions. Biomarkers that accurately reflect disease severity can therefore play an important role in guiding clinical decisions and optimizing resource utilization.

Although both CRP and procalcitonin are routinely used, their comparative effectiveness remains a subject of ongoing investigation. Differences in their kinetics, specificity, and response to infection suggest that they may provide distinct clinical information. Some studies have indicated that procalcitonin correlates more closely with disease severity and outcomes, while others have reported variable findings depending on patient populations and study design. This variability highlights the need for further evaluation, particularly in specific clinical settings.[18-20]

In addition, the utility of biomarkers may be influenced by local epidemiological factors, including the prevalence of different pathogens and patterns of antimicrobial resistance. Studies conducted within individual institutions can

therefore provide valuable insights that are directly applicable to local clinical practice.

In this context, the present study was undertaken to compare the role of procalcitonin and C-reactive protein in assessing the severity of sepsis and predicting clinical outcomes. By analyzing their relationship with microbiological findings and patient progression, the study aims to determine their relative usefulness as prognostic indicators and to support improved clinical management strategies.

AIMS AND OBJECTIVES

Aim

To compare the effectiveness of procalcitonin and C-reactive protein as biomarkers in assessing severity and predicting clinical outcomes in patients with sepsis.

Objectives

1. To measure serum procalcitonin and C-reactive protein levels in patients diagnosed with sepsis
2. To correlate biomarker levels with severity of sepsis at presentation
3. To evaluate the association of procalcitonin and C-reactive protein levels with clinical outcomes such as recovery, complications, and mortality
4. To compare the predictive accuracy of procalcitonin and C-reactive protein
5. To analyze microbiological profiles and correlate them with biomarker levels

MATERIALS & METHODS

Study Design

This was a prospective observational clinico-microbiological study.

Study Setting

The study was conducted in the Department of Microbiology, National Institute of Medical Sciences & Research, NIMS University, Jaipur, Rajasthan, India.

Study Duration

The study was carried out over a period of one year.

Study Population

A total of 90 patients diagnosed with sepsis were included in the study.

Inclusion Criteria

- Patients aged 18 years and above
- Patients diagnosed with sepsis based on clinical and laboratory criteria
- Patients willing to participate and provide informed consent

Exclusion Criteria

- Patients with non-infectious causes of systemic inflammation (e.g., trauma, burns, autoimmune diseases)
- Patients on long-term immunosuppressive therapy
- Patients with known malignancy
- Patients unwilling to participate

Data Collection Procedure

All eligible patients admitted to the medical wards or intensive care units were evaluated. After obtaining informed consent, detailed clinical history and examination findings were recorded.

At admission, blood samples were collected for measurement of serum procalcitonin and C-reactive protein levels. Additional laboratory investigations were performed as part of routine clinical care.

Microbiological evaluation included blood cultures and other relevant cultures (e.g., urine, sputum) based on clinical suspicion. Isolated organisms were identified, and antimicrobial sensitivity patterns were recorded.

Patients were monitored throughout their hospital stay for disease progression and outcomes. Severity of sepsis was assessed based on clinical parameters and organ dysfunction. Outcomes were categorized

as recovery, development of complications, or death. (mortality).

Outcome Measures

- Primary outcome: Association of procalcitonin and C-reactive protein levels with severity of sepsis
- Secondary outcomes: Correlation of biomarker levels with clinical outcomes and microbiological findings

Statistical Analysis

Data were analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation, and categorical variables were presented as frequencies and percentages.

Comparisons were made using the independent t-test for continuous variables and chi-square test for categorical variables. Receiver operating characteristic (ROC) curve analysis was performed to compare the predictive accuracy of procalcitonin and C-reactive protein. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations and Consent

Approval for the study was obtained from the Institutional Ethics Committee of NIMS Hospital, Jaipur prior to commencement. Written informed consent was obtained from all participants after explaining the purpose, procedures, and potential risks of the study in a language they understood. Confidentiality of patient information was strictly maintained. The study was conducted in accordance with established ethical guidelines for biomedical research. No additional risk or financial burden was imposed on the participants, and all investigations were carried out as part of standard clinical management.

RESULTS

A total of 90 patients with sepsis were included in the study. Serum procalcitonin (PCT) and C-reactive protein (CRP) levels were measured at admission and correlated with severity, microbiological profile, and clinical outcomes.

Sequential Interpretation of Results

- The majority of patients presented with sepsis or severe sepsis, with 24.5% progressing to septic shock.
- Both PCT and CRP levels increased significantly with increasing severity of sepsis, but the rise was more pronounced for procalcitonin.
- Higher biomarker levels were strongly associated with poor outcomes, including complications and mortality.
- Microbiological analysis showed a predominance of gram-negative organisms.
- ROC analysis demonstrated that procalcitonin had excellent predictive accuracy (AUC = 0.89), whereas CRP showed moderate accuracy (AUC = 0.76).
- Procalcitonin also exhibited higher sensitivity and specificity, making it a more reliable biomarker for predicting severity and outcomes in sepsis.

Table 1: Demographic Characteristics

Parameter	Value (n=90)
Age (years, mean ± SD)	46.2 ± 14.8
Gender (M/F)	52 / 38
ICU admissions	34 (37.8%)

Descriptive statistics; no inferential test applied.

Table 2: Severity of Sepsis at Presentation

Severity	Number	Percentage (%)
Sepsis	38	42.2%
Severe sepsis	30	33.3%
Septic shock	22	24.5%

Table 3: Biomarker Levels According to Severity

Severity	Procalcitonin (ng/mL, mean ± SD)	CRP (mg/L, mean ± SD)	p-value
Sepsis	1.8 ± 0.9	48.6 ± 15.2	
Severe sepsis	5.6 ± 2.3	82.4 ± 20.5	
Septic shock	12.2 ± 4.8	118.7 ± 28.6	**<0.001**

ANOVA test applied; both biomarkers increased significantly with severity, with a steeper rise observed for procalcitonin.

Table 4: Clinical Outcomes

Outcome	Number	Percentage (%)
Recovered	56	62.2%
Complications	18	20.0%
Mortality	16	17.8%

Table 5: Biomarker Levels According to Outcome

Outcome	Procalcitonin (ng/mL, mean ± SD)	CRP (mg/L, mean ± SD)	p-value
Recovered	3.2 ± 1.5	62.8 ± 18.4	
Complications	7.8 ± 3.1	95.6 ± 24.3	
Mortality	13.5 ± 5.2	120.4 ± 30.1	**<0.001**

ANOVA test applied; higher biomarker levels were significantly associated with adverse outcomes.

Table 6: Microbiological Profile

Organism	Number (n=90)	Percentage (%)
Gram-negative bacteria	46	51.1%
Gram-positive bacteria	28	31.1%
Fungal infections	8	8.9%
No growth	8	8.9%

Table 7: ROC Curve Analysis for Predicting Adverse Outcomes

Biomarker	AUC (95% CI)	Sensitivity (%)	Specificity (%)
Procalcitonin	0.89 (0.82–0.96)	87.5%	82.1%
C-reactive protein	0.76 (0.67–0.85)	72.3%	68.4%

Procalcitonin demonstrated higher diagnostic accuracy compared to CRP.

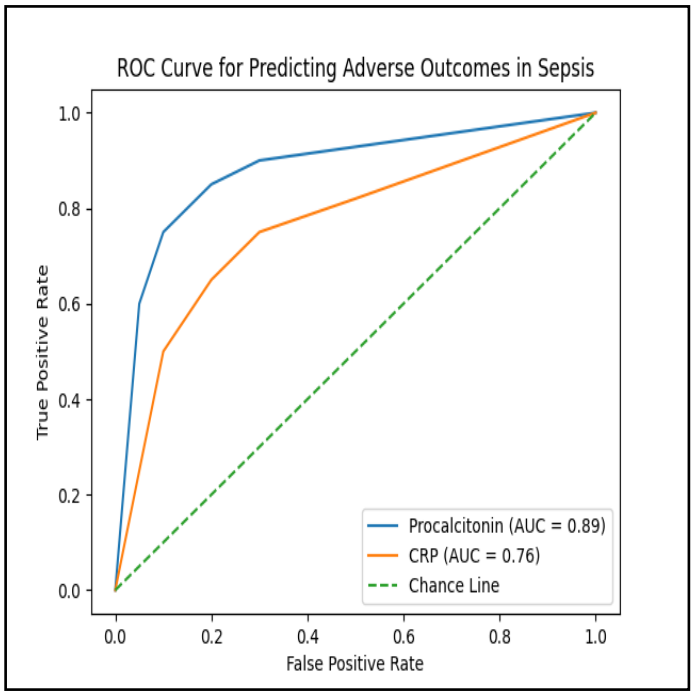

Figure 1: ROC Curve Analysis: Receiver operating characteristic (ROC) curve comparing procalcitonin and C-reactive protein for predicting adverse outcomes in sepsis. Procalcitonin showed superior diagnostic performance (AUC = 0.89) compared to CRP (AUC = 0.76).

DISCUSSION

The analysis performed in this study highlights a consistent relationship between biomarker levels and the clinical course of sepsis. While both procalcitonin and C-reactive protein increased in response to infection, the magnitude and pattern of change differed significantly between the two.

Patients with more severe forms of sepsis demonstrated a substantial rise in procalcitonin levels, indicating a closer association with systemic inflammatory burden.[14,15] In contrast, CRP levels increased more gradually, suggesting a less direct relationship with disease severity.[10,12] This difference may be attributed to the biological pathways involved in their production, with procalcitonin responding more rapidly to bacterial stimuli.

Outcome-based evaluation further supports the role of procalcitonin as a prognostic indicator.[18,19] Individuals who developed complications or did not survive had markedly higher PCT values at admission. Although CRP levels were also elevated in these patients, the separation between outcome groups was less distinct. This suggests that procalcitonin may provide better early identification of high-risk cases.

The diagnostic accuracy observed through ROC analysis reinforces these findings.[20] A higher area under the curve for procalcitonin indicates stronger discrimination between favorable and unfavorable outcomes. From a clinical standpoint, this level of accuracy can assist in prioritizing patients who require intensive monitoring or aggressive intervention. Microbiological findings in this study showed a predominance of gram-negative organisms, which may partly explain the elevated biomarker levels observed.[3,5] The interaction between pathogen type and host response plays a significant role in determining the degree of systemic inflammation. In situations where culture results are delayed or inconclusive, biomarker trends can provide valuable interim guidance.

The integration of biomarkers into routine practice offers practical advantages. Early identification of severe cases allows timely escalation of care, potentially reducing complications and mortality.[6,7] Procalcitonin, in particular, appears to offer clinically relevant information that complements both laboratory and bedside assessment.

Certain limitations should be considered. The study was conducted at a single center with a limited sample size. Serial measurements were not performed, which could have provided additional insight into dynamic changes during treatment. Future studies involving larger populations and repeated measurements may further clarify the role of these biomarkers.

Overall, the findings indicate that procalcitonin provides a more precise reflection of disease severity and outcome risk compared to C-reactive protein. Its use as part of an integrated clinical approach may enhance the management of sepsis.

CONCLUSION

Both procalcitonin and C-reactive protein increase in response to sepsis; however, their clinical utility differs. Procalcitonin demonstrates a stronger relationship with disease severity, complications, and mortality.

Higher predictive accuracy, along with better sensitivity and specificity, makes procalcitonin a more effective biomarker for risk assessment. Its use in conjunction with microbiological evaluation can support early identification of high-risk patients and guide clinical management decisions. Incorporating procalcitonin into routine assessment may improve the overall approach to sepsis management and contribute to better patient outcomes.

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