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To study the Diagnostic Accuracy of Procalcitonin and C-Reactive Protein in Sepsis with special reference to its Microbial Etiology and Antimicrobial Biomarker Profiles in Blood Culture Positive Sepsis Patients

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ABSTRACT

Background: Early and accurate diagnosis of sepsis is critical for prompt management and improved prognosis. Procalcitonin (PCT) and C-reactive protein (CRP) are widely used biomarkers for infection, but their comparative diagnostic utility in culture-positive sepsis requires further evaluation.

Objective: To assess the diagnostic accuracy of PCT and CRP in sepsis and septic shock, and to correlate biomarker levels with blood culture findings.

Methods: A case-control study was conducted on 80 participants, comprising 40 sepsis patients and 40 age- and sex-matched healthy controls. Demographic data, blood culture results, and PCT and CRP levels were recorded. ROC curve analysis determined the sensitivity, specificity, and optimal cut-off values.

Results: The mean age was significantly higher in the sepsis group compared to controls (54.8 ± 18.9 vs 46.3 ± 15.4 years; $p<0.01$). Blood culture was positive in 13 (32.5%) patients, with Gram-negative bacteria predominating (84.6%), particularly Escherichia coli (38.5%). Culture-positive patients had significantly higher PCT levels (median 8.96 ng/ml) compared to culture-negative (1.99 ng/ml) and controls (0.049 ng/ml). CRP levels were also elevated in culture-positive patients but showed less discriminatory power. PCT demonstrated excellent diagnostic accuracy for sepsis vs control (AUC 0.93) and moderate accuracy for culture-positive vs culture-negative (AUC 0.79). CRP had lower discriminatory capacity (AUC 0.85 for sepsis vs control; 0.53 for culture-positive vs culture-negative).

Conclusion: PCT is a superior biomarker to CRP for distinguishing sepsis from controls and

for differentiating culture-positive from culture-negative sepsis. Its early application may enhance diagnostic precision and improve patient outcomes.

Keywords: Diagnostic Accuracy, Procalcitonin, C-Reactive, Protein, Sepsis, Microbial Etiology Antimicrobial Biomarker, Blood Culture, Positive Sepsis Patients

INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection, with mortality rates exceeding 25% despite advances in intensive care management [1]. Early diagnosis is essential for timely initiation of antimicrobial therapy, which significantly improves survival [2]. Blood culture remains the gold standard for identifying causative pathogens, but its utility is limited by delayed turnaround time, low sensitivity, and susceptibility to contamination [3].

Biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) have emerged as valuable adjuncts for early sepsis detection. CRP, an acute-phase reactant produced in the liver in response to interleukin-6, rises within 6–8 hours after infection onset, but lacks specificity as it is elevated in various inflammatory conditions [4,5]. In contrast, PCT, a precursor of the hormone calcitonin, is markedly increased in bacterial infections due to systemic inflammatory activation, and its levels correlate with sepsis severity [6,7].

Several studies have reported that PCT demonstrates superior specificity and prognostic value compared to CRP in bacterial sepsis [8,9]. However, the comparative performance of these biomarkers in differentiating culture-positive from culture-negative sepsis remains inconsistent, particularly in resource-limited settings [10,11]. Moreover, the association of biomarker levels with specific microbial etiologies is not well established in Indian populations.

This study aimed to evaluate the diagnostic accuracy of PCT and CRP in sepsis and septic shock, correlate biomarker levels with blood culture results, and determine their predictive value for various pathogens.

MATERIAL AND METHODS

This hospital-based case-control study was conducted in the Department of Microbiology and Intensive Care Unit of a tertiary care centre over a period of 12 months. Ethical clearance was obtained from the institutional ethics committee, and written informed consent was taken from all participants.

Study population: The study included 40 patients aged ≥18 years diagnosed with sepsis or septic shock according to Sepsis-3 criteria, and 40 healthy age- and sex-matched controls without clinical or laboratory evidence of infection.

Inclusion criteria: Patients admitted to ICU with clinical features of sepsis, positive or negative blood cultures, and no recent major surgery or trauma.

Exclusion criteria: Patients with chronic inflammatory diseases, autoimmune disorders, recent major surgery, burns, or immunosuppressive therapy.

Sample collection and laboratory analysis:

Blood culture: Two sets of blood samples were collected aseptically before initiation of

antibiotics and processed using automated blood culture systems. Identification of isolates and antimicrobial susceptibility testing were performed as per CLSI guidelines.

Biomarker estimation: Serum PCT was measured using an electrochemiluminescence immunoassay, and CRP was quantified via immunoturbidimetry.

Statistical analysis: Data were analysed using SPSS software. Continuous variables were expressed as mean ± SD or median (IQR). ROC curves determined diagnostic accuracy, area under the curve (AUC), sensitivity, specificity, and optimal cut-off values. $p<0.05$ was considered statistically significant.

RESULTS

The mean age of the sepsis group was 54.8 ± 18.9 years, significantly higher than controls (46.3 ± 15.4 years; $p<0.01$). Gender distribution was comparable between groups. Blood culture positivity was observed in 13 (32.5%) sepsis patients, with Gram-negative bacteria accounting for 84.6% of isolates. *Escherichia coli* (38.5%) was the most common pathogen, followed by *Klebsiella pneumoniae* (23.1%), *Pseudomonas aeruginosa* (15.4%), *Acinetobacter baumannii* (7.7%), and *Staphylococcus aureus* (15.4%).

Median PCT levels were highest in culture-positive patients [8.96 (4.68–26.62) ng/ml], followed by culture-negative patients [1.99 (0.41–6.16) ng/ml] and controls [0.049 (0.04–0.13) ng/ml]. Median CRP levels were also elevated in culture-positive patients [36.12 (26.38–54.33) mg/L] compared to culture-negative [34.53 (25.65–40.90) mg/L] and controls [8.61 (2.64–20.62) mg/L], though the difference between culture-positive and culture-negative groups was minimal.

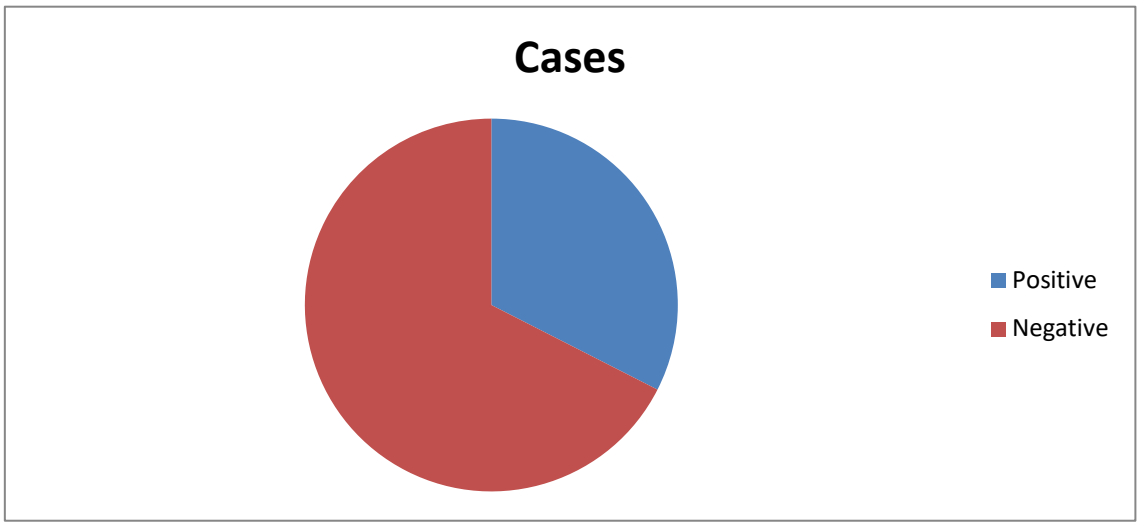
ROC analysis for PCT showed excellent diagnostic accuracy for sepsis vs control (AUC 0.93; cut-off >0.393 ng/ml; sensitivity 86.3%; specificity 86.3%), moderate accuracy for culture-positive vs culture-negative (AUC 0.79; cut-off >3.53 ng/ml; sensitivity 80.8%; specificity 72.2%), and fair accuracy for sepsis vs septic shock (AUC 0.76). CRP demonstrated lower discriminatory performance, particularly for culture-positive vs culture-negative cases (AUC 0.53).

TABLE 1. Demographic Profile

Parameter	Sepsis Group (n=40)	Control Group (n=40)	p-value
Mean Age (years)	54.8 ± 18.9	46.3 ± 15.4	<0.01
Male	18 (45%)	17 (42.5%)	0.75
Female	22 (55%)	23 (57.5%)	

TABLE 2. Blood Culture Positivity

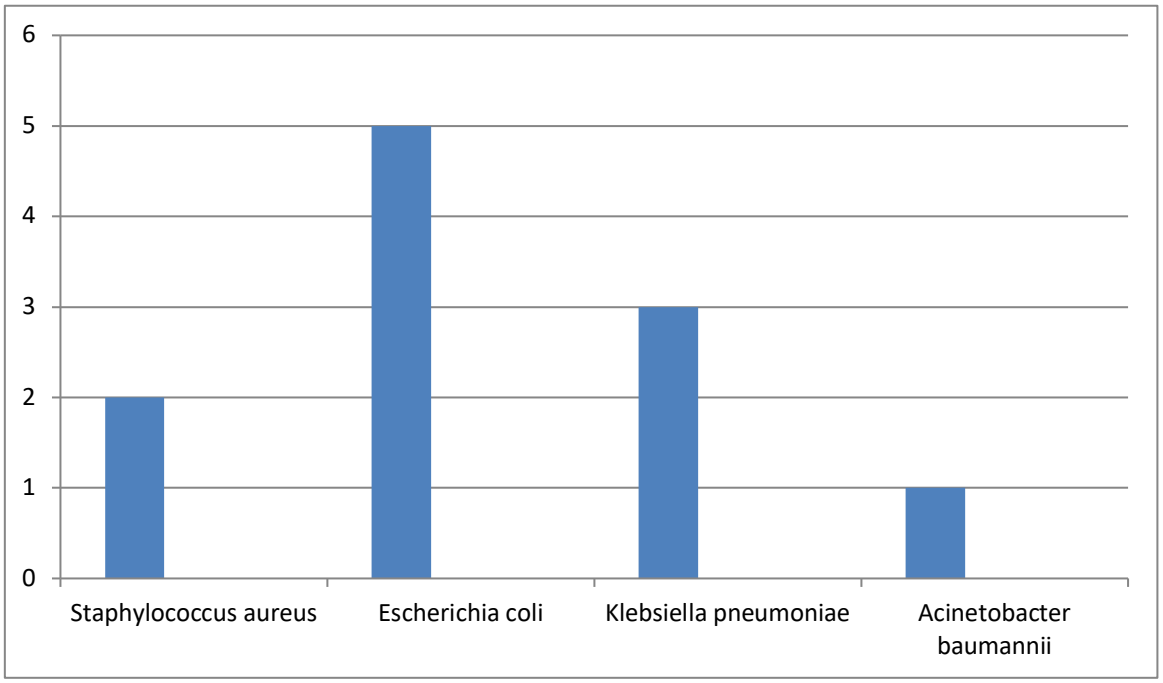
Blood Culture Result	Number	Percentage
Positive	13	32.5%
Negative	27	67.5%



Graph No. 1: Graphical Representation of of Isolated Organisms

Table 3 : Isolated Organisms

Organism Type	No. of Isolates	Percentage
Gram +ve Bacteria	2	15.4%
Staphylococcus aureus	2	15.4%
Gram -ve Bacteria	11	84.6%
Escherichia coli	5	38.5%
Klebsiella pneumoniae	3	23.1%
Acinetobacter baumannii	1	7.7%
Pseudomonas aeruginosa	2	15.4%



Graph No. 2: Graphical Representation of Isolated Organisms

TABLE 4. PCT and CRP Levels by Pathogen

Pathogen	Median PCT (ng/ml)	Median CRP (mg/L)
Gram +ve (n=2)	4.06	38.22
Gram -ve (n=11)	12.56	35.91
E. coli (n=5)	18.22	31.73
K. pneumoniae (n=3)	17.43	33.18
A. baumannii (n=1)	11.75	55.34
P. aeruginosa (n=2)	5.85	32.56

TABLE 5. Biomarkers Across Groups

Group	Mean PCT (ng/ml) (mg/L)	Median (IQR)	Mean CRP	Median (IQR)
Culture Positive	15.39 ± 14.53	8.96 (4.68–26.62)	40.22 ± 18.54	36.12 (26.38–54.33)

Culture Negative	4.84 ± 7.16	1.99 (0.41–6.16)	38.21 ± 18.84	34.53 (25.65–40.90)
Control	0.17 ± 0.23	0.049 (0.04–0.13)	14.80 ± 15.32	8.61 (2.64–20.62)

TABLE 6. ROC Diagnostic Performance of PCT

Comparison	AUC	Sensitivity	Specificity	Cut-off (ng/ml)
Control vs Sepsis	0.93	86.3%	86.3%	>0.393
Culture +ve vs Culture –ve	0.79	80.8%	72.2%	>3.53
Sepsis vs Septic Shock	0.76	100%	60.7%	>2.42

TABLE 7. ROC Diagnostic Performance of CRP

Comparison	AUC	Sensitivity	Specificity	Cut-off (mg/L)
Control vs Sepsis	0.85	100%	66.3%	>15.70
Culture +ve vs Culture -ve	0.53	46.2%	72.2%	>38.08
Sepsis vs Septic Shock	0.88	84.2%	85.2%	>39.43

DISCUSSION

Our study demonstrates that PCT outperforms CRP in differentiating sepsis from controls and in distinguishing culture-positive from culture-negative sepsis. The predominance of Gram-negative bacteria, especially E. coli and K. pneumoniae, is consistent with previous Indian ICU studies [1,2].

PCT elevation in bacterial infections is attributed to the systemic inflammatory response triggered by microbial endotoxins, making it a more reliable marker for bacterial sepsis than CRP, which can rise in viral infections, trauma, and autoimmune diseases [3,4]. Multiple meta-analyses have confirmed the superior specificity of PCT over CRP in diagnosing sepsis, with pooled AUC values above 0.85 [5,6].

Our ROC findings align with the results of Liu et al. [7], who reported an AUC of 0.92 for PCT in distinguishing sepsis from controls, compared to 0.81 for CRP. Similarly, a multicentre

European study found that PCT was significantly better in identifying bacteremia than CRP, particularly in Gram-negative infections [8].

The limited performance of CRP in differentiating culture-positive from culture-negative cases in our study mirrors the findings of Hoeboer et al. [9], suggesting that CRP is less influenced by bacterial load and more by systemic inflammation. The higher PCT levels in Gram-negative infections, as observed in our study, have been linked to the potent endotoxin-mediated induction of the CALC-1 gene [10].

CONCLUSION

Procalcitonin is a more reliable biomarker than CRP for diagnosing sepsis and differentiating culture-positive from culture-negative cases. Its superior specificity, particularly in Gram-negative infections, supports its early use in sepsis workup. Integration of PCT measurement with clinical assessment and blood culture may expedite diagnosis, guide antibiotic therapy, and improve outcomes.

DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study
Consent to participate: There is consent to participate.
Consent for publication: There is consent for the publication of this paper.
Authorscontributions: Author equally contributed the work.

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