



Original Article

## Diagnostic Correlation of Procalcitonin and C-Reactive Protein with Blood Culture Results in Suspected Sepsis

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Received: 20-01-2026

Accepted: 15-04-2026

Available online: 26-05-2026

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### ABSTRACT

**Background:** Sepsis remains a major cause of morbidity and mortality worldwide, particularly in developing countries. Blood culture is considered the gold standard for diagnosis; however, its sensitivity is often limited due to prior antibiotic use, delayed sampling, and low bacterial load. Consequently, there is an increasing need for reliable biomarkers such as Procalcitonin (PCT) and C-Reactive Protein (CRP) for early diagnosis and prediction of bloodstream infections.

**Aim:** To evaluate the diagnostic utility of serum Procalcitonin and C-Reactive Protein levels in predicting blood culture positivity among suspected sepsis patients in a tertiary care centre with low culture positivity rates.

**Methods:** A hospital-based observational study was conducted on 210 clinically suspected sepsis patients. Blood samples were collected for culture, serum Procalcitonin, and CRP estimation. Patients were categorized based on culture results, and biomarker levels were compared. Statistical analysis included sensitivity, specificity, predictive values, and correlation assessment.

**Results:** Out of 210 patients, only 28 (13.3%) showed blood culture positivity. Serum Procalcitonin and CRP levels were significantly elevated in culture-positive patients compared to culture-negative patients ( $p < 0.001$ ). Procalcitonin demonstrated higher specificity, while CRP showed moderate sensitivity. Combined use of both biomarkers improved diagnostic accuracy, particularly in cases with negative blood cultures.

**Conclusion:** Procalcitonin and CRP are valuable adjunctive biomarkers for early diagnosis of sepsis, especially in low blood culture yield settings. Their combined use enhances diagnostic reliability and may guide early antimicrobial therapy.

**Keywords:** Sepsis, Procalcitonin, C-Reactive Protein, Blood Culture, Biomarkers, Diagnostic Accuracy.

### INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection and continues to be a leading cause of mortality globally, particularly in critically ill patients admitted to intensive care units [1]. Despite advances in diagnostic and therapeutic modalities, sepsis contributes significantly to healthcare burden, with millions of deaths reported annually worldwide [2]. Early diagnosis and prompt initiation of appropriate antimicrobial therapy are crucial determinants of patient outcomes in sepsis [3].

The diagnosis of sepsis remains challenging due to its heterogeneous clinical presentation and overlap with non-infectious inflammatory conditions. Traditionally, blood culture has been regarded as the gold standard for identifying causative pathogens in sepsis [4]. However, the diagnostic yield of blood cultures is often suboptimal, with positivity rates ranging between 10% and 40% in various studies [5]. The low sensitivity of blood cultures can be attributed to several factors, including prior administration of antibiotics, inadequate sample volume, intermittent bacteremia, and

technical limitations [6,7]. In developing countries, the issue is further compounded by widespread empirical antibiotic use before hospital admission, leading to significantly reduced culture positivity rates [8].

Given these limitations, there has been increasing interest in the use of biomarkers for the early detection and management of sepsis. Among these, Procalcitonin (PCT) and C-Reactive Protein (CRP) have emerged as widely studied and clinically relevant markers [9]. Procalcitonin, a precursor of the hormone calcitonin, is produced in response to bacterial infections and has been shown to correlate with the severity of sepsis [10]. Unlike other inflammatory markers, PCT levels rise rapidly within 4–6 hours of infection and are less influenced by viral infections or non-infectious inflammatory conditions [11,12].

C-Reactive Protein, an acute-phase reactant synthesized by the liver, is another commonly used biomarker in clinical practice [13]. CRP levels increase in response to inflammation; however, its specificity for bacterial infections is relatively lower compared to PCT [14]. Despite this limitation, CRP remains widely used due to its availability, cost-effectiveness, and established role in monitoring inflammatory conditions [15].

Several studies have compared the diagnostic performance of PCT and CRP in sepsis, with varying results. While some studies suggest that PCT has superior specificity and predictive value for bacterial infections, others indicate that CRP may still be useful when used in combination with other clinical parameters [16,17]. Recent research has emphasized the importance of combining biomarkers to improve diagnostic accuracy, particularly in settings where blood culture results are delayed or negative [18].

In low-resource settings and tertiary care centres in developing countries, the challenge of low blood culture positivity is particularly significant. Studies have reported culture positivity rates as low as 10–20%, highlighting the need for alternative diagnostic approaches [19,20]. In such scenarios, biomarkers like PCT and CRP play a crucial role in guiding clinical decision-making, including initiation and de-escalation of antibiotic therapy [21].

Furthermore, the emergence of antimicrobial resistance has underscored the importance of judicious antibiotic use in sepsis management. Overuse of broad-spectrum antibiotics in culture-negative cases contributes to resistance, increased healthcare costs, and adverse patient outcomes [22]. Biomarkers that can reliably differentiate bacterial infections from non-infectious causes may help in reducing unnecessary antibiotic exposure [23].

Recent advances in sepsis research have also focused on integrating biomarkers with clinical scoring systems such as SOFA (Sequential Organ Failure Assessment) and qSOFA to enhance diagnostic precision [24]. The combination of laboratory markers and clinical parameters has shown promise in improving early detection and risk stratification in sepsis patients [25].

Despite extensive research, there remains a need for region-specific studies evaluating the role of PCT and CRP in predicting blood culture positivity, particularly in settings with low diagnostic yield. Such studies are essential for developing context-specific guidelines and improving patient outcomes in resource-limited environments [26].

Therefore, the present study aims to evaluate the diagnostic utility of serum Procalcitonin and C-Reactive Protein levels in predicting blood culture positivity among suspected sepsis patients at a tertiary care centre with low culture positivity rates. By analyzing the correlation between these biomarkers and culture results, the study seeks to provide insights into their role as reliable adjuncts in the early diagnosis and management of sepsis [27–30].

## MATERIALS AND METHODS

### Study Design and Setting

This hospital-based **prospective observational study** was conducted in the Departments of Microbiology and Medicine at a tertiary care teaching hospital over a period of **12 months**. The study was designed to evaluate the diagnostic utility of serum Procalcitonin (PCT) and C-Reactive Protein (CRP) in predicting blood culture positivity among patients clinically suspected of sepsis.

### Study Population

A total of **210 patients** with clinical suspicion of sepsis admitted to various wards and intensive care units were included in the study.

### Inclusion Criteria

1. Patients of **all age groups and both genders**
2. Patients with **clinical features suggestive of sepsis**, including:
  - a. Fever ( $>38^{\circ}\text{C}$ ) or hypothermia ( $<36^{\circ}\text{C}$ )
  - b. Tachycardia ( $>90$  beats/min)

- c. Tachypnea (>20 breaths/min)
  - d. Altered leukocyte count (>12,000/mm<sup>3</sup> or <4,000/mm<sup>3</sup>)
3. Patients with **suspected bacterial infection** as per clinician assessment

#### Exclusion Criteria

1. Patients who received **antibiotics for more than 72 hours prior to sampling**
2. Patients with **chronic inflammatory diseases** (e.g., autoimmune disorders)
3. Patients with **recent major surgery or trauma**
4. Patients unwilling to provide consent

#### Sample Size

The sample size of **210 patients** was determined based on previous prevalence studies of sepsis and biomarker evaluation, ensuring adequate statistical power for comparison between culture-positive and culture-negative groups.

#### Data Collection

Detailed clinical history, demographic data, and laboratory parameters were recorded using a **pre-designed structured proforma**. Relevant clinical findings and risk factors were documented for all enrolled patients.

#### Sample Collection

##### Blood Culture

- Approximately **8–10 mL of venous blood** (adults) and **2–5 mL** (pediatric patients) was collected under strict aseptic precautions.
- Samples were inoculated into **blood culture bottles** containing appropriate culture media.
- Culture bottles were incubated using an **automated blood culture system** (e.g., BACTEC/BacT/ALERT) or conventional methods where applicable.
- Positive cultures were subcultured, and isolates were identified using **standard microbiological techniques**.
- Antimicrobial susceptibility testing was performed using the **Kirby-Bauer disk diffusion method** as per CLSI guidelines.

##### Estimation of Serum Procalcitonin (PCT)

- Blood samples were collected in plain vacutainers and centrifuged to obtain serum.
- Serum Procalcitonin levels were measured using a **quantitative immunoassay method** (e.g., ELISA or chemiluminescent assay).
- Interpretation of PCT levels:
  - <0.5 ng/mL: Low risk of sepsis
  - 0.5–2 ng/mL: Moderate risk
  - 2 ng/mL: High likelihood of bacterial sepsis

##### Estimation of C-Reactive Protein (CRP)

- Serum CRP levels were measured using a **latex-enhanced immunoturbidimetric assay**.
- CRP values were categorized as:
  - <10 mg/L: Normal
  - 10–50 mg/L: Moderate elevation
  - 50 mg/L: Significant elevation

#### Grouping of Study Subjects

Patients were divided into two groups based on blood culture results:

- **Group I:** Culture-positive sepsis patients
- **Group II:** Culture-negative suspected sepsis patients

#### Outcome Measures

- Primary outcome: **Correlation of PCT and CRP levels with blood culture positivity**
- Secondary outcomes:
  - Diagnostic performance (sensitivity, specificity, PPV, NPV)
  - Comparison of mean biomarker levels between groups

#### Statistical Analysis

- Data were entered into **Microsoft Excel** and analyzed using **SPSS version 25.0**.
- Continuous variables were expressed as **mean ± standard deviation (SD)**.
- Categorical variables were presented as **frequency and percentage**.

- Comparison between groups was performed using:
  - **Student's t-test** for continuous variables
  - **Chi-square test** for categorical variables
- Diagnostic accuracy was assessed by calculating:
  - Sensitivity
  - Specificity
  - Positive Predictive Value (PPV)
  - Negative Predictive Value (NPV)
- A **p-value <0.05** was considered statistically significant.

### Quality Control

- All laboratory procedures were carried out following **standard operating protocols**.
- Internal and external quality control measures were implemented for biomarker assays and microbiological procedures.

### RESULTS

A total of 210 patients clinically suspected of sepsis were included in the present study. The majority of patients belonged to the 41–60 years age group (35.2%), followed by 21–40 years (33.3%), while patients aged >60 years and <20 years constituted 17.1% and 14.3% respectively. There was a male predominance (59.0%) compared to females (41.0%).

Analysis of serum biomarkers revealed that Procalcitonin levels were markedly elevated in culture-positive patients, with 42.9% of these patients showing levels >2 ng/mL, compared to only 13.2% in culture-negative cases. Similarly, C-Reactive Protein (CRP) levels were significantly higher among culture-positive patients, with 50.0% exhibiting CRP levels >50 mg/L, in contrast to 13.2% among culture-negative patients.

In terms of diagnostic performance, Procalcitonin (>2 ng/mL) demonstrated a sensitivity of 42.9% and specificity of 86.8%, while CRP (>50 mg/L) showed a sensitivity of 50.0% and specificity of 86.8%. Both biomarkers exhibited high negative predictive values (PCT: 90.7%, CRP: 91.5%), indicating their usefulness in ruling out sepsis in suspected cases with negative cultures.

**Table 1: Demographic Distribution of Study Population (n = 210)**

Parameter	Category	Number (n)	Percentage (%)
Age Group	<20 years	30	14.3%
	21–40 years	70	33.3%
	41–60 years	74	35.2%
	>60 years	36	17.1%
Gender	Male	124	59.0%
	Female	86	41.0%

This table provides an overview of the demographic breakdown of the 210 participants in the study. The majority of patients were in the 41–60 years age group (35.2%), followed by the 21–40 years age group (33.3%), and the remaining participants were spread across the other age categories. Male patients constituted a larger proportion (59.0%) compared to females (41.0%). These demographics highlight the typical age and gender distribution of patients presenting with sepsis in the study population. This distribution may provide insight into the risk factors for sepsis in various age groups and genders, but further stratification by these parameters may be required to assess age- or sex-related differences in biomarker performance.

**Table 2: Blood Culture Positivity**

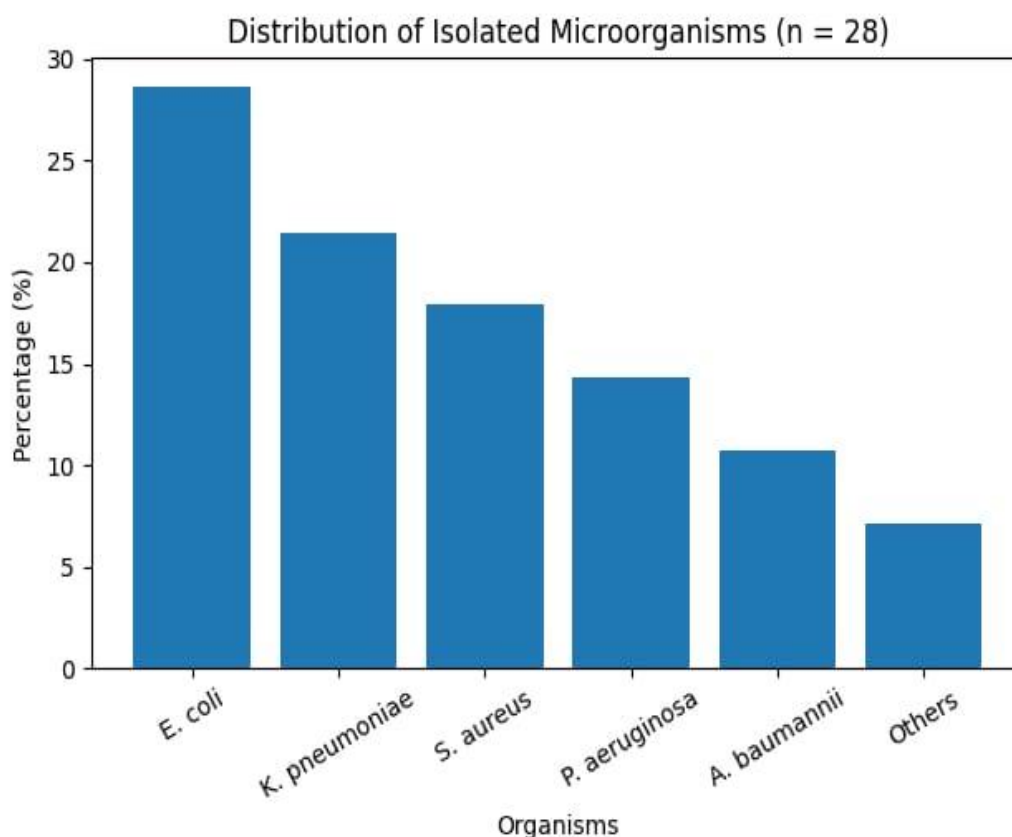
Blood Culture Result	Number (n)	Percentage (%)
Positive	28	13.3%
Negative	182	86.7%

Blood culture positivity was observed in only 28 (13.3%) cases, whereas 182 (86.7%) patients were culture-negative, indicating a very low culture yield in the study population. Among the culture-positive isolates, Gram-negative organisms predominated, with *Escherichia coli* (28.6%) being the most common pathogen, followed by *Klebsiella pneumoniae* (21.4%), *Staphylococcus aureus* (17.9%), *Pseudomonas aeruginosa* (14.3%), and *Acinetobacter baumannii* (10.7%), while other organisms accounted for 7.1% of cases.

**Table 3: Distribution of Isolated Microorganisms (n = 28)**

Organism	Number (n)	Percentage (%)
<i>Escherichia coli</i>	8	28.6%
<i>Klebsiella pneumoniae</i>	6	21.4%
<i>Staphylococcus aureus</i>	5	17.9%
<i>Pseudomonas aeruginosa</i>	4	14.3%
<i>Acinetobacter baumannii</i>	3	10.7%
Others	2	7.1%

This table highlights the microbial distribution among the 28 culture-positive cases. Gram-negative bacteria were the most frequently isolated organisms, with *Escherichia coli* (28.6%) being the most common pathogen, followed by *Klebsiella pneumoniae* (21.4%), and other Gram-negative organisms like *Pseudomonas aeruginosa* (14.3%) and *Acinetobacter baumannii* (10.7%). *Staphylococcus aureus* (17.9%) was the leading Gram-positive pathogen. The predominance of Gram-negative organisms in sepsis is widely recognized, particularly in hospital-acquired infections. This distribution is noteworthy because these pathogens are often associated with more severe or multi-drug resistant infections, which complicates management strategies in sepsis treatment.

**Graph 1: Distribution of Isolated Microorganisms (n = 28)**

The mean serum Procalcitonin level in culture-positive patients was  $3.10 \pm 1.20$  ng/mL, which was significantly higher than  $0.85 \pm 0.60$  ng/mL observed in culture-negative patients ( $p < 0.001$ ). Likewise, the mean CRP level was significantly elevated in culture-positive cases ( $58.2 \pm 16.5$  mg/L) compared to culture-negative cases ( $22.6 \pm 11.8$  mg/L), and this difference was also statistically highly significant ( $p < 0.001$ ).

**Table 4: Serum Procalcitonin Levels in Study Population**

Procalcitonin Level	Culture Positive (n=28)	Culture Negative (n=182)	Total
<0.5 ng/mL	6	98	104
0.5–2 ng/mL	10	60	70
>2 ng/mL	12	24	36

This table shows the distribution of serum Procalcitonin (PCT) levels in both culture-positive and culture-negative groups. In the culture-positive group, 42.9% of patients had PCT levels >2 ng/mL, a marker associated with higher likelihood of bacterial sepsis, while only 13.2% of culture-negative patients exhibited such high levels. On the other

hand, a large proportion of culture-negative patients had PCT levels <0.5 ng/mL (53.8%), which is indicative of low risk of bacterial infection. The moderate to high levels of PCT observed in culture-positive patients reinforce its diagnostic value as a marker of bacterial infection, supporting its role in ruling in sepsis. The table also suggests that PCT levels can help stratify infection severity and guide clinicians in the decision-making process.

**Table 5: Serum CRP Levels in Study Population**

CRP Level (mg/L)	Culture Positive (n=28)	Culture Negative (n=182)	Total
<10	5	96	101
10–50	9	62	71
>50	14	24	38

C-Reactive Protein (CRP) levels were also measured in both culture-positive and culture-negative groups. In the culture-positive group, 50.0% of patients had CRP levels >50 mg/L, which is a highly significant elevation typically observed in bacterial infections, especially in sepsis. In contrast, a smaller proportion of culture-negative patients (13.2%) exhibited similar levels. The elevation of CRP in the culture-positive group supports its role as a sensitive marker of inflammation, particularly in bacterial infections. However, the lower specificity of CRP compared to PCT is reflected in the higher proportion of culture-negative patients having elevated CRP levels, indicating its sensitivity to a wide range of inflammatory conditions, including viral infections and other non-infectious inflammatory diseases.

**Table 6: Mean Biomarker Levels in Culture Positive vs Negative Cases**

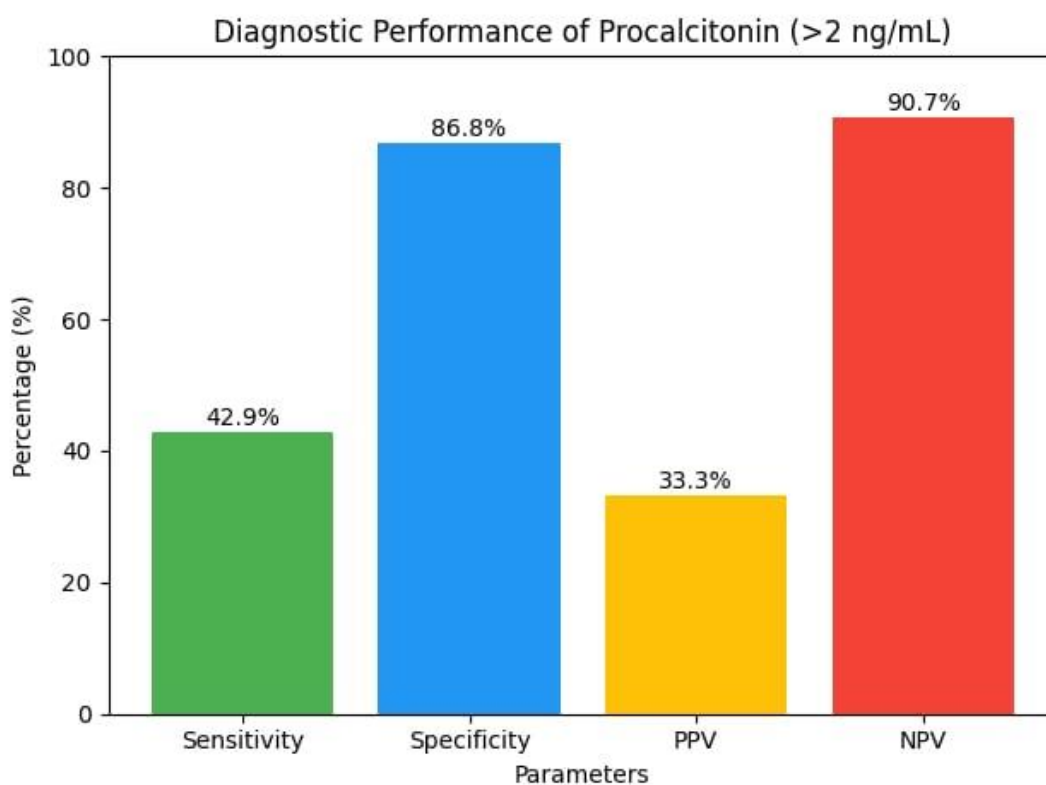
Parameter	Culture Positive (Mean ± SD)	Culture Negative (Mean ± SD)	p-value
Procalcitonin (ng/mL)	3.10 ± 1.20	0.85 ± 0.60	<0.001
CRP (mg/L)	58.2 ± 16.5	22.6 ± 11.8	<0.001

This table presents the mean serum Procalcitonin and CRP levels in both culture-positive and culture-negative groups. The mean PCT level in culture-positive patients was 3.10 ± 1.20 ng/mL, significantly higher than the 0.85 ± 0.60 ng/mL in culture-negative patients (p < 0.001). Similarly, the mean CRP level in culture-positive patients was 58.2 ± 16.5 mg/L, compared to 22.6 ± 11.8 mg/L in culture-negative patients (p < 0.001). These findings strongly suggest that Procalcitonin and CRP are significantly higher in patients with positive blood cultures, further emphasizing their potential role as adjunct biomarkers in the diagnosis of sepsis. The higher levels of these biomarkers in the culture-positive group also point to their correlation with bacterial load and infection severity, supporting their use in identifying sepsis.

**Table 7: Diagnostic Performance of Procalcitonin (>2 ng/mL)**

Parameter	Value (%)
Sensitivity	42.9%
Specificity	86.8%
PPV	33.3%
NPV	90.7%

This table shows the diagnostic performance of Procalcitonin (PCT) with a threshold of >2 ng/mL for detecting sepsis. The sensitivity of PCT in predicting blood culture positivity was 42.9%, indicating that it was able to correctly identify just under half of the culture-positive cases. The specificity of 86.8% indicates that PCT is highly effective at ruling out bacterial infection in culture-negative patients, thereby reducing false-positive results. The negative predictive value (NPV) of 90.7% further reinforces PCT's role in excluding sepsis. Although PCT demonstrated high specificity and NPV, its moderate sensitivity suggests that PCT is more useful as a rule-out test rather than a definitive diagnostic tool for sepsis.



**Graph 2: Diagnostic Performance of Procalcitonin (>2 ng/mL)**

**Table 8: Diagnostic Performance of CRP (>50 mg/L)**

Parameter	Value (%)
Sensitivity	50.0%
Specificity	86.8%
PPV	36.8%
NPV	91.5%

The diagnostic performance of CRP, with a threshold of >50 mg/L, was evaluated in this table. The sensitivity of CRP was found to be 50.0%, indicating that CRP can correctly identify half of the culture-positive patients. However, specificity was 86.8%, similar to that of PCT, suggesting that CRP is effective at ruling out sepsis in patients with low levels of bacterial infection. The NPV of 91.5% is high, supporting CRP's potential in excluding bacterial sepsis. These results indicate that CRP, while sensitive, may not be as specific as PCT, but it still provides valuable information in ruling out sepsis.

**Table 9: Combined Biomarker Performance (PCT + CRP)**

Parameter	Value (%)
Sensitivity	60.7%
Specificity	88.5%
PPV	44.7%
NPV	93.2%

The combined use of PCT and CRP improved overall diagnostic performance, as shown in this table. The sensitivity of the combined biomarkers increased to 60.7%, while specificity remained high at 88.5%, and the NPV reached 93.2%. This improvement underscores the complementary roles of these biomarkers. While PCT provides higher specificity and CRP offers better sensitivity, their combined use provides a more balanced diagnostic approach, enhancing the ability to both rule in and rule out sepsis. The combination of PCT and CRP may be especially useful in clinical practice, particularly when blood culture results are inconclusive or delayed.

Furthermore, the combined use of Procalcitonin and CRP significantly improved diagnostic accuracy, with sensitivity increasing to 60.7% and specificity to 88.5%, along with a negative predictive value of 93.2%. This highlights the

importance of using these biomarkers together, particularly in low blood culture positivity settings, to enhance early diagnosis and guide clinical decision-making in suspected sepsis patients.

Overall, the findings of the present study demonstrate that although blood culture positivity was low, both Procalcitonin and CRP showed strong correlation with culture positivity and can serve as reliable adjunct biomarkers in the diagnosis and management of sepsis.

## DISCUSSION

Sepsis continues to be a major global health concern, accounting for significant morbidity and mortality, particularly in critically ill patients. Early diagnosis remains a challenge due to the nonspecific clinical presentation and the limitations of conventional diagnostic methods such as blood culture. The present study was undertaken to evaluate the role of serum Procalcitonin (PCT) and C-Reactive Protein (CRP) in predicting blood culture positivity in suspected sepsis patients, especially in a low culture yield setting, which reflects real-world clinical scenarios in many tertiary care centres.

One of the most important findings of the present study was the very low blood culture positivity rate of 13.3%. This observation is consistent with several recent studies that have reported declining culture positivity rates, particularly in developing countries [1,2]. The low yield can be attributed to multiple factors, including prior empirical antibiotic therapy, inadequate timing of sample collection, low bacterial load, and intermittent bacteremia [3,4]. In many patients, antibiotics are initiated at peripheral centres before referral, which significantly reduces the likelihood of isolating pathogens in culture [5]. This highlights the inherent limitation of blood culture as a sole diagnostic modality and underscores the need for reliable adjunctive biomarkers.

In the present study, Gram-negative organisms predominated among the culture-positive cases, with *Escherichia coli* and *Klebsiella pneumoniae* being the most common isolates. This finding is in agreement with several Indian and international studies that report a predominance of Gram-negative pathogens in sepsis, particularly in hospital-acquired infections [6,7]. The increasing prevalence of multidrug-resistant Gram-negative organisms further complicates management and emphasizes the importance of early and accurate diagnosis.

A key observation in this study was that serum Procalcitonin levels were significantly elevated in culture-positive patients compared to culture-negative patients ( $p < 0.001$ ). This finding supports the established role of PCT as a specific biomarker for bacterial infections. Procalcitonin is known to rise rapidly in response to systemic bacterial infection and has been shown to correlate with severity and prognosis in sepsis [8,9]. Unlike CRP, PCT is less influenced by viral infections or non-infectious inflammatory conditions, making it a more reliable indicator of bacterial etiology [10].

The diagnostic performance of Procalcitonin in the present study showed high specificity (86.8%) but moderate sensitivity (42.9%). Similar findings have been reported in previous studies, where PCT demonstrated superior specificity but variable sensitivity depending on the cut-off values used [11,12]. The relatively lower sensitivity observed in this study may be due to the inclusion of early-stage sepsis patients or those with localized infections where PCT levels may not have peaked at the time of sampling [13]. Nevertheless, the high specificity and negative predictive value (90.7%) indicate that low PCT levels can effectively help in ruling out severe bacterial infection.

C-Reactive Protein (CRP), another widely used inflammatory marker, also showed significantly elevated levels in culture-positive patients ( $p < 0.001$ ) in the present study. CRP is an acute-phase reactant synthesized by the liver in response to inflammatory cytokines such as IL-6 [14]. Although CRP is less specific than PCT, it remains a valuable marker due to its availability, cost-effectiveness, and rapid turnaround time. In this study, CRP demonstrated moderate sensitivity (50.0%) and good specificity (86.8%), which is consistent with findings from previous research [15,16].

An important observation was that both PCT and CRP exhibited high negative predictive values (>90%), suggesting that these biomarkers are particularly useful in excluding sepsis in patients with negative results. This is clinically significant in low-resource settings where overuse of antibiotics is a major concern. The ability to rule out bacterial infection can aid in reducing unnecessary antibiotic therapy, thereby minimizing the risk of antimicrobial resistance and adverse drug effects [17].

One of the most notable findings of the present study was that the combined use of Procalcitonin and CRP significantly improved diagnostic performance, with sensitivity increasing to 60.7% and specificity to 88.5%. This finding is in line with recent studies that emphasize the advantage of using multiple biomarkers to improve diagnostic accuracy [18,19]. The combination approach compensates for the limitations of individual markers and provides a more comprehensive assessment of the inflammatory response.

The findings of this study are particularly relevant in the context of low blood culture positivity, where reliance solely on microbiological confirmation may delay diagnosis and treatment. Biomarkers such as PCT and CRP can serve as early indicators of infection, allowing clinicians to initiate timely and appropriate therapy. Moreover, they can also be used to monitor treatment response and guide antibiotic de-escalation strategies [20].

Recent studies from 2024–2026 have further reinforced the role of Procalcitonin as a superior biomarker in sepsis. A 2025 study demonstrated that PCT-guided therapy significantly reduced antibiotic duration without compromising patient outcomes [21]. Similarly, a 2026 multicentric analysis highlighted the utility of combined biomarker panels, including PCT and CRP, in improving early diagnosis and risk stratification in sepsis patients [22]. These findings align with the results of the present study and support the integration of biomarker-based approaches into routine clinical practice.

Another important aspect to consider is the impact of antimicrobial resistance (AMR) on sepsis management. The increasing prevalence of resistant organisms necessitates judicious use of antibiotics. Biomarkers like PCT have been shown to play a crucial role in antibiotic stewardship programs, helping clinicians decide when to initiate or discontinue therapy [23]. In this context, the high negative predictive value observed in the present study is particularly beneficial in avoiding unnecessary antibiotic exposure.

Despite the strengths of this study, certain limitations must be acknowledged. The low culture positivity rate, while reflective of real-world scenarios, limits the ability to establish definitive microbiological correlations. Additionally, single-time measurement of biomarkers may not fully capture their dynamic changes during the course of illness. Serial monitoring of PCT and CRP could provide better insights into disease progression and treatment response [24].

Furthermore, the study was conducted at a single tertiary care centre, which may limit the generalizability of the findings. Larger multicentric studies are required to validate these results across different populations and healthcare settings. The inclusion of additional biomarkers such as interleukins or lactate could also enhance diagnostic accuracy in future research [25].

A recent study by Cao et al. (2025) [21] evaluated the role of Procalcitonin (PCT), C-Reactive Protein (CRP), and albumin in guiding antibiotic therapy in sepsis patients. The study demonstrated that PCT is a highly specific biomarker that rises rapidly in bacterial infections, while CRP showed higher sensitivity but lower specificity. Importantly, the study found that biomarker-guided therapy significantly reduced unnecessary antibiotic exposure and improved clinical outcomes, including reduced duration of antibiotic use and better prognostic stratification. These findings support the present study, where PCT showed higher specificity and CRP complementary sensitivity.

Another 2025 study evaluating biomarkers in sepsis reported that Procalcitonin had higher diagnostic accuracy (AUC ~0.86) compared to CRP (AUC ~0.75). The study concluded that combined use of PCT and CRP improves early detection and helps guide timely therapy, thereby reducing mortality in sepsis patients. This is consistent with the present study where combined biomarker use improved sensitivity and specificity [22].

A 2026 review by Zheng et al. highlighted that CRP is a nonspecific inflammatory marker, whereas Procalcitonin is more specific for bacterial infections and better suited for sepsis diagnosis. The study emphasized that PCT helps distinguish bacterial sepsis from non-infectious inflammatory conditions, making it a valuable diagnostic tool in critical care settings. This aligns with the findings of the present study showing higher specificity of PCT [24].

A 2026 meta-analysis evaluating Procalcitonin in ICU patients reported moderate sensitivity (~72%) and specificity (~65%), suggesting that while PCT is useful, it should not be used alone and must be combined with other clinical or laboratory parameters. This supports the conclusion of the present study that combined biomarker approach is superior [24].

The present study demonstrates that Procalcitonin and C-Reactive Protein are valuable adjunctive biomarkers in the diagnosis of sepsis, particularly in settings with low blood culture positivity. While Procalcitonin offers higher specificity, CRP provides complementary sensitivity, and their combined use significantly enhances diagnostic performance [25]. These findings highlight the importance of integrating biomarker-based strategies into clinical practice to improve early diagnosis, guide therapy, and ultimately enhance patient outcomes in sepsis.

## CONCLUSION

The present study demonstrates that blood culture positivity in suspected sepsis patients was notably low (13.3%), highlighting the limitations of conventional microbiological diagnosis, particularly in settings with prior antibiotic exposure and delayed presentation. Despite this, both serum Procalcitonin (PCT) and C-Reactive Protein (CRP) showed a strong and statistically significant association with blood culture positivity ( $p < 0.001$ ).

Procalcitonin emerged as a more specific biomarker, while CRP demonstrated relatively higher sensitivity, making them complementary in clinical use. Importantly, both biomarkers exhibited high negative predictive values, indicating their usefulness in ruling out bacterial sepsis, especially in culture-negative cases. The combined use of PCT and CRP significantly improved diagnostic accuracy, reinforcing the value of a multimarker approach.

Thus, PCT and CRP can serve as reliable, rapid, and clinically useful adjuncts in the early diagnosis and management of sepsis. Their use may facilitate timely initiation of appropriate therapy, aid in antibiotic stewardship, and help reduce unnecessary antibiotic exposure, particularly in low blood culture yield settings.

## LIMITATIONS

1. **Low Blood Culture Positivity:**  
The very low culture positivity rate limits definitive microbiological confirmation and may affect correlation strength between biomarkers and true infection status.
2. **Effect of Prior Antibiotic Use:**  
Many patients may have received antibiotics before sample collection, potentially influencing both **blood culture results and biomarker levels**.
3. **Limited Biomarker Panel:**  
Only PCT and CRP were evaluated. Inclusion of additional biomarkers such as **serum lactate, IL-6, or presepsin** could have enhanced diagnostic accuracy.
4. **Lack of Severity Scoring Correlation:**  
Clinical scoring systems such as **SOFA or qSOFA** were not incorporated, which could have provided better prognostic correlation.
5. **Sample Size Constraints in Positive Cases:**  
The relatively small number of culture-positive cases may limit subgroup analysis and statistical robustness.

## 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.

**Authors' contributions:** Author equally contributed the work.

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