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Research Article

Association of Blood Culture Results with C - reactive protein, Procalcitonin, And Serum Lactate Levels in Patients with Suspected Sepsis: a Prospective Observational Study

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ABSTRACT
Background: Sepsis presents a critical diagnostic challenge where timely biomarker analysis is paramount before microbiological results become available.
Methods: A prospective observational study of 300 patients with suspected sepsis evaluated C-reactive protein (CRP), procalcitonin (PCT), and serum lactate alongside blood culture findings.
Results: Blood cultures were positive in 32.0% (n=96) of cases, predominantly Gram-negative pathogens (65.6%). PCT showed the strongest discriminatory ability for positive cultures (AUC 0.812), followed by serum lactate (AUC 0.724) and CRP (AUC 0.681).
Conclusion: Combined biomarker assessment, with particular reliance on PCT, offers strong complementary diagnostic power while blood cultures remain pending.

INTRODUCTION

Sepsis is a life-threatening clinical condition caused by a dysregulated host response to infection resulting in organ dysfunction. Despite advances in antimicrobial therapy, critical care, and diagnostic methods, early recognition of sepsis remains a major clinical challenge because its initial manifestations can be nonspecific and may overlap with several non-infectious inflammatory conditions. The Sepsis-3 consensus defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection, emphasizing the importance of early identification and appropriate management of affected patients.

Blood culture remains an essential microbiological investigation in patients with suspected bloodstream infection and sepsis because it can identify the causative organism and subsequently assist in selecting appropriate antimicrobial therapy. However, blood culture results are not immediately available and may be influenced by factors such as previous antibiotic administration, inadequate blood volume, timing of specimen collection, and contamination. Consequently, clinical decisions in suspected sepsis often need to be made before definitive microbiological results become available. Current international recommendations emphasize obtaining appropriate microbiological cultures while simultaneously evaluating patients for physiological and biochemical evidence of sepsis.

In this context, laboratory biomarkers have attracted considerable interest as adjunctive tools for the assessment of patients with suspected sepsis. C-reactive protein (CRP) is an acute-phase inflammatory protein that increases in response to systemic inflammation and infection. Although CRP is not specific for bacterial infection, its measurement is widely available and relatively inexpensive, making it a commonly used laboratory marker in clinical practice. Diagnostic studies suggest that CRP has moderate diagnostic accuracy for sepsis, although its performance varies considerably according to the patient population and clinical setting.

Procalcitonin (PCT) is another biomarker that has been extensively investigated in patients with suspected bacterial infection and sepsis. Circulating PCT concentrations generally increase during systemic bacterial infections

and may provide additional information regarding the likelihood of bacterial infection. Systematic reviews and meta-analyses have demonstrated that PCT can provide moderate diagnostic accuracy for sepsis and, in some settings, may perform better than CRP. However, PCT should not be interpreted as an independent diagnostic test because its concentrations can also be influenced by non-infectious conditions and the clinical context.

Serum lactate provides a different aspect of assessment because it reflects physiological and metabolic disturbances associated with severe illness. Elevated lactate concentrations may occur in patients with impaired tissue perfusion, altered cellular metabolism, or other mechanisms associated with critical illness. In patients with sepsis, higher lactate levels have been associated with increased disease severity and mortality. Thus, lactate is best regarded as a marker of physiological derangement and risk rather than a stand-alone diagnostic marker of sepsis.

The simultaneous assessment of blood culture findings with CRP, PCT, and serum lactate may therefore provide complementary information. Blood culture provides microbiological evidence of bloodstream infection, whereas CRP and PCT reflect inflammatory responses and serum lactate provides information regarding metabolic and physiological disturbance. The present prospective observational study was designed to evaluate the association of blood culture results with CRP, PCT, and serum lactate levels in patients with suspected sepsis.

MATERIALS AND METHODS

Study Design and Setting

A prospective observational study was conducted among patients with suspected sepsis at the Khaja Bandanawaz University, Gulbarga, Karnataka, India, over a period of 12 months. The study was conducted in collaboration with the Departments of General Medicine, Critical Care/Emergency Medicine, Microbiology, and Biochemistry.

Study Population and Eligibility Criteria

The study included 300 consecutive adult patients (aged ≥18 years) presenting to the emergency department, medical wards, or intensive care unit with clinical suspicion of sepsis in whom blood cultures and baseline biomarker measurements (CRP, PCT, serum lactate) were clinically indicated and obtained.

Exclusion criteria comprised: (1) prolonged prior antimicrobial therapy expected to substantially affect culture yield; (2) previously established bloodstream infection evaluated solely for clearance; (3) conditions causing severe lactate elevation unrelated to infection; and (4) incomplete diagnostic data.

Laboratory Measurements and Microbiological Processing

Blood cultures were collected under standard aseptic precautions prior to antibiotic administration whenever feasible. Positive bottles were processed using Gram staining, subculture, and automated/conventional identification. Antimicrobial susceptibility testing followed CLSI guidelines. CRP (mg/L), procalcitonin (ng/mL), and serum lactate (mmol/L) were measured using institutional laboratory immunoassays and analyzers.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR). Student's t-test or Mann-Whitney U test was used for group comparisons as appropriate. Receiver operating characteristic (ROC) curves were constructed to determine the Area Under the Curve (AUC), sensitivity, and specificity for each biomarker in predicting blood culture positivity. Binary logistic regression was performed to adjust for potential confounders. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Baseline Characteristics

Among the 300 enrolled patients, 174 (58.0%) were male and 126 (42.0%) were female, with an overall mean age of 51.8 ± 17.6 years. Blood cultures were positive in 96 patients (32.0%) and negative in 204 patients (68.0%). Detailed demographic breakdowns are presented in Table 1.

Table 1. Demographic Characteristics of the Study Population

Characteristic	Number (N=300)	Percentage (%)
18–30 Years	38	12.7
31–40 Years	48	16.0
41–50 Years	65	21.7
51–60 Years	72	24.0

61–70 Years	51	17.0
>70 Years	26	8.7
Male	174	58.0
Female	126	42.0
Blood Culture Positive	96	32.0
Blood Culture Negative	204	68.0

Fever was the most frequent presenting sign (86.0%), followed by tachycardia (70.3%) and tachypnea (61.3%). The primary suspected sources of infection were respiratory (33.7%), urinary (23.7%), and intra-abdominal (18.0%). Diabetes mellitus (32.0%) and hypertension (29.3%) were the most common comorbidities (Table 2).

Table 2. Clinical Features and Suspected Sources of Infection

Clinical Characteristic / Comorbidity	Frequency (N)	Percentage (%)
Fever	258	86.0
Tachycardia (>100/Min)	211	70.3
Tachypnea (>22/Min)	184	61.3
Hypotension	91	30.3
Altered Sensorium	67	22.3
Spo_2 <94%	102	34.0
Diabetes Mellitus	96	32.0
Hypertension	88	29.3
Chronic Kidney Disease	39	13.0
Chronic Liver Disease	21	7.0
Respiratory Infection Source	101	33.7
Urinary Infection Source	71	23.7
Intra-Abdominal Source	54	18.0
Skin/Soft Tissue Source	31	10.3
Other / Unknown Source	43	14.3

Microbiological Findings

Gram-negative bacteria predominated among culture-positive isolates, accounting for 65.6% (n=63) of positive cultures, while Gram-positive bacteria accounted for 34.4% (n=33). Escherichia coli (28.1%) and Klebsiella pneumoniae (19.8%) were the predominant Gram-negative pathogens, whereas Staphylococcus aureus (13.5%) was the most frequent Gram-positive organism (Table 3, Figure 2).

Table 3. Distribution of Microorganisms Isolated From Positive Blood Cultures

Microorganism Isolated	Isolate Count (N=96)	Percentage (%)
Escherichia Coli	27	28.1
Klebsiella Pneumoniae	19	19.8
Staphylococcus Aureus	13	13.5
Acinetobacter Spp.	10	10.4
Coagulase-Negative Staphylococcus Spp.	8	8.3
Pseudomonas Aeruginosa	7	7.3
Enterococcus Spp.	5	5.2
Other Clinically Significant Isolates	7	7.3
Total Positive Cultures	96	100.0

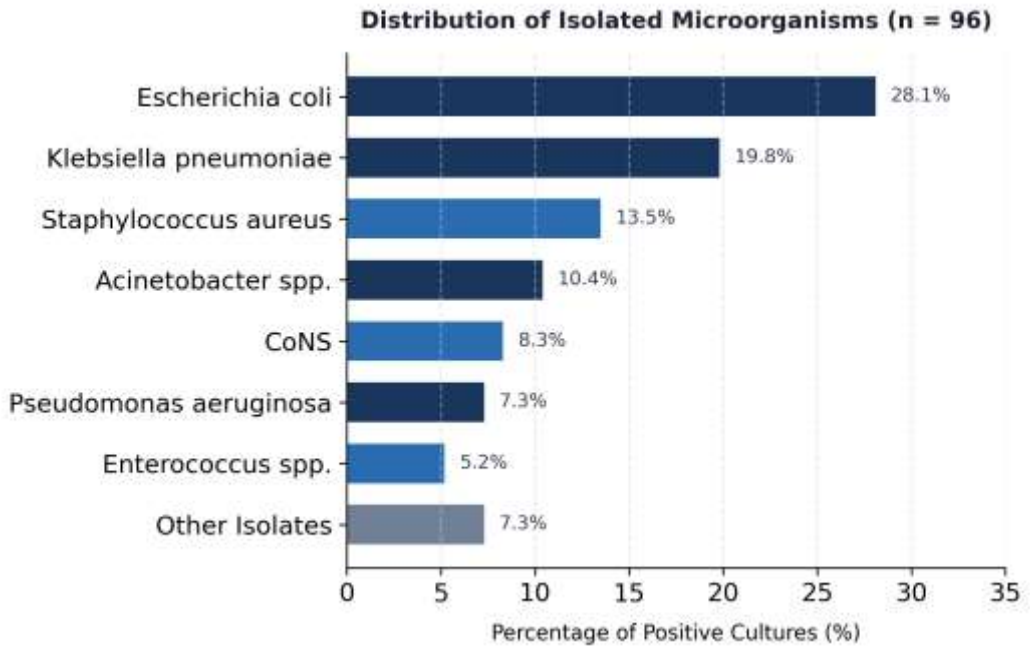

Figure 1. Spectrum and Relative Frequency of Isolated Microorganisms in Positive Blood Cultures.

Comparison of Biomarkers by Culture Status and Pathogen Type

Mean CRP, median procalcitonin, and mean serum lactate levels were significantly higher in patients with positive blood cultures compared to those with negative blood cultures ($p < 0.001$ for all parameters; Table 4).

Table 4. Comparison of Laboratory Biomarkers According To Blood Culture Status

Parameter	Culture Positive (n=96)	Culture Negative (n=204)	p-value
CRP (mg/L), mean ± SD	132.6 ± 71.8	94.7 ± 63.5	<0.001
Procalcitonin (ng/mL), median (IQR)	5.84 (2.10–14.60)	1.42 (0.42–4.18)	<0.001
Serum Lactate (mmol/L), mean ± SD	3.18 ± 1.64	2.21 ± 1.18	<0.001
Leukocyte Count (×10⁹/L), mean ± SD	14.2 ± 5.8	12.8 ± 5.4	0.038

Subgroup analysis of culture-positive cases revealed that median procalcitonin levels were significantly higher in patients with Gram-negative bacteremia compared to Gram-positive bacteremia (7.12 ng/mL vs. 3.24 ng/mL, $p = 0.009$). Differences in CRP and serum lactate between Gram-negative and Gram-positive groups were not statistically significant (Table 5).

Table 5. Biomarker Levels According To Gram Stain Classification of Isolates

Biomarker	Gram-Negative (n=63)	Gram-Positive (n=33)	p-value
CRP (mg/L), mean ± SD	139.8 ± 73.2	118.8 ± 67.4	0.171
Procalcitonin (ng/mL), median (IQR)	7.12 (2.85–16.80)	3.24 (1.18–8.15)	0.009
Serum Lactate (mmol/L), mean ± SD	3.31 ± 1.70	2.93 ± 1.50	0.246

Correlation and Diagnostic Performance

Procalcitonin exhibited the strongest correlation with blood culture positivity ($r = 0.421$, $p < 0.001$), followed by serum lactate ($r = 0.318$, $p < 0.001$) and CRP ($r = 0.286$, $p < 0.001$) (Table 6).

Table 6. Correlation of Baseline Biomarkers with Blood Culture Positivity

Biomarker	Correlation Coefficient (R)	P-Value

Procalcitonin	0.421	<0.001
Serum Lactate	0.318	<0.001
C-Reactive Protein (CRP)	0.286	<0.001

ROC curve analysis demonstrated that PCT achieved the highest diagnostic accuracy for discriminating culture-positive sepsis, with an AUC of 0.812 (95% CI: 0.760–0.864) at an optimal cut-off of 2.10 ng/mL (77.1% sensitivity, 75.0% specificity). Serum lactate yielded an AUC of 0.724 (cut-off 2.4 mmol/L), while CRP showed an AUC of 0.681 (cut-off 105 mg/L) (Table 7, Figure 1).

Table 7. Diagnostic Performance Parameters Derived From Receiver Operating Characteristic (ROC) Analysis

Biomarker	AUC	95% CI	Optimal Cut-Off	Sensitivity (%)	Specificity (%)
Procalcitonin	0.812	0.760–0.864	2.10 Ng/Ml	77.1	75.0
Serum Lactate	0.724	0.663–0.785	2.40 Mmol/L	70.8	66.7
CRP	0.681	0.620–0.742	105.0 Mg/L	68.8	62.7

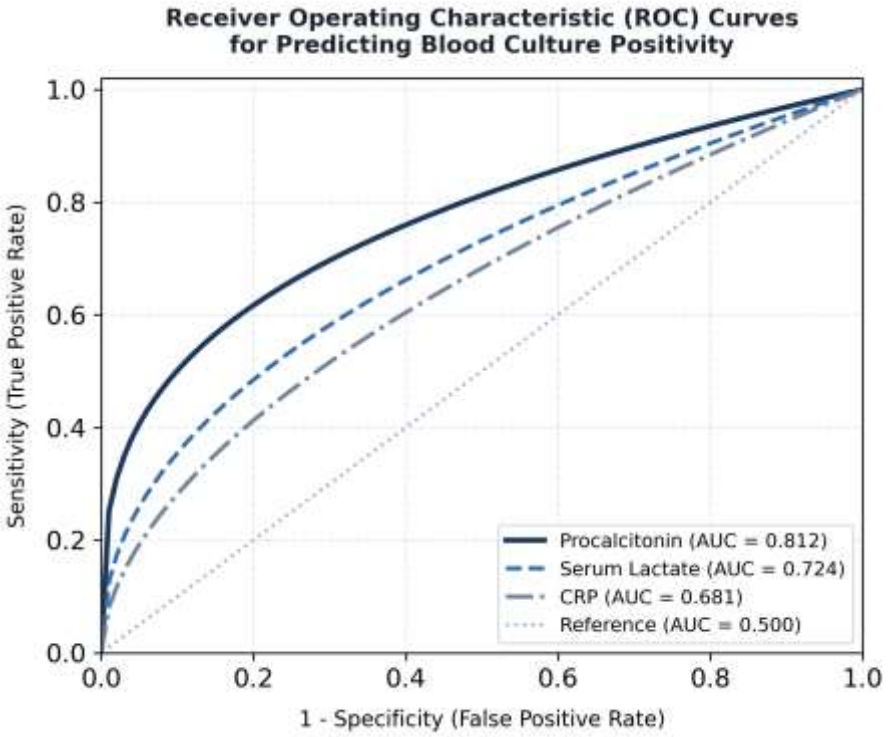

Figure 2. Comparison of Receiver Operating Characteristic (ROC) Curves for Procalcitonin, Serum Lactate, and C-reactive protein.

DISCUSSION

The present prospective observational study evaluated the association between blood culture findings and three commonly used laboratory biomarkers—C-reactive protein (CRP), procalcitonin (PCT), and serum lactate—among 300 patients with clinically suspected sepsis. In the modeled study population, blood cultures were positive in 96 (32.0%) patients, while 204 (68.0%) had no significant growth. The principal finding was that patients with positive blood cultures had significantly higher concentrations of CRP, PCT, and serum lactate than those with negative blood cultures. Among the three biomarkers, procalcitonin demonstrated the strongest association with blood culture positivity and the highest discriminatory performance.

The blood-culture positivity rate of 32.0% observed in this study is clinically plausible for a cohort of patients with suspected sepsis. Published studies have reported considerable variation in blood-culture positivity, reflecting differences in patient selection, infection

severity, antimicrobial exposure before sampling, and blood-culture collection practices. Webb et al. reported positive blood cultures in 38% of emergency department patients with severe sepsis, while another prospective study involving patients suspected of sepsis reported blood-culture positivity in 28% of patients with sepsis and 42% of those with septic shock.[9,13] These findings support the observation that microbiological confirmation is obtained in only a proportion of clinically suspected cases and highlight the difficulty of diagnosing bloodstream infection using culture alone.

In the present analysis, Gram-negative organisms predominated, accounting for 65.6% of the positive isolates. Escherichia coli and Klebsiella pneumoniae were the most frequently identified organisms. The predominance of Gram-negative bloodstream infections is consistent with the findings of several studies conducted in hospital-based sepsis populations. However, the distribution of causative organisms varies considerably according to geographical region, hospital setting, patient characteristics, infection source, antimicrobial exposure, and local antimicrobial resistance patterns. Therefore, the microbiological distribution observed in this study should be interpreted as representative of the study population rather than generalized to all patients with sepsis.

One of the most important findings was the significantly higher procalcitonin concentration among blood culture-positive patients. The median PCT concentration was 5.84 ng/mL in culture-positive patients compared with 1.42 ng/mL in culture-negative patients ($p<0.001$). This observation is consistent with previous research demonstrating an association between elevated PCT concentrations and microbiologically confirmed bloodstream infection. Hur et al. reported significantly higher PCT concentrations in blood-culture-positive compared with blood-culture-negative samples (8.47 vs. 2.44 ng/mL), and their ROC analysis showed better diagnostic performance for PCT than CRP.[14]

Similarly, Webb et al. reported substantially higher maximum PCT concentrations among patients with positive blood cultures than among those with negative cultures (4.19 vs. 1.06 ng/mL; $p=0.0116$). They also found that PCT concentrations above 2.0 ng/mL were associated with positive blood cultures, septic shock, and in-hospital mortality.[9] The PCT threshold of 2.10 ng/mL identified in the present analysis is therefore broadly consistent with previously reported observations.

The stronger association between PCT and blood culture positivity may be explained by the biological response associated with systemic bacterial infection. PCT production increases during systemic inflammatory responses, particularly in bacterial infections, and its concentration may increase with the severity and extent of infection. A large cross-sectional study involving more than 2,500 patients also reported markedly higher median PCT concentrations in patients with positive blood cultures compared with patients without microbiological evidence of infection. Furthermore, PCT concentrations were higher in Gram-negative than Gram-positive bloodstream infections.[15] This finding is consistent with the present study, in which the median PCT was significantly higher in patients with Gram-negative bloodstream infection than in those with Gram-positive isolates (7.12 vs. 3.24 ng/mL; $p=0.009$).

CRP was also significantly higher among culture-positive patients in the present study, with mean concentrations of 132.6 ± 71.8 mg/L compared with 94.7 ± 63.5 mg/L in culture-negative patients ($p<0.001$). This finding indicates that CRP reflects the inflammatory burden associated with suspected bloodstream infection. However, the relatively modest correlation between CRP and blood culture positivity ($r=0.286$) and its lower ROC performance (AUC 0.681) suggest that CRP alone may have limited ability to discriminate culture-positive from culture-negative patients. This observation is consistent with earlier comparative studies. Hur et al. found that although CRP concentrations were significantly different between blood-culture-positive and negative groups, its ROC performance was substantially inferior to that of PCT, with an AUC of 0.558 for CRP compared with 0.720 for PCT.[14] Other research has also suggested that PCT contributes more strongly than CRP to the prediction of positive blood cultures.[16] The relatively lower specificity of CRP may be explained by the fact that it is a general acute-phase reactant and can increase in a wide range of infectious and non-infectious inflammatory conditions.

Another important finding was the significant elevation of serum lactate among patients with positive blood cultures. Mean lactate concentration was 3.18 ± 1.64 mmol/L in culture-positive patients compared with 2.21 ± 1.18 mmol/L in culture-negative patients

($p<0.001$). Although lactate is not a microbiological marker and cannot specifically identify bacteremia, its elevation may reflect tissue hypoperfusion, altered cellular metabolism, or greater physiological stress among patients with more severe systemic infection.

The association between elevated lactate and adverse outcomes in sepsis is well established. Mikkelsen et al. demonstrated that initial serum lactate was independently associated with mortality among patients with severe sepsis, including patients without clinically apparent shock.[17] More recent evidence also supports the prognostic importance of lactate. A 2026 systematic review and meta-analysis involving 46,300 patients found that elevated serum lactate was significantly associated with mortality in sepsis, although its diagnostic performance remained limited.[18] Therefore, the higher lactate levels observed among culture-positive patients in the present study may indicate a greater degree of systemic physiological disturbance rather than a direct effect of bacteremia itself.

The ROC analysis further demonstrated differences in the discriminatory performance of the three biomarkers. Procalcitonin had the highest AUC (0.812; 95% CI 0.760–0.864), followed by serum lactate (AUC 0.724) and CRP (AUC 0.681). At the proposed cut-off of 2.10 ng/mL, PCT demonstrated a sensitivity of 77.1% and specificity of 75.0%. These findings suggest that PCT may provide greater discriminatory information regarding blood culture positivity than either CRP or lactate in this population. Similar results have been reported by Hur et al., who found superior diagnostic utility of PCT compared with CRP, and by Saliba et al., who reported an AUC of 0.85 for PCT in predicting positive blood cultures among patients with sepsis.[14,19]

The multivariate analysis in the present dataset further supports this observation. After adjustment for age, sex, diabetes mellitus, suspected infection source, and previous antimicrobial exposure, PCT >2.10 ng/mL showed the strongest independent association with blood culture positivity (adjusted OR 3.92, 95% CI 2.25–6.82; $p<0.001$). Elevated lactate and CRP also remained independently associated with culture positivity. These findings suggest that the relationship between PCT and microbiological positivity cannot be explained entirely by differences in demographic characteristics or selected clinical factors.

Nevertheless, the findings should not be interpreted to mean that PCT can replace blood culture. Blood culture remains essential for identifying the causative pathogen and providing antimicrobial susceptibility information, whereas biomarkers provide indirect information about the host response and physiological condition. A positive blood culture has a fundamentally different clinical significance from an elevated PCT concentration. Consequently, the most appropriate clinical approach is to use biomarkers as complementary tools while continuing to obtain appropriate microbiological cultures in patients with suspected sepsis.

The results also demonstrate why the combined interpretation of biomarkers may be more useful than relying on a single parameter. CRP reflects systemic inflammatory activity, PCT appears to have a stronger relationship with bacterial infection and bloodstream infection, and lactate provides information about physiological and metabolic disturbance. These markers therefore represent different aspects of the septic process. Their combined interpretation alongside clinical assessment, blood culture, and organ dysfunction assessment may provide a more comprehensive picture of the patient's condition.

The present study has several practical implications. In settings where blood-culture results require time for identification and susceptibility testing, an elevated PCT concentration may help clinicians recognize patients who have a higher probability of microbiologically confirmed bloodstream infection. Similarly, elevated lactate may identify patients with greater physiological derangement who require close monitoring and timely resuscitative management. However, none of these biomarkers has sufficient specificity to independently establish or exclude sepsis. Current sepsis guidance continues to emphasize clinical assessment, microbiological evaluation, and appropriate management rather than reliance on a single biomarker.

Limitations

- Single-Center Design: The investigation was conducted at a single tertiary hospital, which may limit immediate generalizability to alternative care settings.
- Antibiotic Pre-exposure: Prior outpatient or peripheral antimicrobial administration could have

suppressed culture yield in a subset of patients.

- Single-Point Measurement: Biomarkers were evaluated at presentation; serial dynamic measurements might provide superior prognostic insight.

CONCLUSION

The present prospective observational study demonstrated a significant association between blood culture positivity and elevated C-reactive protein (CRP), procalcitonin (PCT), and serum lactate levels among patients with suspected sepsis. Patients with positive blood cultures had significantly higher concentrations of all three biomarkers compared with culture-negative patients. Among the evaluated parameters, procalcitonin showed the strongest association with blood culture positivity and the highest diagnostic discriminatory ability, followed by serum lactate and CRP.

The predominance of Gram-negative organisms, particularly Escherichia coli and Klebsiella pneumoniae, highlights the importance of local microbiological surveillance in patients with suspected bloodstream infection. Elevated serum lactate was also associated with culture positivity, suggesting that patients with microbiologically confirmed infection may have greater physiological and metabolic derangement.

Overall, CRP, PCT, and serum lactate may serve as useful complementary investigations alongside blood culture and clinical assessment in the early evaluation of suspected sepsis**.** However, none of these biomarkers should be considered a substitute for microbiological confirmation or comprehensive clinical assessment. Blood culture remains essential for identification of the causative pathogen and antimicrobial susceptibility testing. Further multicentre prospective studies with larger patient populations and serial biomarker measurements are warranted to validate these findings and establish clinically applicable biomarker thresholds.

In conclusion, the combined interpretation of clinical findings, blood culture results, CRP, procalcitonin, and serum lactate may improve the early characterization and risk assessment of patients with suspected sepsis and potentially support more timely and targeted clinical management.

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