RESEARCH ARTICLE

Diagnostic Performance of Procalcitonin, Interleukin-6 and C-Reactive Protein for Predicting Blood Culture Positivity in Patients with Suspected Sepsis: A Prospective Cross-sectional Study

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ABSTRACT
Sepsis is a potentially life-threatening condition and is one of the leading causes of mortality and morbidity worldwide, as it occurs in response to infection with a dysregulated host response. Thus, it is essential to discover accurate biomarkers that facilitate timely identification. We attempted to assess the diagnostic value of C-reactive protein (CRP), interleukin-6 (IL-6) and procalcitonin (PCT) for predicting blood culture positivity in patients with suspected sepsis. Of 196 patients, 84 (43%) had positive blood cultures. Patients with blood culture-positive patients had significantly higher mean values of PCT (29.1 ± 11.9 ng/mL), IL-6 (836.8 ± 265.6 pg/mL), and CRP (225.5 ± 44.7 mg/L) compared with culture-negative patients ($p < 0.001$). The most frequently identified isolate was methicillin-resistant Staphylococcus aureus (MRSA) (42%), followed by Klebsiella pneumoniae (26%) and Escherichia coli (21%). ROC (Receiver operating characteristic) investigation showed that PCT with significant diagnostic efficacy (AUC: 0.893; 95% CI, [0.84--0.93]) with a sensitivity of 79.8% and specificity of 83.9% at a cut-off value of ≥ 20 ng/mL used in severe sepsis method for diagnosis. For PCT, CRP and IL-6 had the highest specificity (99.1%) with cut-off value at 876 pg/mL; while CRP showed a higher sensitivity (91.7%) than other two markers with a cut-off value at 167 mg/L. Spearman's correlation analysis of each marker demonstrated that PCT was most positively correlated with blood culture positivity ($\rho = 0.675$), followed by interleukin-6 ($\rho = 0.633$) and C-reactive protein ($\rho = 0.600$). The results suggest that in patients with sepsis, procalcitonin has better diagnostic accuracy than interleukin-6 and C-reactive protein for predicting blood culture positivity. In bloodstream infection, significant associations were found for each biomarker; but balance between sensitivity/specificity was best for PCT. In conclusion, inclusion of PCT, IL-6 and CRP into routine clinical assessment may help in the early diagnosis of sepsis and improve antimicrobial stewardship regarding the future management of this patient population.

Keywords: Antimicrobial stewardship; C-reactive protein, Interleukin-6; Procalcitonin; Sepsis
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Introduction

Sepsis, often known as bloodstream infections, is a severe, life-threatening infection with a mortality rate of up to 50%. It is a complex, heterogeneous syndrome characterised by the Sepsis-3 consensus statement as "life-threatening organ dysfunction due to a dysregulated inflammatory host response to infection" and remains a noteworthy health concern worldwide (Authia *et al*., 2025; Gupta *et al*., 2026; Jalal *et al*., 2025; Sharma and Duggal, 2019). This vulnerability is based on two intertwined processes:

inflammation and immunosenescence. Immunosenescence, aggravated by a state of persistent pro-inflammatory conditions referred to as inflammaging, leads to suppression of immune responses (Wacker *et al*., 2013; Wang *et al*., 2026; Sinha *et al*., 2011; Logan and Weinstein, 2017; Lu and Lu, 2023). Untreated or inadequately managed infections can lead to poor infection control, excessive inflammation, endothelial damage, organ failure, sepsis, septic shock, and perhaps death. Sepsis is a prominent cause of illness and death worldwide (Todi *et al*., 2010). Recent Global Burden of Disease (GBD) estimates indicate that there are 166 million cases of sepsis globally each year, resulting in over 21 million fatalities (Authia *et al*., 2025). Sepsis is a significant public health concern, as noted by the World Health Organisation (WHO), which advocates for increased awareness and improved treatment methods (Kumar *et al*., 2026).

Although bacterial pathogens most frequently precipitate sepsis, the condition may also arise from severe viral, fungal, or parasitic infections. The sepsis symptoms, signs and clinical results are non-specific as a result ~40% of patients diagnosed microbiologically with septic shock or sepsis (Duncan *et al*., 2021; La Via eta al., 2026; Lafon *et al*., 2026). In addition, non-infectious conditions associated with SIRS can obscure or simulate sepsis, making it difficult to diagnose correctly. A further obstacle is culture-negative bacterial infection, which complicates the confirmation of sepsis (Chang *et al*., 2024). Recent advances in medical care have not lowered the incidence or mortality of sepsis, which remain alarmingly high. Currently, clinical management is based on antibiotic therapy, organ support, and fluid resuscitation. There are no treatments for the pathophysiology of sepsis Duncan *et al*., 2021; Jekarl *et al*., 2013; Demir *et al*., 2025).

To improve detection, researchers have investigated microbiological techniques as well as biomarkers and molecular markers. It is significant to note that bacterial blood culture, regarded as the gold standard for sepsis diagnosis, is laborious and has a poor positive rate, which delays management (Iskander *et al*., 2013). Hence, it is important to find out the rapid and accurate biomarkers for early diagnosis, assess the effect of the disease and prognosis of the patient to improve outcomes.

Antibiotic therapy in people with assumed bacterial infections is predominantly provided analytically, owing to the unspecific nature of infection presentations, the treatment in emergency settings and the absence of precise, rapid diagnostic procedures to mitigate uncertainty (Sun *et al*., 2025). Current blood tests cannot accurately differentiate between bacterial infections, viral infections and inflammation, with a lag time (12-24 hours) to bacterial infections.

The occurrence of antimicrobial resistance (AMR) is a key contributor to the global problem of infection caused by drug-resistant bacteria. The impact of antimicrobial resistance, quantified by case numbers, associated fatalities and disability-adjusted life years, influences all demographics, with the highest occurrence in infants, followed by individuals aged 65 and above. Excessive and unnecessary antibiotic prescribing accelerates the emergence of antimicrobial resistance (Evans *et al*., 2021; Cao and Sun, 2025). Hence, reducing the duration of antibiotic therapy has become a fundamental intervention in hospital-based antimicrobial stewardship initiatives.

Serological biomarkers represent the host immune responses to infection (Todi *et al*, 2010; Cao and Sun, 2025). Procalcitonin (PCT) is a sensitive & specific marker for bacterial infection, secreted in response to inflammatory signals, with increased concentration found in severe bacterial infections (Kaukonen *et al*., 2014; Knapstein *et al*., 2022). It has been used to support clinical decision-making in critically ill patients. However, studies have reported variable findings regarding its role in predicting treatment response. In contrast to CRP, procalcitonin (PCT) is a reliable biomarker with an early increase in bacterial infection & correlates very well with disease progression (Wang *et al*., 2025). The dynamic changes of its signal allow ongoing tracking of bacterial infection and response to therapy, thus assisting clinical decisions on initiation, change, or discontinuation of antimicrobial therapy. Procalcitonin (PCT) is one of the most accurate biomarkers studied. The sensitivity & specificity of PCT differ greatly depending on the cut-off values & severity of infection, ranging from 35.0% to 96.5% for sensitivity and 70.0% to 100% for specificity. Furthermore, the literature has shown mixed results regarding PCT.

The most common point-of-care marker is C-reactive protein (CRP) to assess patients who present with fever in emergency departments. However, its clinical usefulness is limited by a relatively slow response to bacterial infections and its increase in other non-infectious inflammatory conditions, limiting its diagnostic specificity (Miguel-Bayarri *et al*., 2012). CRP has been recommended as a biomarker linked to sepsis with PCT. The reported ranges of specificity and sensitivity for CRP were 74.0% - 84.4% and 63.5%- 76.0%, respectively (Jeganathan, 2022; Daud *et al*., 2024).

Interleukin-6, a key pro-inflammatory cytokine, has also been found to be useful in the diagnosis of infections and can improve the recognition of infectious processes when combined with clinical assessment. So, IL-6 is a valuable additional biomarker, particularly in the early stage of infection, and the combination of IL-6 with PCT & CRP may improve the diagnostic accuracy for sepsis (Singer *et al*., 2016). The prognosis of septic patients after treatment is of clinical importance. In several studies of septic or critically ill patients, PCT has been suggested to be an important prognostic marker. However, few studies have examined the predictive value of ESR, IL-6, CRP, or WBC counts in patients with sepsis (Prucha *et al*., 2015).

Our current study aimed to evaluate the efficiency of the inflammatory biomarkers C-reactive protein, Procalcitonin

and Interleukin-6 in distinguishing sepsis from Systemic Inflammatory Response Syndrome (SIRS). These markers were further evaluated for their utility in monitoring the success of antimicrobial treatment and as prognostic predictors.

Material and methods

The prospective cross-sectional study has been conducted in the Department of Microbiology at Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Salem, Tamil Nadu. The study was approved by the institutional Ethical Review Committee Tracking No.VMKVMC&H/IEC/22/64. The study has been documented in accordance with STARD 2015 (Standards for Reporting Diagnostic Accuracy Studies) guidelines. Patients were enrolled after informed consent.

Sample size

The team of primary investigators collected the data using preformatted forms. Patients were enrolled after providing informed consent. A sample size of n=196 was calculated using the PASS sample size software, with precision, specificity, prevalence, and sensitivity.

Inclusion criteria

Adult female and male individuals between the ages of 18 to 70, and those under 18 and clinically suspected of having sepsis, were recruited using a purposive non-probability sampling technique. Patients were enrolled within 24 hrs of ICU admission from November 2022 to December 2024. Suspected sepsis was characterised by the presence of a minimum of two of the following clinical criteria upon admission: body temperature ≥38°C or <36°C, white blood cell count <4 × 10^9/L (<4,000/mm^3), or >12 × 10^9/L (>12,000/mm^3), respiratory rate >20 breaths per minute and heart rate >90 beats per minute. A positive blood culture results subsequently validated the diagnosis of sepsis. We also recorded and analysed sepsis-related laboratory indicators, including blood culture, white blood cell (WBC) counts, and C-reactive protein (CRP) levels, at admission as part of standard clinical therapy.

Exclusion criteria

Patients with no clinical signs or symptoms of sepsis were excluded. Patients over 70 years of age were excluded because of 'immune senescence' in the elderly, which results in a different presentation of bacteraemia. In addition to other patients, the study excluded patients with organ failure, who received blood transfusions before tertiary care, and who were discharged before 24 h.

Sample collection and processing

Blood cultures were evaluated using the BD BACTEC FX system following manufacturer and laboratory protocols. Aseptically collected blood volumes were 15–20 mL for adults and 2–5 mL for children. Each vial (aerobic and anaerobic) was inoculated with 8-10 mL (adult) or 1-3 mL (paediatric) blood and mixed well. The system was used to monitor microbial growth by measuring changes in fluorescence associated with CO_2 every 10 min over 5 days. Gram staining was performed on positive flags, followed by subculture to solid media (blood agar and MacConkey agar) for further testing including antimicrobial susceptibility and identification.

Subculturing

Blood culture bottles flagged as positive by the automated system (e.g. BD BACTEC FX system) were Gram-stained to determine the morphology of the organism. Polymicrobial cultures have more than one distinct morphological organism, whereas monomicrobial cultures have only one type of organism. A small volume of broth is inoculated aseptically onto solid media (e.g., blood agar, MacConkey agar) & incubated at 35 to 37 °C for 18 to 48 hours. Regular inspections are made for growth, and characteristic colonies are selected for identification, biochemical profiling and antimicrobial susceptibility testing.

Antibiotic susceptibility

Antibiotic susceptibility testing was performed by using the Kirby–Bauer disc diffusion method in accordance with Clinical & Laboratory Standards Institute (CLSI) guidelines. Mueller-Hinton agar (MHA) media plates were prepared, & the bacterial inoculum was standardised to a McFarland standard of 0.5. A confluent lawn was inoculated on the MHA surface, followed by the placement of antibiotic discs. Plates were incubated at 35 to 37 °C for 16–24 hrs, after which inhibition zones were measured & interpreted as susceptible (S), intermediate (I), or resistant (R) according to CLSI criteria. Quality control was ensured by testing with reference strains like *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 25923 and *Escherichia coli* ATCC 25922, by verifying the validity of the results.

Biomarkers testing

Blood was collected in serum separator tubes, allowed to clot & centrifuged at 1500- 2000 × g for 10 minutes. The serum was separated & stored at −80 °C until analysis. After thawing at room temperature, samples were gently mixed and tested. Serum PCT levels were measured by chemiluminescent microparticle immunoassay (CMIA) on an automated analyser. Using a semi-automatic nephelometric analyser the serum CRP levels were measured by a latex-enhanced nephelometric immunoassay. Plasma interleukin-6 levels were determined by chemiluminescent immunoassay (CLIA) on an automated platform. All measurements were performed in duplicate with proper calibration and quality controls, showing acceptable precision (CV <10–15%).

Sensitivity, specificity, PPV, & NPV were used to evaluate the diagnostic accuracy with blood culture as the gold standard. Receiver operating characteristic curves (ROC) were also used to compare different cut offs. The data were

analysed using SPSS version 22. Chi-square test will be used to assess the association of qualitative variables. Statistical significance was defined as a *p*-value.

Results

Demographic and clinical characteristics of the studied group

The primary study population consisted of people aged 18–59 years, with 105 participants (54%). Individuals aged 60 years and above comprised 67 cases (34%), whereas paediatric patients under 18 years accounted for the smallest cohort, with 24 cases (12%). This signifies that the study cohort primarily consisted of adults, with a significant representation of older individuals. The mean age of the participants, derived from aggregated data approximation utilising class midpoints, was predicted to be roughly 45–48 years. The median age is situated inside the 55-year category, as this group encompasses the cumulative midpoint of the sample.

Over a third of study participants' samples were from the General Medicine department (31%), Emergency Medicine (26%), and 20% from General Surgery. Of the 196 samples, 43% yielded positive blood culture results, whereas 57% yielded negative results. Over fifty percent (57%) were male, while only 43% were female. There was no significant relation between the age, sex & departments of sample collecting of participants and blood culture (p value >0.05). (Table 1).

Distribution of microorganisms in blood samples

Out of the 196 individuals in the study, n=84 (43%) had bacterial isolates grown from blood cultures with both Gram-negative and Gram-positive bacteria, & 112 (57%) had no bacterial growth. A total of 84 bacterial isolates from the blood cultures of patients were included in the investigation. Among the Gram-positive isolates, MRSA was the most prevalent strain, accounting for 42%, followed by *Enterococcus* species, which represented 1%. Additionally, the most common Gram-negative bacterium identified was *K. pneumoniae*, making up 26% of the isolates. Other frequently encountered gram-negative bacteria included *P. aeruginosa* (10%) and *E. coli* (21%). The distribution of microorganisms, as well as Gram-negative & Gram-positive bacteria, is presented in (Figure 1).

Distribution of Multidrug Resistant (MDR) pathogen

A total of 48 multidrug-resistant (MDR) pathogens were identified among the study isolates. The most predominant MDR organism was MRSA, accounting for n=35 (73%) isolates. Among the extended-spectrum beta-lactamase (ESBL) positivity rate was (8%) in *E. coli* isolates, followed by *K. pneumoniae* with n=2 (4%) isolates and *P. aeruginosa* with n=1 (2%) isolate. Additionally, Carbapenem-resistant organisms were also detected, including carbapenem-resistant *E. coli* in (8%) isolates, while carbapenem-resistant *K. pneumoniae* and carbapenem-resistant *P. aeruginosa* were identified in (2%) isolate each. Overall, MRSA constituted the major proportion of MDR pathogens in the study population (Figure 2).

Antimicrobial susceptibility profile of Gram-positive bacterial isolates obtained from blood culture-positive study participants

The drug susceptibility profile of Gram-positive bacteria isolated from blood culture-positive study participants, including MRSA and *Enterococcus faecalis*, was presented in (Figure 3). Among the MRSA isolates, complete susceptibility was observed for teicoplanin, linezolid and vancomycin, with all n=35 (100%) isolates sensitive to these antibiotics. Significant susceptibility was also noted for doxycycline hydrochloride (86%) and ciprofloxacin (63%). Gentamicin exhibited moderate susceptibility at 43%, but lower susceptibility rates were recorded for penicillin (29%), co-trimoxazole (29%), clindamycin (26%), and erythromycin (14%). Methicillin resistance was confirmed by the resistance of all MRSA isolates to cefoxitin.

The single isolate of *E. faecalis* demonstrated 100% susceptibility to ciprofloxacin, levofloxacin, high-level gentamicin, teicoplanin, linezolid, and vancomycin. However, it was resistant to ampicillin, penicillin, doxycycline hydrochloride, and erythromycin. Overall, glycopeptides and oxazolidinones, specifically vancomycin, teicoplanin, and linezolid, had remarkable efficacy against Gram-positive isolates, but resistance to beta-lactam antibiotics and macrolides was frequently noted among MRSA isolates.

Antimicrobial susceptibility profile of Gram-Negative bacterial isolates obtained from blood culture-positive study participants

The maximum susceptibility among *K. pneumoniae* isolates was observed for imipenem and meropenem, with 95% of isolates exhibiting sensitivity to each treatment. High susceptibility was also noted for amikacin and gentamicin, each showing sensitivity in n=18 (81%) isolates. Lower susceptibility rates were observed for ciprofloxacin and ampicillin. Imipenem and meropenem had the greatest susceptibility against *Escherichia coli*, with n=14 (78%) isolates sensitive to each drug. Amikacin, gentamicin, and piperacillin–tazobactam exhibited sensitivity in n=12 (67%) isolates, but ciprofloxacin displayed sensitivity in n=11 (61%) isolates. The least susceptibility was observed for cefuroxime and ampicillin.

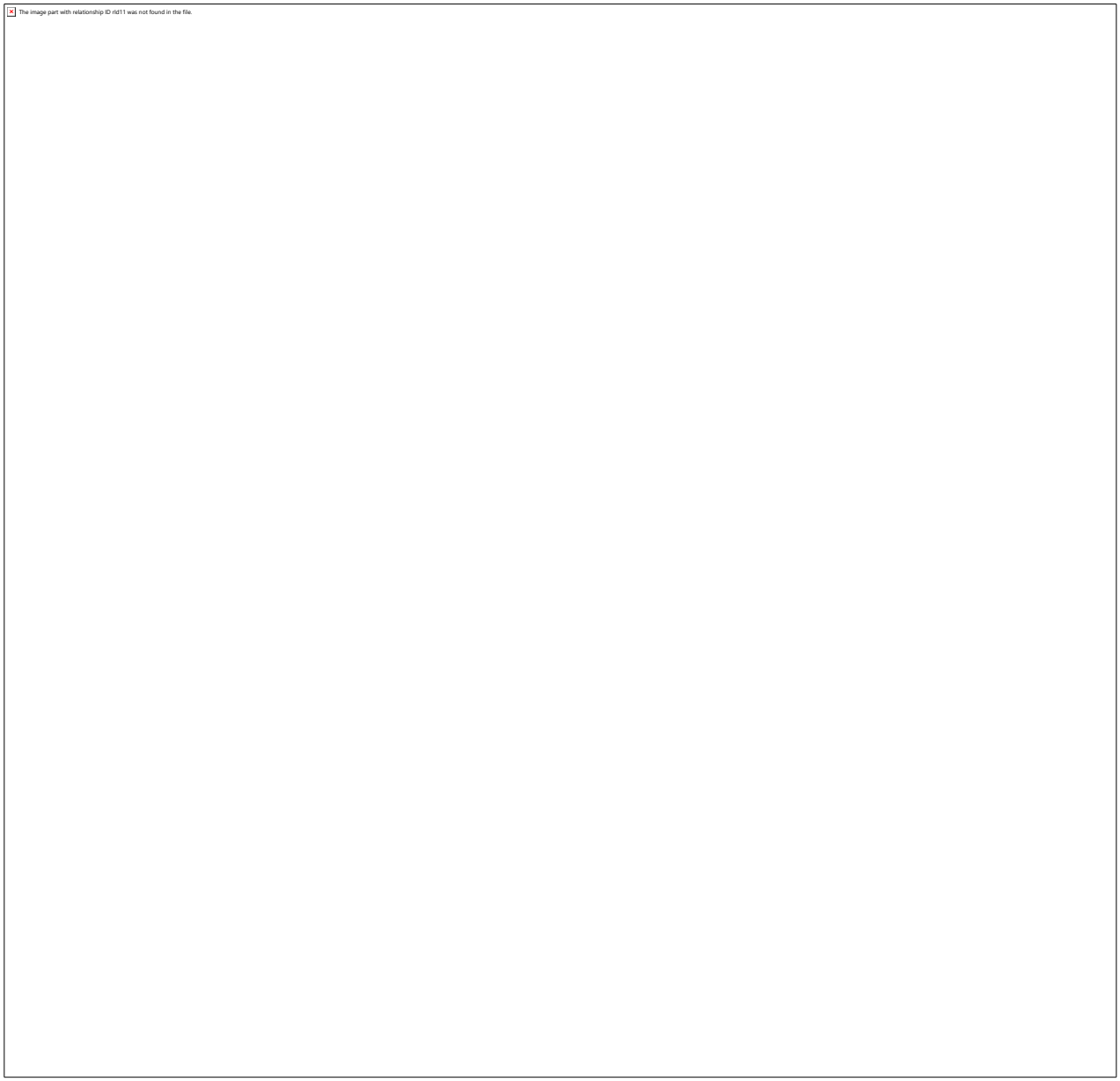
Among *P.aeruginosa* isolates, the greatest susceptibility was observed for ceftazidime and cefepime, each with n=7 (88%) sensitive isolates. Piperacillin–tazobactam, cefuroxime, imipenem and meropenem each showed sensitivity in n=6 (75%) isolates. Notably, complete resistance was observed against ciprofloxacin and levofloxacin, with no isolates sensitive to these antibiotics. Overall, carbapenems (imipenem and meropenem) displayed the highest antimicrobial activity against most

Gram-negative isolates, whereas fluoroquinolones demonstrated comparatively lower susceptibility rates, particularly among *P. aeruginosa* (Figure 4).

According to the severity of sepsis the PCT values has been categorised into four categories (Anand *et al*., 2015; Singh *et al*., 2025).

Procalcitonin Levels

PCT > 10 ng/ml	Indicates severe bacterial sepsis or septic shock.
PCT 2-10 ng/ml	Suggests a severe systemic inflammatory response, most likely due to sepsis.
PCT 0.5-1.9 ng/ml	Represents systemic inflammatory response syndrome (SIRS), a systemic infection cannot be ruled out.
PCT < 0.5 ng/ml	Suggest the possibility of a local bacterial infection, making sepsis less likely.



Distribution of procalcitonin levels

As shown in (Figure 5), among n=196 patients, procalcitonin was tested positive in individuals. The procalcitonin values ranged from 0.5 to 10 ng/ml (minimum

to maximum), and the mean was 20.6 ng/ml. Procalcitonin levels below 0.5 ng/ml were found in n=4 patients. In addition, n=5 patients had procalcitonin levels between 0.5 and 1.9 ng/ml. Moreover, procalcitonin levels ranged from 2 to 10 ng/ml in n=24 patients. Of note, 163 patients had procalcitonin levels >10 ng/ml.

Distribution of IL-6 and CRP concentrations across procalcitonin severity categories

To evaluate the relationship between the biomarkers were divided into four PCT groups. The minimum and maximum levels of IL-6 were 40.75 pg/ml and 681.89 pg/ml, respectively. The mean ± SD for IL-6 in n=24 septic patients were 244.95, and the mean IL-6 value in n=163 severe sepsis patients were 681.89. The lowest value of CRP was 56 mg/l and the highest was 202 mg/l. Mean ± SD for CRP in the n=24 sepsis patients were 103.58 and in the n=163 septic shock patients it was 202.65 (Table 2).

Baseline inflammatory biomarker profile of the study population

The inflammatory biomarkers in the study cohort (n= 196) demonstrated elevated mean values with moderate variability. The mean serum PCT level was 20.6 ± 11.8 ng/ml, with a median value of 19.6 ng/ml. The mean concentration of interleukin-6 (IL-6) was 599 ± 322.2 pg/ml, while the median IL-6 level was 520 pg/ml. C-reactive protein levels showed a mean value of 184 ± 61.9 mg/l and a median of 193.5 mg/l. Among the evaluated biomarkers, IL-6 demonstrated the highest variability, as indicated by its larger standard deviation. The median values of PCT, CRP, and IL-6 were relatively comparable to their respective mean values, indicating a moderately consistent distribution of biomarker levels among the study participants (Table 3).

Comparison of inflammatory biomarker concentrations between blood culture-positive and negative patients

A statistically significant association was identified between blood culture positive and increased levels of inflammatory biomarkers among the study participants (n=196). Participants with positive blood cultures (n=84) exhibited markedly elevated serum levels of PCT, CRP, and IL-6 in comparison to those with negative blood cultures (n=112) (Table 4).

The mean serum PCT level among blood culture-positive participants was 29.1 ± 11.9 ng/ml, which was markedly elevated than that observed in blood culture-negative participants (14.1 ± 6.6 ng/ml). The mean rank for PCT was significantly increased in the positive culture samples (142.5 vs. 65.5), with a Z value of −9.427 and a highly significant *p* value (<0.001). Similarly, IL-6 levels were significantly elevated in blood culture-positive participants, with a mean value of 836.8 ± 265.6 pg/ml in contrast to 420.7 ± 234.1 pg/ml in blood culture-negative participants. The mean rank values were 139.2 and 67.9, respectively, with a Z value of −8.842, signifying robust statistical significance ($p < 0.001$).

CRP values exhibited a notable elevation in blood culture-positive participants (225.5 ± 44.7 mg/l) in contrast to blood culture-negative participants (152.9 ± 54.5 mg/l). The corresponding mean rank values were 137.5 and 69.3, respectively, with a Z value of −8.382 and a highly significant *p* value (<0.001). Overall, elevated levels of PCT, CRP, and IL-6 were significantly correlated with blood culture positivity, indicating that these inflammatory biomarkers may be effective predictors of bloodstream infection and systemic inflammatory response (Table 4).

Biomarkers in the Diagnosis of Sepsis by ROC Curve Analysis

At a critical value of 20 ng/ml, the area under the PCT curve was 0.893 (P<0.05) with sensitivity and specificity of 79.8% and 83.9%, respectively, indicating good overall diagnostic accuracy with balanced sensitivity and specificity. The area under the receiver operating characteristic curve was 0.848 (P<0.05) with 91.7% sensitivity and 63.4% specificity at a cut-off value of 167 mg/L. The area under the IL-6 curve was 0.864 (P<0.05) with a sensitivity of 71.4% and specificity of 99.1% at critical value of 876 pg/ml (Figure 5). Overall, IL-6 demonstrated the highest specificity, CRP showed the highest sensitivity, and PCT provided the best balance between sensitivity and specificity among the three biomarkers evaluated.

Spearman's rank correlation coefficients (ρ) analysis between variables and blood culture positivity

The strongest correlation with blood culture positivity was demonstrated by PCT ($\rho = 0.675$), followed by IL-6 ($\rho = 0.633$) and CRP ($\rho = 0.600$) among the biomarkers. The findings indicate that all three biomarkers were significantly connected with blood culture positive, with PCT exhibiting the strongest correlation strength among the evaluated markers.

Discussion

Despite advances in diagnostic modalities and therapeutic interventions, early detection of sepsis remains a significant challenge because of its heterogeneous clinical manifestations and rapid progression (Samraj *et al*., 2013). Numerous sepsis biomarkers are emerging to facilitate early detection. Biomarkers like PCT, CRP, and ESR serve as indications of bacterial infections (Prucha *et al*., 2015). Studies indicate that biomarkers, in conjunction with gold standard blood cultures, would facilitate a more rapid detection of the bacterial aetiology of sepsis (Duncan *et al*., 2021).

Among the 196 enrolled patients, 43% had positive blood cultures, and all three biomarkers were significantly higher in culture-positive compared with culture-negative patients. ROC analysis demonstrated that Procalcitonin had the highest overall diagnostic accuracy (AUC = 0.893),

providing the best balance between sensitivity (79.8%) and specificity (83.9%), whereas IL-6 exhibited the highest specificity (99.1%) and CRP showed the highest sensitivity (91.7%). Furthermore, PCT demonstrated the strongest correlation with blood culture positivity ($\rho = 0.675$), followed by Interleukin-6 ($\rho = 0.633$) and C - reactive protein ($\rho = 0.600$). These findings suggest that although all three biomarkers are associated with bloodstream infection, PCT is the best single biomarker to predict positivity of blood culture in patients with suspected sepsis.

The previous study by the researcher to assess PCT, CRP, and IL-6 levels in sepsis-related bacteraemia included a cohort comprising 70% male and 30% female participants, with a mean age of 47 years, paralleling the demographics of this study. This study comprised 57% of males and 43% of females, with a mean age of the subjects was 48 years. The present study reported that the mean age of the participants was 48 years and median age was 55 years. A comparable distribution was noted in various global investigations. The average age of a study of severe sepsis in India was 58.17 years (Todi *et al*., 2010).

The blood culture positivity rate in our cohort was 43%, aligning with previous data from Indian and other Asian tertiary care facilities, where positivity rates typically range from 35 to 50% (Hammond *et al*., 2022). A substantial percentage of patients (41.2%) were culture-negative, highlighting a recognised limitation of blood culture. False-negative results may arise from previous antibiotic treatment, low microbial load, or infections caused by fastidious or intracellular pathogens. The dominance of Gram-positive bacilli, with MRSA, and the relatively high proportion of Gram-negative isolates, with *K. pneumoniae* and *E. coli* as the leading organisms in our study, underscore the dual epidemiological burden in sepsis, where both Gram-negative and Gram-positive organisms remain clinically significant (Liboria *et al*., 2024). This pattern is like that described in several multi-centre studies of microbial epidemiology. Both organisms are well known to carry extended-spectrum β-lactamases (ESBLs) and carbapenem resistance, making treatment challenging (Cao and Sun, 2025; Booraphun *et al*., 2021). The prevalence of sepsis was 4.7% (929 out of 19961) due to Gram-positive bacteria (Knapstein *et al*., 2022). Another investigation showed that the predominant type of GND was *Klebsiella* species (12.7%) (Pepys and Hirschfield, 2003) similar to our results. In our investigation, the predominant Gram-negative bacteria were *Klebsiella* and *E. coli*. The discrepancies observed between the current study and earlier reports may be due to differences in geographic settings and patterns of antibiotic administration (Jekarl *et al*., 2013).

Among the biomarkers evaluated, PCT demonstrated the best diagnostic performance for predicting blood culture positivity. Culture-positive patients had significantly higher mean PCT concentrations than culture-negative patients (29.1 ± 11.9 vs. 14.1 ± 6.6 ng/mL; $p < 0.001$), and PCT achieved the highest AUC (0.893) with balanced sensitivity and specificity. Most participants (83%) demonstrated PCT values >10 ng/ml. The estimated mean PCT level was approximately 20.6 ± 11.8 ng/ml, with the median value 19.65 ng/ml falling within the >10 ng/category. The strong positive correlation between PCT and blood culture positivity supports its close association with invasive bacterial infection. According to Zaki *et al*. (2024). PCT was a more reliable diagnostic tool than CRP or interleukin-6 (IL-6), with PCT having higher sensitivity and specificity for bacterial infections than other biomarkers.

IL-6 concentrations were also significantly increased in culture-positive patients confirming its important role as an early mediator of the inflammatory response during sepsis. The overall diagnostic accuracy of IL-6 was slightly lower than PCT (AUC = 0.864), but its specificity at the optimal cut-off value was remarkably high (99.1%). This suggests that markedly elevated levels of IL-6 are highly indicative of bloodstream infection and may be particularly useful in confirming bacterial sepsis in clinically equivocal cases. The mean value ± SD of IL-6 in sepsis was 244.95 pg/ml and in septic shock was 681.89 pg/ml, supporting the high PCT values in these groups thus helping in the diagnosis of sepsis and septic shock. Li *et al*., (2021) demonstrated that PCT is useful in the diagnosis of bacterial infections in sepsis patients, but IL-6 is better for monitoring of antibiotic therapy. Patients with sepsis and septic shock showed increased IL-6 levels.

The levels of CRP were significantly increased in patients with positive blood cultures and showed the highest sensitivity among the three biomarkers examined. The minimum CRP value recorded was 56.00 mg/l, while in 24 patients with sepsis, it was 103.58 mg/l, and in 163 patients with septic shock, it was 202.65 mg/l. CRP levels were elevated in all three groups. This indicates that elevated CRP levels corroborated the high PCT values, hence facilitating the diagnosis of sepsis, SIRS and septic shock. Our findings were analogous to those of other investigations (Schupp *et al*., 2024).

When blood culture was considered as the gold standard, the sensitivity of PCT was 79.8% and specificity was 83.9% (cut off value 20ng/ml, $P < 0.0001$). CRP (cut-off 167mg/l) and IL-6 (cutoff value 876pg/ml) on the other hand has sensitivity of 91.7% and specificity of 63.4%. and sensitivity of 71.4% and specificity of 99.1%. Respectively. Our study results agree with the results of Sharma *et al* and Mehta *et al*., (2024). This shows the effectiveness of PCT in diagnosis of sepsis.

ROC analysis revealed that PCT is more accurate than CRP (0.796–0.902) and IL-6 (0.809–0.919) in diagnosing sepsis, with a peak AUC of 0.893 (95% CI, 0.849 – 0.936). The better diagnostic accuracy of PCT (AUC 0.87) in comparison to CRP (AUC 0.74) strengthens the increasing evidence for its involvement in the early identification of sepsis (Thummala *et al*., 2023). This finding aligned with recent studies that highlighted the enhanced predictive

power of PCT for sepsis relative to IL-6 and CRP, with sensitivity of 73% and specificity of 70% at a threshold of 0.5 ng/ml (Carcò *et al*., 2022). A meta-analysis of 30 studies encompassing 3244 patients demonstrated a sensitivity of 77% and a specificity of 79%, highlighting the importance of PCT as an important biomarker for early detection of sepsis (Wacker *et al*., 2013).

The present study reveals a positive link between PCT levels and blood culture positivity, in contrast to the correlations shown for IL-6 and CRP. The correlation coefficients for PCT, IL-6, and CRP were 0.675, 0.633, and 0.600, respectively, demonstrating a strong connection with bacteraemia ($p < 0.001$). Prucha *et al*. (2015) found that procalcitonin was a more specific biomarker of bacteraemia than IL-6 and CRP with a correlation coefficient of 0.7263 (p-value < 0.05), corroborating our results. PCT not only efficiently identified infections but also had a substantial correlation with illness severity. Mehta *et al*. (2024) documented significantly higher PCT levels in septic patients (3.65 ng/mL vs. 0.4 ng/mL, $p < 0.0001$), demonstrating enhanced diagnostic accuracy (AUC 0.925 vs. 0.677) and a more robust connection with disease severity (Spearman's rho 0.73 vs. 0.41) in comparison to CRP. Similarly, increased PCT levels in severe infections (6.7 ng/mL compared to 0.6 ng/mL, p=0.0075), demonstrating enhanced specificity and sensitivity at a threshold of 0.245 ng/mL, were observed by Massaro *et al*. (2007).

The present results have implications for the early diagnosis and management of sepsis. In the present study, PCT had the best sensitivity/specificity balance and the strongest association with blood culture positivity, having the highest overall diagnostic accuracy. Even though blood culture is the gold standard for diagnosis, its utility in immediate clinical decision-making is limited by a delayed turnaround time and limited sensitivity, especially in patients on prior antibiotic therapy. These findings support the role of Procalcitonin as a reliable adjunct biomarker for early recognition of sepsis and timely initiation of empiric antimicrobial therapy. Also, the high specificity of IL-6 indicates it may be useful in confirming bloodstream infection, while the high sensitivity of CRP makes it a useful first-line screening marker.

The strengths of the current study include the prospective evaluation of three clinically relevant inflammatory biomarkers, PCT, IL-6 and CRP, in a well-characterised cohort of 196 patients with suspected sepsis. The diagnostic performance was comprehensively evaluated by ROC curve analysis, sensitivity, and specificity and correlation analyses, simultaneously with blood culture as the reference standard. Microbiological culture results and antimicrobial susceptibility profiles gave useful information on the local epidemiology of bloodstream infections and multidrug-resistant pathogens.

This study was performed in a single tertiary care unit, which may limit the generalisability to other patient populations. Furthermore, biomarker levels were not evaluated in relation to clinical endpoints such as 28-day mortality, length of stay in a tertiary care unit, organ dysfunction scores and response to antibiotics. Second, molecular diagnostic methods for pathogen detection were not employed, and therefore, culture-negative sepsis could not be further defined in detail. The limitations of this study suggest that further research is needed to address these gaps comprehensively. Further studies are required to validate the findings and to develop biomarker-guided diagnostic algorithms for sepsis; these include multicentre studies with larger patient cohorts, serial biomarker monitoring, molecular microbiological techniques and assessment of long-term clinical outcomes.

Conclusion

Infection prevention initiatives, encompassing both community-acquired and healthcare-associated illnesses, can diminish the occurrence of sepsis. Sepsis is manageable, and prompt execution of specific therapies enhances outcomes. The World Health Assembly has called on member states to enhance initiatives for the identification, documentation, prevention, and treatment of sepsis. Among the biomarkers tested, CRP, PCT and IL-6 showed the best diagnostic accuracy, but their performance depends on the timing of onset of symptoms and presence of fever. In this study, individual biomarkers were not adequate to definitively confirm or exclude infection. These findings underscore the necessity for a sophisticated interpretation of biomarkers in diagnosing infections within the tertiary care unit. Integrating biomarker assays into clinical workflows can facilitate early identification, strengthen antimicrobial stewardship, and ultimately boost patient survival. PCT can aid in diagnosing bacterial infections, particularly in patients with septic shock and severe sepsis. IL6 demonstrated superior kinetics for assessing the efficacy of antibiotic therapy. In conclusion, routine use of PCT, IL-6 and CRP in clinical practice may help in early diagnosis of sepsis and improved antibiotic stewardship for future management of this population of patients.

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Conflict of interest

The authors declare that they have no conflict of interest.

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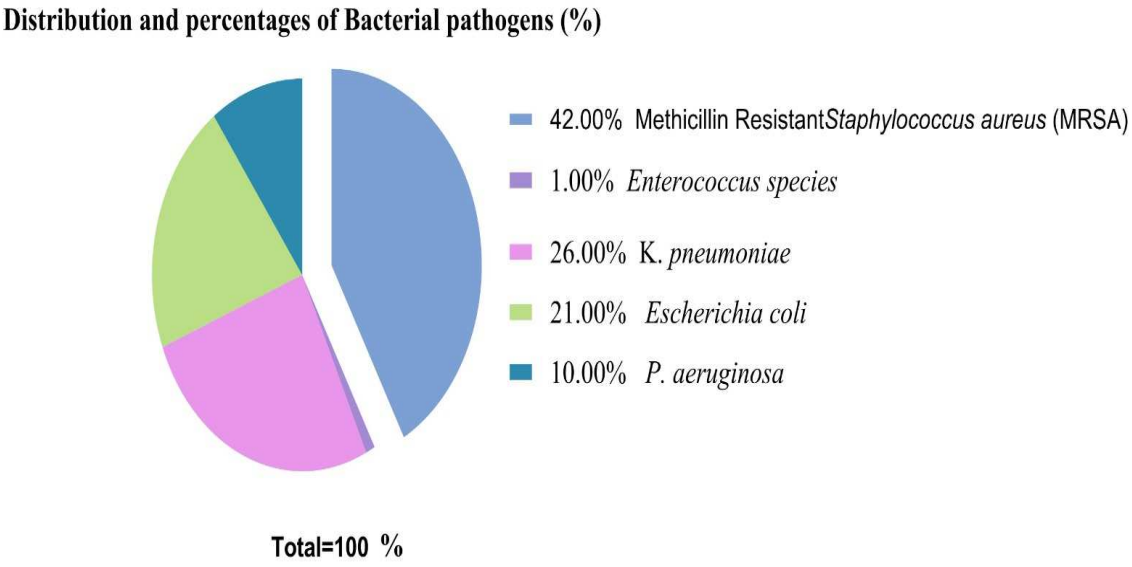


Figure 1: Distribution of organisms present in the blood samples among the study participants (N = 84)

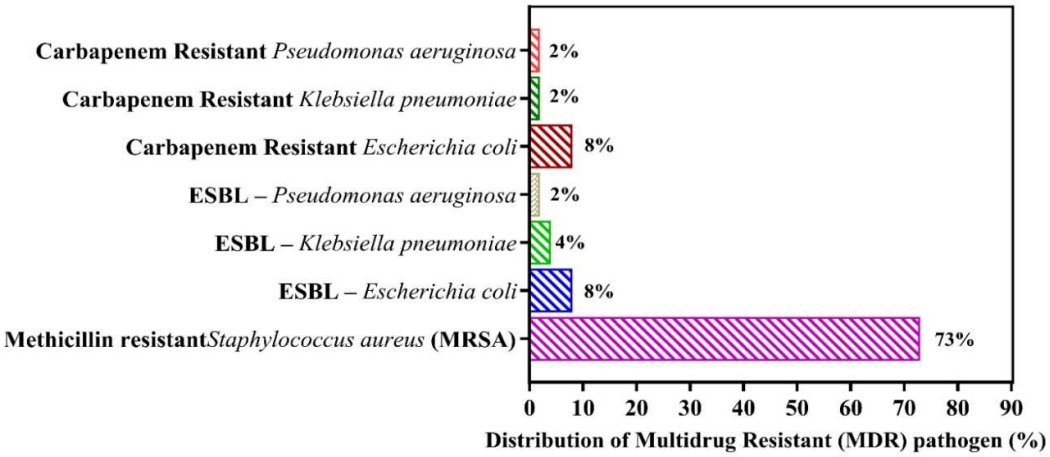


Figure 2: Distribution of Multidrug Resistant (MDR) pathogen



Figure 3: Antimicrobial susceptibility of Gram-positive organisms among blood culture-positive study participants

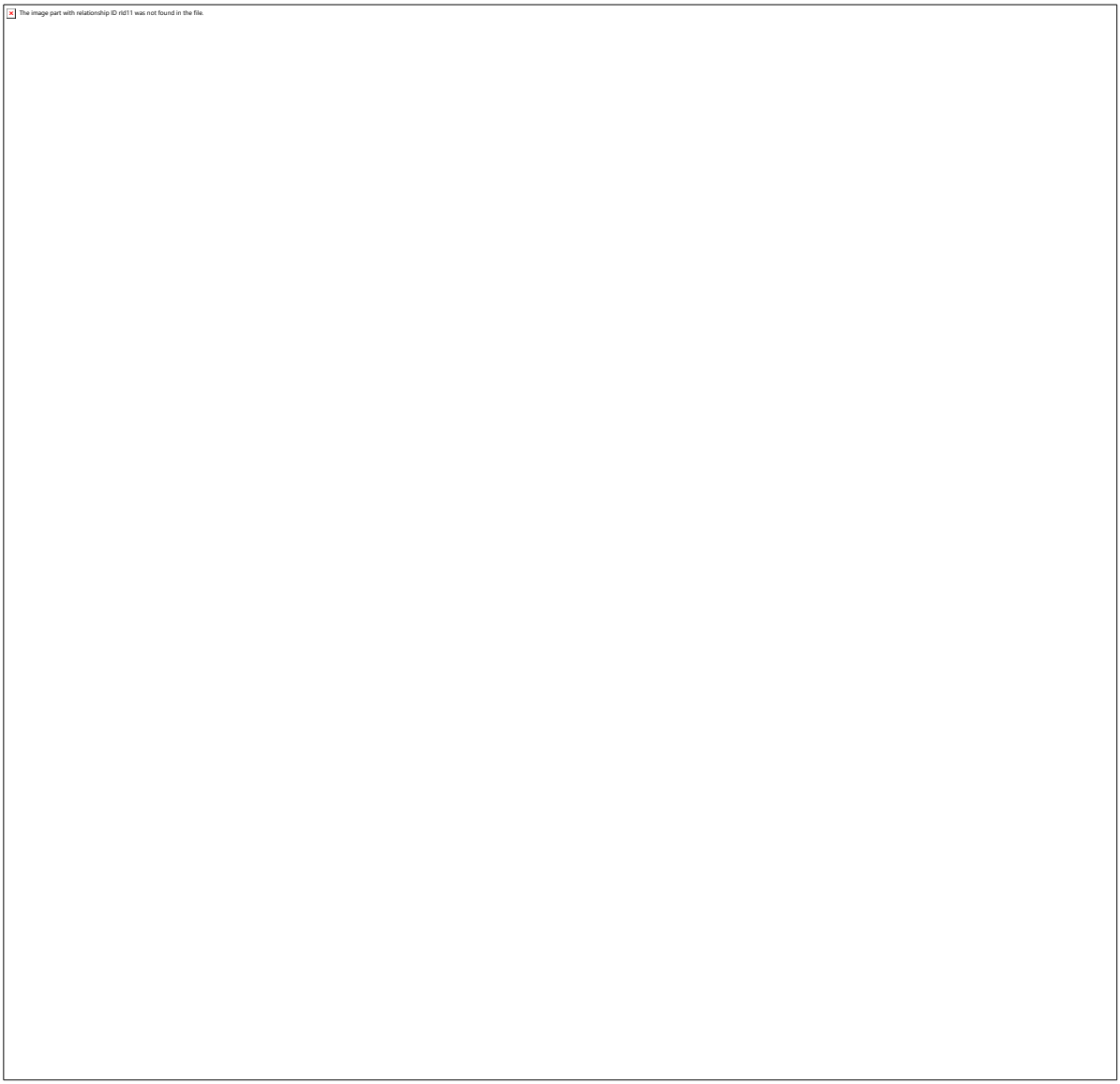


Figure 4: Antimicrobial susceptibility of Gram-Negative Organisms among blood culture positive study participants

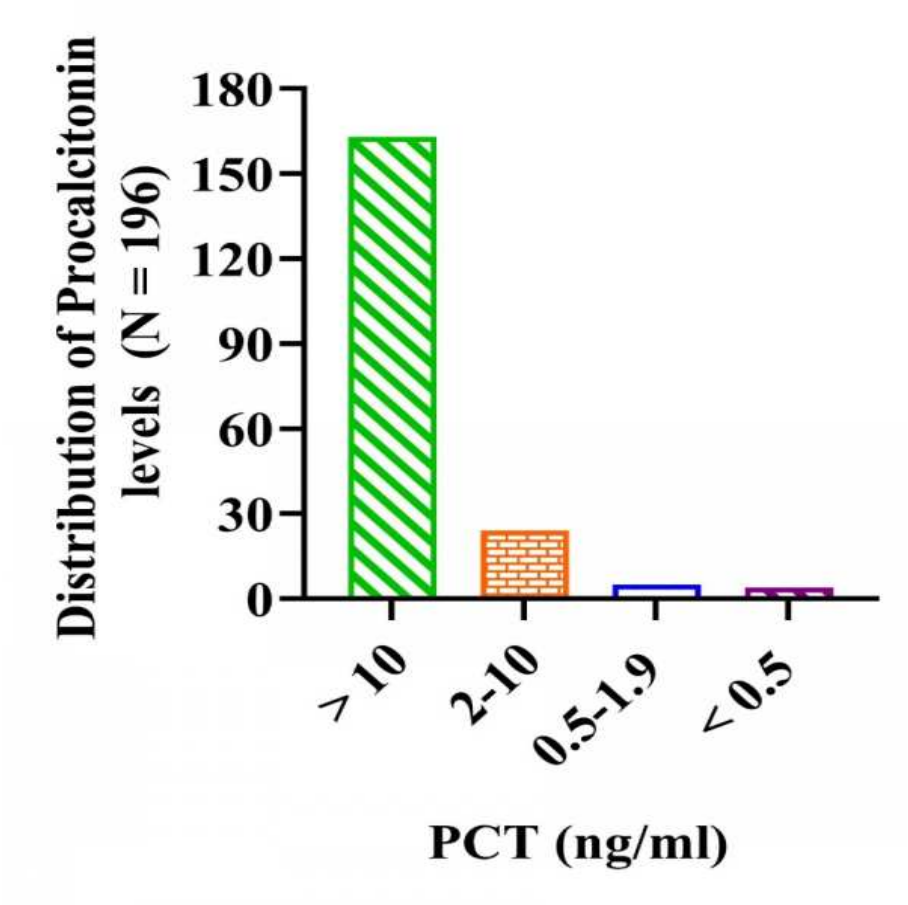


Figure.5: Procalcitonin levels distribution (N = 196)

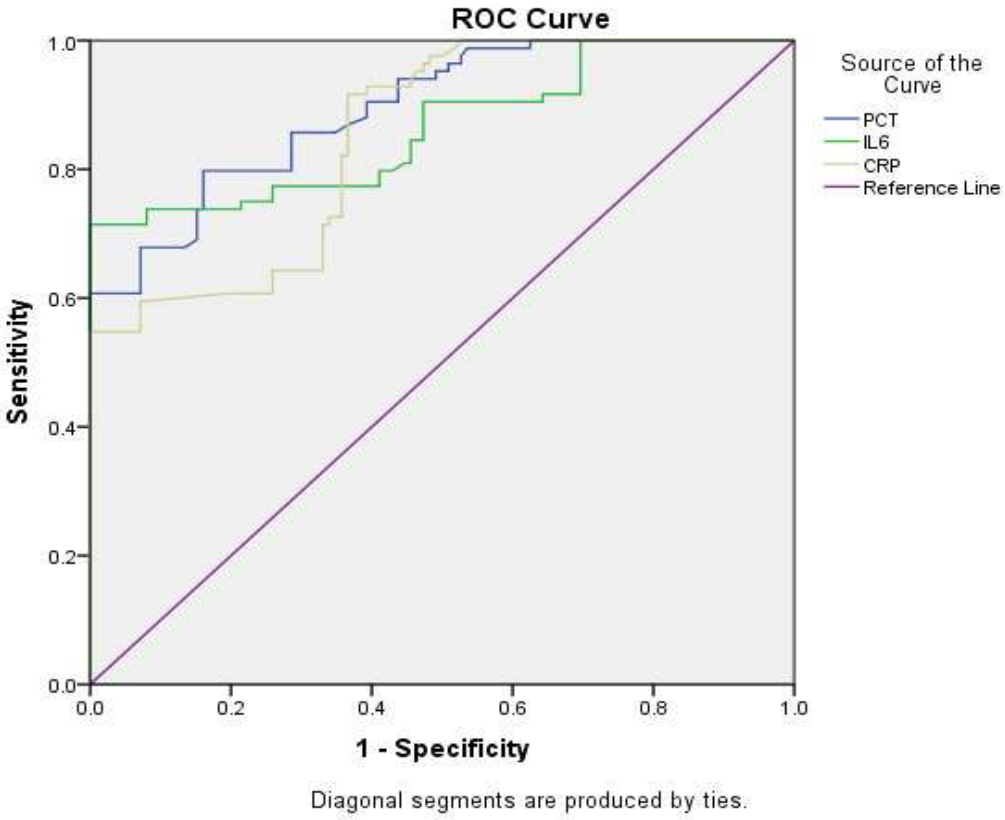

ROC Curve
Sensitivity
1 - Specificity
0.0
0.2
0.4
0.6
0.8
1.0
Source of the Curve
PCT
IL6
CRP
Reference Line
Diagonal segments are produced by ties.

Figure 6: ROC curves demonstrating diagnostic performance of PCT, IL-6 and CRP for prediction of bloodstream infection (N =196)

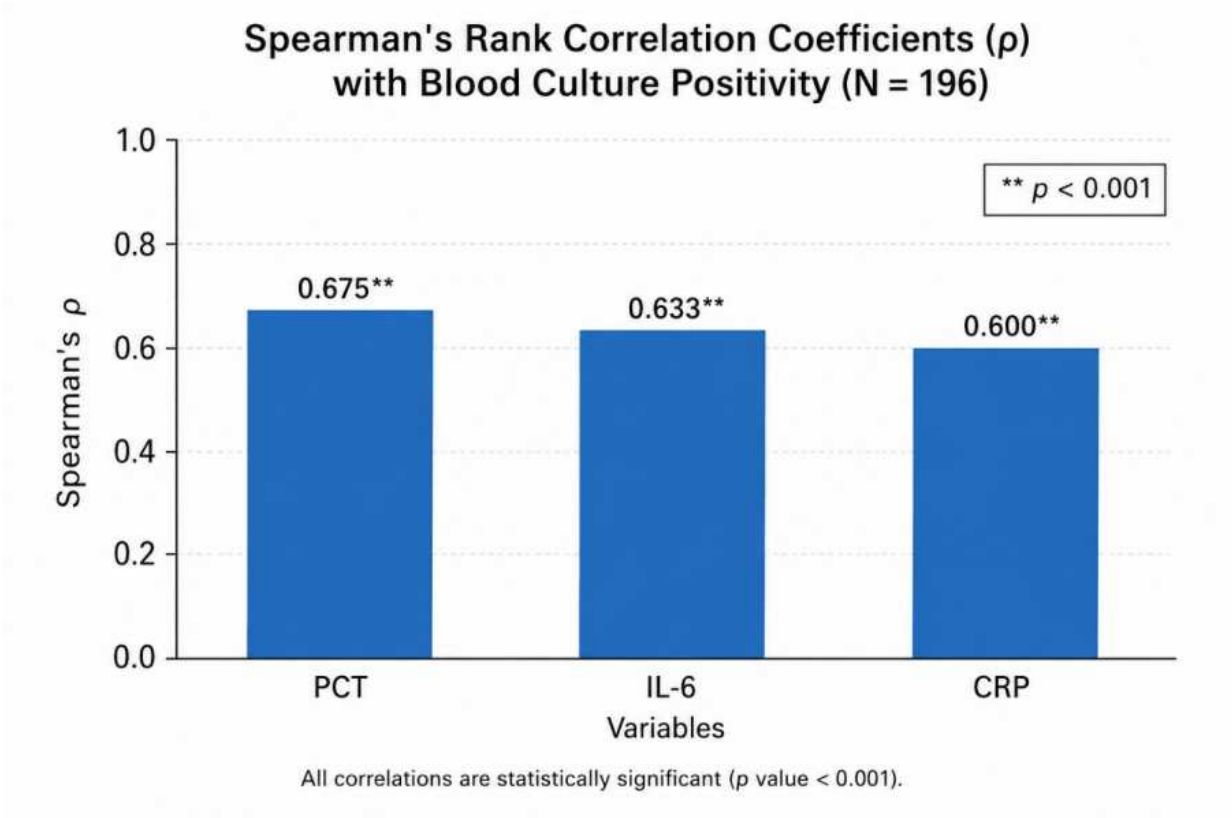


Figure .7: Spearman's rank correlation coefficients (ρ) between the variables Age, PCT, IL-6, CRP, with Blood Culture positivity (N = 196)

Table 1: Demographic and clinical characteristics (N =196)

Variable (n)		Blood Culture		Chi square	*p* value
		Positive N=84 (%)	Negative N=112 (%)		
Age (years)	< 18 (24)	10 (42)	14 (58)	0.02	0.9
	18 - 59 (105)	45 (43)	60 (57)		
	≥ 60 (67)	29 (43)	38 (57)		
Sex	Male (112)	42 (38)	70 (62)	2.1	0.15
	Female (84)	42 (50)	42 (50)		
Department	General Medicine (61)	28 (46)	33 (54)	1.8	0.7
	Emergency Medicine (51)	23 (45)	28 (55)		
	General Surgery (40)	18 (45)	22 (55)		
	Pediatrics (24)	10 (42)	14 (58)		
	Orthopedics (13)	3 (23)	10 (77)		
	Chest & TB (7)	2 (29)	5 (71)		

Table 2: Distribution of IL-6 and CRP concentrations across procalcitonin severity categories

PCT values (ng/ml)	Sample Size (N)	Mean IL-6 values (pg/ml) (Mean ± SD)	Mean CRP values (mg/l) (Mean ± SD)
> 10	163	681.89	202.65
2-10	24	244.95	103.58
0.5-1.9	05	45.18	65.00
< 0.5	04	40.75	56.00

Table 3: Mean PCT, IL-6 & CRP of study participants (N=196)

Clinical Findings	Mean ± SD	Median
PCT (ng/ml)	20.6 ± 11.8	19.6
IL-6 (pg/ml)	599 ± 322.2	520
CRP (mg/l)	184 ± 61.9	193.5

Table 4: Comparison of inflammatory biomarker concentrations between blood culture-positive and blood culture-negative patients (N = 196)

Blood culture		Mean ± SD	Mean Rank	Z value	Chi square	*p* value
PCT (ng/ml)	Positive (84)	29.1 ± 11.9	142.5	- 9.427	88.4	<0.001
	Negative (112)	14.1 ± 6.6	65.5			
IL-6 (pg/ml)	Positive (84)	836.8 ± 265.6	139.2	- 8.842	77.9	<0.001

	Negative (112)	420.7 ± 234.1	67.9			
CRP (mg/l)	Positive (84)	225.5 ± 44.7	137.5	- 8.382	69.4	<0.001
	Negative (112)	152.9 ± 54.5	69.3			