European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: Applied Website:
https://farmclin.com/

ASSOCIATION OF POSITIVE AND NEGATIVE BLOOD CULTURE WITH C-REACTIVE PROTEIN

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ABSTRACT

Background & objectives

Blood culture is the gold standard for diagnosing bloodstream infections but is time-consuming and may yield false-negative results mainly after prior antibiotic use. C-reactive protein (CRP), an acute-phase reactant, may aid early diagnosis. This study evaluated the association between blood culture positivity and quantitative CRP levels in patients with suspected bloodstream infections.

Methods

This cross-sectional study was conducted over a period of 12 months in the Department of Microbiology of a tertiary care teaching hospital in North India, after approval from the Institutional Ethics Committee. A total of 270 blood samples received for culture were included. Blood cultures were processed using the BacT/Alert® automated system, followed by organism identification using standard microbiological methods. Quantitative CRP estimation was performed using a fluorescence immunoassay. CRP values >10 mg/L were considered positive. The association between blood culture results and CRP levels was analyzed using the Chi-square test.

Results

Blood culture positivity was observed in 41 (15.2%) samples, while CRP was elevated in 88 (32.7%). Concordant positivity of blood culture and CRP was seen in 34 (12.6%) cases, and concordant negativity in 175 (65.1%). Discordant results included culture-negative/CRP-positive cases in 54 (19.7%) and culture-positive/CRP-negative cases in seven (2.6%). Higher CRP values (>100 mg/L) were more frequently associated with culture-positive cases, particularly with Gram-negative organisms. A statistically significant association was observed between elevated CRP levels and blood culture positivity ($\chi^2 = 53.883$, $p < 0.001$).

Interpretation & conclusions

Elevated CRP levels showed a significant association with blood culture positivity. Although CRP is non-specific, it serves as a useful adjunct marker for the early assessment of suspected bloodstream infections while awaiting culture results.

KEYWORDS: Blood culture; Bacteremia; C-reactive protein; Inflammation; Microorganisms; Sepsis

How to Cite: Nzanroni Khuvung, Dr. Supriya Mahajan*, Dr. Ayesha Nazar, Dr. Dalip K Kakru, Akanksha Gussain, (2026) ASSOCIATION OF POSITIVE AND NEGATIVE BLOOD CULTURE WITH C-REACTIVE PROTEIN, European Journal of Clinical Pharmacy, Vol.8, No.1, pp. 131-137

INTRODUCTION

Bloodstream infections remain a major cause of morbidity and mortality worldwide and are frequently encountered in hospitalized patients, particularly those in intensive care units [1,2]. Isolation of microorganisms from blood through culture is considered the gold standard for diagnosis of bacteremia and fungemia, as it enables pathogen identification and antimicrobial susceptibility testing [1,2]. However, blood culture is a time-consuming procedure, and its diagnostic yield may be compromised by prior antibiotic therapy, inadequate sample volume, or the presence of fastidious organisms[1-3]. Additionally, contamination of blood cultures by skin commensals further complicates interpretation and may lead to unnecessary antimicrobial use and prolonged hospital stay.

C-reactive protein (CRP) is a widely used acute-phase reactant synthesized by hepatocytes in response to pro-inflammatory cytokines such as interleukin-6. Serum CRP levels rise rapidly within 24–48 hours of significant inflammation and infection, making it a useful marker for early detection and monitoring of infectious processes. Quantitative estimation of CRP is rapid, does not require sterile sampling, and is relatively inexpensive, which makes it particularly useful in resource-limited settings. However, CRP is a non-specific marker and may also be elevated in non-infectious inflammatory conditions, trauma, malignancy, or autoimmune diseases[4].

Several studies have evaluated the diagnostic utility of CRP in suspected infections, with variable results regarding its correlation with blood culture positivity. While markedly elevated CRP levels have been associated with severe bacterial infections, low or moderately elevated values may be seen in localized infections, early disease, or infections caused by low-virulence organisms. Conversely, elevated CRP in the absence of bacteremia may reflect localized infections or non-bacterial inflammatory conditions[4-6]. Therefore, interpretation of CRP values in isolation may be misleading.

In this context, evaluating the association between blood culture results and quantitative CRP levels may help improve early clinical decision-making. The present study was undertaken to assess the relationship between blood culture positivity and CRP levels in patients with clinically suspected bloodstream infections in a tertiary care hospital setting.

MATERIALS AND METHODS

Study design and setting

This cross-sectional study was conducted over a period of 12 months in the Department of Microbiology. The study included 270 blood samples received for blood culture from patients with clinical suspicion of bloodstream infection, comprising both inpatients and outpatients. Ethical approval was obtained from the Institutional Ethics Committee, and the study was conducted in accordance with ethical principles for research involving human participants.

Blood culture processing

Blood culture samples were processed using the BacT/Alert® automated blood culture system (bioMérieux, France). All bottles flagged positive by the system within five days of incubation were subjected to direct Gram staining and subcultured on blood agar, MacConkey agar, and chocolate agar plates. Identification of isolates was performed using standard microbiological and biochemical methods. Cultures that did not show growth after five days of incubation were reported as negative.

C-reactive protein estimation

Quantitative estimation of C-reactive protein was performed using a fluorescence immunoassay (ichroma™ CRP; Boditech Med Inc., Republic of Korea) on serum samples. CRP levels were expressed in mg/L. A CRP value of >10 mg/L was considered positive, and exact quantitative values were recorded for analysis.

Data collection and statistical analysis

Blood culture results were correlated with corresponding quantitative CRP values. Data were entered into Microsoft Excel and analyzed statistically. The association between blood culture positivity and CRP elevation was assessed using the Chi-square test. A p value <0.05 was considered statistically significant.

RESULTS

A total of 270 blood samples were analyzed during the study period. Of these, 156 (58%) were from males and 114 (42%) from females, with a male-to-female ratio of 1.4:1. The median age of the study population was 10 years, and the majority of samples (82.5%) were from patients aged 0–20 years. Most samples were obtained from inpatients (98.1%), reflecting a predominance of hospitalized cases (Table 1).

Table 1: Demographic profile of study population

Parameter	Number (%)
Total Samples	270
Sex Distribution	
• Males	156 (58%)
• Females	114 (42%)
Male : Female Ratio (M:F)	1.4 : 1
Median Age (in years)	10
Patient Type	
• OPD	5 (1.86%)
• IPD	265 (98.14%)

Blood Culture Results	
• Positive	41 (15.2%)
• Negative	229 (84.8%)
CRP Results	
• Positive	88 (32.7%)
• Negative	182 (68.1%)
Correlation Between Blood Culture and CRP	
• Both Culture and CRP Positive	34 (12.6%)
• Culture Positive and CRP Negative	7 (2.6%)
• Culture Negative and CRP Positive	54(19.7%)
• Both Culture and CRP Negative	175 (65.1%)

Blood culture positivity was observed in 41 (15.2%) samples, while 229 (84.8%) samples were culture negative. Elevated CRP levels (>10 mg/L) were detected in 88 (32.7%) cases. Concordant positivity of blood culture and CRP was noted in 34 (12.6%) cases, while concordant negativity was seen in 175 (65.1%). Discordant results included culture-negative/CRP-positive cases in 54 (19.7%) samples and culture-positive/CRP-negative cases in seven (2.6%) samples.

Age-wise analysis showed that most concordant positive and negative results occurred in the 0–20-year age group, consistent with the overall pediatric predominance of the study population. Discordant patterns were also mainly observed in this age group, with minimal representation from older age categories.

Ward-wise distribution revealed that the majority of samples were received from the Neonatal Intensive Care Unit (34.9%) and Pediatric wards (32.0%). Concordant positive cases were predominantly seen in NICU and pediatric units, followed by General Medicine and MICU. Culture-negative/CRP-positive cases were also largely contributed by pediatric and intensive care units(Table 2).

Table 2: Correlation of Blood Culture results with CRP results of different departments

Sl.no	Department	No. Of sample	Blood culture positive + CRP Positive [n(%)]	Blood Culture Negative + CRP Negative [n(%)]	Blood Culture Negative + CRP Positive [n(%)]	Blood Culture Positive + CRP Negative [n(%)]
A	NICU	94(34.94)	8(2.97)	80(29.62)	2(0.74)	4(1.48)
B	MICU	12(4.46)	3(1.11)	5(1.85)	4(1.48)	0(0)
C	SICU	2(0.74)	0(0)	20.74)	0(0)	0(0)
D	PICU	21(7.8)	2(0.74)	11(4.07)	8(2.97)	0(0)
E	EMERGENCY ICU	2(0.74)	0(0)	2(0.74)	0(0)	0(0)
F	DERMATOLOGY	1(0.37)	1(0.37)	0(0)	0(0)	0(0)
G	ENT	1(0.37)	1(0.37)	0(0)	0(0)	0(0)
H	GM	33(12.27)	10(3.70)	10(3.70)	13(4.81)	0(0)
I	GS	1(0.37)	1(0.37)	0(0)	0(0)	0(0)
J	OBS AND GYNAE	12(4.46)	0(0)	12(4.46)	0(0)	0(0)
K	ORTHO	2(0.74)	0(0)	1(0.37)	1(0.37)	0(0)
L	PAED	87(31.97)	7(2.59)	52(19.25)	25(9.25)	3(1.11)
M	RM	2(0.74)	1(0.37)	0(0)	1(0.37)	0(0)
	TOTAL NO.	270	34 (12.6)	175(64.7)	54(19.7)	7 (2.6)

A: Neonatal Intensive Care Unit, **B**: Medical Intensive Care Unit, **C**: Surgical Intensive Care Unit, **D**: Pediatric Intensive Care Unit, **E**: Emergency Intensive Care Unit, **G**: Ear Nose and Throat, **H**: General Medicine, **I**: General Surgery, **J**: Obstetrics and Gynaecology, **K**: Orthopedics, **L**: Pediatric, **M**: Respiratory Medicine

Among CRP-positive samples, most values were within the 10–50 mg/L range (48.8%), followed by levels >100 mg/L (32.6%) and 51–100 mg/L (18.6%). Blood culture positivity increased with higher CRP levels, with the highest proportion of culture-positive cases observed in patients with CRP values >100 mg/L(Table 3).

Table 3: Distribution according to CRP Quantitative value in Blood Culture Positives and Negatives

CRP Level Range (mg/L)	No of CRP Samples[n(%)]	No. of Blood Culture Positive[n(%)]	No. of Blood Culture Negative[n(%)]
10-50	44(48.8)	14(15.90)	30(33.72)
51-100	16(18.6)	7(8.13)	9(10.46)
>100	28(32.55)	13(14.77)	15(17.44)
Total(n)	88(100)	34(38.37)	54(61.62)

A total of 41 isolates were recovered from blood culture–positive samples. Gram-negative bacilli constituted the majority of isolates, followed by Gram-positive cocci and yeasts(Figure 1). The most common organism isolated was *Staphylococcus epidermidis* (26.8%), followed by *Escherichia coli* (12.2%), *Salmonella Typhi* (12.2%), and *Klebsiella pneumoniae* (9.8%). Higher mean CRP levels were associated with Gram-negative organisms such as *E. coli* and *Klebsiella pneumoniae*, whereas comparatively lower CRP values were observed with coagulase-negative staphylococci and *Candida* species (Table 4).

Figure 1: Distribution of blood culture isolates in the total study population.

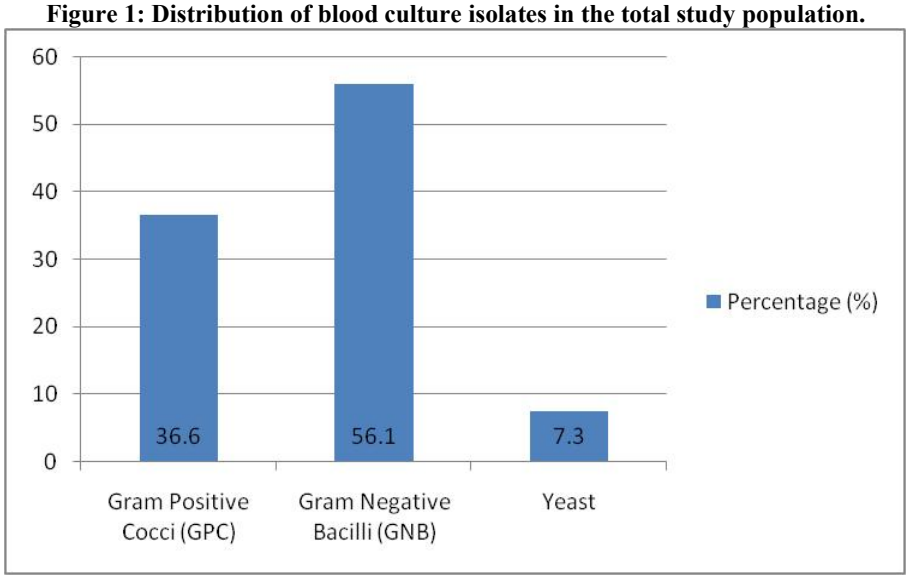

Table 4: Overall isolates from Positive Blood Culture

Isolates	Blood Culture Positive[n(%)]	Total CRP Positive[n(%)]	Mean value of CRP(mg/L)
Escherichia coli	5(12.20)	5 (12.20)	214.6
Klebsiella penumoniae	4(9.76)	4 (9.76)	206.87
Klebsiella oxytoca	1(2.44)	1 (2.44)	19.5
Acinetobacter spp	1(2.44)	1 (2.44)	98.85
Salmonella Typhi	5(12.2)	5 (12.2)	175.89
Salomenella paratyphi A	2(4.88)	2 (4.88)	93.23
Citrobacte rkoserii	1(2.44)	0	-
Proteus mirabilis	2(4.88)	2 (4.88)	45.60
Pseudomonas spp	2(4.88)	2 (4.88)	75.8
MRSA	1(2.44)	1 (2.44)	190.63
MSSA	2(4.88)	1 (2.44)	13.07
Enterococcus spp	1(2.44)	1 (1.22)	20.08
Staphylococcus epidermidis	11(26.83)	7 (17.07)	63.68
Candida spp	3(7.32)	2 (4.88)	11.6

Statistical analysis demonstrated a significant association between elevated CRP levels and blood culture positivity (Pearson's $\chi^2 = 53.883$; $p < 0.001$), indicating a strong correlation between CRP elevation and the presence of bloodstream infection.

DISCUSSION

In this study, 270 blood samples were analyzed to assess the correlation between blood culture results and CRP levels in patients with clinically suspected sepsis. Of these, 156 (58%) were males and 114 (42%) females, showing a slight male predominance (1.38:1), similar to findings by Hassan H et al., [7] and Rani R et al., [8]. The median age was 10 years, with most samples from pediatric and neonatal ICUs, which aligns with observations by Rani et al. [8] and Agarwal A et al.[9] who reported a higher incidence of bloodstream infections among neonates and pediatric patients, attributed to their immature immune systems and the frequent need for invasive interventions in critical care settings.

Blood culture positivity was observed in 41 (15.2%) cases. The relatively low yield may be due to prior antibiotic use, low sample volume, or fastidious organisms that do not grow in routine media[10]. CRP was positive in 88 (32.7%) cases, highlighting its role as an acute-phase reactant produced by hepatocytes in response to inflammation [11].

In this study, the two extreme CRP ranges, markedly elevated values (>100 mg/L) and very low values (<20 mg/L) showed notable associations with blood culture outcomes. Higher CRP range (>100 mg/L), were predominantly associated with clinically significant bacterial pathogens i.e. *Klebsiella spp*., *Escherichia coli*, and *Staphylococcus aureus*. These organisms are known to trigger strong systemic inflammation, which explains their clustering in the markedly elevated CRP category[12]. At the lower end of the spectrum, isolates such as *Staphylococcus epidermidis*and Candida spp. were linked with mean CRP values of 20.1 mg/L and 11.6 mg/L, respectively. Similar findings were reported by Colakoğlu et al.,[13]and Wang et al.,[14], who demonstrated significantlylower CRP responses in fungal and low-virulence bacterial infections compared to severe bacterial sepsis.

Quantitatively, CRP levels above 100 mg/L were strongly associated with culture positivity—46.4% of patients in this category were blood-culture positive. Similar observations were made by Ali AA et al., [15]and Monga N et al.,[16]who found CRP >50 mg/L to be a good predictor of bloodstream infections. Although CRP is non-specific, it is a sensitive marker of early bacterial infection and sepsis.

Most culture-positive isolates in this study were Gram-negative bacilli (56.1%), followed by Gram-positive cocci (36.6%) and yeasts (7.3%), a pattern similar to that seen in studies byLai et al.,[17] and Rani et al. [8]. The most frequent organisms were *Staphylococcus epidermidis* (26.8%), *E. coli* (12.2%), *Salmonella Typhi* (12.2%), and *Klebsiella pneumoniae* (9.8%). In this study, *Staphylococcus epidermidis* was considered as significant only when two consecutive blood cultures showed positivity. The predominance of *Staphylococcus epidermidis*, especially from NICU samples, may represent genuine infections in immunocompromised patients[18].

A few cases in this study were blood culture positive but CRP negative. Possible explanations may include early sampling before CRP had risen to detectable levels where CRP typically increases 6–8 hours after infection onset[11], localized or low-grade bacteremia with limited systemic inflammatory response as Immunocompromised patients or those with hepatic dysfunction may have impaired CRP synthesis [18].Technical factors, such as delayed processing or inadequate serum storage or faulty kit may also influence CRP results. Similar discordance wasbeen noted by Apurva AD et al., [12]where 39.8% neonates showed discordant CRP and blood culture results likely due to early infection or delayed CRP response.This underscores that CRP alone is not a definitive diagnostic tool and should be interpreted alongside blood culture results.

A considerable number of cases showed elevated CRP despite negative blood culture. The possible reasons may include prior antibiotic therapy, which can sterilize blood cultures but not suppress the inflammatory response[19][20]andlocalized infections likepneumonia, meningitis, urinary tract infections that produce systemic inflammation without bacteremia. Non-bacterial causes such as viral infections, autoimmune diseases, trauma, or post-surgical inflammation can also elevate CRP nonspecifically [21]. Another reason could be the presence of fastidious or anaerobic organisms that are not detected in routine culture conditions. Studies byAhmed et al.[22] and Husain et al.[23] also reported similar findings, with 15–25% of patients showing CRP positivity despite sterile cultures, emphasizing that CRP alone cannot distinguish bacterial from non-bacterial inflammation.

Importantly, statistical analysis in the present study demonstrated a significant association between CRP elevation and blood culture positivity (Pearson's Chi-square = 53.883, df = 1, $p < 0.001$). This indicates that higher CRP levels were strongly correlated with bloodstream infections, supporting the clinical utility of CRP as an early marker of bacteremia. However, despite this significant association, CRP should serve as an adjunct rather than a standalone diagnostic tool. Its interpretation must always be integrated with clinical findings and microbiological investigations.

Overall, this study demonstrates a significant positive correlation between blood culture positivity and CRP elevation($p < 0.001$). Although CRP is not specific, it is a valuable indicator for early detection and monitoring of bloodstream infections—especially in settings where culture results are delayed. When used together, blood culture and CRP measurement enhance diagnostic accuracy and support rational antibiotic use.

Limitations

This study was limited by its single-center design and the absence of serial CRP measurements, which may have provided additional insight into disease progression and treatment response. Molecular diagnostic techniques were not employed, which could have improved detection of fastidious organisms.

Conclusion

This study demonstrates a significant association between elevated C-reactive protein levels and blood culture positivity in patients with suspected bloodstream infections. Although CRP is a non-specific marker, higher CRP values—particularly above 100 mg/L—were more frequently associated with culture-proven bacteremia, especially due to Gram-negative organisms. CRP estimation, when used alongside blood culture results and clinical findings, serves as a valuable adjunct for early assessment and management of suspected bloodstream infections.

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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