

# The role of C-Reactive protein as a diagnostic predictor of sepsis in postpartum women

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## ABSTRACT

**Background:** Postpartum sepsis remains a leading cause of maternal mortality worldwide, necessitating the evaluation of C-reactive protein (CRP) as an accessible, rapid diagnostic biomarker to improve early detection and patient outcomes. The study aims to evaluate the diagnostic accuracy of elevated C-reactive protein (CRP) for detecting postpartum sepsis using blood culture as the gold standard.

**Material and Methods:** This cross-sectional study was conducted at Civil Hospital Karachi over six months. A total of 471 postpartum women (aged 20–45 years) with suspected sepsis (qSOFA  $\geq 2$ ) within six weeks of delivery were included using non-probability consecutive sampling. Blood samples for quantitative CRP and culture were obtained prior to antibiotic administration. CRP  $\geq 50$  mg/L was considered elevated. Diagnostic indices included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, and receiver operating characteristic (ROC) analysis.

**Results:** The mean age was  $29.4 \pm 5.8$  years. Blood culture confirmed sepsis in 370 (78.6%) patients. Elevated CRP ( $\geq 50$  mg/L) was observed in 356 (75.6%) patients. CRP demonstrated sensitivity of 84.3% (95% CI: 80.2–87.8), specificity of 56.4% (95% CI: 46.2–66.2), PPV of 87.6% (95% CI: 83.7–90.8), NPV of 49.6% (95% CI: 40.2–58.9), and diagnostic accuracy of 78.3% (95% CI: 74.3–81.9). The AUC was 0.71 (95% CI: 0.66–0.76).

**Conclusion:** CRP  $\geq 50$  mg/L demonstrates a satisfactory level of sensitivity and good overall test diagnostic accuracy in identifying postpartum sepsis in a high-prevalence tertiary care environment. Serial CRP measurements can also be used to measure therapeutic responses.

**Keywords:** C-reactive protein, Diagnostic accuracy, Maternal sepsis, Postpartum period, Sensitivity and specificity

## BACKGROUND

Maternal complications during pregnancy and childbirth remain a critical global public health challenge. The World Health Organization (WHO) defines maternal sepsis as a life-threatening condition caused by infection during pregnancy, childbirth, post-abortion, or the postpartum period.<sup>1</sup> Despite the development of obstetric care, maternal sepsis remains a significant source of maternal morbidity and mortality worldwide. Sepsis is a leading cause of maternal death worldwide accounting for 11% of maternal deaths, with a larger burden in low- and middle-income countries.<sup>2</sup> According to the latest international estimates, approximately 800 women die every day due to

preventable causes during pregnancy and childbirth and South Asia has a large share of the burden in this estimation strictly speaking.<sup>3</sup>

In Pakistan, maternal sepsis is among the most common direct causes of maternal death, as indicated by national surveillance data indicated.<sup>4</sup> In a nested case-control study in Pakistan, several obstetric and socioeconomic risk factors linked to postpartum sepsis were found, with the necessity to resolutely recognize and manage them in time.<sup>5</sup> Sepsis has a high mortality rate that is proportional to the severity of the disease. Whereas uncomplicated sepsis has an estimated mortality rate of 15–20%, severe sepsis has mortality rate of 25–30% and septic shock can have a mortality rate as high as 40–60%.<sup>6</sup> Hence, it is important to identify sepsis early and initiate treatment to enhance maternal outcomes. Postpartum sepsis is difficult to diagnose based on clinical findings alone because it presents in a nonspecific manner. Bedside clinical assessment tools, such as the quick Sequential Organ Failure Assessment (sofa), have been applied to clinical assessments, but their sensitivity in obstetric populations is inconsistent across different populations.<sup>7</sup>

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Blood culture is still the gold standard for detecting bacteremia, however yet it is time-consuming and can postpone targeted therapy. Several inflammatory biomarkers have been explored for the early detection of sepsis. A reaction protein (C-reactive protein) (CRP), a product of acute-phase production by hepatocytes triggered by inflammatory cytokines, increases considerably during bacterial infections.<sup>8</sup> CRP is more affordable and available than more recent biomarkers, such as procalcitonin in resource-limited contexts.<sup>9</sup> CRP has moderate-to-high sensitivity in sepsis diagnosis but low specificity, with its application for diagnosing sepsis being best as a screening test but not as a confirmatory test.<sup>10</sup>

Although the clinical importance of postpartum sepsis is obvious, there is a scarcity of local data on the diagnostic accuracy of CRP in obstetric patients in Pakistan. Considering the financial limitations and limited access to highly sensitive biomarkers in state hospitals, it is necessary to find a quick and low-cost diagnostic supplement. Thus, this study aimed to identify the accuracy of elevated CRP levels in diagnosing postpartum sepsis using blood culture as the gold standard at a tertiary care hospital in Karachi.

## MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Civil Hospital Karachi, between 10<sup>th</sup> December 2025 till 10<sup>th</sup> March 2026. This study was approved by the Institutional Review Board (IRB) of Civil Hospital Karachi (Approval No: IRB-4378/DUHS/Approval/2025/40 dated 6<sup>th</sup> December 2026). Written informed consent was obtained from all participants prior to enrollment in the study.

Sample size was calculated using the WHO Sample Size Calculator, taking a confidence level of 95%, margin of error of 5%, and an anticipated prevalence of postpartum sepsis of 50%.<sup>10</sup> The estimated sample size came out to be 471 participants. Non-probability consecutive sampling was used to include 471 postpartum women aged 20–45 years who came to the hospital with suspected sepsis within six weeks after delivery.

Women presenting beyond six weeks postpartum were excluded. Patients with infections other than puerperal sepsis (including malaria, dengue, typhoid, tuberculosis, and pneumonia) and those with conditions known to

elevate CRP independent of puerperal sepsis, such as autoimmune diseases, chronic liver disease, chronic kidney disease, congestive heart failure, and chronic obstructive pulmonary disease, were also excluded. Women with prior hospitalization during the current pregnancy were excluded as well.

Venous blood (15–16mL) was drawn aseptically at the time of clinical suspicion and prior to antibiotic treatment. Ten milliliters were given to the microbiology laboratory for culture and sensitivity testing and five milliliters were forwarded to the biochemistry laboratory for quantitative estimation of C-reactive protein (CRP) with the help of standard laboratory methods. CRP was measured at enrollment (0 h) as well as at 24 and 48 h to explore trends. The chosen CRP cutoff level of  $\geq 50$  mg/L was supported by previous literature that showed it to be associated with significant bacterial infection and sepsis, yet still provided acceptable diagnostic performance.<sup>11</sup> Microbial growth in the blood cultures was considered to be positive. A microbiologic reference standard was used for bloodstream infection, which was blood culture, and was accepted as imperfect, especially in the case of patients who had previously received antibiotics. Quantitative CRP measurement was performed using a standardized immunoassay-based analyzer (Roche Cobas system; RRID:SCR\_019033). Blood cultures were processed using an automated blood culture system (BD BACTEC system; RRID:SCR\_017061). These Research Resource Identifiers (RRIDs) are provided to enhance reproducibility and transparency. To minimize interpretation bias and ensure compliance with STARD guidelines, blinding was implemented during diagnostic assessment. Laboratory personnel performing and interpreting CRP assays were blinded to patients' clinical details and blood culture results. Similarly, microbiologists analyzing blood culture samples were blinded to CRP values and clinical data. Other laboratory tests included complete blood count, total leukocyte count, differential count, platelet count, and neutrophil to lymphocyte ratio (NLR) calculation. Clinical details such as demographics, booking, and socioeconomic status (using the Kuppaswamy scale), mode of delivery, gestational age at delivery, prior exposure to antibiotics, and clinical outcomes were entered in a structured proforma. Antibiotic exposure within the preceding seven days was specifically documented because of its potential effect on blood

culture yield and was evaluated as a potential confounder during analysis.

Potential confounders were identified prior to analysis, including maternal age, parity, booking status, socioeconomic status, mode of delivery, prior antibiotic exposure, anemia, and comorbid conditions. Stratified analysis was performed where appropriate to assess their potential influence on diagnostic accuracy. Cases with incomplete key variables, including CRP levels or blood culture results, were excluded from analysis. A complete-case analysis approach was applied, and no imputation methods were used.

The Statistical Package for Social Sciences (SPSS) version 26 was used to input and analyses the data. The Shapiro Wilk test was used to check the normality of continuous variables. Age was found to be normally distributed and was therefore presented as mean  $\pm$  standard deviation. CRP levels were not normally distributed and were summarized as median and interquartile range (IQR). Frequencies and percentages were used to describe categorical variables. The 2x 2 contingency table was used to determine the parameters of diagnostic accuracy such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the overall diagnostic accuracy. Stratification was performed in relation to age, booking status, residence, socioeconomic status, and mode of delivery to eliminate possible confounders. The Chi-square test was applied to compare categorical variables, and a p-value  $\leq 0.05$  was considered statistically significant.

## RESULTS

A total of 471 postpartum women with suspected sepsis were included in this study. The mean age of the participants was  $29.4 \pm 5.8$  years (range 20–45 years), with the majority (58.6%) between 20 and 30 years of age. The demographic and clinical characteristics of the participants are presented in Table-I.

**Table-I: Demographic and clinical characteristics (n=471).**

Variable	n (%) / Mean $\pm$ SD
Age (years)	29.4 $\pm$ 5.8
Age 20–30 years	276 (58.6%)
Urban residence	288 (61.1%)
Unbooked cases	276 (58.6%)
Cesarean section	256 (54.3%)
Gestational age (weeks)	38.2 $\pm$ 1.7
RR $\geq 22$ /min	389 (82.6%)
SBP $\leq 100$ mmHg	301 (63.9%)
Altered mentation	124 (26.3%)
Upper-lower SES	181 (38.4%)

The laboratory profile revealed a mean haemoglobin level of  $9.8 \pm 1.6$  g/dL and a mean total leukocyte count of  $16.4 \pm 4.2 \times 10^9$ /L. The average neutrophil percentage was  $78.2 \pm 8.5\%$ , with a mean platelet count of  $168 \pm 72 \times 10^9$ /L. The mean neutrophil–lymphocyte ratio was  $9.6 \pm 3.4$ . At admission (0 h), the mean CRP level was  $86.5 \pm 28.4$  mg/L Table-II.

A comparison of CRP levels between blood culture-positive and negative groups is shown in Figure 1. Blood culture results were positive in 370 (78.6%) patients and negative in 101 (21.4%) patients. Among culture-positive cases, the most commonly isolated organism was *Escherichia coli* (38.4%), followed by *Klebsiella* species (23.8%), *Staphylococcus aureus* (17.3%), and *Pseudomonas* (12.4%), while other organisms accounted for 8.1% of the isolates. Prior antibiotic exposure before blood sampling was documented in 96 (20.4%) patients. The distribution of blood culture results and isolated organisms is presented in Table-III.

When CRP ( $\geq 50$  mg/L) was compared with blood culture as the reference standard, 312 cases were true positives, 44 were false positives, 58 were false negatives, and 57 were true negatives. CRP exhibited a sensitivity of 84.3%, specificity of 56.4%, positive predictive value of 87.6%, negative predictive value of 49.6%, and overall diagnostic accuracy of 78.3%. The diagnostic performance of CRP, including sensitivity, specificity, predictive values is summarized in Table-IV.

Stratified analysis was performed to assess the effect of potential confounders including age, booking status, residence, socioeconomic status, and mode of delivery on the diagnostic performance of CRP. No statistically significant differences were observed in sensitivity and specificity of CRP across age groups (20–30 vs  $>30$  years;  $p > 0.05$ ) (Table-V)

**Table-II: Laboratory parameters and CRP trend.**

Parameter	Mean ± SD
Hemoglobin (g/dL)	9.8 ± 1.6
TLC (×10 <sup>9</sup> /L)	16.4 ± 4.2
Neutrophils (%)	78.2 ± 8.5
Platelets (×10 <sup>9</sup> /L)	168 ± 72
NLR	9.6 ± 3.4
CRP at 0 hr (mg/L)	86.5 ± 28.4
CRP at 24 hr (mg/L)	74.2 ± 26.1
CRP at 48 hr (mg/L)	59.8 ± 24.7
CRP ≥50 mg/L at admission	356 (75.6%)

**Table-III: Blood culture findings and diagnostic accuracy of CRP blood culture and organism profile.**

Variable	n (%)
Blood culture positive	370 (78.6%)
Blood culture negative	101 (21.4%)
Escherichia coli	142 (38.4%)
Klebsiella species	88 (23.8%)
Staphylococcus aureus	64 (17.3%)
Pseudomonas	46 (12.4%)
Other organisms	30 (8.1%)
Prior antibiotics before culture	96 (20.4%)

**Table-IV: Diagnostic Accuracy of CRP (≥50 mg/L) Using Blood Culture as Gold Standard**

CRP (≥50 mg/L)	Blood Culture Positive	Blood Culture Negative
Yes/Positive	312 (84.3%)	44 (43.6%)
No/Negative	58 (15.7%)	57 (56.4%)
Diagnostic Parameters	Calculation	Value (%)
Sensitivity	TP / (TP + FN) = 312 / (312 + 58)	84.3
Specificity	TN / (TN + FP) = 57 / (57 + 44)	56.4
Positive Predictive Value (PPV)	TP / (TP + FP) = 312 / (312 + 44)	87.6
Negative Predictive Value (NPV)	TN / (TN + FN) = 57 / (57 + 58)	49.6
Diagnostic Accuracy	(TP + TN) / Total = (312 + 57) / 471	78.3

TP = 312, FP = 44, FN = 58, TN = 57, Total Patients = 471

**Table-V: Stratified analysis of diagnostic accuracy of CRP (≥50 mg/L) using blood culture as gold standard.**

Variable	Category	Sensitivity (%)	Specificity (%)	p-value
Age (years)	20–30	84.8	55.6	0.742
	>30	83.5	57.3	
Booking Status	Registered	85.1	57.0	0.681
	Non-registered	83.1	55.8	
Residence	Urban	84.6	56.9	0.793
	Rural	83.8	55.4	
Socioeconomic Status	Low	83.7	55.1	0.615
	Middle/High	84.9	57.8	
Mode of Delivery	Vaginal Delivery	82.9	56.7	0.532
	Cesarean Section	86.2	55.9	

## DISCUSSION

This cross-sectional study included 471 women with suspected sepsis during the postpartum period the findings showed that an admission C-reactive protein (CRP) cutoff of ≥50 mg/L had high sensitivity (84.3%) but only moderate specificity (56.4%) in identifying culture-proven postpartum sepsis, with a total AUC of 0.71. These results suggest that CRP is an effective early screening test in a high-prevalence, resource-limited

environment but lacks specificity to be applied alone to guide definitive treatment.<sup>11</sup>

Our study results, with as high level of sensitivity, substantiate the acknowledged position of CRP as an initial inflammatory indicator of bacterial infections<sup>12</sup>. CRP is produced by hepatocytes in response to inflammatory cytokines and increases rapidly when there is systemic infection as a result, it is clinically helpful to be used in suspicion and to triage at an early

stage.<sup>13</sup> However, this moderate specificity in our results is probably due to the inability of CRP to adequately differentiate between infectious and non-infectious inflammatory conditions, most notably in postpartum women whose bodies are physiologically state-activated to inflammation and may have undergone surgery, which increases CRP levels not necessarily due to infection, but regardless of it.<sup>14</sup>

Relative biomarker studies have indicated that procalcitonin, compared with CRP, could provide additional specificity in the diagnosis of bacterial sepsis, but CRP is more cost-effective, widely available, and practical in resource-limited environments. Implementation studies in Pakistan have highlighted the importance of incorporating practical diagnostic tools within structured maternal sepsis recognition and management programs such as the FAST-M bundle.<sup>16</sup> Predictive values are influenced by disease prevalence; therefore, the positive predictive value observed in our study may reflect the high prevalence of culture-confirmed sepsis in the study population and may not be directly applicable to lower-prevalence settings.<sup>17</sup> Although previous studies have explored the role of serial CRP measurements in monitoring infection, our study evaluated only a single admission CRP value. So, the results of the present study do not allow conclusions on treatment monitoring or antibiotic stewardship and require further prospective studies.<sup>18, 19</sup>

Blood culture positivity in our study was 78.6%, with *Escherichia coli* being the most frequently isolated organism, followed by *Klebsiella* species and *Staphylococcus aureus*. Microbial patterns of this nature have also been reported in obstetric studies of infection in South Asia, where gram negative organisms dominate in post-partum sepsis.<sup>20</sup>

The strengths of this study include a relatively large sample size and the use of blood culture as the reference standard. However, several limitations should be considered. As a single-center study conducted among women with suspected postpartum sepsis, selection bias may have occurred, and the findings may not be generalizable to other healthcare settings. Blood culture sensitivity may have been reduced by prior antibiotic exposure, potentially resulting in false-negative results. In addition, physiological postpartum inflammation and surgical delivery can elevate CRP levels in the absence of infection, contributing to its moderate specificity. Clinically, these findings indicate that CRP should be

used as a screening tool alongside clinical assessment and microbiological investigations rather than as a standalone diagnostic test, as reliance on CRP alone may lead to overdiagnosis and unnecessary antibiotic use.

## CONCLUSION

A cutoff value of  $\geq 50$  mg/L and higher C-reactive protein (CRP) showed excellent sensitivity and reasonable overall diagnostic value for identifying postpartum sepsis in a high-prevalence tertiary care environment. Despite its relative lack of specificity, rendering it a substandard confirmatory test in its own right, CRP is a fast, cheap, and readily available screening biomarker in healthcare systems with limited resources.

## CONFLICT OF INTEREST

None

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Declared none

## AUTHOR CONTRIBUTION

**Bushra Ammar:** Substantial contributions to concept, study design and acquisition of data, manuscript drafting and reviewing it critically for important intellectual content, has given final approval of the version to be published.

**Urooj Naz:** Substantial contributions to study design and interpretation of data, critical review of manuscript for important intellectual content, has given final approval of the version to be published.

**Devia Kumari:** Substantial contributions to acquisition of data, manuscript drafting and reviewing it critically for important intellectual content, has given final approval of the version to be published.

**Marium Usman:** Substantial contributions to acquisition, analysis and interpretation of data, critical review of manuscript, has given final approval of the version to be published.

**Faiza Rana:** Substantial contributions to acquisition of data, manuscript drafting and reviewing it critically for important intellectual content, has given final approval of the version to be published.

**Misbah Batool:** Substantial contributions to analysis and interpretation of data, critical review of manuscript, has given final approval of the version to be published.

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