MedPulse Spectrum
Volume 1, Issue 2 (July-December 2025)
https://jouex.com/index.php/medpulspect
p-ISSN: 3105-4226
e-ISSN: 3105-4234

Original Article

DIAGNOSTIC ACCURACY OF C-REACTIVE PROTEIN IN NEONATAL SEPSIS USING BLOOD CULTURE AS GOLD STANDARD: A CROSS-SECTIONAL STUDY

Bintul Huda✉, Rabia Munir[1], Anum Arif[2], Umar Rasool [3]
Department of Paediatrics, College of Medicine and Dentistry at the Hills, Abbottabad, KP Pakistan, [1]Bhatti International Teaching Hospital, Kasur, Punjab Pakistan, [2]Shalamar Hospital, Lahore Pakistan, [3]Ittefaq Hospital, Lahore Pakistan[3]

Background: Neonatal sepsis is a life-threatening but treatable condition if diagnosed early, though its nonspecific signs can delay detection. C-reactive protein (CRP) is a helpful marker, but its diagnostic accuracy varies. This study evaluates CRP's accuracy in diagnosing neonatal sepsis, using blood culture as the gold standard. **Methods:** This cross-sectional study was conducted at the Paediatric department of Ittifaq Hospital, Lahore, over a six-month period. A total of 150 patients were included. After fulfilling the study criteria, Informed consent from either parent, as well as a detailed history and a blood sample, were taken for CRP and blood culture tests. All data were analysed using SPSS-24. The data were stratified by age and gender to address the issue, and a chi-square test was applied with a $p \leq 0.05$ considered significant. **Result:** Among the total 150 patients, the mean age was 14.46±7.61 days, with 64 (42.7%) females, and the mean CRP was 10.97±13.23. CRP was found positive in 47 (31.33%) patients, whereas Blood culture was positive in 45 (30.00%). The sensitivity and specificity of CRP were 93.33% and 95.24% respectively, with an overall diagnostic accuracy of 94.67%. A significant association was also found between blood culture and CRP, $p<0.001$. **Conclusion:** CRP is a good diagnostic tool for diagnosing neonatal sepsis. Using this simple test, an accurate and timely diagnosis can be made, and it can help initiate early medical treatment for these high-risk cases. These findings support CRP's utility for ruling out sepsis and guiding early antibiotic discontinuation.
Kyewords: Neonatal sepsis; C-reactive protein; blood culture; diagnostic accuracy

✉**Corresponding author: Dr. Bintul Huda,** Department of Paediatrics, College of Medicine and Dentistry at the Hills, Abbottabad. KP Pakistan. **Cell:** +92-332-2336426 **Email:** drbintulhuda@gmail.com

Cite this article: Huda B, Munir R, Arif A, Rasool U. Diagnostic Accuracy of C-Reactive Protein in Neonatal Sepsis Using Blood Culture as Gold Standard: A Cross-Sectional Study. MedPluse Spectrum 2025;1(2):18-21

Submitted: 2nd September 2025 **Revised:** 10th December 2025 **Accepted:** 17th December 2025

INTRODUCTION

Neonatal sepsis is a bloodstream infection among neonates, i.e., aged <28 days, and remains a major cause of mortality and morbidity in low- and middle-income countries.[1,2] Neonates are predisposed to infections during the perinatal period due to a relatively compromised immune system. The burden of neonatal sepsis is attributed to neonatal infections, which vary by geographic region and maternal and neonatal risk factors. Worldwide, it is estimated that more than 1.3 million neonatal deaths annually are the consequence of neonatal sepsis.[3] Its incidence varies worldwide but remains between 1 and 5 in 1000 live births.[4]

There are mainly two types of neonatal sepsis: early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS remains a common and serious problem for neonates, especially preterm infants. Group B streptococcus (GBS) is the most common etiologic agent, while *Escherichia coli* is the most common cause of mortality. LOS attributable to Gram-positive organisms, including coagulase-negative *Staphylococci* and *Staphylococcus aureus*, is also associated with increased morbidity and mortality among premature infants.[1,5]

Early diagnosis of neonatal sepsis is often difficult because of the nonspecific symptoms and signs.[6] Traditional methods, such as blood culture, though it's a gold standard but its accuracy is being questioned because of spurious positive results due to contamination, negative blood cultures even sometimes in fatal cases, and the time it takes to get a result.[7] Thus, in addition to blood culture, different laboratory tests are evaluated in the diagnosis of EOS, of which complete blood count with different neutrophil parameters and C-reactive protein (CRP) are most frequently used.[8]

The diagnostic accuracy of CRP for neonatal sepsis shows significant variability across studies, influenced by cutoff values, the timing of sepsis onset,

and testing. A recent Pakistani study highlights this heterogeneity: Irshad *et al*, reported a sensitivity of 77.6% and a specificity of 73.8%, while Aslam *et al*, documented 94% sensitivity and 74% specificity at a cutoff of >10 mg/L.[9,10] Earlier work by Hisamuddin *et al,* showed lower sensitivity, i.e., 76.92% and specificity 53.8%.[11] Conversely, some studies report higher accuracy, such as Younis S *et al*, with sensitivity and specificity both 95%, though these findings are less consistent with recent literature.[12] Overall, CRP's negative predictive value (NPV) tends to be robust (81.2%-93.7%), supporting its role in ruling out sepsis, while variables' positive predictive value (PPV) limits its confirmatory utility.

It is now evident that CRP is a potential diagnostic tool for neonatal sepsis, as supported by a meta-analysis by Liu Y *et al*. However, the literature shows wide variation in reported diagnostic accuracy, creating uncertainty about CRP's true reliability in clinical practice.[13] While blood culture remains the gold standard for diagnosing neonatal sepsis, it is time-consuming, often taking 48 hours to 6 days til result, during which critical delays in treatment may worsen neonatal outcomes. Timely and accurate diagnosis remains a challenge, and given the limitations of blood culture and the variability in CRP's reported for accuracy, this study was conducted to determine the diagnostic accuracy of CRP for diagnosing neonatal sepsis, using blood culture as the gold standard.

METHODOLOGY

This cross-sectional study was conducted at the Department of Paediatrics, Ittifaq Hospital, Lahore, over a six-month period from January 1, 2023, to June 30, 2023.

After obtaining ethical approval from the institute ethical board, and through purposive sampling, a total of 150 patients were taken in this study using WHO sample size calculator, which determined that a minimum of 147 participants was required based on an expected sensitivity of 77.6%, specificity of 95%, a predicted prevalence of 50%, a desired precision of 10% and a 95% confidence interval.[9,12]

All patients of either gender, aged 0 to 28 days, who presented with suspected neonatal sepsis were included. Neonates with major congenital anomalies, e.g., heart defects, neural tube defects, Down syndrome, very low birth weight (<1000 g), or underlying surgical conditions, like intussusception, imperforate anus, were excluded based on clinical presentation and radiographic investigation.

After fulfilling the criteria, Informed consent was obtained from either parent, and a detailed history was taken, including their age, gender, and address, in a standardised form. CRP and blood cultures were obtained from all patients at admission and sent to the laboratory free of charge. After all aseptic measures, 2 cc of blood was taken and inoculated into a blood culture bottle containing brain heart infusion (BHI). For CRP estimation, blood was taken using a 3 cc syringe. CRP was performed by latex agglutination assay in Ittefaq hospital laboratory, and a value more than 6 mg/L was considered as raised or positive. Diagnosis of neonatal sepsis on culture was based on the presence of bacteria or fungi; cultures with>105 colonies/HPF were labelled positive for neonatal sepsis. Blood culture (positive/negative) and CRP (raised/not raised) were also noted in the same form by the researcher herself.

All the data collected were entered and analysed using SPSS-24. For qualitative variables, such as patient gender, neonatal sepsis on blood culture, and CRP levels greater than 6, results were presented as frequencies and percentages. For quantitative variables such as age and CRP levels, the mean ± SD was calculated. A 2×2 table was made for CRP (>6) and blood culture (positive, negative). Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated manually for CRP using blood culture as the gold standard. The data were stratified by age and gender to address potential effect modifiers, and a post-stratified chi-square test was applied to determine significance ($p \leq 0.05$).

RESULTS

Among total 150 patients, with mean age of the patients was 14.46±7.61 days(min 1 and max 28 days), females 64 (42.7%) and males 86 (57.3%) participated, with a mean value of CRP 10.97±13.23 (min 1 and Max 70) it was found positive in 47 (31.33%) patients, whereas Blood culture was positive in 45 (30.00%), Table-1. Among the 47 (31.3%) positive CRP cases, blood culture was found to be positive in 42 (89.4%), as shown in Table-2**.** The sensitivity and specificity of CRP were 93.33% and 95.24% respectively. The positive and negative predictive values were 89.36% and 97.09%, respectively, with an overall diagnostic accuracy of 94.67% Table-3. When data was stratified for age group and Gender significant association between blood culture and CRP was found, $p<0.001$, Table-4.

Table-1: Descriptive statistics of sample n=150

Variable		n (%)
Age	**14.46±7.613 (1–28)**	
CRP Value	**10.97±13.259 (1–70)**	
Gender	**Female**	64 (42.7)
	Male	86 (57.3)
Age group	**0–14 days**	86 (57.33%)
	15–28 days	64 (42.67%)
Blood culture	**Negative**	105 (70%)
	Positive	45 (30%)
CRP value	**Negative**	103 (68.7%)
	Positive	47 (31.3)

Table-2: Comparison between CRP and blood culture

Variable	Blood culture	Total

		Positive	Negative	
CRP	**Positive**	42 (93.3%)	5 (4.8%)	47(31.3%)
	Negative	3 (6.7%)	100 (95.2%)	103 (68.7%)
Total		45 (100%)	105 (100%)	150 (100%)

Table-3: Diagnostic metrics of CRP and blood culture

Matrics	Point Estimate	95% CI
Sensitivity	93.33%	(82.14, 97.71)
Specificity	95.24%	(89.33, 97.95)
Positive Predictive Value	89.36%	(77.41, 95.37)
Negative Predictive Value	97.09%	(91.78, 99)
Diagnostic Accuracy	94.67%	(89.83, 97.27)

Table-4: Comparison between CRP and age group with respect to blood culture, n=150

Variable	Blood culture		Total	*p*
	Negative	Positive		
Age-group				
1–14 days	59 (56.2%)	27 (60%)	86 (57.3%)	0.666
15–28 days	46 (43.8%)	18 (40%)	64 (42.7%)	
CRP				
Negative	100 (95.2%)	3 (6.7%)	103 (68.7%)	0.000
Positive	5 (4.8%)	42 (93.3%)	47 (31.3%)	

DISCUSSION

This cross-sectional study demonstrates exceptionally high sensitivity (93.33%) and specificity (95.24%) of CRP for diagnosing neonatal sepsis, using blood culture as the gold standard. While these results suggest CRP's utility as a diagnostic tool, they must be contextualised within existing literature and evaluated for methodological influences. Below, we analyse each key finding through comparative literary analysis.

The observed sensitivity (93.33%), specificity (95.24%), and diagnostic accuracy (94.67%) are notably high and comparable to a similar study conducted nearby, which reported a sensitivity of 97.3%, specificity of 95.2%, and a diagnostic accuracy of 96.6% for CRP. Twelve other studies reported lower values, including 77.6% sensitivity, 76.92% sensitivity, 73.8% specificity, and 53.99% specificity, as well as 75% and 70.07% diagnostic accuracy of CRP, by Irshad *et al*, and Al-Atwi SS *et al*, respectively.[9,14] Our findings exceed these benchmarks, aligning with only a few single-centre studies that reported similarly high CRP sampling (14-day mean age, likely at peak infection phase) or variability in CRP thresholds and assay methods, which meta-regression suggests may significantly influence accuracy.[15] Still, the strong diagnostic metrics support CPR's potential utility, albeit requiring validation in larger, more representative cohorts.

Our high NPV (97.09%%) suggests CRP effectively rules out sepsis, supporting antibiotic discontinuation in negative cases. This aligns with recent evidence that serial CRP measurements reduce antibiotic exposure by 7 (17%).[16] However, the PPV (89.36%%) may be inflated by variability in CPR cut-offs and assay methods, which can yield false positives in the presence of non-infectious inflammation, such as birth trauma, intraventricular hemorrhage.[17] Crucially, blood culture's limitations as a gold standard-false negative occurs in 30-70% of sepsis cases due to low bacteremia volumes—may misclassify the true sepsis cases as false negatives, artificially elevating PPV.[18]

The strong association between CRP and blood culture positivity ($p<0.005$) reinforces CRP's diagnostic relevance. Yet, the imperfect sensitivity of blood cultures necessitates cautious interpretation. Studies indicate that maternal antibiotics reduce culture sensitivity, which may explain why only 4.8% of our CRP-positive cases had blood culture-negative infants with clinical symptoms.[19] Thus, while CRP correlates with culture results, its true value may lie in identifying culture-negative sepsis.

The absence of an association between CRP accuracy and gender/age group suggests consistent performance across neonatal subgroups. This contrasts with the literature, which shows that gestational age significantly affects CRP kinetics, with preterm infants exhibiting delayed and attenuated CRP responses.[20] Our findings may reflect homogeneous sampling (mean age 14 days; term infants), missing EOS where age effects are pronounced. Future studies should stratify by onset type to clarify demographic interactions.

Although enrolling 150 neonates yields moderate precision (95% CI ±10–15%), relying on a single CPR measurement at a mean age of 14 days likely misses the early inflammatory peak, which occurs around 36–48 hours post-infection.[21] As is clearly evident, the difference in values of diagnostic accuracy of CPR measured at the time of admission and after 72 hours, reporting higher values at 72nd hours.[22] Moreover, neonatal blood cultures often fail to detect low-grade bacteremia (<4CFU/mL), leading to false negatives that inflate CPR's apparent accuracy.[23] Nevertheless, the high NPV supports CRP's use to rule out sepsis and reduce antibiotic duration—serial CRP protocol has cut treatment courses by up to 48–54% in similar cohorts.[24] To enhance confiramatroty power, future strategies should integrate CRP with early-phase markers (e.g., IL-6, procalcitonin) and standardise serial sampling at symptom onset and 24 hours later.

CONCLUSION

CRP provens high diagnostic accuracy and excellent NPV for neonatal sepsis compared to the blood culture. These findings support the utility of CRP in ruling out sepsis to guide early antibiotic discontinuation. However, the variability in CPR thresholds and assay methods, as well as a single CRP measurement, limits generalizability. Future prospective studies with serial measurements and multi-marker approaches are warranted to validate these findings. CPR remains a valuable- though not a standalone—adjunct in neonatal sepsis diagnosis.

REFERENCES

1. Raturi A, Chandran S. Neonatal sepsis: aetiology, pathophysiology, diagnostic advances and management strategies. Clin Med Insights Pediatr 2024;25;18:11795565241281337. DOI: https://doi.org/10.1177/11795565241281337
2. Celik IH, Hanna M, Canpolat FE, Mohan Pammi. Diagnosis of neonatal sepsis: the past, present and future. Pediatr Res 2022;91(2):337–50. DOI: https://doi.org/10.1038/s41390-021-01696-z
3. Fleischmann C, Reichert F, Cassini A, Horner R, Harder T, Markwart R, *et al*. Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. Arch Dis Child 2021;106(8):745–52. DOI: https://doi.org/10.1136/archdischild-2020-320217
4. Odabasi IO, Bulbul A. Neonatal Sepsis. Sisli Etfal Hastan Tip Bul 2020;54(2):142–58. DOI: https://doi.org/10.14744/SEMB.2020.00236
5. Singh M, Alsaleem M, Gray CP. Neonatal Sepsis. 2022 Sep 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
6. Kosmeri C, Giapros V, Serbis A, Baltogianni M. Application of advanced molecular methods to study early-onset neonatal sepsis. Int J Mol Sci 2024;25(4):2258. DOI: https://doi.org/10.3390/ijms25042258
7. Du LZ. Early diagnosis and management of neonatal sepsis: a perspective. World J Pediatr 2024:20: 303–6. DOI: https://doi.org/10.1007/s12519-024-00803-4
8. Ahmed KA, Khan MA, Naqvi SZ, Mughal IA, Zia MS, Idrees A. Combining complete blood count with differential count, C-reactive protein, and band neutrophils in the diagnosis of early-onset neonatal sepsis. Pak J Med Health Sci 2022;16(9):168–9. DOI: https://doi.org/10.53350/pjmhs22169168
9. Irshad M, Hayat M, Parvez H, Ihsan Ullah, Zia ur Rehman. Neonatal sepsis: diagnostic accuracy of C-reactive protein (CRP) in the diagnosis of neonatal sepsis. Professional Med J 2019; 26(4):608–14.DOI: https://doi.org/10.29309/TPMJ/2019.26.04.3362
10. Aslam F, Sipra MWK, Zakir FA, Anwar ZUA, Shaukat A. The clinical significance of CRP and IL-6 in early recognition of neonatal sepsis. Pak J Pathol 2024; 35(1):13–19. DOI: https://doi.org/10.55629/pakjpathol.v35i1.775
11. Hisamuddin E, Hisam A, Wahid S, Raza G. Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. Pak J Med Sci 2015;31(3):527–1. DOI: https://doi.org/10.12669/pjms.313.6668
12. Younis S, Shiekh MA, Raza AA. Diagnostic Accuracy of C-Reactive Protein in Neonatal Sepsis. J Bioresour Manag 2014;1(1):33–42 DOI: https://doi.org/10.35691/JBM.4102.0001
13. Liu Y, Zhao L, Wu Z. Accuracy of C-Reactive Protein Test for Neonatal Septicemia: A Diagnostic Meta-Analysis. Med Sci Monit 2019;25:4076–81. DOI: https://doi.org/10.12659/MSM.916968
14. Al-Atwi SS, Al-Atwi MA, Al-Balawi MS, Al-Balaw MK. Assessing the diagnostic accuracy of C-reactive protein (CRP) in neonatal sepsis detection. J Popul Ther Clin Pharmacol 2023;30(1): 415–23. DOI: https://doi.org/10.53555/jptcp.v30i1.4681
15. Eichberger J, Resch E, Resch B. Diagnosis of neonatal sepsis: The role of inflammatory markers. Front Pediatr 2022;10:840288. DOI: https://doi.org/10.3389/fped.2022.840288
16. Bunduki GK, Adu-Sarkodie Y. The usefulness of C-reactive protein as a biomarker in predicting neonatal sepsis in a sub-Saharan African region. BMC Res Notes 2020;13(1):194. DOI:https://doi.org/10.1186/s13104-020-05033-1
17. Mouliou DS. C-reactive protein: pathophysiology, diagnosis, false test results and a novel diagnostic algorithm for clinicians. Diseases 2023;11(4):132. DOI: https://doi.org/10.3390/diseases11040132
18. Samuel L. Direct-from-Blood detection of pathogens: a review of technology and challenges. J Clin Microbiol 2023;61:e00231–21. DOI: https://doi.org/10.1128/jcm.00231-21
19. Vieira RC, Procianoy RS, Mulle LD, Prado CH. Repercussão da antibioticoterapia materna intraparto no diagnóstico de sepse neonatal precoce [The influence of intrapartum antibiotic therapy on the diagnosis of early-onset neonatal sepsis]. J Pediatr (Rio J). 1997;73(3):171–5. Portuguese. DOI: https://doi.org/10.2223/jped.527
20. Herzlich J, Waksman Y, Marom R, Berliner S, Mandel D, Mangel L. Determinants of CRP measurements and CRP dynamics during early neonatal sepsis workup. Sci Rep 2025;15,18031. DOI: https://doi.org/10.1038/s41598-025-02337-9
21. Weitkamp JH, Aschner JL. Diagnostic Use of C-Reactive Protein (CRP) in Assessment of Neonatal Sepsis. Neoreviews 2005;6(11):e508–15. DOI: https://doi.org/10.1542/neo.6-11-e508
22. Kumar D, Khan M, Shaikh M, Hanif M, Hussain W. Sensitivity and specificity of C-reactive protein against blood culture in patients with neonatal sepsis - A hospital-based study. Liaquat Natl J Prim Care 2024;6(1):14–7.
23. Paolucci M, Landini MP, Sambri V. How Can the Microbiologist Help in Diagnosing Neonatal Sepsis?, Int J Pediatr 2012;2012:120139. DOI: https://doi.org/10.1155/2012/120139
24. Siddaiah P, Shetty PN, Karishna NW, Jagadeeshwara S. A study on validity of C-reactive protein in deciding the duration of antibiotic therapy in suspected neonatal bacterial infection. Int J Contemp Pediatr 2017;4(5):1838–43. DOI: https://doi.org/10.18203/2349-3291.ijcp20173796

Authors' contribution: BH: Significant contribution to study design, data collection, or analysis; Drafted or critically revised the manuscript; Approved the final version for publication; Agrees to take responsibility for the work's integrity and accuracy. **TM, AA, MUR**: Drafted or critically revised the manuscript; Approved the final version for publication; Agrees to take responsibility for the work's integrity and accuracy.

Conflict of interest: declared NONE
Source of funding: declared NONE

Published version: approved by authors