e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 908-911

Original Research Article

Validity of CRP in Deciding Antibiotic Usage Duration Among The Suspected Neonatal Bacterial Infection

Srujan Kukkadapu[1], Uppalapati Sushma[2], Srikanth Kumar Elagandula[3]

[1]Assistant Professor, Department of Paediatrics, Chalmeda Anand Rao Institute of Medical Sciences Bommakal, Karimnagar

[2]Assistant Professor, Department of Paediatrics, K. D. Medical College, Hospital & Research Center, Mathura, Uttar Pradesh

[3]Assistant Professor, Department of Paediatrics, Chalmeda Anandrao Institute of Medical Sciences, Karimnagar

Received: 17-07-2025 / Revised: 16-08-2025 / Accepted: 17-09-2025
Corresponding Author: Dr. Srikanth Kumar Elagandula
Conflict of interest: Nil

Abstract:

Introduction: Neonatal septicemia is challenging to diagnose due to nonspecific signs and limited lab accuracy, often leading to prolonged antibiotic use. CRP, a short half-life inflammatory marker, may help tailor treatment duration. This study evaluates CRP's role in safely guiding antibiotic discontinuation in suspected neonatal bacterial infections.

Methods: This prospective cohort study at Prathima Institute included neonates with suspected sepsis. Based on CRP levels after 24–48 hours, neonates were grouped for antibiotic duration. Relapse was monitored over four weeks. CRP's negative predictive value was assessed to determine its reliability in guiding safe antibiotic discontinuation and minimizing overtreatment.

Results: Among 50 neonates, 44% were culture-positive, predominantly with Staphylococcus aureus and Klebsiella. CRP >6 mg% correlated with infection; Group 1 neonates with CRP <6 mg% showed no relapse, yielding 100% NPV. Antibiotics were safely stopped within 7 days in 54%, supporting CRP's role in guiding treatment duration.

Conclusion: CRP is a reliable, cost-effective biomarker for guiding antibiotic duration in suspected neonatal sepsis. A CRP level <6 mg% showed 100% negative predictive value, supporting early antibiotic discontinuation without relapse. Incorporating CRP monitoring can reduce unnecessary antibiotic use and hospital stay, improving neonatal care and combating antibiotic resistance.

Keywords: Neonatal Septicemia, C-Reactive Protein, Antibiotics, Blood Culture.

Introduction

Neonatal septicemia, previously referred to as sepsis neonatorum, is defined as a clinical syndrome resulting from the systemic inflammatory response to a suspected or proven bacterial infection during the first four weeks of life. Although it was traditionally identified by positive blood cultures, limitations in diagnostic precision due to nonspecific clinical signs and suboptimal laboratory parameters still pose a significant challenge in neonatal sepsis (NS) diagnosis and management [1]. The incidence of NS in India is substantially high, ranging from 11 to 24.5 per 1000 live births, reflecting a substantial burden on neonatal health care [2].

The uncertainty in diagnosing NS often leads to the indiscriminate and prolonged use of antibiotics, thereby contributing to the emergence of antimicrobial resistance. Current treatment guidelines suggest a 48–72 hour antibiotic course in neonates with negative blood cultures and 7–14 days in confirmed or clinically suspected cases, though these durations lack strong evidence-based validation [3]. Given the dynamic interaction between pathogens and the immature neonatal immune system, a uniform duration of therapy may not be ideal for all cases [4].

C-reactive protein (CRP), an acute-phase reactant synthesized in the liver in response to inflammatory cytokines, has a short half-life and rapidly declines upon effective infection control, making it a promising biomarker for individualizing antibiotic duration [3, 4]. This study evaluates the validity of CRP in guiding antibiotic cessation in suspected neonatal bacterial infections.

Methods

This was a prospective cohort study, conducted in department of Pediatrics, Prathima Institute of Medical Sciences, Karimnagar. This research was carried from September 2017 to 2018, 1 year. Study protocol was approved by the institutional Ethics committee. An informed written consent was taken from the parent.

Neonates (< 28 days) with suspected septicemia, birth weight > 1500grams were included in this study. Neonates who had undergone surgical procedures, those diagnosed with meningitis were excluded.

Following admission, all neonates underwent thorough evaluation including blood collection for culture and sensitivity testing, chest X-ray, and urine culture sensitivity. Empirical broad-spectrum antibiotic therapy was initiated immediately with injection Ampicillin and Gentamicin. CRP levels were estimated between 24 to 48 hours after initiation of antibiotics. Based on the CRP values, neonates were categorized into three groups: Group 1 with CRP levels <6 mg%, in whom infection was deemed unlikely. In these cases, antibiotics were discontinued regardless of other clinical or laboratory findings, unless the attending consultant decided otherwise. Group 2 consisted of neonates with CRP levels >6 mg%, indicating likely infection. This group was further divided into two subgroups. Group 2a followed a CRP-guided therapy approach, where CRP was monitored every alternate day, and antibiotics were stopped once the CRP value dropped below 6 mg%. In contrast, Group 2b followed a fixed 7-day antibiotic regimen, with CRP measured on the seventh day; antibiotics were discontinued if the CRP level was <6 mg% and the neonate remained asymptomatic, subject to the consultant's discretion.

Post-therapy monitoring involved observation for at least 48 hours after cessation of antibiotics to assess for recurrence of clinical features suggestive of septicemia. Additionally, all neonates were followed for four weeks of post-discharge to monitor for signs of relapse. Non-relapsed was considered if no symptoms of septicemia within four weeks or if antibiotics were administered for unrelated diagnoses. The primary outcome of the study was the proportion of infectious relapses occurring within four weeks after stopping antibiotic therapy. To assess the reliability of CRP as a guide for determining the safe duration of antibiotic use, the negative predictive value (NPV) of CRP in relation to subsequent infection was calculated. This approach allowed evaluation of whether CRP levels could reliably predict resolution of infection and safe discontinuation of antibiotics, potentially reducing unnecessary antibiotic exposure. Blood sample collection, culture, CRP estimation was carried as per the institutional protocol.

Statistical analysis: The data was analysed using SPSS, version 19. Chi-square (χ^2) test was used for statistical analysis, P <0.05 was considered statistically significant.

Results

Among 50 neonates, 64% were male (32) and 36% female (18). Group 1 had 17 males, group 2a had 11 females, and group 2b had 8 males. Fourteen presented within 72 hours, and 11 had early-onset septicemia (EOS). Most (45) were term. Birth weights ranged from 1.5 kg to over 3 kg, with 25 neonates weighing between 2.5–2.9 kg. Late-onset septicemia (LOS) was observed in 39 cases.

All 23 cases in group I were blood culture-negative (CN), while group IIa had 9 culture-positive (CP) and 4 CN cases, and Group IIb had 12 CP and 2 CN cases. Of the 22 CP cases (44%), 17 grew Gram-positive organisms, most commonly Staphylococcus aureus (13.6%) and 5 grew Gram-negative organisms, predominantly Klebsiella (28.57%), followed by E. coli and Pseudomonas. A total of 29 neonates (58%) showed BNR > 0.2, which was statistically significant (P < 0.05). CRP was positive in 24% on day 5 (not significant) and 22% on day 7 (P < 0.05), correlating with LOS. Group 1 neonates (n=24) with CRP <6 mg% were CN with no relapse, showing 100% negative predictive value. Groups 2a and 2b (13 each) had CRP >6 mg%, were mostly CP, and had no relapses. Antibiotics were stopped within 7 days in 27 cases (54%), demonstrating CRP's utility in guiding therapy.

Discussion

In this study of 50 neonates with suspected septicemia, the majority were male (64%), which aligns with previous findings that male neonates are at a higher risk for sepsis due to factors such as the immunomodulatory effects of testosterone and X-linked immune response genes [5]. Group-wise distribution showed that Group 1, characterized by low CRP and culture negativity, predominantly consisted of males (17 out of 24), whereas Group 2a had a higher proportion of females (11 out of 13), suggesting possible sex-based immune variability in the inflammatory response. EOS, occurring within 72 hours of birth, was observed in 11 neonates (22%), while the majority, 39 neonates (78%), presented with LOS, a pattern consistent with earlier Indian studies emphasizing the burden of nosocomial or postnatal infections [6]. The timing of presentation also reflects the challenges in perinatal care and infection control practices in resource-limited settings.

Regarding birth weight, 25 neonates (50%) had weights between 2.5–2.9 kg, and only 7 weighed over 3 kg, while 18% had weights under 2.5 kg. Low birth weight is a well-established risk factor for NS, due to immature immune defense mechanisms and

frequent invasive procedures [7]. Most neonates (90%) were full-term, which may imply that in this cohort, postnatal environmental exposure played a larger role than prematurity in sepsis onset. These findings highlight the importance of sex, gestational age, and birth weight in understanding sepsis epidemiology and planning targeted interventions.

In the current study evaluating suspected neonatal septicemia, blood culture findings revealed that all 23 neonates in group I were CN, affirming the reliability of CRP as a marker for ruling out infection in this subgroup. Conversely, group IIa had 9 CP and 4 CN cases, and Group IIb had 12 CP and 2 CN cases, reflecting a strong correlation between elevated CRP (>6 mg%) and confirmed infection. Among the 22 culture-positive neonates (44% of the cohort), Gram-positive organisms were isolated in 17 cases, with Staphylococcus aureus being the most frequently identified (13.6%). This aligns with previous literature that emphasizes the predominance of Staphylococcus aureus and coagulase-negative staphylococci in neonatal bloodstream infections, particularly in LOS due to their environmental and nosocomial origin [8, 9]. The remaining 5 culture-positive cases grew Gram-negative bacteria, predominantly Klebsiella (28.57%), followed by Escherichia coli and Pseudomonas aeruginosa. These organisms are frequently implicated in early and late-onset neonatal infections and are associated with high morbidity, particularly in low- and middle-income countries [10, 11]. The pattern observed in our study reflects the regional burden of both Gram-positive and Gram-negative organisms, with Gram-negative sepsis often linked to poor hygiene and invasive procedures during delivery and postnatal care [7].

In addition to culture findings, hematological parameters supported clinical diagnosis. A total of 29 neonates (58%) had a Band-to-Neutrophil Ratio (BNR) > 0.2, a statistically significant finding ($P < 0.05$) that supports its utility as an early diagnostic marker of infection. Elevated BNR, a marker of left shift in neutrophilic response, reflects bone marrow stimulation due to infection and has been well validated in prior neonatal studies [12]. The concordance of elevated CRP and BNR in culture-positive cases adds robustness to the diagnostic approach, allowing clinicians to initiate timely antibiotic therapy. Notably, the combination of CRP >6 mg% and BNR >0.2 was highly predictive of blood culture positivity in groups IIa and IIb. This also emphasizes the potential of using these markers to stratify risk and tailor treatment duration more precisely. The results suggest that integrating CRP with hematological markers such as BNR provides a practical, low-cost approach to improving early diagnosis and management of NS, especially in resource-constrained settings. Furthermore, the absence of relapse in CRP-guided early antibiotic cessation groups (group I and some in group IIa) underscores the safety of individualized therapy durations and highlights the potential of CRP as a tool for antimicrobial stewardship. Such strategies are essential in the current era of rising antimicrobial resistance.

The findings from this study underscore the diagnostic and prognostic value of CRP in managing neonatal septicemia. CRP positivity was noted in 24% of neonates on day 5 (statistically not significant) and in 22% on day 7, with the latter showing significant correlation ($P < 0.05$) with LOS. These observations highlight the dynamic role of CRP as a biomarker, particularly in LOS, where symptoms may evolve more gradually and laboratory confirmation is often delayed. The delayed CRP response also supports previous reports that CRP levels typically peak 24–48 hours after onset of infection and normalize rapidly upon resolution, making it a useful marker for monitoring therapeutic response [13, 14]. Group 1 neonates (n=24), who had CRP values <6 mg% within 24–48 hours and were all blood CN, showed no clinical relapse during follow-up. This 100% negative predictive value (NPV) of CRP reinforces its reliability in ruling out ongoing bacterial infection and justifies early discontinuation of antibiotics in these cases.

Group 2a and 2b neonates (n=13 each) had CRP values >6 mg%, indicating a higher likelihood of infection. The majority of these were CP, confirming the association between elevated CRP and proven infection. Importantly, none of the neonates in these groups experienced clinical relapse after completion of therapy, regardless of whether CRP-guided therapy (group 2a) or fixed 7-day therapy (group 2b) was followed. This outcome supports previous studies that advocate for the safe use of serial CRP measurements to tailor the duration of antibiotic treatment in NS, ultimately minimizing unnecessary antibiotic exposure without compromising safety [15]. Additionally, this practice has significant implications for reducing the emergence of antimicrobial resistance, lowering healthcare costs, and shortening hospital stays [16]. In this study, antibiotics were discontinued within 7 days in 27 neonates (54%), including 24 cases in group 1 who stopped treatment after 48 hours based on CRP <6 mg%. This outcome demonstrates that CRP can serve as an effective tool not only for diagnosis but also for rationalizing treatment duration. In the current era of antimicrobial stewardship, such individualized treatment strategies are highly valuable, especially in resource-limited settings where prolonged antibiotic use remains widespread due to diagnostic uncertainty [17].

Furthermore, the absence of relapse among all neonates supports the hypothesis that CRP is a

reliable marker for both infection clearance and therapeutic monitoring. This also validates its utility in distinguishing between bacterial and non-bacterial causes of neonatal illness, thereby avoiding unnecessary treatment in CRP-negative infants. By integrating CRP-based decision-making with clinical judgment and culture findings, clinicians can confidently adopt a shorter, evidence-based treatment protocol that ensures both safety and efficacy in managing NS.

Conclusion: This study confirms the utility of CRP in guiding antibiotic therapy among neonates with suspected septicemia. A CRP level <6 mg% within 48 hours reliably predicted absence of infection, with 100% negative predictive value and no relapse during follow-up. CRP-guided therapy allowed early discontinuation of antibiotics in over half the cases, reducing unnecessary exposure and hospital stay. These findings support the integration of CRP into routine clinical protocols to optimize antibiotic use, minimize risks of antimicrobial resistance, and enhance individualized neonatal care. Further large-scale studies are warranted to validate these findings across diverse clinical settings.

References:

1. Raturi A, Chandran S. Neonatal Sepsis: Aetiology, Pathophysiology, Diagnostic Advances and Management Strategies. Clin Med Insights Pediatr. 2024 Sep 25; 18: 11795565241281337.
2. Murthy S, Godinho MA, Guddattu V, Lewis LES, Nair NS. Risk factors of neonatal sepsis in India: A systematic review and meta-analysis. PLoS One. 2019; 14(4): e0215683.
3. Siddaiah P, Shetty P N, Jagadeeshwara S. A study on validity of C-reactive protein in deciding the duration of antibiotic therapy in suspected neonatal bacterial infection. International Journal of Contemporary Pediatrics. 2017; 4(5): 1838 – 43.
4. Ahmed E, Rehman A, Ali MA. Validation of serum C-reactive protein for the diagnosis and monitoring of antibiotic therapy in neonatal sepsis. Pak J Med Sci. 2017; 33(6): 1434 – 7.
5. Melvan JN, Bagby GJ, Welsh DA, Nelson S, Zhang P. Neonatal sepsis and neutrophil insufficiencies. Int Rev Immunol. 2010; 29(3): 315 – 48.
6. Thaver D, Zaidi AK. Burden of neonatal infections in developing countries: a review of evidence from community-based studies. Pediatr Infect Dis J. 2009; 28: S3 – 9.
7. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. Clin Microbiol Rev. 2014; 27(1): 21 – 47.
8. Stoll BJ, Hansen NI, Sánchez PJ, Faix RG, Poindexter BB, Van Meurs KP, et al. Early onset neonatal sepsis: the burden of group B Streptococcal and E. coli disease continues. Pediatrics. 2011; 127(5): 817 – 26.
9. Dong Y, Speer CP. Late-onset neonatal sepsis: recent developments. Arch Dis Child Fetal Neonatal Ed. 2015; 100(3): F257 – 63.
10. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. Lancet. 2005; 365(9465): 1175 – 88.
11. Majigo M, Makupa J, Mwazyunga Z, Luoga A, Kisinga J, Mwamkoa B, Kim S, Joachim A. Bacterial Aetiology of Neonatal Sepsis and Antimicrobial Resistance Pattern at the Regional Referral Hospital, Dar es Salam, Tanzania; A Call to Strengthening Antibiotic Stewardship Program. Antibiotics (Basel). 2023; 12(4): 767.
12. Zea-Vera A, Ochoa TJ. Challenges in the diagnosis and management of neonatal sepsis. J Trop Pediatr. 2015; 61(1): 1 – 13.
13. Philip AG, Mills PC. Use of C-reactive protein in minimizing antibiotic exposure: experience with infants initially admitted to a well-baby nursery. Pediatrics. 2000; 106(1): E4.
14. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics. 1998; 102(4): E41.
15. Gaunekar RA, Borker SS, Rodrigues S. Role of C-reactive protein in neonatal septicemia. IOSR Journal of Dental and Medical Sciences. 2023; 22: 35 – 41.
16. Stocker M, van Herk W, El Helou S, Dutta S, Schuerman FABA, et al. C reactive protein, Procalcitonin, and white blood count to rule out neonatal early-onset sepsis within 36 hours: a secondary analysis of the neonatal procalcitonin intervention study. Clin Infect Dis. 2021; 73(2): e383 – e390.
17. Polin RA, Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. Pediatrics. 2012; 129(5): 1006 – 15.