e-ISSN: 0976-822X, p-ISSN:2861-6042

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

International Journal of Current Pharmaceutical Review and Research 2023; 15(1); 63-67

Original Research Article

Hospital Based Prospective Comparison of CRP against Blood Culture in Diagnosis of Neonatal Sepsis

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Received: 18-11-2022 / Revised: 17-12-2022 / Accepted: 22-01-2023
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Conflict of interest: Nil

Abstract

Aim: The Aim of the study was to compare CRP against blood culture in diagnosis of neonatal Sepsis.

Methods: The present study was conducted in the Department of Microbiology, Narayan Medical College and Hospital, Sasaram, Rohtas, Bihar, India, India for 10 months. 100 neonates suspected of septicaemia were included in the study, information on demographic data, blood culture and the level of CRP was extracted.

Results: Of the 100 neonates studied, 60 were blood culture positive while 40 were CRP positive. The sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of CRP were 84%, 40%, 44%, 82% and 65% respectively.

Conclusion: The specificity and sensitivity of CRP against blood culture strengthen the use of this acute phase protein in the diagnosis of neonatal sepsis and would help the clinicians to fix the period of antibiotic treatment and medical management to reduce the liver damage due to antibiotic exposure, development of bacterial resistance and neonatal mortality.

Keywords: C-reactive protein, Neonates, Neonatal Sepsis.

Introduction

Sepsis is a major cause of morbidity and mortality among neonates. It is one of the leading cause of death in neonates in our country.1 Neonatal septicaemia is defined as localized or systemic condition resulting from adverse reaction to the presence of an infectious agent(s) or its toxin(s). [1] Clinical manifestations of neonatal sepsis are non-specific, therefore, clinical diagnosis of sepsis is difficult and laboratory help is required. The gold standard for diagnosis of bacterial sepsis is blood culture, may be primary or secondary to a focal infection (osteomyelitis, gastroenteritis, pyelonephritis, and endocarditis). [2] The clinical manifestation of neonatal sepsis are not specific and usually occur in the late stages of the infection. [3]

C-reactive protein (CRP) is a part of a protein group called acute phase reactants that is produced by the liver and is considered as an inflammatory marker. C-reactive protein is commonly elevated during an infection but are not specific for infection and do not identify any specific

infection. These tests can be used to monitor response to therapy. [3] The half-life of CRP is 19 hours and in acute response its level increases up to thousand fold and comes down rapidly as the source is removed. After effective treatment, its levels can fall rapidly in 5-7 hours. CRP crosses through placenta in very low quantities, so any elevation in a newborn always represents endogenous synthesis. [4]

The newborn infants host resistant mechanism particularly that of preterm infant may be immature and easily overcome by invading organisms. Infection therefore becomes fulminant and causes death within few hours or days. A variety of organisms including bacteria, viruses, fungi and protozoa are the etiological agents. Etiological agents vary in different geographical area. [5]

CRP was first demonstrated in 1930 by Tillet and Francis at Rockefeller University. [6] It is an acute phase reactant and an inflammatory marker synthesised in the liver in response to inflammatory cytokines (IL-1, IL-6 and TNF-α) and plays a major role in innate immunity. [7] CRP stimulates cell-mediated cytotoxicity. It leads to the activation of neutrophils, promotion of platelet degranulation and enhancement of natural killer cell activity. It is produced rapidly after a single stimulus by the hepatic cells. The half-life of CRP is 19 hours and in acute response its level increases up to thousand fold and comes down rapidly as the source is removed. After effective treatment, its levels can fall rapidly in 5-7 hours. CRP crosses through placenta in very low quantities, so any elevation in a newborn always represents endogenous synthesis. [8]

The Aim of the study was to compare CRP against blood culture in diagnosis of neonatal Sepsis.

Methods

The present study was conducted in the Department of Microbiology, Narayan Medical College and Hospital, Sasaram, Rohtas, Bihar, India for 10 months. 100 neonates suspected of septicaemia were included in the study, information on demographic data, blood culture and the level of CRP was extracted.

Inclusion criteria

All newborns who were diagnosed with septicaemia with a positive blood culture and CRP level to validate and confirm the diagnosis and those neonates who were also diagnosed with septicaemia with a negative blood culture and CRP levels.

Exclusion criteria

Neonates who had received antibiotics before collection of blood samples having surgical problems, chromosomal or congenital anomalies were excluded from the study. Blood culture bottles that were received from paediatrics department were incubated at 37◦C aerobically. After overnight incubation blood culture bottles were examined for indicators of growth like turbidity, haemolysis or discrete colonies on the surface of sedimented red cells.

If any of these were present subculture was done on to blood agar and MacConkey agar. If indicators of growth were not present primary subculture was done after 48 hours of incubation on blood agar and MacConkey agar. If no growth occurred on plates after overnight incubation, bottles were incubated further and observed daily for indicators of growth till 7 days. A final subculture was done at the end of day 7 or at appearance of indicators of growth which ever was earlier. The colonies grown on blood agar and MacConkey agar were identified by conventional methods according to the standard laboratory protocol, including colony morphology, Gram staining and biochemical reactions5 C-reactive protein was estimated semi quantitatively by using the CRP latex kit manufactured by the

Pathozyme diagnostics (P) Limited. The CRP latex reagent was standardized to detect serum CRP level of >=6 ug/ml, which was considered the lowest concentration of clinical significance. CRP level can be calculated in term of micrograms per ml by multiplying the highest dilution giving clear cut agglutination with a factor of 6.

Results

Table 1: Demographic details of patients with neonatal sepsis

Demographic Details (n=100)	No. of Neonates
Gender	
Male	64
Female	36
Age	
0-7	70%
8-14	10%
15-21	5%
22-28	15%
Preterm (<37 weeks)	55%
Term (>37 weeks)	45%

Table 2: Comparison of blood culture and CRP in patients with neonatal septicaemia

Variables	Blood culture positive	Blood culture negative
CRP positive	45	20
CRP negative	15	15
Total	60	40

45(45%) neonates had sepsis with positive blood culture, and positive CRP level. 20(20%) neonates with clinical signs of sepsis but their blood culture was negative and positive CRP level. Culture positive but CRP negative samples are 15 (15%) & CRP negative & culture negative are 15(15%).

Table 3: Sensitivity, specificity, PPV, NPV and diagnostic accuracy of CRP

Test	Sensitivity	Specificity	PPV	NPV	Diagnostic
CRP	84%	40%	44%	82%	65%

Discussion

Neonatal sepsis is the major and common cause of morbidity and mortality. The incidence is much higher in the developing world. Early diagnosis and effective treatment is the best way to reduce morbidity and mortality. The delay in diagnosis and initiating therapy are the main reasons for high mortality. Blood culture is still regarded as a gold standard for diagnosis. Different hematologic parameters, multiple inflammatory cytokines and acute phase reactants levels are used in this regard.

According to one study, CRP had the sensitivity and specificity of 58.33% and 56.52% respectively. The test had a positive predictive value of 67.74% and 48.27%. [9]

In our study, incidence of septicaemia was higher in preterm neonates (55%) compared to term neonates (45%). Our results were consistent with studies conducted by Patel BM et al., [10] and Shah AJ et al. [11], who reported 67.37% and 70% blood culture positivity rates respectively in preterm babies. Preterm neonates are more prone to septicaemia because they have increased susceptibility to infection due to an immature immune system, inefficient neutrophil function and

lack of antigen type-specific antibodies to pathogens in their environment. [12-14]

The study group consists of 64 males (64%) and 36 females (36%). Males have been reported to be more likely than females to develop septicaemia as revealed in this study. Faridi et al. also reported 66.67% males and 33.33% females out of 63 cases of neonatal septicemia. [15] And also similar to findings of other studies reported from India. [10,16] In our study, out of the 53 blood culture positive samples, 46 (86.7%) were positive for CRP which was similar to studies done by Gowsami Y et al., [17] and Hisamuddin E et al., [18]

In this study CRP reported to have Sensitivity of 84%, Specificity of 40%, Positive Predictive Value of 44%, Negative Predictive Value of 82% and diagnostic accuracy of 65% against blood culture these result are similar to studies done by Younis S et al., [19] and Chauhan S et al. [20,21]

For definitive diagnosis of septicaemia, blood culture is the gold standard method but it takes at least 48-72 hours for reporting and by that time the infection may progress, especially if antibiotic treatment is not started. So there is a need of a screening test which can diagnose septic neonates rapidly and prevent injudicious antibiotic therapy in non-septic neonates.

Conclusion

Early diagnosis of neonatal sepsis with the aid of biomarkers like CRP may serve as an important tool in reducing the mortality and morbidity among neonates. So the estimation of CRP can help in providing a presumptive diagnosis as to whether a gram negative or gram positive organism is the cause of septicaemia and the antibiotic therapy can be started even before the blood culture comes positive.. The specificity and sensitivity of CRP against blood culture strengthen the use of this acute phase protein in the diagnosis of neonatal sepsis and would help the clinicians to fix the period of antibiotic treatment and medical management to reduce the liver damage due to antibiotic exposure, development of bacterial resistance and neonatal mortality.

References

1. Meherban S. Perinatal Infections. In: Care of the Newborn. New Delhi: Sagar Publication; 2010.
2. Marcdante K, Kliegman RM. Nelson essentials of pediatrics e-book. Elsevier Health Sciences; 2014 Feb 25.
3. Prashant A, Vishwanath P, Kulkarni P, Sathya Narayana P, Gowdara V, Nataraj SM, Nagaraj R. Comparative assessment of cytokines and other inflammatory markers for the early diagnosis of neonatal sepsis–a case control study. PloS one. 2013 Jul 15;8(7):e68426.
4. Patel U, Patel VK, Patel NP, Verma J, Ratre BK, Verma SP. To evaluate C-Reactive Protein and other Hematological parameters for diagnosis of Neonatal Sepsis. Int J Med Res Rev. 2014;2(4):1–10.
5. Asindi AA, Bilal NE, Fatinni YA, Al-Shehri MA, Mannan N, Habeeb SM. Neonatal septicemia. Saudi medical journal. 1999 Dec 1;20(12):942-6.
6. Tillet WS, Francis T. Serological Reactions in Pneumonia with a Non-Protein Somatic Fraction of Pneumococcus. J Exp Med.1930;52(4): 561-71.
7. Jan AZ, Zahid SB, Ahmad S. Role of C-Reactive Protein in diagnosing Neonatal Sepsis. Khyber Med Univ J. 2012;4(4):161-64.
8. Patel U, Patel VK, Patel NP, Verma J, Ratre BK, Verma SP. To evaluate C-Reactive Protein and other Hematological parameters for diagnosis of Neonatal Sepsis. International Journal of Medical Research and Review. 2014;2(4):1-10.
9. Mahmood A, Karamat KA, Butt T. Neonatal Sepsis: High antibiotic

resistance of the bacterial pathogens in a Neonatal Intensive Care Unit in Karachi. J Pak Med Assoc. 2002;52 (8):348-50
10. Rajendraprasad BP, Basavaraj KN, Antony B. Bacterial spectrum of neonatal septicemia with their antibiogram with reference to various predisposing factors in a tertiary care hospital in Southern India. Ann Trop Med Public Health. 2013 Jan 1;6(1): 96.
11. Shah AJ, Mulla SA, Revdiwala SB. Neonatal sepsis: High antibiotic resistance of the bacterial pathogens in a neonatal intensive care unit of a tertiary Care hospital. J Clin Neonatol. 2012;1(2):72-75.
12. Nagata E, Brito ASJ, Matsuo T. Nosocomial infections in a neonatal intensive care unit: Incidence and risk factors. Am J Infect Control. 2002 ;30 (1):26-31.
13. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. Pediatrics. 2002; 110(2 Pt 1):285-91.
14. Tsai MH, Chu SM, Lee CW, Hsu JF, Huang HR, Chiang MC, et al. Recurrent late-onset sepsis in the neonatal intensive care unit: incidence, clinical characteristics and risk factors. Clin Microbiol Infect. 2014;20(11): O9 28-35.
15. Faridi MM, Gupta PI, Bhargava SK. Chest radiographs in neonatal septicemia. Indian pediatrics. 1992 Jul 1;29(7):871-4.
16. Sharma A, Kutty CV, Sabharwal U, Rathi SU, Mohan H. Diagnostic and prognostic role of CRP and m-ESR in neonatal septicemia. Indian pediatrics. 1993 Mar 1;30(3):347-50.
17. Goswami Y, Jadav P, Rathod B. Study on Significance of C-Reactive Protein Estimation in Early Diagnosis of Neonatal Septicemia. Mortality. 2014; 15(50):10-5.
18. Hisamuddin E, Hisam A, Wahid S, Raza G. Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. Pakistan journal of medical sciences. 2015 May;31(3):527.
19. Younis S, Sheikh MA, Raza AA. Diagnostic accuracy of C-reactive protein in neonatal sepsis. Journal of Bioresource Management. 2014;1(1):1.
20. Chauhan SB, Vaghasia V, Chauhan BB. C-reactive protein (CRP) in early diagnosis of neonatal septicemia. National journal of medical research. 2012 Sep 30;2(03):276-8.
21. Tamubango Kitoko H. Accouchement prématuré aux cliniques universitaires de Lubumbashi de 2011-2019: fréquence et prise en charge. Journal of Medical Research and Health Sciences, 2023; 6(2): 2457–2470.