

A Hospital Based Comparative Assessment of CRP against Blood Culture in Diagnosis of Neonatal Sepsis

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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, Anugrah Narayan Magadh medical College and Hospital, Gaya, Bihar, India for 18 months from March 2019 to Aug. 2020. 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

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Introduction

Septicaemia is a recognized cause of morbidity and mortality in the new-borns in the developing countries. [1] Septicaemia is well-defined as a “clinical syndrome characterized by systemic signs/symptoms and bacteraemia during the 1st month of life”. Septicaemia is known as ‘early onset’ disease if present during 5-7 days of life and considered as ‘late onset’ if it follows after the first week. [2]

Neonatal septicemia is a serious illness but curable if identified early. The primary threatening signs and symptoms are mostly nonspecific and can easily be mixed up with the non-infective causes. Nonspecific signs/symptoms make it very challenging to formulate a timely clinical diagnosis. [3] Neonatal physician after evaluating many tests are looking for a test that would help in neonatal sepsis diagnosis and also quickly confirms it and also that decisively

rules it out. [4] Diagnostic test like blood cultures are time consuming so correct diagnosis gets delayed and problematic.

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.

Materials and Methods

The present study was conducted in the Department of Microbiology, Anugrah Narayan Magadh medical College and Hospital, Gaya, Bihar, India for 18 months from March 2019 to Aug. 2020. 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 sub culture 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 reactions. 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]

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. [22]

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.

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