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COMPARISON OF C-REACTIVE PROTEIN (CRP) WITH BLOOD CULTURE IN THE DIAGNOSIS OF NEONATAL SEPSIS

Microbiology

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ABSTRACT

Purpose: Neonatal Sepsis is a serious and life threatening condition. Mortality and morbidity due to sepsis can be prevented by early diagnosis and timely management. Blood culture is the gold standard test in the diagnosis of sepsis but it is time consuming, require well equipped laboratory and trained personnel. C-reactive protein is an important early diagnostic marker of sepsis which help in early assessment of infection in neonates. We aim to assess the diagnostic accuracy and its association with blood culture in clinically suspected cases of neonatal septicaemia. **Method:** It was a hospital based observational study conducted during June 2021 to May 2022 in the department of Microbiology, SMS Medical College, Jaipur. Hundred fourty cases of suspected neonatal septicemia admitted in Neonatal ICU's of Sir Padampat Mother and Child Care Hospital were enrolled and processed by BACT/ALERT- 3D Automated Blood Culture system and CRP rapid slide latex agglutination method. **Results:** Out of 140 enrolled cases of neonatal septicaemia, 60(42.85%) were considered as the Culture proven neonatal sepsis cases. Out of these culture proven neonatal septicemia, 52 (86.66%) were CRP Positive. The sensitivity and specificity of CRP in the diagnosis of neonatal septicemia were 86.66% and 45% respectively. The positive and negative predictive value were 54.16% and 81.81% respectively. The diagnostic accuracy was 62.85%. **Conclusion:** Serum CRP is a screening tool for the early diagnosis of neonatal septicaemia that can easily available, rapid method with good sensitivity and negative predictive value. Hence it can be used by clinicians for treatment of sepsis.

KEYWORDS

Neonatal sepsis, C- Reactive Protein, Blood Culture.

INTRODUCTION

Neonatal sepsis is defined as a clinical syndrome of bacteremia characterized by systemic signs and symptoms of infection in the first 28 days of life[1,2]. Neonatal sepsis include various systemic infections like septicemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infection of the newborn. Neonatal sepsis is responsible for about 30-50% of the total neonatal deaths in developing countries like India. Nearby 20% of neonates develop sepsis and approximately 1% deaths occur due to sepsis related causes[3,4]. The incidence of neonatal sepsis in India, according to the data from national neonatal perinatal database (NNPD) is 30 per 1000 live births and was reported three times higher in developing countries as compared to developed countries[5]. Clinically diagnosing neonatal sepsis is a challenge because of subtle and non specific signs and symptoms.Mortality and morbidity due to sepsis can be prevented with early diagnosis, rational antimicrobial therapy and aggressive supportive care.

Blood culture is the gold standard in the diagnosis of neonatal sepsis. It helps in microbial identifiction and antibiotic susceptibility testing but it is time consuming, require well equipped laboratory and trained personnel[6,7]. Early diagnostic markers of sepsis like C-reactive protein (CRP), pro-calcitonin (PCT), interleukins (IL-6,8) and tumour necrosis factor which help in early assessment of infection and also helps in reducing the mortality and sequelae. CRP was first described in 1930 by Tillet and Francis at Rockefeller University[8]. C- reactive protein (CRP) is an acute-phase reactant that is synthesized by the liver within 6 hours after the onset of inflammation and tissue necrosis. Serum CRP level increases within 6- 10 hours in neonates after exposure to infection and peaks at 2-3 days followed by a decrease in level as source is removed. CRP crosses through placenta in very low quantities so any elevation in a newborn always represent endogenous synthesis[9]. CRP helps to discriminate bacterial infections from viral infections and monitor the response to antibiotics[10]. In many study, CRP has high sensitivity for diagnosis of sepsis, but there was limited studies conducted in Rajasthan,India. This study was conducted to compare CRP against blood culture in diagnosis of neonatal sepsis.

MATERIAL & METHODS

This was a Hospital based observational study carried out in the Department of Microbiology, SMS Medical College, Jaipur, Rajasthan, India from June 2021 to May 2022. One hundred forty, cases of suspected neonatal septicemia admitted in Neonatal ICU's of Sir Padampat Mother and Child Care Hospital were included in the study. The study protocol was approved by the Ethics Committee of Sawai Man Singh Hospital, Jaipur (letter no 1157/MC/EC/2021 dated 03/12/2021). After obtaining informed consent from the patients' parents, all details regarding clinical presentation and history were filled on a structured proforma. Two blood samples were drawn from each patient one for blood culture and other for CRP test following strict aseptic precautions.

AIM & OBJECTIVES

To compare C- Reactive Protein (CRP) against blood culture in diagnosis of neonatal sepsis.

Inclusion Criteria we included neonates with risk factors like prolonged rupture of membranes (PROM) >18 hours, more than 3 vaginal examinations after rupture of membranes, intrapartum fever, foul smelling liquor, maternal UTI within 2 weeks prior to delivery and clinically suspected neonates with one or more sign and symptoms (refusal to feed, poor cry, irritable, lethargy, fever or hypothermia, respiratory distress, diarrhea, vomiting.

Exclusion Criteria were neonates with gestational age < 28 weeks, neonates with birth weight < 1000 gms, neonates with congenital anomalies and malformation and birth asphyxia.

Blood Culture:

Blood culture bottles were incubated at 37˚C aerobically and examined for turbidity, hemolysis and discrete colonies on the surface of sedimented red cells (indicators of growth). Primary subculture was done on Blood agar and MacConkey agar after 48 hrs of incubation irrespective of the presence or absence of indicators of growth in the blood culture bottles. If there is no sign of growth on Blood agar and MacConkey agar, bottles were again be incubated at 37˚C and monitored daily for indicators of growth. Subculture on Blood agar and MacConkey agar plate were done if any growth indicator is positive on or before day seven. The colonies on Blood agar and MacConkey agar were identified by conventional methods according to the standard laboratory protocol including colony morphology, gram stain and biochemical reaction. CRP was estimated semi-quantitatively by using the CRP latex kit manufactured by Precision Biomed Pvt. Ltd.

RESULTS

In our study, 140 neonates with suspected sepsis were enrolled. Information like demographic details,blood culture and CRP results were extracted. Males were more affected compared to females with

2.2:1. PROM(37.85%) and febrile illness(21.42%) were the commonest maternal risk factor associated with neonatal septicemia followed by prematurity(12.85%)(Table 1). Out of 60 culture proven neonatal septicemia, 52(86.66%) were CRP Positive(Table 2). The sensitivity and specificity of CRP in the diagnosis of neonatal septicemia was 86.66% and 45% respectively. The positive and negative predictive value were 54.16 % and 81.81% respectively.The diagnostic accuracy was 62.85%(Table 3).

Table 1: Demographic details of patients with neonatal sepsis

Demographic Details(n=140)	No. of Neonates
Gender	
Male	97(69.28%)
Female	43(30.71%)
Gestational age	
Term (>37 weeks)	22(36.67%)
Preterm (<37 weeks)	38(63.33%)
Birth Weight (Kg)	
≥2.5Kg	17(28.33%)
<2.5(LBW)	43(71.67%)
RISK FACTORS	
PROM(Premature rupture of membrane)	53(37.85%)
Febrile illness	30(21.42%)
Prematurity	18(12.85%)
Prolong labour	12(08.57%)
Meconium stained liqor(MSL)	10(07.14%)
Obstructed labour	5(03.57%)
Chorioamnionitis	4(02.85%)
Factor not known	8(05.71%)
ONSET	
EOS	95(67.85%)
LOS	45(32.14%)

Table 2: Comparison of blood culture and CRP in neonatal sepsis

	Blood Culture Positive	Blood Culture Negative	Total
CRP Positive	52	44	96
CRP Negative	8	36	44
Total	60	80	140

Table 3: Predictive values of CRP in patients with neonatal sepsis.

Parameters	Value
Sensitivity	86.66%
Specificity	45%
Positive Predictive Value	54.16%
Negative Predictive Value	81.81%
Diagnostic Accuracy	62.85%

DISCUSSION

In the present study out of 140 clinically suspected neonatal sepsis cases, increased prevalence was found in male infants (69.28%) than in female infants(30.71%) in the ratio of 2.2:1.Male predominance was also observed in similar studies conducted by Boma A West et al[11] with male to female ratio 1.85:1, Jyoti P et al [12] 1.89:1, Azza Labib[13] 1.5:1 , Ashish Bodhke et al [14] 1.85:1 and Gupta B et al [15] (1.3:1). In the present study among 60 culture positive cases septicemia was more common among neonates with low birth weight i.e < 2.5 kg (71.67%) as compared to neonates with normal birth weight i.e >2.5kg (28.33%). Similar result had been reported in a comparative study by Mamta Jajoo et al [16] where 68% neonates have low birth weight and 32% cases have normal birth weight. Other similar study was done by Tallur, et al [17] in which 54.55% sepsis cases had low birth weight. Blood culture positivity was higher in preterm neonates (63.33%) as compared to term neonates(36.67%). It is similar to other study done by Pandit B R et al and Jigar A S et al and Avyact et al [18] who reported 73% , 70% and 81.4% positivity rates respectively in preterm babies. premature rupture of the membran (PROM) with 37.85% cases was the commenest maternal risk factor associated with neonatal septicemia followed by febrile illness(21.42%) , prematurity(12.85%) and Prolong labour(08.57%).The similar study of maternal risk factors was done by Dhaneria M et al[19] in which he observed 14% cases with PROM, 10.6% foul-smelling liquor, 9.33% had prolonged labour. In the present study, 68.6% of the suspected cases were CRP positive and out of 60 culture proven neonatal septicemia, 52(86.66%) were CRP Positive. Sensitivity and Specificity of CRP in the diagnosis of neonatal septicemia was 86.66% and 45% respectively. The positive and negative predictive value were 54.16% and 81.81% respectively. The diagnostic accuracy was 62.85%. Effat et al (2015)[20] studied that the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy was found to be 76.92%, 53.49%, 80%, 48.94% and 70.07% respectively. Similar study was done by Lamichhane, A. and A. Mishra[21] (sensitivity 88.5%, specificity 46.1%, positive predictive value 54.8%, negative predictive value 84.1 ,diagnostic accuracy 64.1%) and Bunduki, G. K., & Adu-Sarkodie Y.[22] (sensitivity 95.7%, specifcity 82.4%, positive and negative predictive values were 70.2% and 97.8% respectively) and Gupta et al[23] (sensitivity 86.7%, specificity 42%, positive predictive value 45.5%, negative predictive value 85%, diagnostic accuracy 69%).

CONCLUSION

CRP considered as a good diagnostic and therapeutic tool due to its high sensitivity and a good negative predictive value so that antibiotic can be started as early as possible. This helps to reduce the delay in instituting antibiotic therapy which reduces the mortality and morbidity by neonatal septicaemia.

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Conflict of interest: Nil

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