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CRP In The Diagnosis Of Neonatal Sepsis In A Tertiary Care Hospital: An Observational Study.

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ABSTRACT

Neonatal sepsis is still one of the major causes of morbidity and mortality, despite recent advances in the health care system. Culture methods to identify the causative agents are time-consuming and take 2 days. The role of C-reactive protein (CRP) as a marker of neonatal sepsis has been studied at Government Medical College and Hospital, Cuddalore, Tamil Nadu, a tertiary care hospital, in the year 2023. Neonates with clinical suspicion of sepsis or who were at high risk of developing sepsis were included in the study (135 neonates). Significant values for screening tests were taken as C – reactive protein > 0.6 mg/dl. A statistical evaluation was done. In our study, 86.2% of culture-proven cases were CRP positive and 18.2% of culture-negative cases were CRP positive. 13.8% of culture-positive cases were CRP negative and 81.8% of culture-negative cases were CRP negative. The P value was < 0.001 which shows CRP was significant in our study. Neonatal sepsis screening is required for the detection of infection as the blood culture report may not be positive in all cases and is time-consuming. CRP showed high sensitivity and was a reliable marker in the diagnosis of neonatal sepsis.

Keywords: neonatal intensive care, CRP, infectious disease, neonatal sepsis.

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INTRODUCTION

Neonatal sepsis, defined as a systemic infection occurring in newborns within the first 28 days of life, is the second major cause of mortality among neonates. Globally, the incidence of neonatal sepsis has been increasing by 12% every year [1] and our country has the highest incidence of neonatal sepsis ie 17,000/100,000 live births. It is a serious illness but curable if identified early. Diagnostic tests like blood cultures are time-consuming and the occurrence of culture-negative sepsis is on the increase due to the irrational use of antibiotics. CRP is sensitive in detecting cases of culture-negative neonatal sepsis. Sepsis is categorized as early onset if diagnosed within the first 72 hours of life and is often due to perinatal risk factors and late onset sepsis if diagnosed after 72 hrs of life which may be secondary to nosocomial risk factors. Clinical features of neonatal sepsis are non-specific. Culture results take up to 48 hours and have the risk of false negativity which in turn affects the treatment and prognosis of the child. In resource-limited settings, the diagnosis of neonatal sepsis can be made by non-culture methods like estimation of CRP, procalcitonin, and serum amyloid. Despite the advances in neonatal care, early-onset neonatal sepsis remains a serious and potentially life-threatening disease with a mortality rate ranging from 1.5% in term to almost 40% in very low-birthweight infants [2]. The signs and symptoms of neonatal sepsis may be subtle and nonspecific being clinically indistinguishable from various noninfectious conditions such as respiratory distress syndrome or maladaptation. The current practice of starting empirical antibiotic therapy in all neonates showing infection-like symptoms results in their exposure to adverse drug effects, nosocomial complications, and the emergence of resistant strains [3]. Laboratory sepsis markers complement the evaluation of clinical signs and risk factors in the diagnosis of neonatal sepsis. No currently available test can provide perfect diagnostic accuracy, and false-negative as well as false-positive results may occur. For example, in a critically ill newborn a negative test result will not give much additional information on its infectious status, and in a good infant, a positive result will not dramatically increase the probability that the child is infected. Diagnostic tests will be most useful in infants with clinically unclear infectious status [4]. There is great interest in rapid diagnostic tests that can distinguish infected from uninfected newborns, especially in the early phase of the disease [5]. A delayed start of the antibiotic treatment may no longer be able to stop the fulminant clinical course with the development of septic shock and death within hours after the first clinical symptoms [6]. In the era of multi-resistant microorganisms, it is also important to avoid the unnecessary use of antibiotics in sepsis-negative infants. There is an abundance of studies evaluating laboratory markers in the diagnosis of neonatal sepsis. C-reactive protein (CRP) is the most extensively studied acute-phase reactant so far, and despite the ongoing rise (and fall) of new infection markers, its wide availability and its simple, fast, and cost-effective determination make it one of the preferred indices in many neonatal intensive care units (NICUs) [7] for the treatment of sepsis.

MATERIALS AND METHODS

This study was conducted in Government Medical College And Hospital, Cuddalore district, Tamil Nadu, India between Jan 2022 and Dec 2023 on 135 neonates, both inborn and referred cases. The children who presented before 28 days of life with clinical suspicion of sepsis or who were at high risk of developing sepsis were included. Significant values of screening tests were taken as CRP>0.6mg/dl. and statistical evaluation was done.

Inclusion Criteria

- Inborn neonates admitted to the ward or NICU with sepsis.
- Neonates were referred to the hospital for sepsis.

Exclusion Criteria

- Neonates with congenital malformations.
- Babies referred to this hospital with infection but above 1 month in age.

Two ml of blood was collected by venipuncture from the newborn. Samples were transported without any delay to the microbiology laboratory for CRP estimation. CRP was estimated by the latex agglutination method, which is rapid, economical, and easy to perform.

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Data collection and analyses: Clinical data were collected using a questionnaire. Data were analyzed using SPSS software. For all statistical analyses, the P-value was considered to be significant at $p < 0.05$

RESULT

Table 1: Prevalence Of Neonatal Sepsis (N=135)

Isolates in culture	Frequency	Percentage
Present	58	42
Absent	77	58
Pearson's chi-square test used; p-value <0.05 is significant.		

Table 2: Relationship between CRP and blood culture in Neonatal sepsis

CRP	Neonatal sepsis				χ2	p-value
	Culture positive (n=58)		Culture negative (n=77)			
	No	%	No	%		
Positive	50	86.2	14	18	61.39	**<0.001**
Negative	8	13.8	63	81.8		
Pearson's chi-square test used; p-value <0.05 is significant.						

Table 3: Bacteriology of isolates (n=135)

	Frequency	Percentage
Staph. aureus	22	37.9
Enterococci faecalis	3	5.2
Klebsiella pneumoniae	14	24.1
E.coli	5	8.6
CONS	7	12.1
Pseudomonas aeroginosa	1	1.7
Enterobacter aerogens	2	3.4
Acinetobacter baumani	3	5.2
Citrobacter koseri	1	1.7

DISCUSSION

It is generally acknowledged that neonatal sepsis remains an important diagnostic consideration in many infants. CRP rises in response to inflammation or tissue necrosis [8,9]. Although it is a nonspecific marker, it has repeatedly been shown to increase with bacterial sepsis &meningitis [10-12]. So, it is difficult to ignore the use of antibiotics during the the early neonatal period [13,14]. Some centers use serial CRP measurements to determine the length of antibiotic treatment for infants with culture-negative clinical sepsis. Serial CRP measurements can help monitor the response to treatment in infected neonates, determine the duration of antibiotic therapy, and recognize possible complications [15]. Several studies are currently assessing laboratory inflammatory markers in the diagnosis of neonatal sepsis. Recent studies have suggested the use of CRP biomarkers for the precocious diagnosis of neonatal sepsis. It has been shown that no combination of biomarkers performs well in diagnosing sepsis-like CRP alone. Current diagnostic tools are not so useful in the decision to initiate empiric antibiotic therapy in neonates suspected of sepsis but may help in the decision to discontinue antibiotic therapy. CRP helps decrease antibiotic use [16]. In the present study, 135 neonates who were suspected of neonatal septicemia were investigated. Our study showed 42% culture-positive neonatal sepsis. Blood cultures were found to be positive in 42% and negative in 58%. This correlates with the study conducted by Mythri et al [17]. *Staphylococcus aureus* 37% was the most common organism isolated followed by *Klebsiella pneumoniae* 24.1%. this is in correlation with the study conducted by Paulomi Dutta et al [18] and Karthikeyan et al [19]. In our study CRP estimation was done and compared with the results of blood culture and the

following results were obtained. CRP shows a sensitivity of 86% and specificity of 84%, positive predictive value of 84%, and negative predictive value of 86% and is in correlation with the study conducted by Santhakumar et al [20]. In our study 86.2% of culture-proven cases were CRP positive and 18% of culture-negative cases were CRP positive. 13.8% of culture-positive cases were CRP negative and 82% of culture-negative cases were CRP negative. The P value was < 0.001 which shows CRP was significant in our study.

CONCLUSION

Neonatal sepsis is a bloodstream infection occurring in infants under 28 days old. It is a serious medical condition that may turn life-threatening if not treated promptly for which an early diagnosis of sepsis is required. Blood culture reports may not be positive in all cases, and even if positive it may take 2 days to identify the organism. CRP is a rapid, highly sensitive, and specific test that can be used in the diagnosis of neonatal sepsis. An early diagnosis and the use of the appropriate antibiotics will be life-saving in the case of neonatal sepsis. Estimation of CRP can be done for early diagnosis and prompt treatment of neonatal sepsis. CRP cannot be considered as a single test for diagnosis but can be made as a part of a scoring system that will include hematological parameters along with clinical criteria. This will not only help in the early detection of neonatal sepsis but will also reduce antibiotic abuse and the delay in the initiation of therapy which may be life-saving to the patient.

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