ORIGINAL RESEARCH

Evaluation of CRP with blood culture in the diagnosis of neonatal septicemia in institutional deliveries predisposing with maternal risk factors

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ABSTRACT

Introduction: Neonatal sepsis is a blood infection that occurs in an infant younger than 90 days old. Early-onset sepsis is seen in the first week of life. Late onset sepsis occurs after 1 week through 3 months of age..It is one of leading cause of morbidity and mortality. Therefore, early diagnosis and provide good management prevent fatal outcome. C-reactive protein is an important biomarker that aids in the timely diagnosis of neonatal septicaemia. Aim: The present study was carried out to evaluate the CRP in the diagnosis of neonatal septicaemia with blood culture.

Materials and Methods: 221 neonates diagnosed with neonatal sepsis were included in the study over a period of 1year . Blood culture and semi- qualitative assessment of CRP was done for all the patients.

Results: Of the 221 neonates studied, 90 were blood culture positive while 131 were CRP positive. The sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of CRP were 86.7%, 43%, 45.5%, 85% and 69% 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.

Key Words: Septicemia, Preterm delivery, Chorioamnionitis,

Introduction

Neonatal sepsis is localized or systemic condition resulting from adverse reaction to thepresence of an infectious agent(s) or its toxin(s) that occurs in an infant younger than 90 days old. Early-onset sepsis is seen in the first week of life. Late onset sepsis occurs after 1 week through 3 months of age.It is one of leading cause of morbidity and mortality in our country. 1 Early-onset neonatal sepsis most often appears within 24 to 48 hours of birth. The baby gets the infection from the mother before or during delivery. The following increase an infant's risk of early-onset bacterial sepsis:

- GBS colonization during pregnancy
- Preterm delivery
- Water breaking (rupture of membranes) longer than 18 hours before birth
- Infection of the placenta tissues and amniotic fluid (chorioamnionitis).

Babies with late-onset neonatal sepsis are infected after delivery. The following increase an infant's risk for sepsis after delivery:

- Having a catheter in a blood vessel for a long time
- Staying in the hospital for an extended period of time

Clinical presentation of neonatal sepsis are non-specific, therefore, clinical diagnosis of sepsis is difficult and laboratory help isrequired. The gold standard for diagnosis of bacterial sepsisis blood

culture, may be primary or secondary to a focal infection (osteomyelitis, gastroenteritis, pyelonephritis, andendocarditis)3 4 An acute phase reactants produced by the liver it's a marker of inflammation known as C-reactive protein (CRP). This marker is commonly elevated during an infection but its is unspecific .These tests can be used to monitor response to therapy. 5 The half life of CRP is around 18-20 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.

Aims & Objective

Aim of the study was to

1. Evaluate CRP against blood culture in identifying of neonatal Sepsis.
2. Isolation of organism responsible for the disease.

Materials and Methods

An observational Study design was used to study on detection of CRP and blood culture in early diagnosis of neonatal sepsis. This is a hospital based study conducted in Department of Microbiology, in colleberation with Department of Obstetrics & Gynecology and Dept, of Pediatrics in Maharani Laxmi Bai Medical College, Jhansi, Uttar Pradesh, India

Inclusion criteria

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

Temperature instability, lethargy, feeding intolerance, respiratory distress, hemodynamic instability, convulsion, hypotonia, irritability, or bleeding diathesis were all signs of sepsis. Prematurity (37 weeks), low birth weight (2000 g), history of resuscitation at birth, rupture of membrane for more than 18 h (PROM), antepartum fever, foul-smelling liquor, and frequent (three or more) dirty per vaginal inspections were all considered risk factors for neonatal sepsis.

Exclusion criteria

- All newborn who had received antibiotics before collection of blood samples.
- Newborn who were admitted for other diseases i.e.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 determinations were performed on serum from capillary, venous or arterial blood,often as small as sample as 0.5ml of blood, and was estimated semi quantitatively by using the CRP latex kit manufactured by the RHELAX-CRP Tulip Diagnostics Pvt. Limited.6 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

221 neonates born in the institution and presented with maternal risk factors & neonates suspected for septicemia were included in the study, information on demographic data, blood culture andthe level of CRP was extracted.

Table 1: Demographic data of the study population.

Variables	**Sex**	
	Male(%)	Female (%)
Sepsis	57(25)	41(18)
Clinical sepsis	78(35)	45(20)
Total	135(61)	86(38)

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

Variables	Blood culture positive	Blood culture negative
CRP positive	87	61
CRP negative	14	59
Total	101	120

As shown in Table 2. 87(39%) neonates had sepsis with positive blood culture, and positive CRP level. 53(23%) neonates with clinical signs of sepsis but their blood culture was negative and positive CRP level. Culture positive but CRP negative samples are 7 (6%) & CRP negative & culture negative are 40(26%).

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

Test	Sensitivity	Specificity	PPV	NPV	Diagnostic
CRP	86.1%	43%	46.4%	86%	71%

Table: 4 Maternal and neonatal risk factors associated with neonatal sepsis.

S.no	Variables		Septicemia Present	CRP Positive
1.	Maternal age			
	a.) >35	98	34	32
	b.) <35	123	53	53
2.	Educational level			
	a.) Non educated	78	45	45
	b) Educated	143	42	42
3.	Parity			
	a.) >3	53	27	27
	b) <3	163	60	60

Table: 5 Mode of Birth with associated CRP & Blood Culture Findings

S.no	Variables			Blood Culture Positive	CRP Positive
1.	Vaginal delivaries	127		45	45
2.	Cesarean Section	56		26	26
3	Assisted Vaginal Delivaries				
	a.) Vaccum	22		07	07
	b.) Forceps	16		09	09
	Total	221		87	87

Discussion

The study group consist s of 135 males(61%)and86 females(39%). Males have been reported to be more likely than females to develop septicemia as revealed in this study. Fari di et al. also reported 66.67% males and 33.33% females out of 63 cases of neonatal septicemia. [6]And also similar to findings of other studies reported from India. [7,8] In our study, out of the 101 blood culture positive samples, 87(86.1%) were positive for CRP which was similar to studies done by Gowsami Y etal., [9]and Hisamuddin E et al., [10] In this study CRP reported to have Sensitivity of 86.1%,Specificity of 43%, Positive Predictive Value of 46.4%,Negative Predictive Value of 86% and diagnostic accuracy of 71% against blood culture these result are similar to studies done by Younis S et al.,[11-12],ZipurskyAet al.[13] The current study finding showed that premature rupture of membrane (PROM) was significantly associated with the risk of neonatal sepsis which in agreement with other study in Bangladesh and Nepal.[15–17] That is may explained by increased the risk of the chance of ascending infection from the birth canal into the amniotic fluid. The present study is in line with Adatara et al.[14] and Siakwa et al.,[15] they found parity (primiparous) significantly linked with the occurrence of neonatal sepsis, as parity increases neonatal sepsis decreases. It may be explained by prolonged delivery duration among primiparous compared to multiparous, which increases exposure to infection. Maternal age above 35 years was a predisposing risk factor for neonatal sepsis, which as reported by Mogollón et al.[16] study. Maternal age (more than 35 years) is linked to a higher risk of poor baby outcomes. It may explained by, maternal age greater than 35 years is linked to the occurrence of significant medical health problems related to pregnancy, such as gestational hypertension, diabetes, cardiac disease, congenital abnormalities and genetic problems, multiple

pregnancies, premature birth. Our study revealed that neonates gender significantly associated with neonatal sepsis, which in agreement with Adatara et al.[14] results which reported that, males neonates were at more risk compared to females. But our results inconsistent with a hospital based cross-sectional study in Nepal.[16]

Limitation

This study has several limitations, these limitationsisrelatedtotheobservationalnatureofthisres earchandlow sample size. Many factors such as gestational age , antibiotic use , third trimester follow up, other biomarkers like,alpha-fetoprotein,procalcitonin,CD64 & CD11b cell surface antigen, were not recorded. Such factors would be helpful to examine such association in depth.

Conclusion

The specificity and sensitivity of CRP against blood culture strengthen the use of this acute phase reactant 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.

Prematurity predispose to high risk of neonatal sepsis which is in agreement Yismaw et al.[17] and Manandhar et al.[18] results that is may due to underdeveloped innate immune responses as well as a lack of maternally produced, passively acquired antibodies.

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Conflict of Interest

None

Reference

1. Meherban S. Perinatal Infections. In: Care of the Newborn. New Delhi:Sagar Publication;2010.p.223–33.
2. Chauhan S, Vaghasia V, Chauhan B.C-reactive protein in arly diagnosis of neonatal septicemia. *Natl J Med Res*.2012;2(3):276–8.
3. Jaye DL, Waites KB. Clinical applications of C reactive protein in pediatrics .Pediatrc Infect DisJ.1997;16(8):735-47.
4. Reed AH, Henry RJ, Mason WB. Influencezo fstat istical method used on the resulting estimate of normal range. ClinicChemist.1971;17(4):275-84.
5. Lin DS, Huang SH, Lin CC, Tung YC, Huang TT, ChiuNC,etal.Urinarytractinfectioninfebrileinfantsyoung erthaneightweeksofage.Pediatr.2000;105(2):20.
6. Collee JG .Mackie and Mccartney Practical Medical Microbiology.14thed.Elsevier;1996.
7. Faridi MMA, Gupta P, Bhargava SK. Chest radiograph in neonatalsepsis.*IndianPediatr*.1972;29(7):871–4.
8. Sharma A, Kutty CV, Sabharwal U, Rathi S, Mohan H.D iagnosti cand prognostic role of CRP and ESR in neonatal septicemia.*IndianPediatr*.1993;30(3):347–50.
9. Rajend raprasad M, Basavaraj KN, Antony B, Patel 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 ealth*.2013;6(1):96.doi:10.4103/1755-6783.115204
10. Goswami Y, Jadav P, Rathod B. Study on significance of CRP estimation in early diagnosis of neonatal septicemia. *IJSR*.2014;3(8):388–90
11. Hisamud din E, Hisam A, Wahid S, Raza G. Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. *Pak J Med Sci*.2015;31(3):527–31.
12. Younis S, Sheikh MA, Raza AA. Raza Diagnostic Accuracy ofC-Reactive Protein in Neonatal Sepsis A.*J Bioresource Manage*.2014;1(1):33–42.
13. Zipursky A,Palko J, Milner R, Akenzua GI. The hematology of bacterial infections in premature infants. Pediatr.1976;57(6):839-53.
14. Adatara P, Afaya A, Salia SM, et al. Risk factors associated with neonatal sepsis: a case study at a specialist hospital in Ghana. *Sci World J* 2019; 2019: 1–8. [PMC free article] [PubMed] [Google Scholar]
15. Rafi MA, Miah MM, Wadood MA, et al. Risk factors and etiology of neonatal sepsis after hospital delivery: a case-control study in a tertiary care hospital of Rajshahi, Bangladesh. *PLoS One* 2020; 15(11): e0242275. [PMC free article] [PubMed] [Google Scholar]
16. Yadav NS, Sharma S, Chaudhary DK, et al. Bacteriological profile of neonatal sepsis and antibiotic susceptibility pattern of isolates admitted at Kanti Children's Hospital, Kathmandu, Nepal. *BMC Res Notes* 2018; 11(1): 301. [PMC free article] [PubMed] [Google Scholar]
17. Yismaw AE, Abebil TY, Biweta MA, et al. Proportion of neonatal sepsis and determinant factors among neonates admitted in University of Gondar comprehensive specialized hospital neonatal Intensive care unit Northwest Ethiopia 2017. *BMC Res Notes* 2019; 12(1): 1–5. [PMC free article] [PubMed] [Google Scholar]
18. Manandhar S, Amatya P, Ansari I, et al. Risk factors for the development of neonatal sepsis in a neonatal intensive care unit of a tertiary care hospital of Nepal. *BMC Infect Dis* 2021; 21(1): 1. [PMC free article] [PubMed] [Google Scholar]