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C-Reactive Protein (CRP) in Early Diagnosis of Neonatal Septicemia

Harshali H. Bendgude*, Charushila S. Halgarkar**

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Author Affiliation
* Resident, **Assistant Professor ,
Department of Microbiology,
S.R.T.R. Medical College,
Ambajogai, Dist.Beed,
Maharashtra, India.

Reprint Request
Charushila S. Halgarkar
Assistant Prpfessor, S R T R Medical college, Ambajagai, Dist, Beed.
Maharashtra 431517.
E-mail:
dr.charushilahalgarkar@gmail.com

Abstract

A study was conducted to evaluate C-reactive protein(CRP) as a screening tool for neonatal sepsis. CRP is one of the most studied and most used laboratory tests for neonatal sepsis. As part of the acute phase reaction to infection, it plays a central role in the humoral response to bacterial invasion. CRP is useful for monitoring the response to treatment and guiding antibiotic therapy. 75 neonates with risk factors and clinical features suggestive of CRP sepsis were selected as per operational definition and fulfilling the inclusion and exclusion criteria. Detailed physical examination was carried out. Blood sample for culture and CRP was taken from all neonates. CRP performed by semi quantitative latex agglutination method. Positive culture were the 'gold standard' against which the performance of CRP, abnormal white blood cell count (WBC) and platelet count were compared. Among 75 septic screens, 40 (53.33%) neonates had positive cultures. The sensitivity, specificity and positive predictive value of CRP was 92.5%, 89.74%, 90.24% respectively. Abnormal platelet count had lowest specificity(62.86%) and sensitivity(37.5%) among them. CRP assay is a valuable adjuvent in screening for neonatal sepsis, complementing clinical decision-making.

Keywords: C-Reactive Protein; Acute Phase Reactant; Neonatal Sepsis.

Introduction

Neonatal septicemia remains a significant cause of neonatal morbidity and mortality [1]. The most important risk factors for neonatal sepsis are prematurity, low birth weight, invasive medical procedures and prolonged hospitalization. Neonatal sepsis presents in diverse ways. It may present with fever, poor feeding, abdominal distention, diarrhea, tachypnea, oliguria, tachycardia or bradycardia, hypotension, irritability, seizures, bulging fontanelle or bleeding [2]. Although various hematological indices had been utilized to screen for sepsis, most were neither highly sensitive nor specific and were commonly affected by perinatal factors like maternal hypertension, asphyxia and hemolytic disease. C-reactive protein (CRP) has been used as an acute phase reactant to diagnose and follow the course of infection in neonates. Its advantages that its very low serum levels in normal infants, a rapid rise within 12 to 24 hours of sepsis and a large incremental increase thereafter [3]. C reactive protein production is a very early and sensitive response to most forms of microbial infection [4]. There is great interest in rapid diagnostic tests that are able to safely distinguish

infected from uninfected newborns, especially in the early phase of the disease [5,6]. Although blood culture is gold standard for diagnosis of neonatal sepsis and allows targeted antimicrobial therapy, its result may be delayed for up to 48 hours and it may yield negative results in many cases of septic shock. Also, contamination rates are high due to the technical difficulty of obtaining a sterile sample from small babies. On the other hand, unnecessary antibiotics increase the risk of drug side effects and contribute to emergence of microbial resistance [2].

Measurement of CRP allows rapid identification of infected patients, does not require a sterile sample, and a normal value may help in early exclusion of infection. Serial measurements of CRP have a prognostic value, and show the effectiveness of antibiotic therapy [2].

Materials and Methods

The present study was conducted in the Department of Microbiology, SRTR Medical College, Ambajogai from December 2014 to May 2015. 75 suspected septic neonates were included with the age group of first 28 days (4 weeks) of life in study.

For identification of suspected neonatal sepsis, two or more of the following clinical features were used: Respiratory and cardiovascular compromise, metabolic and neurologic changes. Exclusion criteria include, age at the time of admission is greater than 28 days, neonates who received antibiotic dose prior to septic setup and neonate diagnosed to have congenital malformation. Blood samples were drawn prior to administration of antibiotic therapy for blood culture by trained staff with all aseptic precaution in blood culture bottle and should be observed for 5 days for culture growth and after that they are reported as sterile, complete hemogram and routine biochemical investigations including glucose level [3].

CRP value was estimated by semi quantitative latex agglutination slide method with CRP kit manu-factured by BEACON Diagnostics Pvt. Ltd. as per instructions in the manual provided by company. Results are given as negative, 0.6mg/dl, 1.2mg/dl etc. by serial dilution of serum of patients. Total leukocyte count and indices were counted on a cell counter.

Results

During study period, total 75 neonates admitted in neonatal intensive care unit were studied. They were divided into 3 groups based on clinical features and blood culture reports- proven sepsis, probable sepsis, clinically sepsis.

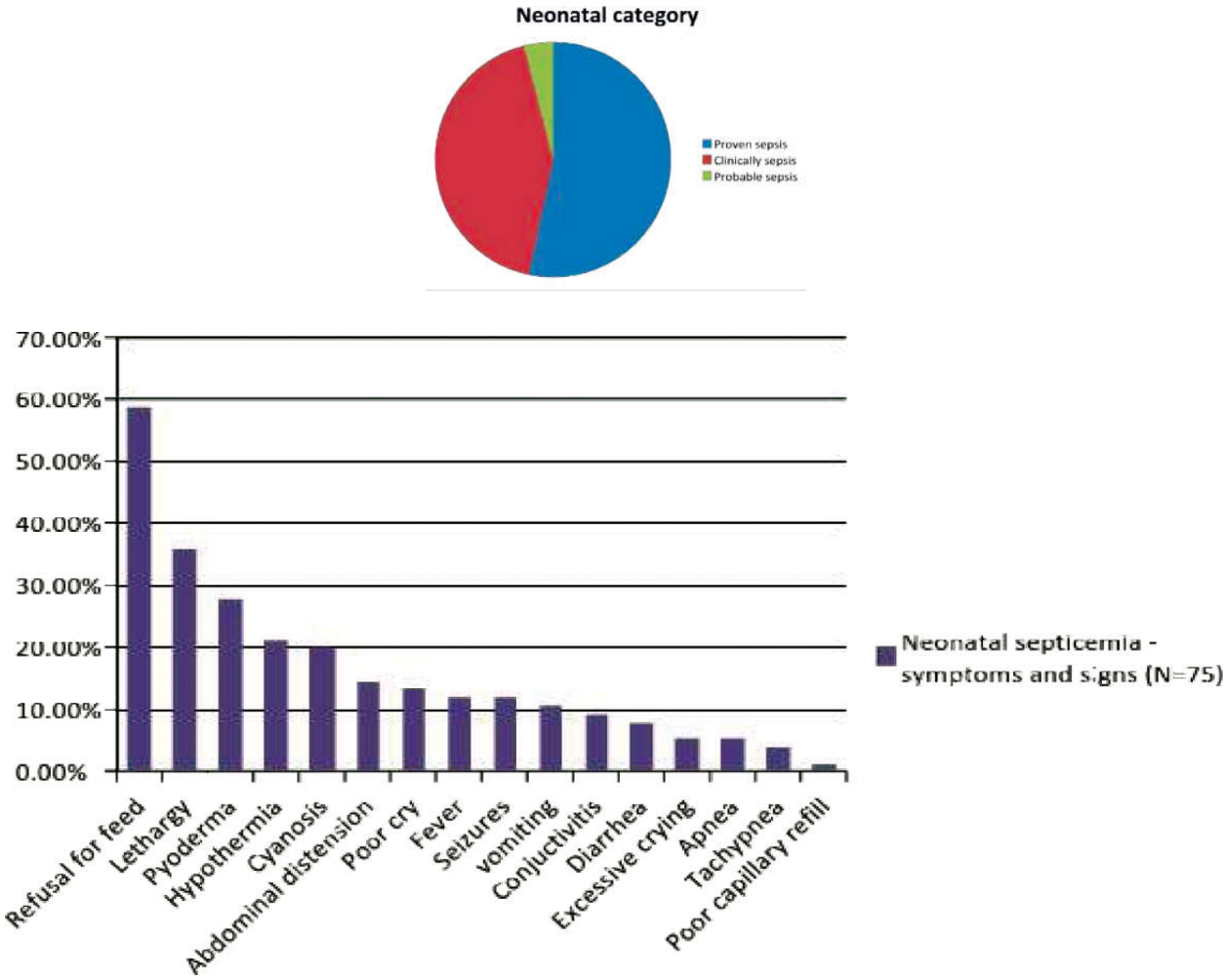
Table 1: Relation between birth weight and sepsis

Sr. No.	Neonatal category	Low birth weight (<2500 gm)	Normal birth weight (>2500 gm)
1	Proven sepsis (%)	72.5% (29/40)	27.5% (11/40)
2	Probable sepsis (%)	66.67% (2/3)	33.33% (1/3)
3	Clinically sepsis (%)	71.88% (23/32)	28.13% (9/32)

Table 2: Neonatal septicemia - symptoms and signs (N=75)

Symptoms*	N	(%)
Refusal for feed	44	58.67
Lethargy	27	36
Poor cry	10	13.33
Diarrhea	6	8
Vomiting	3	4
Fever	5	6.67
Excessive crying	2	2.67
Signs*	N	(%)
Pyoderma	21	28
Hypothermia	16	21.33
Cyanosis	15	20
Abdominal distension	11	14.67
Seizures	9	12
Conjunctivitis	7	9.33
Vomiting	5	6.67
Fever	4	5.33
Apnea	4	5.33
Tachypnea	3	4
Excessive crying	2	2.67
Poor capillary refill	1	1.33

*More than one sign or symptom were present together



Proven Sepsis: These are the patients among suspected neonatal sepsis in which blood culture confirms sepsis or there is definite evidence of localized infection.

Probable Sepsis: These are the suspected septic patient with CRP and/or hematological parameters suggestive of septicemia but negative culture.

Clinically Sepsis: These are the suspected septic patient with CRP <0.6 mg/dl, almost normal hematological parameters and sterile blood culture.

Out of 75 total cases 40 cases were proven sepsis, 3 cases have probable sepsis and rest of 32 cases having clinically sepsis. Study confirms that low birth weight babies are prone to develop neonatal sepsis as compared with normal birth weight.

Refusal for feed, lethargy and pyoderma were the main presenting features followed by poor cry, hypothermia and cyanosis. In this study, commonest organism for neonatal sepsis was coagulase negative Staphylococcus followed by *Klbsiella pneumonia, E.coli, Pseudomonas aeruginosa* and *Acinetobacter.*

Sensitivity of CRP, abnormal WBC Count, Platelet Count were 92.5%, 37.5%, 22.5% respectively. Specificity of CRP, abnormal WBC Count, Platelet Count were 89.74%, 62.86%, 42.86%. Positive predictive value of CRP, WBC Count, Platelet Count were 90.24%, 83.33%, 31.03%.

Table 3: Sensitivity, Specificity, Positive predictive value

Investigation	Sensitivity	Specificity	Positive predictive value
CRP >= 0.6mg/dl	92.5%	89.74%	90.24%
Abnormal WBC Count (<5000/ml or >20000/ml)	37.5%	62.86%	83.33%
Platelet Count (<1.51/cumm)	22.5%	42.86%	31.03%

Discussion

Neonatal septicemia is very common in the present Indian set-up. The disease has got high morbidity and mortality but it is unfortunate that none of laboratory parameters available till are rapid, specific, sensitive, cheap and simple enough to confirm the diagnosis and to asses the prognosis or therapeutic response in this condition. The present work was concluded to assess the efficacy and reliability of CRP in neonatal septicemia and values of the CRP as a tool of prognosis in neonatal septicemia. CRP production is very early and sensitive response to most form of microbial infections(7).

Comparison of the performance of CRP and abnormal hematology was thus made against well defined 'gold standard'. Majority of infecting organisms were Staphylococcus, which form a leading cause of nosocomial infections in the susceptible neonate. The calculation of both sensitivity and specificity depend on knowing which infants were already septic when CRP assay was performed. Platelet counts had the lowest sensitivity (22.5%) and lowest specificity (42.86%) among the indices. These indices render them less valuable than CRP for screening purpose, as abnormal hematology may be affected by non-septic processes like steroid treatment as part for chronic lung disease. Commonly used anti-inflammatory or immunosuppressive drugs including steroids, unless these drugs affect actively of underlying diseases do not affect the CRP response.

Sensitivity, specificity and positive predictive value for CRP were 92.5, 89.74 and 90.24% respectively; while for WBC Count, Platelet Count they were markedly less.

A good response of treatment was assessed by rapid fall in CRP level whereas, insignificant rise of CRP suggested that either the treatment was inadequate or some complications had developed.

Conclusion

C-reactive protein has high sensitivity and specificity for establishing the diagnosis of neonatal septicemia which is comparable with other indices. With the added benefit of early test result availability, it is highly recommendable that it should be used routinely in the evaluation of neonates with any features suggestive of sepsis to reliably include or exclude the diagnosis of neonatal septicemia.

CRP levels are useful in monitoring the course of neonatal septicemia. It provides an early indication of response of treatment. It can help in decision of initiating or discontinuing antibiotic therapy. The persistence or insignificant decline of serum CRP with treatment signifies about inadequate treatment or development of complications.

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