

Estimation of C-reactive protein in Neonates with Suspected Septicemia at Bhuj, Kutch, Gujarat, India- A Prospective Study



Medical Science

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ABSTRACT

Background and Aim: Despite the promising results for some diagnostic markers, current evidence suggests that none of them can consistently diagnose 100% of infected cases. Present study was performed with an aim to estimate C-reactive protein in Neonates with Suspected Septicemia at Bhuj, Kutch, Gujarat, India.

Material and Methods: This prospective study was conducted in the neonatal unit of general hospital from December 2014 to December 2015 at Department of Pediatrics, Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat, India. Approximately 5ml of blood was collected from the umbilical cord after clamping & cutting of the cord. About 48hrs after birth, approximately 2ml of blood was collected by venipuncture from the newborn. Samples were transported without any delay to the laboratory for CRP estimation. CRP value was calculated at birth. Newborn babies were observed for signs of sepsis for at least 48h. Clinical data were collected using a questionnaire

Results: The main presenting symptoms in child include the Refusal to feed, lethargy and poor cry. CRP was positive in 45 patients at admission; 25 of whom remained positive at 48 hours. Of the 85 neonates with suspected neonatal septicemia, CRP was ≤ 6 mg/L at 48 hours in 65 cases; 15 of these showed positive blood culture.

Conclusion: CRP is most widely & extensively used marker of neonatal sepsis. Intrapartum risk factors for early onset sepsis can cause elevation of cord & neonatal CRP levels in the absence of infection.

Introduction

C-reactive protein (CRP) is an annular (ring-shaped), pentameric protein found in blood plasma, whose levels rise in response to inflammation. It is an acute-phase protein of hepatic origin that increases following interleukin-6 secretion by macrophages and T cells. Its physiological role is to bind to lysophosphatidylcholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex.¹

CRP is synthesized by the liver in response to factors released by macrophages and fat cells (adipocytes).² It is a member of the pentraxin family of proteins. It is not related to C-peptide (insulin) or protein C (blood coagulation). C-reactive protein was the first pattern recognition receptor (PRR) to be identified.³

A high-sensitivity C-reactive protein (hs-CRP) test, which is more sensitive than a standard test, also can be used to evaluate your risk of developing coronary artery disease, a condition in which the arteries of your heart are narrowed. Coronary artery disease can eventually lead to a heart attack. A simple blood test measures C-reactive protein. Some researchers think that treating people with high C-reactive protein levels will lessen their risk of heart attack or stroke.⁴

Neonatal septicemia is a critical disease in neonatal period. Its incidence among live births is between 1 and 8 per 1000. Mortality of neonatal septicemia may be as high as 50% for infants who are not treated.⁵ The early diagnosis of neonatal sepsis presents a clinical dilemma. There is no reliable method to distinguish babies that are actually infected from those with suspected sepsis.

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-birth weight infants.⁶ 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 in the emergence of resistant strains.⁷

Laboratory sepsis markers represent a helpful tool in the evaluation of a child with clinical signs and complement the evaluation of a neonate with a potential infection. During the last decades efforts were done to improve laboratory sepsis diagnosis and a variety of the above mentioned markers and more were studied with different success.⁶ Despite the promising results for some of them current evidence suggests that none of them can consistently diagnose 100% of infected cases. C-reactive protein (CRP) is the most extensively acute phase reactant studied so far and despite the ongoing rise (and fall) of new infection markers it still remains the preferred index in many neonatal intensive care units.⁸

There is an abundance of studies evaluating laboratory markers in the diagnosis of neonatal sepsis. Despite the promising results for some diagnostic markers, current evidence suggests that none of them can consistently diagnose 100% of infected cases. 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.

Material & Methods

This prospective study was conducted in the neonatal unit of general hospital from December 2014 to December 2015 at Department of Pediatrics, Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat, India. Subjects included were all the babies who were evaluated and treated for suspected neonatal sepsis within the first 4 months of life. The standard unit protocol for management of infants with suspected sepsis was to obtain a complete blood count including differential white blood cell count and platelets, CRP and a blood culture, before antibiotic treatment. Serum CRP levels were obtained at the initial evaluation and at 24 hours later. The CRP was measured qualitative-

ly. Baby who had suffered birth asphyxia, very low birth weight <1500 grams, extremely premature <32 weeks gestation and neonates who already had taken antibiotics were excluded from the study. Positive blood culture was considered as the "Gold Standard" against which the performance of CRP was compared. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Approximately 5ml of blood was collected from the umbilical cord after clamping & cutting of the cord. About 48hrs after birth, approximately 2ml of blood was collected by venipuncture from the newborn. Samples were transported without any delay to the laboratory for CRP estimation. CRP was estimated by turbidometry method.

Data collection and analyses: CRP value was calculated at birth. Newborn babies were observed for signs of sepsis for at least 48h. 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 $p < 0.05$

Results:

Out of the 85 neonates who were admitted to the neonatal care unit with suspicion of septicemia, 25 weighed between 1000 g and 2000 g, 25 were 2001–3000 g and 45 were > 2500 g. In the present study the Table 1 shows demographic data of study samples. Table 2 shows the symptoms and signs present in the children. The main presenting symptoms include the Refusal to feed, lethargy and poor cry; these symptoms were followed by tachypnoea, fever and jaundice. Blood culture was found to be positive in 40 neonates, out of which 21 were Gram-positive and 19 were Gram-negative. All 21 isolated Gram-positive cases were *Staphylococcus aureus*, while among the Gram-negative cases, *E. coli* was found in 8, *Klebsiella pneumoniae* in 7 and *Pseudomonas aeruginosa* in 3. CRP was positive in 45 patients at admission; 25 of whom remained positive at 48 hours. Table 3 shows the CRP values at birth and blood culture findings in relation to CRP values. Of the 85 neonates with suspected neonatal septicemia, CRP was ≤ 6 mg/L at 48 hours in 65 cases; 15 of these showed positive blood culture

Table 1 Demographic data of neonates with suspected neonatal septicemia (n = 85)

Characteristics	No.
1. Sex	85
Male	55
Female	30
2. Gestational age	85
Preterm	35
Term	45
3. Residence	
Rural	63
Urban	22
4. Onset of Sepsis	
Early onset	22
Late onset	58

Table 2 Distribution of clinical signs and symptoms in neonates with suspected neonatal septicemia (n = 85)

Symptoms	No.
Refusal to feed	43
Lethargy	32
Poor cry	38
Fever	34
Vomiting	27
Diarrhea	10
Tachypnea	38
Jaundice	29

Cyanosis	16
Vomiting	27
Seizures	4

Table 3: Analysis of CRP in cord blood

Percentile	Mb/L CRP Value	Culture Positive
25 th	3.50	0
50 th	3.80	8
75 th	4.30	12
95 th	4.60	20

Discussion:

CRP was first described in 1930 by Tillet and Francis at Rockefeller University. They observed a precipitation reaction between serum from patients suffering acute pneumococcal pneumonia and the extracted polysaccharide fraction C from the pneumococcal cell wall. This reaction could not be observed when using serum of neither healthy controls nor the same pneumonia patients after they had recovered. In view of the fact that the polysaccharide fraction was a protein the C-reactive component in the serum was named C-reactive protein. By the 1950s CRP had been detected in more than 70 disorders including acute bacterial, viral, and other infections, as well as non-infectious diseases such as acute myocardial infarction, rheumatic disorders, and malignancies. All of these disorders of disparate etiology had in common the theme of inflammation and/or tissue injury.

The present study was designed to evaluate the usefulness of serum CRP levels as a screening test in guiding the duration of treatment in suspected neonatal septicemia. It is generally acknowledged that neonatal sepsis remains an important diagnostic consideration in many infants. CRP rises in response to inflammation or tissue necrosis. Although it is a nonspecific marker, it has repeatedly shown to increase with bacterial sepsis & meningitis. So it is difficult to ignore use of antibiotic during early neonatal period. The present study was designed to evaluate the normal pattern of CRP during initial days of birth in healthy neonates & to have a cut off value. In our study CRP value significantly increases in first 48hrs of life in healthy babies with a median value of 6.05mg/L & 95th percentile of 13.10mg/L. This shows wide variation of CRP value. CRP value can rise up to 13.10mg/L even if sepsis is not there.

Wasunna et al⁹ found no evidence that intraventricular haemorrhage was associated with elevation of CRP in neonates with no evidence of infection. Schouten- Van Meeteren et al¹⁰ demonstrated no significant difference between the CRP levels of neonates with perinatal asphyxia, prolonged rupture of membranes, hyperbilirubinemia or respiratory distress syndrome, and those of a control group. Xanthou et al¹¹ also found no difference between the CRP levels in neonates with asphyxia compared to controls. Gestational maturity & sex of baby did not influence the cord blood CRP or CRP at 48hrs. Chiesa et al showed that mean CRP concentration at birth was increased by a factor of 1.50 (95% CI, 1.32 to 2.03) if the 5-min Apgar score was 18 hours.

Conclusion

CRP is most widely & extensively used marker of neonatal sepsis. Intrapartum risk factors for early onset sepsis can cause elevation of cord & neonatal CRP levels in the absence of infection. Maternal & fetal factors should be kept in mind while considering CRP as an indicator of sepsis.

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