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# Study on Significance of C- Reactive Protein Estimation in Early Diagnosis of Neonatal Septicemia

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**Abstract:** ***Background:*** *Septicemia is major problem in neonates. Clinical criteria alone could not establish the diagnosis of neonatal septicemia. However, empirical treatment should not be delayed because of the high mortality. C- reactive protein, an acute phase protein , increases in inflammatory disorders and tissue injury.* ***Objectives:*** *1. To evaluate the diagnostic accuracy of CRP in neonatal sepsis METHOD: A prospective study included newborn infants, aged < 30 days and diagnosed with septicemia, who were admitted in neonatal intensive care unit at Sir T Hospital, Bhavnagar during 8- month period. This study included 200 cases in which 100 were culture proven septicemia and 100 normal newborn. Investigations for infection included CBC, blood culture and urine culture.* ***Results:*** *As per present study, sensitivity of Serum CRP is 91% and specificity being 94% with NPV of 91.2% suggesting its beneficial role in diagnosing sepsis. As per the study, Serum CRP was positive in 91% of culture proven sepsis and negative in 9% of cases. p value of the test applied for the statistical significance is < 0.05 which implies that the result is statistically significant for CRP.* ***Conclusion:*** *CRP is most commonly used laboratory test for neonatal bacterial infection and despite the continuing emergence of new infection markers it still plays a central role in the diagnosis of early onset neonatal septicemia.*

**Keywords:** C-reactive protein (CRP), Neonatal septicemia

## 1. Introduction

Neonatal period is essentially that period during which the baby is physiologically adjusting from an intrauterine to extrauterine environment. Neonatal septicemia remains an important cause of morbidity & mortality – even today – especially in developing countries[1].Neonatal septicemia refers to systemic bacterial infection in association with positive blood culture in first 30 days of life. Its incidence is 1-8/1000 live births with mortality of about 25%. It is one of the leading causes of death and over 80% of late neonatal deaths in hospitals are caused by septicemia. In developing countries-because of prevailing MCH services, unhygienic delivery practices, social customs & taboos, illiteracy, poverty, false believes & prejudices there are higher chances of infection in neonatal period. Neonatal septicemia is a disease that starts with usually minimal & nonspecific symptoms & poses a high risk of morbidity & mortality due to its fulminant course. The early and efficient diagnosis of neonatal bacterial sepsis still remains a difficult task. A number of laboratory tests have been used in attempts to facilitate the early diagnosis of septicemia. However there is not a single laboratory test that will identify with certainty about sepsis, nor is there any one technique that excludes bacterial disease. C–Reactive protein is simple rapid and easily available technique and is recommended for routine screening of all clinically suspected cases of neonatal septicemia. Moreover, CRP along with other hematological tests included in sepsis screen like total count, ANC, I: T ratio, platelets can help in definitive diagnosis of septicemia. Therefore, this study was selected to assess efficiency of CRP in early detection of neonatal septicemia.

## 2. Literature Survey

Neonatal septicemia is a clinical syndrome characterized by systemic signs of infection and accompanied by bacteremia in the first month of life.[2] W.A. Silverman in 1959 described septicemia as a clinical diagnosis of probable bacteremia with a serious clinical status with or without apparent focus of infection.[3] Bhakoo et al described neonatal septicemia as a persistent or recurrent bacteremia due to inability of body mechanism to localise the infection leading to an acute fulminant and for sometimes protracted illness with significant mortality.[4] The term neonatal sepsis encompasses diagnosis of septicemia, meningitis and pneumonia in newborn. According to national neonatal perinatal database, in India, the incidence of neonatal sepsis is 3.9% of all intramural births, out of which 20-30% develop meningitis.[5] Septicemia/meningitis is primary cause of neonatal death in 19.3% of all neonatal admissions in NICU. On the other hand, in developed countries, neonatal sepsis is high risk but low incidence disease. It is 1-8/1000 live births in developed countries compared to 30-40/1000 live births in developing countries.[6,7,8] Depending on the age of onset, neonatal sepsis is classified as follows:

**Table 1:**

| | Early Onset | Late Onset |
|---|---|---|
| Age | Birth – 72 hours | After 72 hours |
| Risk factors | Prematurity, Amnionitis Maternal infection or colonisation. | Prematurity |
| Source of organism | Maternal genital tract | Postnatal environment |
| Presentation | Fulminant Multisystem Pneumonia frequent | Slowly progressive Focal Meningitis frequent. |
| Mortality | 15-50% | 10-15% |

Early diagnosis and treatment of the newborn infant with suspected sepsis are essential to prevent severe and life threatening complications. In this era of multidrug resistance, it is mandatory to avoid unnecessary use of antibiotics to treat non-infected infants. Thus rapid diagnostic test(s) that differentiate infected from non-infected infants, particularly in the early newborn period, have the potential to make a significant impact on neonatal care. Various accurate and timely diagnosis of early onset neonatal sepsis remains challenging to the clinician and the laboratory. A test with a rapid turnaround time with 100% sensitivity rather than high specificity , which allows accurate diagnosis and appropriate antimicrobial treatment or which allows antibiotics to be safely withheld in non infected infants is desirable. Many potential markers (acute phase reactants ,cell surface markers, cytokines ) are not routinely available to the laboratory and most likely combinations of markers will ensure greater diagnostic accuracy. CRP is a hepatic glycoprotein and it has its name to the ability of this protein to precipitate pneumococcal C-polysaccharide in presence of calcium.[9]Its levels rise within 6-8 hours of inflammation. As infection is the most likely cause of inflammation in neonate, elevation of CRP is a useful marker of sepsis.[10] Its levels double atleast every 8 hours and reach a peak after about 48-72 hours. After effective treatment levels can fall as rapidly as 5-7 hour, Philipson[11] et al first described presence of CRP in bacterial infection in neonates.Felix et al, Hanson et al, and Seigel observed that CRP[12] increased in neonatal infections.

## 3. Materials and Methods

The present study is conducted at Department of pathology, Sir T Hospital, Bhavnagar. A study is reviewed and approved by Human Ethics Committee of Govt Medical College and Sir T Hospital, Bhavnagar. This study included 200 cases in which 100 were culture proven septicemia and 100 normal newborn. Neonates were admitted during 1st January to 30th august. Newborn with hyaline membrane disease, birth asphyxia, meconium aspiration syndrome were excluded. Detail antenatal, intranatal, thorough clinical examination and maturity scoring system was done in all newborn as per performa.

## 4. Results

**Table 2:** Comparison of CRP (> 0.6 mg/dl) in test group and control group

| | *Mean ± SD* | *p value* | *t value* |
|---|---|---|---|
| Test Group | 1.338±1.304 | <0.05 | 9.7 |
| Control Group | 0.054±0.2272 | | |

p value of the test applied for the statistical significance is coming < 0.05 which implies that the result is statistically significant for CRP.

**Table 3:** CRP in case of neonatal septicemia

| *CRP* | *No. of cases* | *Percentage* |
|---|---|---|
| Positive (> 0.6mg/dl) | 91 | 91% |
| Negative (< 0.6mg/dl) | 9 | 9% |

As per the study, Serum CRP was positive in 91% of culture proven sepsis and negative in 9% of cases.

**Table 4:** Performance of CRP

| *Test* | *Sensitivity ( % )* | *Specificity ( % )* | *Positive predictive value (%)* | *Negative predictive value (%)* |
|---|---|---|---|---|
| Present study | | | | |
| S CRP (>0.6 mg/dl) | 91 | 94 | 93.8 | 91.2 |
| K. Swarnkar et al[43] | | | | |
| S. CRP (>0.6 mg/dl) | 52.3 | 56 | 89 | 14.3 |

As per present study, sensitivity of Serum CRP is coming 91% and specificity being 94% with NPV of 91.2% suggesting its beneficial role in diagnosing sepsis.

**Table 5:** CRP and septicemia with reference to weight

| Weight | Total | Sepsis with CRP positive | Sepsis with CRP negative |
|---|---|---|---|
| <1 kg | 9 | 8% | 1% |
| 1.1 – 1.5 kg | 38 | 33% | 5% |
| 1.51 – 2 kg | 26 | 26% | 0% |
| >2 kg | 27 | 24% | 3% |

**Table 6:** Outcome of neonatal septicemia in relation to CRP

| | *No of cases* | *Survived* | *Expired* | *Percentage expired* |
|---|---|---|---|---|
| CRP positive | 91 | 76 | 16 | 16.48% |
| CRP Negative | 9 | 7 | 1 | 11% |

Above analysis suggests that mortality amongst CRP positive cases is few percentage higher but is not significant.

## 5. Conclusion

CRP is most commonly used laboratory test for neonatal bacterial infection and despite the continuing emergence of new infection markers it still plays a central role in the diagnosis of early onset neonatal septicemia. CRP has the advantage of extensive knowledge on its properties.

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