

Evaluation of C - reactive protein As a Biomarker for Early Detection of Clinically Suspected Cases of Neonatal Sepsis.

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Aim:

The aim of the study is to perform a rapid laboratory test for early detection of clinically suspected neonatal sepsis cases.

Objective(s):

1. Evaluate the usefulness of C-reactive protein as a biomarker for Early diagnosis of neonatal sepsis .
2. To correlate the presence of C-reactive protein in blood culture positive cases of clinically suspected neonatal sepsis.

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I. Introduction

Neonatal sepsis is a leading cause of neonatal mortality in India. Bacterial infection is a major cause of neonatal sepsis. This potentially fatal condition therefore demands early diagnosis to start empirical antimicrobial regime. C-reactive protein being an acute phase reactant is an useful biomarker to detect neonatal sepsis rapidly at an early stage [1,3]. The present study was performed to evaluate the usefulness of C-reactive protein as a neonatal sepsis marker.

II. Review of Literature

Neonatal sepsis is a major threat to newborns, aged less than a month. Because of delay of identification of sepsis in neonates, it leads to dilemma to begin proper therapy and that results in neonatal mortality. This can be dealt with early diagnosis and prompt therapeutic intervention [4].

C-reactive protein is an acute-phase protein produced by liver within 6 - 12 hours after onset of inflammation and tissue damage (acute-phase proteins are chemical mediators released in response to tissue necrosis). The name of the protein is derived from its pattern of recognition activity that is; C-reactive protein (CRP) binds to C-polysaccharide cell-wall component found on a variety of bacteria. This binding activates the complement system resulting into clearance of the microorganism.

The CRP latex agglutination test involves an easy & cost effective procedure. CRP level in serum <0.8 mg/dl is considered as negative result. A decrease in the CRP level in neonates diagnosed with sepsis, after a particular treatment period, indicates that the antibiotic treatment is sufficient. So, the CRP test also has a prognostic value [5]s.

Biomarkers other than C-reactive protein (CRP), such as procalcitonin, tumour-necrosis factor (TNF) - alpha, IL (interleukin) - 1, IL-6, IL-8 can also predict neonatal sepsis[6].

III. Materials and Methods

A total of 312 Neonates (age <30 days) with clinically suspected sepsis admitted to R. G. KAR Medical College (a tertiary medical college) in NICU (Neonatal Intensive Care Unit) and SNCU (Sick Newborn Care Unit), Kolkata, India were included in the present study. The study was performed over a period of six months from 1st December '15 to 31st May '16.

To detect the bacterial pathogen causing neonatal sepsis, two sets of blood samples were collected in brain heart infusion broth and aerobic culture were performed. Simultaneously, Latex agglutination test was done for the particular patient on the same day.

CRP detection was done by passive agglutination test using a uniform suspension of polystyrene latex particles coated with Anti-CRP antibodies. The reagent was standardized to detect CRP concentrations greater than 0.6 mg/dl.

Only serum was used for testing. From blood samples the serum was separated by centrifuging the

samples at 2000 rpm. for 2 minutes.

Serum samples were mixed with the latex reagent and allowed to react. If CRP concentration was greater than 0.8 mg/dl, a visible agglutination was observed and then two fold serial dilutions were performed. Concentration of CRP was calculated as follows:

$$\text{CRP (mg/dl)} = S \times D$$

Where, S = Sensitivity of the reagent i.e. 0.6 mg/dl.

D = Highest dilution of serum showing agglutination.

Data compilation and interpretation were performed as per standard statistical methods.

IV. Results

TABLE 1. No. of blood culture positive cases among suspected cases of neonatal sepsis.

Total no. of samples of neonates (age < 1 month)	Total no. of samples with positive blood culture
316	132

TABLE 2. No. of CRP positive cases among confirmed cases of blood culture for neonatal sepsis.

No. of samples with positive blood culture	No. of CRP test positive samples (CRP level >0.8 mg/dl)
132	126

Results were found to be statistically significant.

V. Discussion

Neonatal sepsis is one of the major causes of neonatal mortality in our country. Blood culture is an essential tool for diagnosis of neonatal sepsis. In the present study, 41.77% (132 / 316) of suspected cases of neonatal sepsis were culture positive. Patel D. et al has reported 32.59% of culture positivity in their study on neonatal sepsis [7]C-reactive protein (CRP) is an acute-phase reactant synthesized by the liver within six hours after the onset of inflammation and tissue damage [8]. Higher CRP level is associated with suspected neonatal sepsis [9]. In our study 95.45% (126 / 132) blood culture positive cases were CRP positive However, recently several workers have suggested that there are great variations in the sensitivity, specificity, and predictive values of CRP detection amongst acutely infected patients, which may compromise its diagnostic accuracy [10-12].

VI. Summary

Neonatal sepsis is a leading cause of neonatal mortality in India. The present study was performed to evaluate the usefulness of C-reactive protein as a neonatal sepsis marker. Correlation was done between the presence of C-reactive protein and blood culture positive cases of clinically suspected neonatal sepsis to suggest the former as an early diagnostic biomarker for neonatal sepsis.

A total of 312 Neonates (age <30 days) with clinically suspected sepsis admitted to R. G. KAR Medical College (a tertiary medical college) in NICU (Neonatal Intensive Care Unit) and SNCU (Sick Newborn Care Unit), Kolkata, India were included in the present study. The study was performed over a period of six months from 1st December 15 to 31st May '16. To detect the bacterial pathogen causing neonatal sepsis, two sets of blood samples were collected in brain heart infusion broth and aerobic culture were performed. Simultaneously, Latex agglutination test was done for the particular patient on the same day.

In the present study, 41.77% (132 / 316) of suspected cases of neonatal sepsis were culture positive. 95.45% (126 / 132) of blood culture positive cases were CRP positive. So, the latex agglutination test showed a good correlation with culture positive cases of suspected neonatal sepsis & so CRP may be used as a biomarker for early diagnosis of neonatal sepsis although findings of this study warrants further evaluation.

VII. Conclusion

The present study was conducted at R G Kar Medical College for a period of six months to evaluate the usefulness of C-reactive protein as a neonatal sepsis marker & to correlate the presence of C-reactive protein in blood culture positive cases of clinically suspected neonatal sepsis. It was found that 41.77% (132 / 316) of suspected cases of neonatal sepsis were culture positive & 95.45% (126 / 132) of blood culture positive cases were CRP positive. So, the latex agglutination test showed a good correlation with culture positive cases of suspected neonatal sepsis & so CRP can be used as a biomarker for early diagnosis of neonatal sepsis although findings of this study warrants further evaluation.

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