Original article:

Diagnostic Veracity of C- reactive protein in the early diagnosis of neonatal sepsis

1Dr.Hurakanwaljeet Singh, 2Dr. SharjaPhuljhele, 3Dr. OnkarKhandwal

1Assistant Professor , Department Of Pediatrics, Pt.J.N.M.Medical College, Raipur, 492001 Chhatishgarh, India
2Professor & Head , Work Place And address: Department Of Pediatrics ,Pt.J.N.M.Medical College, Raipur,492001 Chhatishgarh, India
3Professor, Work Place and address : Department Of Pediatrics ,Pt.J.N.M.Medical College, Raipur,492001 Chhatishgarh, India
Corresponding author : Dr.Hurakanwaljeet Singh

Abstract

Aim: This study was done to assess the role of C- reactive protein (CRP) in early diagnosis of neonatal sepsis.

Background: It is challenging to diagnose neonatal sepsis on the basis of clinical features. Therefore, various investigations are required in high-risk neonates. Usually, presumptive treatment is instituted while awaiting blood culture reports.

Material and Methods: This study was carried out in Neonatal Intensive Care Unit (NICU) of Department of Pediatrics, Pt. JNM Medical College, Raipur, Chhattishgarh, India over a period of one year from January 2014 to December 2014. Total 110 neonates of less than 4 weeks of age, who were suspected to have sepsis were included in to the study. CRP analysis was performed and compared to blood culture, which was considered as gold standard to diagnose neonatal sepsis.

Results: Out of 110 neonates, blood culture was positive in 63(57.2%) of the suspected sepsis patients. The Sensitivity, specificity, positive predictive value, and negative predictive value was found out to be 98.4%, 93.7%, 96.8%, and 97.8% respectively.

Conclusion: CRP level is useful supplementary test in screening the patients of neonatal sepsis and helps to form the clinical decision.

Key words: Neonatal Sepsis, Acute Phase Reactant, C- Reactive Protein, Blood Culture.

Introduction

Neonatal sepsis is a significant cause of neonatal mortality and morbidity. In developing countries, it accounts for 30-50% of all neonatal deaths. The clinical feature of neonatal sepsis are often nonspecific and subtle. The blood culture is gold standard to diagnose neonatal sepsis, although it takes up to 48 hours for the result. Therefore, other supportive diagnostic tests are done, such as, total leucocyte count (TLC), differential count and immature to TLC. Various markers have been evaluated for likely role in early diagnosis of neonatal sepsis such as procalcitonin (PCT), Interleukins (IL-6, IL-8, IL-10) and tumor necrosis factor α.3 C reactive protein (CRP) is an acute phase reactant produced by liver. Its level increases within 10-12 hours of bacterial infection. CRP is most commonly done and readily available diagnostic test for diagnosis of neonatal sepsis. Sequential CRP measurements help in guiding duration of antibiotic therapy.
Material and Methods
This hospital based prospective observational study was conducted in Neonatal Intensive care unit (NICU) of Pt. JNM Medical College, Raipur, Chhattisgarh from January 2014 to December 2015. Total 110 neonates of age less than four weeks were taken in to the study. All neonates were suspected to have neonatal sepsis. Two or more of the following clinical feature were used to diagnose sepsis: Tachycardia, tachypnea, prolonged capillary refill time, oligouria and temperature instability.

Blood samples were collected under strict aseptic precautions, prior to administration of antibiotics. About 2 ml of blood was collected for blood culture in a broth heart infusion bottle. For CRP measurement, 1 ml of blood was taken in plain vial. CRP was measured by latex agglutination assay and a value of more than 0.6 mg/dl was considered elevated. Exclusion criteria includes, neonates with birth weight of less than 1000gm, patients who received antibiotics before septic work up, neonates older than 28 days, babies with gross congenital malformation, inborn error of metabolism and underlying surgical condition.

Blood culture was taken as gold standard. Diagnostic accuracy of CRP is measured in terms of specificity, sensitivity, positive predictive value, and negative predictive value. It was calculated by using different parameters, True Positive (TP): if CRP is elevated and blood culture is positive, True Negative (TN): CRP is normal while blood culture is negative, False Positive (FP): CRP is increased but blood culture is negative, False Negative (FN): blood culture comes positive while CRP is not increased. Mean and standard deviation were calculated for quantitative variables and percentages were calculated for qualitative variables.

Results
A total of 110 neonates with suspicion of sepsis were studied. Among this, 59 (53.6%) were male and 51 (46.4%) were female. Mean weight of the patient was 2.51 ± 0.43 kg and mean age of the patient was 5.37 ± 1.72 days.

The CRP was elevated in 58.18% of the patients, whereas both blood culture positivity and increased level of CRP was found in 56.36% on suspected sepsis cases. Among 64 patients with raised CRP levels, 62 (96.88%) were blood culture positive thus were true positive (TP) whereas blood culture was negative in 2 (3.12%), thus were false positive (FP). About 46 (41.82%) neonates had normal CRP level, amongst which 45 (97.83%) patients were blood culture negative, thus were true negative (TN). Whereas 1 (2.17%) patient had positive blood culture and was false negative (FN). Specificity of CRP (TN/TN+FP) was found out to be 95.7% whereas sensitivity (TP/TP+FN) of the test was found out to be 98.4%. Positive predictive value (TP/TP+FP) was found to be 96.8% while negative predictive value (TN/TN+FN) was calculated to be 97.8%.

Among 110 neonates, blood culture was positive in 63 (57.2%) cases. Among the isolates, 56 (88.9%) were gram negative whereas 7 (11.1%) were gram positive. Most common isolate was Klebsiella pneumoniae in (50.8%) followed by Escherichia coli in (27%) Pseudomonas aeruginosa (11.1%), Staphylococcus aureus (6.3%), Coagulase negative staphylococci (CONS) (3.2%) and Enterococci (1.6%).

Graph 1.
Discussion

It is difficult to diagnose neonatal sepsis on the basis of clinical signs and symptoms. Therefore, it is necessary to start antibiotics in suspected cases of neonatal sepsis on clinical ground and risk factors, without waiting for blood culture results. The use of unnecessary antibiotics lead to increased risk of drug reaction, high health expenditure, and emergence of microbial resistance to antibiotics. The blood culture yield is often low and some times it is contaminated. Abnormal leucocyte count, absolute neutrophil count, platelet count, micro ESR, immature to total leucocyte ratio, and band cell count have low sensitivity and specificity to diagnose neonatal sepsis. Prompt diagnosis of neonatal sepsis will result in early institution of appropriate antibiotics which will help in reducing morbidity and mortality associated with neonatal sepsis. 6

In our study, 53.8% were males which is similar to the observation made by Zakariya et al.

The mean weight of the neonates was 2.51 ± 0.43 kg which is comparable to other studies 4.

The blood culture was positive in 57.1% of neonates which is analogous to the finding made by Prashant et al. where blood culture was positive in 50% of cases. Most common organism in our study was klebsiella aeroginosa which is congruous to other studies 7. Setal B reported that most common organism was Coagulase negative staphylococcus which is not similar to what we found in ours. This may be due to difference in geographical region.

In present study, sensitivity of CRP was found to be 98.4%, which is identical to the finding by Lee et al. In one series of 75 neonates, sensitivity was found to be 92.3%, which is lower than this study 8. Specificity of CRP was found to be 95.7% which is not same as other studies which have reported specificity of 85.7% 8 and 78% 9. Negative predictive value of CRP was found to be 97.8% which is slightly lower than other studies 9. The small difference in our observation may be due to difference in sample size.

<table>
<thead>
<tr>
<th>Organism isolated in blood culture</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klebsiella Pneumoniae</td>
<td>40%</td>
</tr>
<tr>
<td>Escherichia Coli</td>
<td>20%</td>
</tr>
<tr>
<td>Pseudomonas...</td>
<td>10%</td>
</tr>
<tr>
<td>Staphylococcus...</td>
<td>5%</td>
</tr>
<tr>
<td>CONS</td>
<td>5%</td>
</tr>
<tr>
<td>Enterococci</td>
<td>5%</td>
</tr>
</tbody>
</table>
CRP level increases gradually but steadily, during early phase of infection and tissue injury. Serial measurement increases the sensitivity of the test. The half life of CRP is 19 Hours. Alteration in the level of CRP specially declining level from the peak is often indicator of the response to treatment, and helps to decide period of antimicrobial therapy. The CRP is late but specific indicator of neonatal sepsis. Diagnostic accuracy is enhanced by combination of other markers, such as, soluble intercellular adhesion molecule-1, highly sensitive C-reactive protein, soluble E-selectin, and serum amyloid A. CRP level is also increased in autoimmune disorder, meconium aspiration current immunization, maternal pyrexia, prolonged rupture of membrane, chorioamnionitis, and surgery. The serum level of CRP increases more in gram negative organism sepsis than in gram positive organism.

**Conclusion**

None of the markers for neonatal sepsis diagnose it with 100% accuracy. CRP has high sensitivity and specificity in making diagnosis of neonatal sepsis. Because of the ease of availability, low cost and prompt result, it is highly recommended to do CRP level along with other supportive investigation in patients of neonatal sepsis.

**References**