

STUDY OF HAEMATOLOGICAL PARAMETERS AND ACUTE PHASE REACTANTS IN EARLY AND LATE ONSET NEONATAL SEPSIS IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Neonatal sepsis is defined as an invasive bacterial infection which occurs in the first 4 weeks of life. The incidence of neonatal sepsis varies from 11-24.5 /1000 live births in India. Hence alternative fast diagnostic test of serological markers enabling earlier detection of neonatal sepsis might be beneficial. **Materials and Methods:** This cross sectional study was done in Department of Pathology, SKMCH, Muzaffarpur, Bihar. The study period duration was 12 months from January 2018 to December 2019. Informed consent was obtained from the parents. Ethical committee clearance was obtained before the study. Blood was obtained from each neonate prior to the commencement of the antibiotics for the sepsis work up, which included haematological parameters like the micro ESR, total leukocytes count, the absolute neutrophil count (ANC), the immature neutrophils to total neutrophil count ratio (I/T ratio), blood culture and C-reactive protein (CRP) estimation. **Result:** Total 90 cases of neonates were diagnosed with neonatal sepsis. Out 90 cases of infants 48 were male and 42 were female. Total 90 cases who were eligible for the study were classified into two groups viz., probable sepsis 55(61.11%) and proven sepsis 35(38.88%). The results revealed that most of the neonates belong to EOS group. Total 59% of the cases were seen EOS and 41% cases were seen in LOS group. Gender distribution reveals that males constitute 53.33 % are females constitute 46.66%. **Conclusion:** Our study suggests that CRP could be used as a preferred marker in evaluating a neonate for sepsis. CRP along with other laboratory tests and physical examination will be useful in identifying infants with a low probability of infection.

INTRODUCTION

Neonatal sepsis is defined as an invasive bacterial infection which occurs in the first 4 weeks of life. The incidence of neonatal sepsis varies from 11-24.5 /1000 live births in India.^[1] The clinical manifestation of sepsis in newborn infants is usually non-specific. Neonatal sepsis is classified into early onset neonatal sepsis (EONS) and late onset neonatal sepsis (LONS) according to time of onset of signs and symptoms. Early onset neonatal sepsis is defined as the onset of signs and symptoms within the first 72 hours of life. In late onset neonatal sepsis (LONS) clinical signs and symptoms occurs after 72 hours of age. Because of the high morbidity and mortality which is associated with neonatal sepsis.^[2] antibiotic therapy is commenced soon after the onset of the symptoms before the diagnosis is confirmed by blood culture. Initial diagnosis of neonatal sepsis based on clinical signs and symptoms which are nonspecific as other non-infective condition like

aspiration, asphyxia and metabolic disorders may also present with similar signs mimicking sepsis. The problem of symptom wise false positivity in diagnosing sepsis resulting in unwarranted initiation of empirical antibiotic therapy may lead to development of drug resistance, prolonged hospital stay, increased treatment cost and the separation of the neonates from their mothers.^[3] The gold standard method for diagnosis of neonatal sepsis is isolation of microorganism from blood. It is time consuming procedure usually takes more than three days for complete result and also requires well equipped laboratory and trained personnel for better results.^[4] Hence alternative fast diagnostic test of serological markers enabling earlier detection of neonatal sepsis might be beneficial.

MATERIALS AND METHODS

This cross sectional study was done in Department of Pathology, SKMCH, Muzaffarpur, Bihar. The

study period duration was 12 months from January 2018 to December 2019. Informed consent was obtained from the parents. Ethical committee clearance was obtained before the study.

Inclusion Criteria

Infants who were admitted to this NICU with signs which is suggestive of sepsis, or those who developed signs of sepsis while they were in the ward.

Exclusion Criteria

Early death, more than one episode of infection, which were on antibiotic, aspiration syndrome. Blood was obtained from each neonate prior to the commencement of the antibiotics for the sepsis work up, which included hematological parameters like the micro ESR, total leukocytes count, the absolute neutrophil count (ANC), the immature neutrophils to total neutrophil count ratio (I/T ratio), blood culture and C-reactive protein (CRP) estimation.

RESULTS

Total 90 cases of neonates were diagnosed with neonatal sepsis. Out 90 cases of infants 48 were male and 42 were female. Total 90 cases who were eligible for the study were classified into two groups viz., probable sepsis 55(61.11%) and proven sepsis 35(38.88%). The results revealed that most of the neonates belong to EOS group. Total 59% of the cases were seen EOS and 41% cases were seen in LOS group. Gender distribution reveals that males constitute 53.33 % are females constitute 46.66%. Out of the blood samples collected from 90 participants, 35cases were found to be positive for blood culture. The organisms isolated were Klebsiella pneumoniae in 12 neonates (34.28%), Escherichia coli in 8 neonates (22.85%), Pseudomonas aeruginosa in 4 neonates (11.42%), Klebsiella oxytoca in 7neonates (20%), and Staphylococcus aureus in 4 neonates (11.42%). Klebsiella spp was found to be the most common organism in both early and late onset sepsis [Figure 1].

Table 1: Relation between haematological parameters with sepsis groups

Sepsis group Test	Probable sepsis (n=55)	Proven sepsis (n=35)
Elevated micro ESR	18	10
I:T Ratio	10	7
Abnormal WBC count	27	18
Total	55	35

The hematological parameters in the sepsis groups were compared and presented in Table 1. The total WBC count was normal in 17 out of 35 cultures in the proven sepsis cases. An elevated micro ESR level was observed in 18 of probable sepsis and in 10of proven sepsis neonate. An abnormal I/T ratio were observed in 10 probable sepsis and in 7 proven sepsis cases. An abnormal WBC count observed in 27 probable sepsis and in 18 proven sepsis.

Table 2: Relation between CRP with sepsis groups

Sepsis group CRP	Probable sepsis (n=55)	Proven sepsis (n=35)
Positive	26(47.27%)	21(60%)
Negative	29(52.72%)	14 (40%)
Total	55	35

In the present study 60% of the neonates with proven sepsis had raised CRP levels of more than 6 mg/lit. About 47.27 % of the neonates with suspected sepsis had raised CRP levels [Table 2].

Table 2: Comparison of CRP, haematological sepsis score and blood culture

Parameter	No. of Positive (Out of 90)	No. of positive (Out of 35)
CRP	47	21
Elevated Micro ESR	28	10
I:T Ratio	17	7
Abnormal WBC count	45	18
Total	137	56

The sensitivity of CRP in predicting sepsis was 47 out of 90 cases (52.22%). Total 28(31.11%) cases out of 90 was resulted positive in Elevated Micro ESR, total 17 (18.88%) out of 90 was resulted positive in I: T Ratioand total 45 (50%)cases out of 90 was resulted positive in Abnormal WBC count [Table 3].

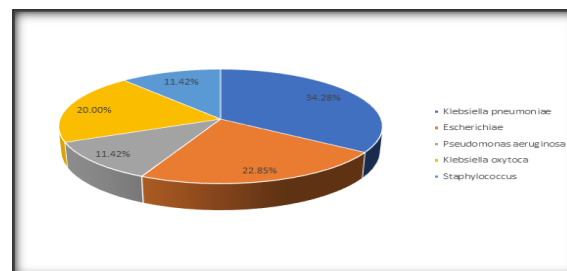


Figure 1: Organism in blood culture

Out of the blood samples collected from 90 participants, 35 cases were found to be positive for blood culture. The organisms isolated were *Klebsiella pneumoniae* in 12 neonates (34.28%), *Escherichia coli* in 8 neonates (22.85%), *Pseudomonas aeruginosa* in 4 neonates (11.42%), *Klebsiella oxytoca* in 7 neonates (20%), and *Staphylococcus aureus* in 4 neonates (11.42%). *Klebsiella* spp was found to be the most common organism in both early and late onset sepsis [Figure 1].

DISCUSSION

The neonatal sepsis is a leading cause of mortality and morbidity in neonates. Early diagnosis of neonatal sepsis helps the clinician in instituting antibiotic therapy at the earliest, thereby reducing the mortality rates in the neonates.^[4] The positive blood culture is the only definitive method of confirming a case of sepsis. Culture and sensitivity tests require a minimum period of 48 hours which is a precious time in making decisions in the treatment of sepsis in new borns. The readily achievable complete blood count and the leukocyte differential assays have a relatively poor specificity for diagnosing sepsis.^[5] Therefore, the need persists for improved diagnostic indicators of neonatal sepsis. There is no single reliable test for the early definite diagnosis of neonatal sepsis, and therefore, there is a continuing search for a new infection marker. The C- reactive protein has been the most analyzed parameter for the detection of bacterial infections for years.^[6,7] The current study shows that among 90 suspected sepsis cases, blood culture was positive in 35 cases (38.88%) and this result shows more valueas compare to the result of 30.8% blood culture positive cases.^[12] In contrast low positivity of blood culture had been reported.^[13] which revealed 16.2% of blood culture positivity in 120 samples.^[14] In the present study the total WBC count was abnormal in 18 out of 35 (51.42%) proven sepsis cases. An elevated micro ESR level was observed in 10 proven sepsis neonates. An abnormal I/T ratio were observed in 7 proven sepsis cases. In a similar study by.^[17,18,19] the total WBC count was abnormal in only one out of 13 cases with proven sepsis. An abnormal I/T ratio were observed only in two cases. Similar results was observed in study.^[8, 9,10,11] The sensitivity of CRP in predicting sepsis was 47 out of 90 cases (52.22 %). Total 28(31.11%) cases out of 90 was resulted positive in Elevated Micro ESR, total 17 (18.88%) out of 90 was resulted positive in I: T Ratio and total 45 (50%)cases out of 90 was resulted positive in Abnormal WBC count (Table 3). This is different to the results of other studies.^[25] showed that C-reactive protein had higher sensitivity and specificity of 92.9% and 85%.^[20,21,22,23,24] in their study said that C-reactive protein was best single marker with an overall sensitivity and specificity of 88% and 84%.^[15,16] The marked difference of result among studies evaluating C-reactive protein as useful marker can be explained by non-availability of universally

acceptable definition of neonatal sepsis, difference in reference range values and environmental influence on the results in different setups.^[26,27] The test for estimation of CRP is easy to perform and results will be available in minutes. Furthermore, it can also be used effectively in neonates who had already used antibiotics.

CONCLUSION

CRP is one of the most widely available, most studied, and most used laboratory tests for neonatal bacterial infection and despite the continuing emergence of new markers of infection, it still plays a central role in the diagnosis of neonatal sepsis. Although blood culture is still a gold standard test in diagnosing sepsis, its main drawback is its delayed result, more chances of contamination, high cost and non-availability in most peripheral setups in our country. Our study suggests that CRP could be used as a preferred marker in evaluating a neonate for sepsis. CRP along with other laboratory tests and physical examination will be useful in identifying infants with a low probability of infection.

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