

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

Afsara Khatoon¹, Drishti², Sujit Kumar Mandal³

^{1,2}Senior Resident, Department of Pathology, Govt. Medical College, Purnea, Bihar, India

³Assistant Professor, Department of Pathology, Govt. Medical College, Purnea, Bihar, India

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Corresponding Author:

Dr. Drishti,

Email: 0029drishti@gmail.com

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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. The gold standard method for diagnosis of neonatal sepsis is isolation of microorganism from blood. 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, Govt. Medical College, Purnea, Bihar. The study period duration was 12 months from March 2022 to February 2023. 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 neutrophil to total neutrophil count ratio (I/T ratio), blood culture and C-reactive protein (CRP) estimation. **Result:** Total 95 cases of neonates were diagnosed with neonatal sepsis .Out 80 cases of infants 43 was male and 37 were female. Total 80 cases who were eligible for the study were classified into two groups viz., probable sepsis 50(62.5%) and proven sepsis 30(37.5%). 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 2 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. **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, Govt. Medical College, Purnea, Bihar. The study period duration was 12 months from March 2022 to February 2023. 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 haematological parameters like the micro ESR, total leukocytes count, the absolute neutrophil count (ANC), the immature neutrophil to total neutrophil count ratio (I/T ratio), blood culture and C-reactive protein (CRP) estimation.

RESULTS

Total 95 cases of neonates were diagnosed with neonatal sepsis .Out 80 cases of infants 43 was male and 37 were female. Total 80 cases who were eligible for the study were classified into two groups viz., probable sepsis 50(62.5%) and proven sepsis 30(37.5). 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 80 participants, 30 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 2 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].

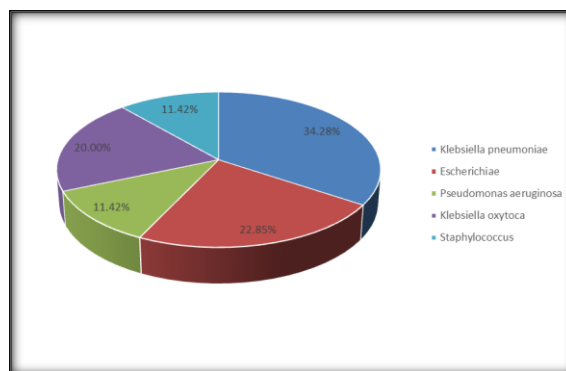


Figure 1: Organism in blood culture

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Table 1: Relation between haematological parameters with sepsis groups

Sepsis group Test	Probable sepsis (n=50)	Proven sepsis (n=30)
Elevated micro ESR	16	9
I:T Ratio	10	6
Abnormal WBC count	24	15
Total	50	30

The haematological parameters in the sepsis groups were compared and presented in [Table 1]. The total WBC count was normal in 16 out of 30 cultures in the proven sepsis cases. An elevated micro ESR level was observed in 18 of probable sepsis and in 10 of 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	23(46.27%)	18(60%)
Negative	27(54.72%)	12 (40%)
Total	50	30

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 3: Comparison of CRP, haematological sepsis score and blood culture

Parameter	No. of Positive (Out of 80)	No. of positive (Out of 30)
CRP	46	20
Elevated Micro ESR	27	9
I:T Ratio	16	6
Abnormal WBC count	44	17
Total	133	52

The sensitivity of CRP in predicting sepsis was 46 out of 80 cases (57.5%). Total 27(33.75%) cases out of 80 was resulted positive in Elevated Micro ESR , total 16 (17.88%) out of 80 was resulted positive in I:T Ratio and total 44 (53%)cases out of 80 was resulted positive in Abnormal WBC count [Table 3].

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 born. 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 80 suspected sepsis cases, blood culture was positive in 30 cases (37.5%) and this result shows more values 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 17 out of 30 (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 12 cases with proven sepsis. An abnormal I/T ratio were observed only in two cases. Similar results were observed in study.^[8,9,10,11]

The sensitivity of CRP in predicting sepsis was 46 out of 80 cases (57 %). Total 27(33.75%) cases out of 80 was resulted positive in Elevated Micro ESR , total 16 (17.88%) out of 80 was resulted positive in I:T Ratio and total 44 (53%)cases out of 80 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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