

# Diagnostic Performance of Various Laboratory Parameters for Neonatal Sepsis in a Tertiary Care Hospital.

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## ABSTRACT

**Background:** Infections commonly cause morbidity and mortality in neonates despite various advances. It accounts for more than a million annual deaths worldwide, more cases from the developing countries have been reported. Around 2% of the fetuses worldwide acquire in utero infection, whereas 10% fetuses get infected in the first month. **Introduction:** Sepsis is rampant in our socioeconomic conditions. Any infection in the neonate can be fatal. It is a challenge for all the health care providers worldwide to reduce the morbidity & mortality caused by neonatal sepsis by a timely diagnosis and appropriate intervention. Early diagnosis of neonatal septicemia helps the clinician in instituting antibiotics therapy at the earliest during its progressive course thereby reducing morbidity and mortality in neonates and also helps in avoiding unnecessary treatment of a non-infected neonate. In the present study an attempt has been made to study the biochemical profile of neonatal sepsis and in evaluation of various biochemical markers to diagnose presence of septicemia. **Methods:** This study included 100 neonates presenting to a tertiary care NICU for presence of sepsis. After examining for risk factors and systemic illness, intravenous sampling was done for screening of sepsis after written informed consent. Diagnostic performance of various laboratory parameters involved was calculated after evaluating their statistical significance. **Results:** All the routine markers are found to be highly specific in diagnosis of neonatal sepsis. The specificity of TLC, ANC, I/T RATIO, MICRO ESR and CRP was found out to be 87.8%, 79.7% 77% 85.1% and 83.7% respectively. MICRO ESR and CRP show a better sensitivity and positive predictive value than other markers in addition to high specificity and negative predictive value. CRP is found to have better sensitivity (73.1%), positive predictive value (61.3%) and negative predictive value (90%) than other used routine markers. **Conclusion:** ?

**Keywords:** Neonatal sepsis, Absolute Neutrophil Count, Total Leucocyte Count, Immature/Total neutrophil ratio, Micro ESR, C- Reactive Protein.

## INTRODUCTION

Infections commonly cause morbidity and mortality in neonates despite various advances. It accounts for more than a million annual deaths worldwide, more cases from the developing countries have been reported. Around 2% of the fetuses worldwide acquire in utero infection, whereas 10% fetuses get infected in the first month.<sup>[1]</sup>

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Epidemiological studies suggest that the incidence, pattern, outcome as well as mortality of neonatal sepsis occurring in developing world, is variably different from that of the developed world.<sup>[2-4]</sup> The most commonly isolated organism from North

America and Europe is Group B Streptococci and other gram positive organisms whereas gram negative infections are constantly being reported from South East Asian subcontinent and other tropical countries.<sup>[5,6]</sup> However it is interesting to note that, over time the epidemiological pattern of neonatal infections changes entirely within a specified geographical area.<sup>[7,8]</sup> Diagnosis and management is complicated by other noninfectious conditions that coexist.<sup>[9]</sup> Manifestations vary clinically in different newborns, depending upon the time of exposure, virulence of the organism involved and immunity of the subject. Newborns may manifest with subclinical infection, localized or systemic infection, and may rarely develop congenital syndromes following in utero insult. Maternal infection is the prime source of transplacental infection. It remains undiagnosed frequently which is attributed to casual attitude and non specific symptoms. Various etiologic agents have been identified in causing neonatal infections

including bacteria, fungi, viruses, protozoa and even mycoplasma. Despite recent advances, newborns are at a continuous risk for acquiring infection in hospital environment. Depending on different ages at onset of infection, neonatal sepsis is categorized as early- onset infection and late- onset infection. Early onset sepsis is acquired before or during child birth which suggests vertical infection i.e from mother to child. Newborn present from birth to 72 hours of life. Late onset sepsis is acquired after child birth from community or the hospital and presentation is after 72 hours of life.<sup>[1]</sup> Very late onset sepsis may present after 1 month of life in premature, low birth weight infants who require prolonged NICU care. Neonatal infections often present as life threatening emergencies, therefore any delay in the diagnosis, evaluation and management can result in unwanted mortality. Surveillance is thus needed to know about the common organism and its antibiotic sensitivity pattern in a specified area. On suspecting sepsis clinically it needs to be evaluated further by laboratory studies. Blood culture is the gold standard for diagnosing sepsis and should be performed in every suspected case prior starting antibiotics. Total leukocyte count with differential cell count, absolute neutrophil count and band cell percentage out of total neutrophils (Immature: total neutrophil ratio) are other tests but they are not sensitive if measured shortly after presentation,<sup>[10]</sup> and it takes about 72 hours for the micro-organism to be isolated from culture studies. Contaminated reports often alter the diagnosis. Therefore starting antibiotics empirically on suspicion of sepsis can reduce mortality as there is around 50% mortality of untreated neonatal infections worldwide.<sup>[11]</sup> Any test that is more sensitive will help in the early diagnosis of sepsis and unnecessary treatment will be avoided. There are various non infective condition that can mimic sepsis just after child birth. Meconium aspiration syndrome, transient tachypnea of newborn (TTN), inborn errors of metabolism (IEM), cyanotic congenital heart disease, intracranial hemorrhage are some of them. Other conditions occurring after few hours which may mimic sepsis are necrotizing enterocolitis, bowel obstruction and metabolic conditions (IEM).

To avoid any delay and considering financial constraints of patients rapid and minimum investigations should only be undertaken. Various leukocyte index studies and acute phase reactants are identified to aid the diagnosis of sepsis. One of the acute phase reactant is CRP and its synthesis takes place in liver. It is a nonspecific marker of inflammation and tissue necrosis. CRP value is elevated in bacterial sepsis and meningitis however a single reading of CRP is neither sensitive nor specific in aiding diagnosis of infection. Series of readings are required at birth, after 12 hrs, 24 hrs and further for managing infants who are at risk for sepsis. Many centers use CRP levels for estimation

of duration of antibiotic therapy and NICU stay. It is also seen that CRP alone is of little value in early onset infections but is considered to be more specific with a much better positive predictive value in late onset infections. This is due to the fact that many cytokines are involved to direct the transcription of CRP.<sup>[12]</sup> Many authors have therefore cited to carefully order CRP estimation in illness lasting less than 12 hours. Currently no single test is adequately sensitive or specific in prediction of which at risk subject will develop culture proven sepsis.

**Aims And Objectives:** Comparison of diagnostic performance of various laboratory parameters for neonatal sepsis in a tertiary care hospital.

## MATERIALS AND METHODS

This study included 100 neonates presenting to a tertiary care NICU for presence of sepsis. After examining for risk factors and systemic illness, intravenous sampling was done for screening of sepsis after written informed consent. Diagnostic performance of various laboratory parameters involved was calculated after evaluating their statistical significance.

### Inclusion criteria

All newborn admitted to NICU with clinical suspicion of sepsis.

### Exclusion criteria

Newborn with gross/apparent congenital anomalies, Parents &/ or attendants not giving written informed consent.

## RESULTS

**Table 1: Comparison of Diagnostic performance of various laboratory parameters.**

Variable s	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV)	Negative predictive value (NPV) (%)
TLC	26.9	87.8	43.7	77.3
ANC	30.8	79.7	34.7	76.6
I:T Ratio	38.5	77	37.0	78
micro-ESR	65.4	85.1	60.7	87.5
CRP	73.1	83.7	61.3	90

As depicted in [Table 1], On comparing the diagnostic performance of sepsis screen following observations were noted:

All the routine markers are found to be highly specific in diagnosis of neonatal sepsis. The specificity of TLC, ANC, I/T RATIO, MICRO ESR and CRP are 87.8%, 79.7% 77% 85.1% and 83.7% respectively.

MICRO ESR and CRP show a better sensitivity and positive predictive value than other markers in

addition to high specificity and negative predictive value.

CRP is found to have better sensitivity (73.1%), positive predictive value (61.3%) and negative predictive value (90%) than other used routine markers.

## DISCUSSION

### Diagnostic performance of laboratory markers

- A. Total leucocyte count (TLC): In our study, TLC showed 26.9% sensitivity, 87.8% specificity, 43.7% PPV and 77.3% NPV respectively [Table 1]. The result is comparable to Anwer et al.<sup>[13]</sup> In their study on rapid identification of neonatal sepsis, they found out 14.28% sensitivity, 93.8% specificity, 60% PPV and 60% NPV respectively for the parameter TLC.
- B. Absolute neutrophil Count (ANC): ANC showed 30.77% sensitivity, 79.7% specificity, 34.7% PPV and 76.6% NPV respectively [Table 1]. Several studies considering ANC (Polin et al<sup>14</sup> (2005) and Varsha et al (2003)) have published similar results.<sup>[15]</sup>
- C. I/T Ratio: I/T ratio showed 38.5% sensitivity, 77% specificity, 37% PPV and 78% NPV respectively [Table 1]. Many variations among different researches are observed for this parameter which can be explained by infection severity, neonatal age, decreased sensitivity if test is undertaken after first week of life, criteria for diagnosis (different among different studies) and different sampling time which differed from study to study.<sup>[16,17]</sup>
- D. Micro-ESR: Micro-ESR showed 65.4% sensitivity, 85.1% specificity, 60.7% PPV and 87.5% NPV of present study comparable to results by other researchers.<sup>[9,16,17]</sup> Variations observed are because of the notion that a minimum of 4 hours are necessary in development of the hematological response after infection onset, thus rendering a different result if blood samples are collected or worked up before this period.<sup>[17]</sup>
- E. C- Reactive Protein (CRP): Positive value for CRP was taken as > 10mg/l. CRP showed 73.08% Sensitivity, 83.7% specificity, 61.3% PPV and 90% NPV respectively [Table 1]. Results of present study were quite similar to those by Gerdes et. al.<sup>[18]</sup>

## CONCLUSION

The gold standard to diagnose neonatal sepsis is demonstration of microorganism by blood culture. Routine blood tests like total leucocyte count, absolute neutrophil count, micro-ESR and I/T ratio although having high specificity have low sensitivity, thus can exclude sepsis but not much beneficial in diagnosing neonatal sepsis. CRP has better sensitivity and hence can detect most cases of neonatal sepsis and better negative predictive value, which will lead to decrease in the number of patients treated unnecessarily. Currently, no single test can be considered as an ideal diagnostic test. So, new

laboratory methods for early diagnosis of neonatal sepsis are needed.

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