

Original Research Article

## **Evaluation of Indirect markers of Sepsis for the Diagnosis of Neonatal Septicaemia**

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**Abstract:** Neonatal sepsis is a serious condition resulting from the effects of severe bacterial infection in the first month of life. The clinical diagnosis of neonatal sepsis is difficult due to nonspecific signs and symptoms. The objective is to evaluate the role of different indirect markers in the early diagnosis of neonatal septicaemia. A Prospective cross sectional study had been done in Kalinga Institute of Medical science, Bhubaneswar, India. Blood was collected for estimation of indirect sepsis markers like, Total platelet count, Total leukocyte count, C-reactive protein(CRP), Immature to total neutrophil ratio(I:T) & micro-ESR & culture sensitivity. Sensitivity, specificity positive predictive value of different test was done. Sensitivity of two tests combination was better than the individual test. CRP+I: T ratio was most sensitive & specific parameter. Three test combinations have no added advantage than two test combination. It was concluded that even if two Indirect Sepsis Markers are positive the neonates should be presumed to have probable sepsis and early intervention should be started immediately to prevent the morbidity and mortality of neonatal sepsis.

**Keywords:** Blood culture, early diagnosis, indirect markers, neonatal sepsis

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**INTRODUCTION:**

Early diagnosis of neonatal septicaemia is very difficult as the clinical characteristics are non-specific [1]. Globally, sepsis is still one of the major causes of morbidity and mortality, in spite of many advances in medical health system [2]. More than 40% of under-five deaths globally occur in the neonatal period, resulting in 3.1 million newborn deaths each year [3]. Incidence of neonatal sepsis in India was 30/1000 live births and is not changed much over the past decade with a mortality of 30% to 65% [4]. Neonatal sepsis is defined as syndrome complex characterized by signs of generalized bacterial infection and documented by positive blood culture during first month of life [5].

Though the gold standard for diagnosing neonatal sepsis is positive blood culture, it requires at least 48-72 hrs for confirming the diagnosis. Again blood cultures are not always positive and facilities for culture are not available in most peripheral health facilities in developing countries [6]. Therapy cannot wait this long in a critically sick neonate. So to diagnose early in neonatal sepsis and rationalize therapy certain indirect early markers of infection like CRP,  $\mu$  ESR, TLC, presence of toxic granules and band cell in neutrophils and I: T ratio have been identified.

Therefore this study has been undertaken with a purpose to evaluate the role of the different indirect markers in the early diagnosis of neonatal septicaemia.

**MATERIALS AND METHODS:****Study type**

A hospital based Prospective cross-sectional study was done in Neonatal Intensive Care Unit of Kalinga Institute of Medical science, Bhubaneswar over a period of one year from June 2014 to July 2015 after approval from the institutional ethics committee.

**Inclusion criteria**

All the newborns less than 28 days, admitted to NICU with feature of refusal to feed, lethargy, vomiting, convulsion, fever with or without history of premature rupture of membrane, foul smelling liquor, and maternal fever were included in this study after taking proper informed consent from the parent.

**Exclusion criteria**

Newborn having other diseases like Neonatal jaundice, birth asphyxia, feeding difficulty or congenital infection without any feature of sepsis, newborn already on antibiotic therapy, & parents refused to give consent were excluded from the study.

**Procedure**

Total 256 newborns were enrolled for this study by consecutive sampling method. Blood was collected for estimation of haemoglobin, total platelet count (TPC), total leukocyte count (TLC), differential count(DC), C-reactive protein(CRP), Band cell count, Immature to total neutrophil ratio(I:T) & micro-ESR. For blood culture with proper aseptic measure, 2 ml of blood was drawn and send to the laboratory for inoculation in to the suitable culture medium.

**Data Analysis**

After data collection, all the data were entered into the excel sheet for analysis of proportion, sensitivity, specificity and positive predictive value (PPV) of different parameter both in single and in combination.

**OBSERVATION:**

Out of 258 cases, 76 cases were blood culture positive & labelled as proven sepsis. 108 cases had blood culture negative but others relevant investigation positive & were levelled as probable sepsis. 74 cases

had neither blood culture was positive nor any other relevant investigation and levelled as no sepsis or control group.

It was found majorities of cases of Group-A was in the first week of life (57.7%). (Table-1) Sepsis was more common in male M: F = 1.7:1.(Table-2) Sensitivity and specificity value in all indirect parameter showed CRP had both maximum sensitivity (81%) & specificity (94%) while TLC had minimum sensitivity (23%) & micro-ESR had minimum specificity (70%). (Table-4) Positive predictive value was highest for TPC (91%) and lowest for TLC (66%). (Table-4) Among two tests combination, CRP+I: T had both highest sensitivity (92%) & highest specificity (81%) in proven sepsis group while CRP+I: T had both highest sensitivity (89.4%) & highest specificity (81%) in probable sepsis group.(Table-5) When three tests were combined, a combination of micro-ESR, CRP and I: T ratio had highest sensitivity (92%) & specificity (84%) while micro-ESR+CRP+Toxic had the lowest sensitivity (84%) and specificity (50%).(Table-6)

**Table 1: Age distribution in different groups in percentage**

Age in days	Group-A (Proven-sepsis) N=76	Group-B (Probable-sepsis) N=108	Group-C (Control-group) N=74
0-7	57.7	52.7	62.5
8-14	23	28.9	18.7
15-21	15.4	13.1	6.2
22-28	3.8	5.3	12.6

**Table 2: sex distribution in different age group in percentage**

Sex	Group-A (proven sepsis)	Group-B (probable sepsis)	Group-C (control group)
Male	65.4	68.4	56.2
Female	34.6	31.6	43.8

**Table 3: Results of parameter studied in percentage**

Parameter	Group-A (proven sepsis)	Group-B (probable sepsis)	Group-C (control group)
CRP	80	60	6
micro ESR( > 10 mm in 1 <sup>st</sup> hr)	69	68	31
I:T ratio(>0.2)	69	60	12
TLC(<5000)	23	57	18
Presence of Toxic granulation	57	68	19
TPC(<100,000/cmm)	42	28	6

**Table 4: Sensitivity, Specificity and PPV of individual test**

test	Sensitivity %	Specificity%	PPV%
CRP	81	94	95
Micro ESR	69	70	78
I:T ratio	69	88	90
TLC	23	81	66
Toxic granulation	58	81	84
TPC	42	93.7	91

**Table 5: two test combination of proven sepsis**

test	Sensitivity%	Specificity%
CRP+ micro ESR	84	69
CRP+ I:T ratio	92	81
CRP+ Toxic granulation	80	75
micro ESR+ I:T ratio	80	62.5
micro ESR+ Toxic granulation	84	50
I:T ratio + Toxic granulation	80	68

**Table 6: three test combination of sepsis proven group**

test	Sensitivity%	Specificity%
CRP+ micro ESR+ I:T ratio	92	62.5
CRP+ micro ESR+ Toxic granulation	84	50

**DISCUSSION:**

The early onset cases in proven sepsis and probable sepsis group were 57.7% and 52.7% respectively in our study. Namdeo *et al.*; reported 45.8% early onset cases were in proven sepsis group [7]. It was observed that neonatal sepsis is more common in male infants both in proven sepsis group (65.4%) and probable sepsis group (68.4%) also supported by similar finding by other studies (74%) Sharma A *et al.*; [8] & (73.17%) Harendra M *et al.*; [9]. In our study CRP had a maximum sensitivity (81%) & specificity (94%). Mondal S also found high sensitivity of CRP (84%) in his study [10]. In a systematic review conducted by Fowlie P *et al.*; it was found the sensitivity and specificity of CRP in diagnosing early onset sepsis were ranges from 43–90% and 70–78% respectively [11].

We found a low sensitivity (69%) and specificity (70%) of micro-ESR compared to CRP while Mondal S found m-ESR had the highest specificity (94%) contrast to our finding [10]. I: T ratio was found as 69% sensitivity, 88% specificity, & PPV of 78% in our study while I/T ratio had the maximum specificity of 87.5% had the maximum positive

predictive value of 42.85% in another study [9]. TLC count was found to be very low sensitive 23% but high specificity (81%) in our study. Also, similar finding had shown by Gerdes *et al.*; 29% sensitivity and 91% specificity [12]. TPC was found to be 42% sensitive and 93.7% specific in our study. Similar presentation also supported by many researchers [12].

We found that two test combinations had better sensitivity than the single test, also specificity and positive predictive value increased when the results of these tests were considered together. The combination of CRP+ I/T ratio were the best combination for screening and diagnosis of sepsis, similar to finding by Mondal *et al.*; [10]. The second best combination was m-ESR and CRP, followed by m-ESR and I/T ratio. Three test combinations had no obvious advantage than two test combination. In our present study sensitivity value of CRP+I: T ratio was 92% while CRP+ micro ESR+ I: T ratio had same 92%.

**CONCLUSION:**

The accurate diagnosis of neonatal sepsis is often difficult as the sign and symptoms are nonspecific. But early diagnosis and prompt treatment

is necessary for reducing neonatal morbidity & mortality. Combinations of two tests are better than the individual test. CRP+I: T ratio was most sensitive & specific parameter found in this study. Three test combinations have no added advantage than two test combination. So it was concluded that even if two Indirect Sepsis Markers are positive the neonates should be presumed to have probable sepsis and early intervention should be started immediately to prevent the morbidity and mortality of neonatal sepsis.

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