

**Original article**

**Early diagnosis of neonatal sepsis in primary health care unit**

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**Abstract:**

**Aim:** The aim of the study is to find out the role of common haematological parameters along with micro-ESR, I/T ratio in diagnosis of neonatal sepsis for initiating early management.

**Methods:** This is a descriptive study consisting of 35 neonates admitted at a sophisticated institute with clinical suspicion of septicaemia along with 40 neonates as the comparison group. The neonatal haematological parameters including total leucocytes count, absolute neutrophil count, immature neutrophil count, I/T ratio, platelet count were measured in all the neonates. Micro-ESR was measured as a bed side test. CRP was also measured using slide agglutination method and the results were compared with turbidimetric method. Blood culture was done as a gold standard test for sepsis. Micro-ESR more than age of the patient in days +3 mm in 1st hour was considered significant for sepsis. I/T ratio more than or equal to 0.2 was considered positive for sepsis.

**Results:** The study revealed that micro-ESR and I/T ratio were significantly higher ( $p < 0.001$ ) in suspected cases of septicaemia as compared to the neonates in the comparison group. Sensitivity and specificity of micro-ESR were 87.09% and 75.0% respectively. Sensitivity and specificity of I/T ratio were 93.54% and 95% respectively.

**Conclusion:** Micro-ESR and I/T ratio can be used effectively as cheap and simple tests to screen for septicaemia in neonate which is possible even in a primary health care centre.

**Keywords:** neonatal sepsis; micro-ESR; I/T ratio

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**Introduction**

Neonates are newborn child within first 28 days of life<sup>1</sup>. Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteraemia within neonatal period<sup>2</sup>. Common causes of neonatal mortality in India are preterm birth(31%), severe infection (25%) , Birth asphyxia(23%), Congenital defects(7%), Neonatal tetanus(3%), Diarrheal diseases(3%), Others (9%)<sup>1</sup>. Sepsis is one of the common causes of neonatal mortality. Nearly 72.8% of Indian population live in rural areas where the health facilities are not up to the mark<sup>3</sup>. In primary health care setting sophisticated

investigations are not available. In most of the cases of septicaemia clinical features are vague and non-specific. For which sometimes treatable condition of septicaemia becomes aggravated.

If we can make an early diagnosis of possible infection in neonates by simple investigations feasible at Primary health care setting, early initiation of therapy will be possible. Blood culture the is the gold standard for definitive diagnosis of septicaemia<sup>4</sup>. But the pitfalls of blood culture are (i) it takes several days, thus delaying initiation of treatment of suspected cases (ii) most of Primary health care units have no infrastructure for Blood culture (iii )

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sometimes, patients are advised oral antibiotics on clinical suspicion of sepsis during outdoor visit before they get admitted or before taking blood samples for culture and the culture report is dubious. The definitive diagnosis of septicaemia is made by a positive blood culture, which requires a minimum of 48-72 hours, yields a positive result in only 10-60% of cases<sup>5</sup>.

During sepsis there are changes in various blood parameters. One of these is immature to total neutrophil ratio (I/T ratio). The positive predictive value of I/T ratio ranges from 71%-100% and the negative predictive value from 57%-63%. The normal I/T ratio is less than 0.2. The specificity of I/T ranges from 0.75-0.91 and the sensitivity ranges from 0.22-0.47( R). Micro-ESR is also a cheap parameter and easy to perform as a bedside test. I/T ratio more than 0.2 was considered positive for sepsis. Sensitivity and specificity of micro-ESR were 63.3% and 60% respectively. Combination of micro-ESR and I/T ratio showed high sensitivity (80%) and specificity (70%). So, studying the I/T ratio & micro-ESR may provide a simple, cost effective tool as a screening test for early diagnosis of neonatal sepsis. Keeping the challenge of septicemia in mind, we evaluated effectiveness of I/T (immature to total neutrophil) ratio & micro-ESR to predict diagnosis of neonatal sepsis in this study. The main idea and objectives of this study are (i) to diagnose neonatal sepsis with the help of routine blood examination, (ii) to detect whether I/T ratio & micro-ESR can predict neonatal sepsis with reasonably good accuracy and (iii) to confirm the role of I/T ratio & micro-ESR in diagnosis of neonatal sepsis.

### **Materials and methods**

This descriptive study was conducted in the Baby Nursery, Department of Paediatric Medicine, Burdwan Medical College & Hospital, Burdwan, West Bengal over a period of 6 months from July 2010 to January 2011 after obtaining the requisite permission of the Ethical Committee of the hospital. Newborn babies with signs and symptoms of septicaemia aged 0 to 28 days were included in this study. The study included 35 neonates who were suspected to have severe sepsis. 40 neonates without sign symptoms of severe infection and admitted for other causes like jaundice, birth asphyxia etc. were taken as a comparison group. Each neonate was examined by a paediatrician who recorded the signs and symptoms of the neonate, predisposing perinatal factors and the clinical assessment of the neonate. Patients with positive blood culture were categorized

as definite sepsis. Patients with negative blood culture but abnormal clinical & laboratory reports suggestive of sepsis were categorized as probable sepsis & those showing no signs of sepsis were categorized as control group. Relevant histories also were taken. When at least three of the following high risk factors were present, the baby was considered to be infected.

1. very low birth weight (<2000 g)/ preterm baby
2. febrile illness in mother during or within two weeks of delivery
3. foul-smelling/meconium stained liquor amnii
4. prolonged rupture of membranes (>12 hrs)
5. >3 vaginal examination in labor
6. Prolonged labor (>24 hours)
7. Birth asphyxia

Laboratory investigations like CRP (both latex fixation slide & turbid metric method) and blood culture were done. Micro-ESR was determined bedside in heparinised capillary tubes. It requires a small amount of blood which can be obtained easily by heel stick and this test is easy to perform. A normal micro-ESR had been considered as 'day of life plus 3 mm/hr' to maximum of 15 mm/hr. Peripheral blood smears were stained by Leishman method. Total leukocyte count (TLC), total neutrophil count (T), differential leukocytes count (DLC), immature neutrophil count (I) (including metamyelocyte and band form) were performed. Degenerative changes & toxic granules in the neutrophils were noted. I/T (immature to total neutrophil) ratio was calculated by dividing the total immature count by total neutrophil count (including both mature and immature neutrophil count). I/T ratio more than or equal to 0.2 was considered positive for sepsis<sup>5</sup>. Total leukocyte count and platelet count were done by automated cell counter as well as compared by visual inspection of the stained slide and manual method.

### **Inclusion criteria for cases:**

- 1) Neonates with provisional diagnosis of sepsis

### **Exclusion criteria for cases:**

- 1) Neonates who have received any antimicrobial therapy prior to taking blood samples for blood culture
- 2) Neonates whose parents did not give consent to be included in the study.
- 3) Neonatal tetanus cases
- 4) Neonates with diarrhea
- 5) Neonates with congenital diseases

### **Inclusion criteria for comparison group:**

Neonates with a provisional diagnosis other than sepsis

**Exclusion criteria for comparison group:**

Neonates whose parents did not give consent to be included in the study including the exclusion criteria mentioned above

The statistical analyses were performed using SPSS version 17.0 for windows.

**Results**

In this study we found that among 35 neonates suspected of sepsis, blood culture is positive in 13(42%) neonates. Males (n=17, 55%) were more commonly affected. Mean values of different parameters are given in Table 1.

cases.

There was no significant difference between the TLC (p=0.326) and ANC (p=0.695) between the cases and comparison group. TLC range varies over a wide range both among cases (3200 – 31000/mm<sup>3</sup>) and in the comparison group (4900-15000/mm<sup>3</sup>). Sensitivity of TLC was only 41.93% and NPV of 67.27%. Variation in ANC values is much more in cases (1152-17670/mm<sup>3</sup>) in contrast to the comparison group (3436-7252/mm<sup>3</sup>).

Platelet count in the cases varies over a wide range with minimum value of 11000/mm<sup>3</sup> to maximum

**Table I–Laboratory and Clinical Characteristics of Cases and comparison group**

Parameters	Mean values	
	Cases Mean±s.d.	Comparison group Mean ±s.d.
1. Age (days)	7.81±6.22	8.25±1.53
2. TLC! (per mm <sup>3</sup> )	10754.84±8117	10410±2141.50
3. Platelet (per mm <sup>3</sup> )	102716.13±47866.95	199775±25452.3
4. Immature cells (%)	18.90±5.46	4.92±4.18
5. ANC*(per mm <sup>3</sup> )	4979.23±4235.89	4882.52±854.60
6. Micro-ESR (mm/hour)	15.84±6.57	5.32±1.87
7. I/T ratio	0.26±0.08	0.087±0.04
8. Neutrophil(%)	33.74±11.38	42.30±6.5
9. CRP (mg/L)	19.32 ±13.0	3.7 ±1.36

! TLC – Total Leukocyte Count

\* ANC – Absolute Neutrophil Count

I/T ratio and immature cells were significantly higher in cases as compared to the controls (P <0.001), correlating well with indicators of sepsis. Micro-ESR was also significantly higher in cases as compared to the controls (P < 0.001). Sensitivity and specificity of micro-ESR were 87.09% and 75 % respectively. Its positive predictive value (PPV) & negative predictive value (NPV) were 72.975% and 88.23% respectively. Sensitivity and specificity of I/T ratio were 93.54% and 95% respectively while its PPV was 93.54% and NPV was 95%.

Values of sensitivity & specificity of CRP (latex agglutination method) were 83.87% & 90% respectively. PPV of CRP was 86.66% and NPV of CRP was 87.80%.

Percentage of immature cells was between 7-30 among the cases while among the comparison group it was mostly less than 10 except in 2 false positive

value of 204000/mm<sup>3</sup> while in the comparison group it is in the normal range (165000-260000/mm<sup>3</sup>). Thrombocytopenia (<1,50,000/mm<sup>3</sup>)<sup>8</sup> has a sensitivity of 75% and NPV 83%.

**Discussion**

Neonatal sepsis is a life-threatening yet treatable condition. Non- infectious disorders may sometimes produce haematological changes similar to those seen with infection. Confirmation by blood culture is a time consuming process and also has restricted availability. Also the clinical features of sepsis are sometimes non-specific. Combining both, haematological alterations in appropriate clinical background may help us to screen infected newborns. These neonates pose a diagnostic and therapeutic dilemma because fatal infections have been reported in the presence of negative blood cultures<sup>5</sup>. The present study evaluates the usefulness of the I/T

ratio & micro- ESR as an early indicator of neonatal septicaemia. This study was undertaken because these are simple bed-side and cost effective tests which can be done even if the baby has had antibiotics. Also early marker I/T ratio is almost as efficient as IL-6<sup>6</sup>. Though blood culture is a gold standard for diagnosing neonatal sepsis, facilities for performing it are not readily available in a resource poor setting whereas I/T ratio & micro- ESR are available in all setups.

Among the different parameters analysed, we found that an elevated I:T ratio was the most reliable indicator of sepsis. This was similar to the observations of many authors<sup>7,8,9</sup>. In present study the reliability of IT ratio was compared with blood culture and the CRP was measured as it is a marker of inflammation. Total leukocyte count (TLC) is of little clinical use in the diagnosis of neonatal infection because of wide variation in values.

Neutropenia (<1000/mm<sup>3</sup>) has been more common in association with sepsis, compared with neutrophilia, probably because of increased adherence to altered endothelial cells and utilization at the site of infection. But in this study, we found minimum neutrophil count to be 1132/mm<sup>3</sup>.

A shift to the left in differential white cell count with a raised immature neutrophil count has been documented in patients with bacterial infection. Degenerative changes in neutrophils like toxic granules have already been documented<sup>10</sup>. In this

study, 26 cases (83%) show presence of toxic granules whereas only 4(10%) of the neonates in the comparison group showed the same.

Among the neonatal hematological parameters, the association of low platelet count with neonatal systemic infection is significant. Neonates with sepsis develop thrombocytopenia, possibly because of disseminated intravascular coagulation (DIC) and the damaging effects of endotoxin on platelets. In this study we found thrombocytopenia in 23 out of 31 cases (74%).

Considering high mortality and morbidity associated with sepsis, tests with high sensitivity and NPV are most desirable because all infants with sepsis have to be identified. In this study, we found micro-ESR and I/T ratio to have high sensitivity and NPV. So these tests can be used as good screening tools.

### **Conclusion**

The I/T ratio and routine haematological profile are simple, quick and cost effective tool in the early diagnosis of neonatal sepsis but its sensitivity is unsatisfactory. Therefore, it cannot provide a guideline for antibiotic therapy. In combination, micro-ESR, I/T ratio and CRP had reasonably good sensitivity. They are also simple, quick and cost effective tools in the early diagnosis of neonatal sepsis and can be done in primary health care unit and treatment can be started early which reduces the neonatal mortality.

**Conflict of interest:** None

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