

# Role of Micro- ESR in the Evaluation of Suspected Sepsis in Neonates

Ghaliyah Aziz Kutty<sup>1</sup>, Anitha S Prabhu<sup>2</sup>, Sahana K S<sup>3</sup>

<sup>1</sup>Final Year Post Graduate, Department of Pediatrics, Yenepoya Medical College Hospital, Mangalore, Karnataka, India

<sup>2</sup>Professor, Department of Pediatrics, Yenepoya Medical College Hospital, Mangalore, Karnataka, India

<sup>3</sup>Associate Professor, Department of Pediatrics, Yenepoya Medical College Hospital, Mangalore, Karnataka, India

**Abstract:** ***Aims:** In a developing country like India, where proper medical care and obstetrical facilities are still scarce in the rural areas, Neonatal sepsis is a major cause of neonatal morbidity and mortality. With limited resources, early diagnosis and treatment, if crucial, may not be achieved. Objective of this study is to evaluate the role of Micro ESR in the diagnosis of suspected neonatal sepsis.*

***Materials and Methods:** A prospective cross-sectional hospital based descriptive study was done in the NICU of Yenepoya Medical College Hospital, Mangalore, Karnataka, India, Between 1st January 2015 to 15<sup>th</sup> July 2015. 50 Newborns with suspected sepsis admitted for septic work up and IV antibiotics were included in the study. Micro ESR was measured with relevant septic screening investigations. The micro ESR value results were compared with Blood culture taken as gold standard and hematological factors such as CRP. **Results:** Out of 50 babies, micro ESR was elevated in 19 (38%) babies out of which Blood culture was positive in 16 cases. Total proven sepsis cases were 16 (32%) and probable sepsis were 34 (68%). Correlation of elevated micro ESR was statistically significant with blood culture positive cases and CRP>6 with a p-value of 0.004 and 0.043 respectively. The sensitivity, specificity, positive and negative predictive value compared with blood culture was 68.8%, 76.5%, 57.9% and 83.9% respectively with a diagnostic accuracy of 74%. **Conclusion:** Micro ESR is simple and cheap bedside evaluation test and relatively sensitive in the prediction of neonatal sepsis and can be a useful test in the early detection of sepsis and can be used as a screening tool for detecting suspected Neonatal Sepsis.*

**Keywords:** Micro-Erythrocyte sedimentation rate, Neonatal Sepsis, CRP, Blood Culture, Screening.

## 1. Introduction

Neonatal sepsis is the most important cause of morbidity and mortality especially among low birth weight and preterm babies in developing countries<sup>1</sup>. The contribution of neonatal sepsis for such high mortality and morbidity makes it quite an important study for research as well as action<sup>1-2</sup>. Various maternal, foetal and environmental factors also contribute towards sepsis in newborns. Some of the maternal factors are premature rupture of membranes, maternal fever within 2 weeks prior to delivery, meconium stained amniotic fluid (MSAF), foul smelling liquor and instrumental delivery<sup>1</sup>. Foetal factors include birth weight, gestation and apgar score. Neonatal sepsis is diagnosed when generalized systemic features are associated with pure growth of bacteria from one or more sites<sup>1</sup>. According to pooled hospital data based on NNPD survey 2002 – 2003, the incidence of neonatal sepsis is around 30 /1000 live births<sup>3</sup>. Although blood culture considered to be the gold standard for diagnosis of septicemia, the technique is time consuming and demands a well equipped laboratory.<sup>4,5</sup>

Present study was undertaken to evaluate the role of Micro-ESR in early diagnosis of neonatal sepsis by determining the predictive value of Micro-ESR in neonatal sepsis by comparing it with blood culture which is gold standard and comparing it with certain other infective markers such as CRP and detect significance. The micro erythrocyte sedimentation rate is an easy and inexpensive bedside screening test for neonatal sepsis<sup>2</sup>.

## 2. Materials and Methods

It was a Prospective hospital based cross-sectional

descriptive study carried out between 1st January 2015 to 15<sup>th</sup> July 2015, in the NICU of Yenepoya Medical College Hospital, Mangalore, Karnataka. A total of 50 newborns admitted in the NICU with a diagnosis of sepsis and suspected sepsis fulfilling the inclusion and exclusion criteria was taken in the study. Inclusion criteria was neonates admitted as suspected neonatal sepsis and with Hb>10gm% and <20gm%. Exclusion criteria was Anaemia (Hb<10gm%) and Polycythemia (Hb>20gm%), neonates with proven chromosomal, genetic or inborn errors of metabolism already on treatment, neonates without any risk factors and clinical criteria for sepsis, newborn weighing <1000g and newborns with gross congenital malformations. Ethical approval was taken from the institution ethics committee before initiation of the study. Positivity of at least two of the following laboratory screening tests were required for inclusion in the study<sup>6</sup>.

The investigations were:<sup>6</sup>

- Total leukocyte count < 5000/mm<sup>3</sup>
- P. Smear Band cells>20%
- Micro ESR ≥ 15 mm/ 1st hour
- C-reactive protein > 6 mg/dL
- Absolute neutrophil count <1800/mm<sup>3</sup>
- Platelet count < 100,000

Neonates suspected of sepsis were enrolled in the study after obtaining written consent from the concerned parent/guardian. The neonates were evaluated by a thorough history from mother, maternal parameters at birth and detail clinical examinations. Gestational assessment was done using Modified Ballard Score. The risk factors for sepsis were divided into Major risk factors - PROM>18hrs, Maternal fever >38°C within 15 days and Foul smelling

liquor. The Minor risk factors - Low birth weight < 1500 gms , Prematurity < 34 wks , and Vaginal swab positive for GBS. Clinical signs and symptoms of sepsis were also taken into consideration, neonates who exhibited a minimum of three out of the given signs and symptoms were taken to be having suspected sepsis. The clinical signs and symptoms were sclerema, lethargy, apnea, hypotonia, poor cry, poor feeding, respiratory distress, grunting, vomiting, fever, mottling of the skin and irritability. For every neonate recruited, Micro-ESR was estimated with capillary blood obtained by heel prick, collected in a standard 75 millimeter heparinised micro-hematocrit tube with internal diameter of 1.1 millimeters. Air was not allowed to interrupt the column of blood to avoid false normal result and one end of the tube was sealed with 2-3 millimeter of clay/plasticine. The capillary tubes were placed on the Micro –ESR stand which was provided along with the Micro-ESR kit. The capillary tubes were anchored firmly with adhesive at the base of the stand with the names of the patients and time of blood collection stated, Thereafter the distance from the highest point of the plasma column to the meniscus of the packed red cell column (height of the plasma column) of each tube was measured with a rule after 1 hour. Micro-ESR was said to be elevated if the height of plasma column measured was greater than the sum of the age in days and a constant (3) for neonates aged 0-5 days, according to Alder and Denton in 1975<sup>7</sup> and greater than 15 mm/hr for all neonates irrespective of age<sup>8,9</sup>. For the present study, any values showing >15mm/1<sup>st</sup> hour irrespective of the neonates age was taken. Complete Hemogram was also done in the Hematology Laboratory for all neonates recruited. Full blood count was suggestive of sepsis if the total leukocyte count was greater than 20 X 10<sup>9</sup>/L or less than 5 X 10<sup>9</sup>/L, Platelet count less than 100 X 10<sup>9</sup>/L, neutrophil count greater than 75% or less than 40% of the total leukocyte count and the presence of more than 20% band forms in the peripheral blood film.<sup>6</sup> Blood culture was performed under strict sterile precautions. Neonates were classified as proven sepsis for those with culture proven sepsis, Probable sepsis for those with clinical impression of sepsis with other abnormal laboratory or radiological results but negative for culture. Antibiotics were started as per the Unit protocol on the on the babies of clinical presentation or obstetric risk factors. The clinical details and results of laboratory investigations were recorded in a pre-designed Proforma.

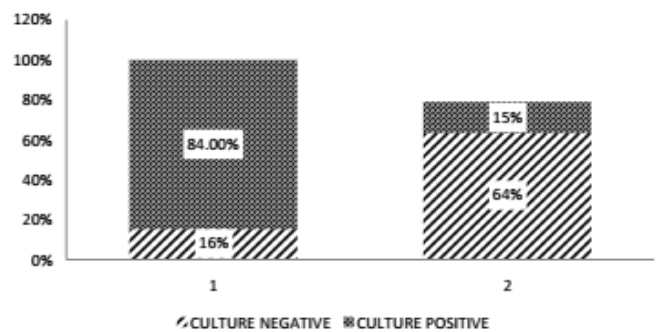
The collected data was entered into SPSS software version 20 and analysis was also done by the same. Main statistical methods used were Pearsons Chi – Square test and comparison using Micro ESR as a dependent variable and other variables as independent variable. Calculation of sensitivity, specificity, Positive Predictive value, Negative Predictive Value with accuracy and agreement using Kappa statistics were done. P value of < 0.05 was considered statistically significant.

### 3. Results

A Total of 50 neonates who fulfilled the inclusion criteria were recruited into the study. Out of the 50 neonates, 24 (48%) were female and 26 (52%) were male. Mean birth weight observed was 2.9±0.8kg and a mean gestational age of 35.8±3.6 weeks. Out of the 50 Neonates, Blood culture

was positive in 16 cases which gives a prevalence rate of 32% for sepsis. 20 neonates (40%) were pre-term while the rest 30 neonates (60%) were born term. Almost all the neonates enrolled in the study were diagnosed to have suspected sepsis within the 1<sup>st</sup> three days of life with the mean days of life being 1.98 days. PROM>18hours was seen in 9 (18%) cases of suspected sepsis and CRP>6 in 22 (44%) of all the cases recruited. 16 (32%) cases had culture proven sepsis, which gives a prevalence rate of 32% in Proven sepsis. The rest of the cases were taken as probable sepsis 34 (64%).

Micro- ESR was elevated (>15mm/1<sup>st</sup> hour) in 19 out of the 50 cases, out of which 16(84%) cases were culture proven sepsis. Micro- ESR was normal in 31 cases out of 50 , out of which 3(15%) were culture proven sepsis. (Fig 1)



**Figure 1:** 1- The No. Micro-ESR elevated cases - 19  
 2- No. of Micro- ESR Normal Cases - 31

Out of the 50 neonates who had clinical symptoms and signs of sepsis, the following Maternal and Obstetrical factors and neonatal clinical signs and symptoms were observed.

(Table -1)

Factors	Present	Absent	Total
Prom >18 Hours	9 (18%)	41 (82%)	50 (100%)
Foul-Smelling Liquor	12 (24%)	38 (76%)	50 (100%)
Maternal Fever	29 (58%)	21 (42%)	50 (100%)
Lethargy	18 (36%)	32 (64%)	50 (100%)
Poor Feeding	28 (56%)	22 (44%)	50 (100%)
Poor Cry	10 (20%)	40 (80%)	50 (100%)

Maternal and Obstetrical factors and neonatal clinical signs and symptoms which were observed. (Table 1).

Co-relation of Elevated Micro – ESR showed statistically significant association with Blood Culture and CRP>6, with a p-value <0.05. (Table – 2)

	Micro ESR – Elevated (>15mm/1st Hour)	Micro – ESR Normal	Total	P-Value
CRP >6 (Elevated)	12 (63.2%) (TP)	10(32.3%) (FN)	22(44%)	0.043
CRP <6 (Normal)	7 (36.8%) (FP)	21(67.7%) (TN)	28(56%)	
Total	19 (100%)	31 (100%)	50 (100%)	
Proven Sepsis	11 (68.8%) (TP)	5 (31.2%) (FP)	16(32%)	0.004
Probable Sepsis	8 (23.5%) (FN)	26(76.5%) (TN)	34(68%)	
Total	19(38%)	31 (62%)	50 (100%)	

Key: TP (True Positive) FP (False Positive) TN (True Negative) FN (False Negative) (Table – 2)

Blood culture was positive in 16 cases in total and 34 suspected sepsis cases had no growth. *Staphylococcus aureus*, *Acinetobacter* and *Citrobacter* was grown in 3 cases each, followed by *Proteus*, *Pseudomonas* and  $\alpha$ -hemolytic streptococcus was isolated in 2 cases each. Coagulase negative *Staphylococcus* was seen in 1 case.

Sensitivity, Specificity, Positive and Negative Predictive values of Micro –ESR and Certain Relevant Hematological Parameters was statistically calculated using Blood culture as a Gold standard. Elevated Micro- ESR compared with blood culture yielded a sensitivity of 68.80%, a specificity of 76.50%, a positive predictive value of 57.90%, negative predictive value of 83.90% and an accuracy and agreement of 74.00%

#### 4. Discussion

Neonatal sepsis is a clinical syndrome. It is characterized by signs and symptoms of infection with or without bacteremia in the first month of life. The diagnosis of neonatal infection is difficult to establish based on the clinical picture alone, yet it is imperative that treatment is instituted early because of the high mortality associated with neonatal infection.<sup>8</sup>

Statistical significance was obtained with comparison of elevated Micro - ESR with the hematological parameter of CRP>6, which was the cut-off taken in the present study, which was seen in 22 (44%) cases and had a significant p-value of .043. This observation is similar to the observations of Hofer et al<sup>11</sup>, and the study conducted by Chauhan et al.<sup>12</sup> The present study showed that Micro-ESR correctly identified 11 out of 16 neonates who had blood culture proven sepsis, giving a sensitivity of 68.8%. This implies that about more than half of the neonates with suspected sepsis was correctly diagnosed with the Micro-ESR technique. This value is comparable with the 79% reported by Misra et al.<sup>13</sup> and 71% by Akpede and Abiodun.<sup>14</sup> It is however higher than the 62.5% documented by Diwarker and Rosul G<sup>9</sup> and 14.3% by Zeeshan et al.<sup>15</sup> These lower sensitivities could be attributed to the difference in the variables and the diagnostic criteria used in these different studies. The cut-off value in the present study was taken as >15mm/1st hour irrespective of the age of the newborn<sup>8,9</sup>. The sensitivity obtained in the present study was lower than the 96.9% documented by Okolo et al. in Benin<sup>16</sup>.

Micro-Erythrocyte sedimentation rate was unable to identify 5 out of 169 neonates who had culture proven sepsis giving a specificity of 76.5%. This is at variance with the 60.9%, 75% and 90% reported by Diwarker and Rosul G<sup>9</sup>, Zeeshan et al.<sup>15</sup> and Okolo et al.<sup>16</sup> The variation in the specificity in the present study as compared to the latter studies<sup>14-16</sup> could be attributed to the different diagnostic criteria and the different cut-off values used compared to the present study. The positive predictive value (PPV) of 57.9% obtained in the present study suggests that neonates with elevated Micro-ESR have 57.9% probability of having sepsis. This value is much higher than the 13.8% reported by Zeeshan et al.<sup>15</sup>. This difference could be attributed to the disparity in the cut-

off values used. The finding in the present study of a Negative Predictive Value (NPV) of 83.1% implies that neonates with normal Micro-ESR have 83.1% probability that sepsis is absent. This value is comparable to the 75.5% reported by Zeeshan et al.<sup>15</sup> It is however lower than the 90% reported by Okolo et al.<sup>16</sup> and 92% reported by Akpede and Abiodun<sup>14</sup>. In the latter study,<sup>14</sup> children aged 1 month to 5 years constituted the study population as opposed to the present study, where neonates aged 0-28 days made up the study population.

#### 5. Conclusion

Micro –ESR is a simple, cheap and relatively sensitive and specific bedside test which can be easily done and which has proved to have good negative predictive value in the prediction of suspected sepsis in neonates. It can be used as a screening tool in a setting with limited resources.

#### References

- [1] Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. Kathmandu Univ Med J. 2006;4:187-189.
- [2] Paudel KP, Adhikari RK. Micro ESR in the evaluation of neonatal sepsis. J Inst Med. 2012;33.1
- [3] NNPD(2002-2003) <http://www.newbornwhocc.org/>
- [4] Buch AC, Srivastava V, Kumar H, Jadhav PS. Evaluation of haematological profile in early diagnosis of neonatal sepsis. Int J Basic App Med Sci. 2011;1:1-6.
- [5] Desai P, Shah AN, Pandya T, Desai P, Pandya T. CRP, immature to total neutrophil ratio and micro ESR in early diagnosis of neonatal sepsis. Int J Biomed Adv Res. 2014;5:364-66.
- [6] Cloherty JP, Eichenwald EC, Hansen AR, Stark AR, Goldsmith JP. Lippincott Manual Series. 7th Ed. Wolters Kluwer Health; 2012. Manual of Neonatal Care; p. 1024.
- [7] Adler SM, Denton RL. The Erythrocyte Sedimentation Rate in newborn period. J Pediatr. 1975;86:942-8.
- [8] Gerdes JS. Clinicopathological approach to the diagnosis of neonatal sepsis. Clin Perinatol. 1991;18:361-81.
- [9] Diwarker KK, Rosul G. Revised look at micro-erythrocyte sedimentation rate in neonates. Indian Pediatr. 1999;36:703-5.
- [10] West BA, Tabansi PN, Ugwu RO, Eneh AU. The predictive value of micro-erythrocyte sedimentation rate in neonatal sepsis in a low resource country. Pediatr Therapeut. 2012; S2:002
- [11] Hofer N, Müller W, Resch B. The Role of C-Reactive Protein in the diagnosis of neonatal sepsis, DOI: 10.5772/54255 ISBN 978-953-51-1124-5, Published: April 30, 2013. Available from: <http://www.intechopen.com/books/neonatal-bacterial-infection/the-role-of-c-reactive-protein-in-the-diagnosis-of-neonatal-sepsis>
- [12] Chauhan SB, Vaghasia V, Chauhan BB. CRP in early diagnosis of neonatal septicemia. Natl J Med Res. 2012;2:276-78.

- [13] Misra PK, Kumar R, Malik GK, Mehra P, Awasthi S. Simple haematological tests for diagnosis of neonatal sepsis. *Indian Pediatr.* 1989;26:156-60.
- [14] Akpede GO, Abiodun PO The micro-erythrocyte sedimentation rate as a screening test for bacteraemia in young children with non-focal infections. *West Afr J Med.* 1995; 14:147-51.
- [15] Zeeshan A, Tariq G, Talal W, Salman A, Shahid A, Shahid M. Diagnostic value of C- reactive protein and other haematological parameters in neonatal sepsis. *J Coll Physicians Surg Pak.* 2005;15:152-6.
- [16] Okolo AA, Scott-Emuakpor AB, Omene JA. The diagnostic value of leukocyte indices and micro-erythrocyte sedimentation rate in neonatal infections. *Trop Geogr Med.* 1988;40:304-8.