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Research Article

Neonatal septicemia- a smooth technique of diagnosis in developing countries

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ABSTRACT

Background: Neonatal septicemia is characterized by clinical signs and symptoms accompanied by bacteremia in the first month of life. As per National Neonatal Perinatal Database (NNPD) 2002-2003, the incidence of neonatal sepsis in India was 30 per 1000 live birth. C-reactive protein (CRP), an acute phase reactant has advantages of low serum levels in normal infants, a rapid rise after 12 to 24 hours of sepsis and a massive rise thereafter as long as inflammatory stimuli persist and followed by immediate fall of serum level as soon as inflammation subside.
Methods: Total 100 cases were studied at NICU, K.R Hospital, Mysore, India. Peripheral blood smear was prepared by heel prick and were stained using Leishman stain. Total leucocyte count was performed by using automated haematology analyzer. I/T (immature to total neutrophil) ratio were calculated by dividing the total immature count by total neutrophil count (including both mature and immature neutrophil count. C reactive protein was assessed by kit using CRP Latex, agglutination slide test. For Micro ESR blood was collected in preheparinised microhematocrit tubes of 75 mm length with an internal diameter of 1.1 mm & external diameter of 1.5 mm by heel prick technique.
Results: Our study revealed that, among 100 children under study, males of low birth weight were commonly affected. Among the investigations I:T ratio and CRP shows a better sensitivity and specificity for early diagnosis of neonatal sepsis.
Conclusions: Amongst all the hematological parameters Immature to total neutrophil (I:T) ratio has a reasonably good predictive value for early diagnosis of neonatal septicemia. This study is done as an endeavor to add to something about our preexisting knowledge of diagnosis of neonatal sepsis early for better management of this group of patients especially in developing countries.

Keywords: CRP, I:T ratio, Micro ESR, Neonatal sepsis

INTRODUCTION

Neonatal septicemia is characterized by clinical signs and symptoms accompanied by bacteremia in the first month of life.[1] Its a clinical syndrome characterized by signs and symptoms of infection, identified and confirmed by positive blood cultures.[2] As per National Neonatal Perinatal Database (NNPD) 2002-2003, the incidence of neonatal sepsis in India was 30 per 1000 live birth.[2] Currently, criteria for neonatal sepsis usually include documentation of infection in a newborn infant with a serious systemic illness in which noninfectious explanations for the abnormal pathophysiologic state are excluded or unlikely.[3] It is normally divided into three categories, depending on time of onset: early onset sepsis (EOS) at <3 days of age, late onset sepsis (LOS) at 3-28 days of age, and late onset sepsis (LLOS) at 29-120 days of age. Of these, LOS is the most common infection,

especially in very low birth weight (VLBW) infants.[4] The gold standard and most reliable diagnostic test for neonatal sepsis is blood culture test for bacteria. While this test takes 48 hours to obtain the results, the treatment must often begin before the results are known. An additional complication is the fact that the blood culture test can be negative for one in five subjects with sepsis.[5] Thus, it is of critical importance to identify better way of diagnosing sepsis in its earliest stages. It is well-known fact that understanding hematology of neonatal sepsis helps in early identification of suspected cases of neonatal sepsis, predicting the prognosis and also helps in decision of line of treatment to these neonates as to have better outcome.[2] The present study was undertaken to assess the role of I:T ratio, CRP, micro ESR in early diagnosis of neonatal septicemia in a cost-effective manner particularly in developing countries like India.

The aim and objective was to evaluate the diagnostic efficacy of hematological parameters especially I: T ratio, CRP and micro ESR to find a suitable parameter in the early diagnosis of neonatal septicemia, so that immediate treatment can be started before results of bacterial culture (The gold standard confirmatory test) become available.

METHODS

The present study was performed on neonates admitted to Neonatal I.C.U., K. R hospital, Mysore during the period of November 2012 to September 2013 and all tests were performed at the department of Pathology, Mysore Medical College, Karnataka. Written informed consent was taken from parents of the included neonates. Total 100 cases were studied. After taking a careful history specified questionnaire was designed and the detailed information was recorded.

Using all aseptic precautions blood was collected from peripheral vein prior to starting antibiotic treatment. Two C.C. blood was collected in plain vial for CRP and EDTA bulb for leucocyte count. Heel prick method was used to obtained blood for preparation of peripheral smears for estimation of Immature: Total neutrophil (I: T) ratio, to see the morphology of neutrophils.

Total leucocyte count was performed by using automated haematology analyzer sysmex K 10 based on principle of Electric impedence.

Peripheral blood smear was prepared by heel prick and were stained using Leishman stain. These were used for determination of the differential leucocyte count by counting 100 cells, Absolute neutrophil count, Band cell count and Immature: Total neutrophil ratio. Degenerative morphologic changes in neutrophils were graded 0 to 4+ according to Zipursky et al.[6] Degenerative changes in neutrophils include vacuolization, toxic granulations,and Dohle bodies. 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 sepsis5.[7] C reactive protein was assessed by kit using CRP Latex, agglutination slide test for manufactured by Reckon Diagnostic Ltd., Vadodara, India. This test detects CRP concentration >0.6 mg/dl. For Micro ESR blood was collected in preheparinised micro-hematocrit tubes of 75 mm length with an internal diameter of 1.1 mm & external diameter of 1.5 mm by heel prick technique. One end was sealed using clay/ wax. The tube was then fixed vertically with the help of sticking plaster & left undisturbed for 1 hour. At the end of 1 hour the fall in the red cell column was measured accurately to the nearest millimeter. The hematological findings were analyzed according to the hematologic scoring system (HSS) of Rodwell et al.[7] Sensitivity, specificity, positive and negative predictive values (PPVs and NPVs) were evaluated for each of the criteria of HSS using standard statistical methods.

Inclusion criteria

- Neonates with features suggestive of sepsis
- Neonates with history of maternal infection

Exclusion criteria

Neonates with

- Major congenital anomaly
- Inborn errors of metabolism
- Hemolytic jaundice

RESULTS

In our study, among 100 cases,

- Males were most commonly affected with male: female ratio was 1.8:1.
- Incidence of neonatal sepsis was higher in low birth weight (≤2500gms) children (68%).
- 58% of children had early onset sepsis, 23% had late onset sepsis and 19% had late onset sepsis
- Out of 100 cases, sepsis was common in preterm babies (73%) compared to term (22%) and post term (05%) babies.
- There was no significant change in TLC but platelet count was significantly reduced. Thrombocytopenia (<1,50,000/mm3) 8 has a sensitivity of 78% and NPV 86%.
- I/T ratio and immature cells were significantly increased with sensitivity and specificity being 93.54% and 95% respectively. While its PPV was 94.74% and NPV was 92%. Among the 100 cases 96% cases had I:T Ratio ≥0.2.
- Amongst 100 neonates with clinical presentation of neonatal sepsis, 67% cases had micro ESR >15 mm at the end of 1st hour. Micro-ESR was also significantly higher with sensitivity and specificity

being 88.49% and 77% respectively. Its positive predictive value (PPV) & negative predictive value (NPV) were 70.97% and 85.24% respectively.

- Amongst 100 neonates with clinical presentation of neonatal sepsis, 80% cases had CRP value≥1mg/dL. Values of sensitivity & specificity of CRP (latex agglutination method) were 84.67% and 93% respectively. PPV of CRP was 89.46% and NPV of CRP was 85.82%.

Table1: Sensitivity and specificity of various hematological parameters.

Test	Sensitivity	Specificity	PPV	NPV
Thromocytopenia <1,50000/cumm	78%	--	--	86%
I: T Ratio ≥0.2	93.54%	95%	94.74%	92%
CRP positive ≥1mg/dl	84.67%	93%	89.46%	82.82%
Micro ESR 15mm/hr	88.49%	77%	70.97%	85.24%

DISCUSSION

Neonatal sepsis is a dangerous condition that affects between 0.1-1% of newborns but extremely common among preterm infants, incidence being as high as 30-40% have been reported. The mortality and morbidity is increased in sepsis with consequences such as poor neurological outcome, bronchopulmonary dysplasia and necrotizing enterocolitis, leading to prolonged hospital stays and increased costs. Diagnosis of neonatal sepsis is based on bacteraemia demonstrated by a positive blood culture, a method with well-known limitations in turnaround time, sensitivity, and specificity. The standard treatment for neonatal sepsis is intravenous broad spectrum antibiotics together with supportive intensive care. If neonatal sepsis was easier to diagnose, fewer infants would receive antibiotic treatment and the overall antibiotic consumption in neonatal intensive care could diminish.[4]

Our study reviewed that sepsis was more common in male children which was consistent with other studies. Male neonates are more prone to neonatal sepsis than female neonates. This is due to the fact that regulating Immunoglobulin (IgG) may be on X – chromosomes. Therefore presence of pair of X – chromosomes in females probably confers a greater genetic diversity to female immunological system and accounts for relatively more strength to fight infection.[8] In our study premature neonates were more prone to acquire sepsis than the full term neonates. Premature infants are more frequently exposed to resuscitation, inhalation therapy and other life supportive measures leading to higher risk of infection. Low birth weight neonates were more prone to sepsis.

I:T ratio had the maximum sensitivity in our study followed by micro ESR. Even CRP stands the next stage which proves that hematological parameters are a must investigation to avoid the misuse of antibiotics in non-septic neonates.

CONCLUSION

I: T ratio analysis is most important parameter which guides the sepsis rate. Combining with it is CRP and micro ESR gives a good analysis of sepsis. It forms a combined tool with a rapid turnaround time with good sensitivity, rather than high specificity, which allows accurate diagnosis and appropriate antimicrobial treatment or which allows antibiotics to be safely withheld in non-infected infants, is desirable.

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REFERENCES

1. Majumdar A, Jana A, Jana A, Biswas S, Bhattacharyya S. Hematologic scoring system (HSS): A guide to decide judicious use of antibiotics in neonatal septicemia in developing countries. Journal of Applied Hematology. 2013;4(3):110-3.
2. Desai P, Shah AN, Pandya T, Desai P, Pandya T. C - Reactive protein, Immature to total Neutrophil Ratio and Micro ESR in early diagnosis of Neonatal Sepsis. International Journal of Biomedical And Advance Research. 2014;05(08):364-6.
3. Chiesa C, Panero A, Osborn JF, Simonetti AF, Pacifico L. Diagnosis of Neonatal Sepsis: A Clinical and Laboratory Challenge. Clinical Chemistry. 2004;50(2): 279-87.
4. FT- Aspects on early diagnosis of neonatal sepsis © Andreas Ohlin, 2010 Title: Aspects on early diagnosis of neonatal sepsis Publisher: Örebro University 2010 www.publications.oru.se page 12

5. Wang K, Bhandari V, Chepustanova S, Huber G, Hara S, Hern C, et al. Which Biomarkers Reveal Neonatal Sepsis?. Plos one. 2013; 8(12):1-8.
6. Zipursky A, Alko J, Mitner R, Akenzua GI. The hematology of bacterial infections in premature infants. Pediatrics. 1976;57:839-53.
7. Rodwell RL, Leslie AL, Tudehope Dl. Early diagnosis of neonatal sepsis using a Hematological scoring system. J Pediatr. 1988;112:161-6.
8. Nelson Waldo: Text book of Paediatrics, 18th ed. 2007;623-39.

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