

Diagnostic efficacy of Nucleated Red blood cell count in the early diagnosis of neonatal sepsis

Abhishek M G^{1,*}, Sanjay M²

¹Associate Professor, ²Assistant Professor, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, B.G. Nagara, Mandya district, Karnataka state, India 571448

***Corresponding Author:**

E-mail: drmgabhishek@gmail.com

ABSTRACT:

Objective: To determine the efficacy of Nucleated Red blood cell count in the Early diagnosis of neonatal sepsis.

Material and Methods: Cross sectional diagnostic study conducted over a period of 1 year from Oct 2013 to Sept 2014, which included 60 neonates with clinical suspicious of sepsis at birth and within 72 hours or had maternal history of infection. The cord blood was collected immediately after delivery for NRBCs count under peripheral smear. Statistical analysis was performed and Sensitivity, specificity, positive predictive value and negative predictive value was calculated.

Result: NRBCs count was higher in all sepsis cases. Sensitivity of NRBC for detecting proven sepsis was 35%, its specificity 53.48%, its positive predictive value was 23.07% and its negative predictive value was 67.64%.

Conclusion: It is a simple and cost effective test in early diagnosis of early neonatal sepsis. It will help the clinicians in early diagnosis and treatment whenever applicable, thereby reducing the neonatal morbidity and mortality.

Keywords: Nucleated red blood cells, Early onset neonatal sepsis, Blood culture, Hematological parameters.

INTRODUCTION

Neonatal sepsis, characterized by systemic response to bacterial infection, is the leading cause of morbidity and mortality among neonates. Incidence in India is 30 per 1000 live births.[1,2]

Usually asymptomatic, it progresses rapidly, there by warranting urgent diagnosis and proper treatment.[3]Gold standard diagnostic modality for neonatal sepsis is blood culture which is time consuming, un available and has low positivity.[4]

As a result there has been a constant search for a simple, rapid, and cost effective test. Dysfunction in the hematologic system, endothelial alterations and platelets activation play major role in pathogenesis of sepsis. Recently research on the role of molecular markers like cytokines, cell surface antigens etc are on but their use in routine practice will be limited by lack of resources in rural areas and high cost.

Much work has been done on assessing the role of various parameters like C reactive protein, hematological parameters as total leukocyte count, total neutrophilic count, immature to total leukocyte ratio, immature to mature cells ratio, platelet count, and toxic granules in diagnosing neonatal sepsis. [5]

The present study aims to determine the efficacy of Nucleated Red blood cell count in the diagnosis of neonatal sepsis in a rural setup.

OBJECTIVE

To determine the efficacy of Nucleated Red blood cell count in the early diagnosis of neonatal sepsis.

MATERIAL AND METHODS

Study design: Cross sectional diagnostic study.

Sample size: 60

Cases: 60 Cases of clinically suspected neonatal sepsis.

Study Population: Neonates with clinical suspicion of sepsis at birth and within 72 hours or had maternal history of infection

Criteria for subject selection:

Inclusion criteria: 60 neonates with clinical suspicion of sepsis at birth and within 72 hours or presenting with maternal history of infection

Exclusion criteria:

1. Neonates diagnosed with inborn errors of metabolism
2. Neonates with congenital anomalies

Methodology details:

Data of 60 neonates with clinical suspicion of sepsis admitted to the NICU, AH & RC was reviewed. Complete clinical perinatal history and demographic data (sex, mode of delivery as to pre

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-6792.2015.00016.2

term/full term, weight and manner of delivery) will be noted.

Clinical criteria for neonatal sepsis:

Neonates from birth till 72 hours of life presenting with respiratory distress syndrome, cyanosis, apnea, pneumonia, birth asphyxia, lethargy, temperature instability and hypoglycemia. Neonates with maternal history of infection such as upper respiratory tract infection, pneumonia, urinary tract infection, vaginitis, with or without antibiotic intake during pregnancy.

Specimens and tests to be performed:

Blood samples were collected in EDTA anti coagulated vials from umbilical cord blood or arterial or venous blood. Peripheral smear was prepared, stained using leishman's stain. NRbc count was done on peripheral smear.

Hematological parameters:

Total leukocyte count, total neutrophilic count, was obtained from fully automated quantitative hematology analyzer Sysmex kX-21 in all the cases. Toxic granules in the neutrophils were obtained in peripheral smear stained with Leishman's stain in all the cases.

Institutional ethical committee:

Approval was obtained from the institutional ethical committee

Statistical tests:

Data was expressed as mean values, Sensitivity, specificity, positive predictive value and negative predictive value were calculated.

SPSS software 16 version was used for analysis.

RESULTS:

Table 1: Comparison of variables between 3 sepsis groups

Type of sepsis	No	Sex		Maturity		Birth weight	
		Male	Female	preterm	term	Low (>2500gm)	Normal
Clinical sepsis	26	18	8	9	17	7	19
Suspected sepsis	20	13	7	7	13	9	11
Proven sepsis	14	7	7	10	4	8	6
Total cases	60	38	22	26	34	24	36
Culture positive	18	10	8	9	9	10	8
Percentage%	30	26.31	36.36	34.62	26.48	41.67	22.23

Table 2: Relation between Haematological parameter and NRbc count in sepsis group

Sepsis group	Clinical sepsis N=26	Suspected sepsis N=20	Proven sepsis N=14
Elevated ESR	3	6	2
Total WBC count	6	5	4
Toxic granules in neutrophils	2	3	4
Increase Nrbc	4	7	6

Table 3: Relation between NRbc count and sepsis group

Sepsis group	Clinical sepsis N=26	Suspected sepsis N=20	Proven sepsis N=14
NRbc/100wbc			
10-19	1	1	1
20-29	2	2	2
>30	2	4	3

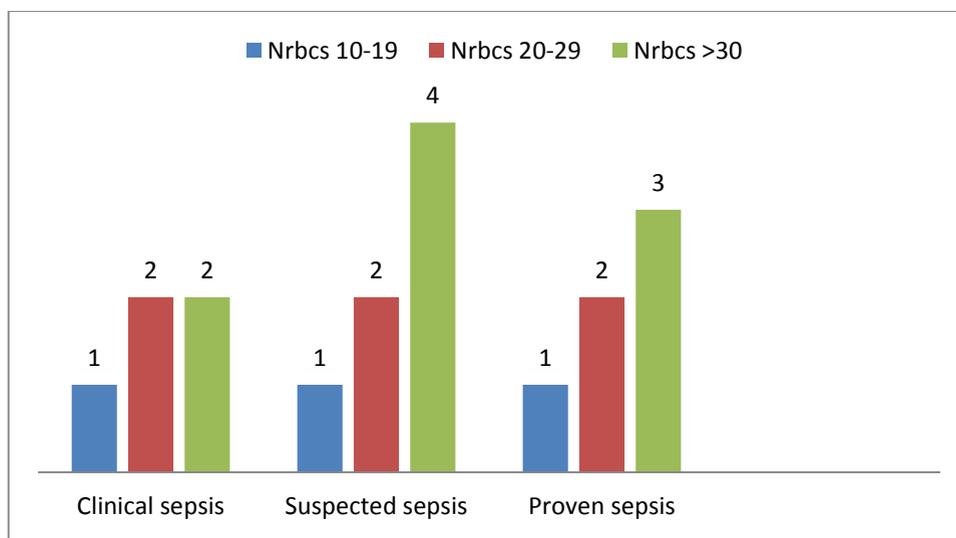


Fig. 1: Graph depicting the comparison of Nrbcs with sepsis

Table 4: Comparison of ESR, Total WBC count, Toxic granules in neutrophils, Nrbcs and positive blood culture

Parameters	No of Positive cases (out of N=60)	Culture positive (out of 14 cases)
Elevated ESR	11	2(14.28%)
Total WBC count	15	4(28.57%)
Toxic granules in neutrophils	9	4(28.57%)
Increase Nrbcs	17	6(42.85%)

ESR: erythrocyte sedimentation rate, **WBC:** White blood corpuscle, **Nrbcs:** Nucleated Red blood cell.

Sensitivity: 35%, Specificity: 53.48%, Positive predictable value: 23.07%, Negative predictable value: 67.64%

Based on clinical findings and laboratory parameters, 60 Neonates were grouped into 3 categories. Namely 1) proven sepsis (14 cases) 2) suspected sepsis (20 cases) and 3) clinical sepsis (26 cases). This classification is based on Chandna A et al.

Table 1: This table depicts comparison of different variables like sex, maturity and birth weight. Among total 60 cases, 22 neonates were female with 7 cases of proven sepsis. The ratio of clinical, suspected and proven sepsis in male and female is 18:13:7 = 8:7:7 (Male: Female) respectively. With respect to maturity and birth weight, 26 neonates were preterm and 24 neonates were weighing less than 2.5kg.

Table 2: This table shows comparison of hematological parameters with NRBC count in sepsis group. The total WBC count was normal in 10 neonates out of 14 proven sepsis cases. Raised ESR value and Toxic granulation in neutrophils were seen in 2 neonates and 4 neonates among proven sepsis cases (N=14). Significant rise of Nrbcs count was seen in 6 neonates among total 14 proven sepsis neonates.

Table 3: In this table, 3 neonates shows more than 30NRBCs/100WBC out of 14 proven sepsis cases. 2 Cases showed 20-29Nrbcs/100WBC among 14 cases of proven sepsis.

Table 4: This table depicts comparison of ESR, Total WBC count and toxic granulation in neutrophils and NRBCs with positive blood culture. Out of all 60 cases, an increase in NRBC count was detected in 17 cases whereas elevated ESR, increased total count was noticed only in 11 and 15 cases respectively. Among 14 positive culture cases, 6 neonates(42.85%) showed increase in NRBC count level, whereas increased total wbc count was seen in 4 neonates (28.5%). Another parameter which is Toxic granulation seen in neutrophils was revealed in only 4(28.5%) cases.

DISCUSSION

Neonatal sepsis, characterized by systemic response to bacterial infection, is the leading cause of neonatal morbidity and mortality. Incidence of neonatal sepsis in developing countries is 30 per 1000 live births. [1,2,.]

1% of neonatal death is due to sepsis. (Shanker M J et al 2008)[6]. The main reason for bacterial sepsis in neonate is due to deficit in their inherent immune mechanism. (Khatua SP et al 1986)[7]. The gold standard diagnostic tool is the blood culture which is time consuming. Hence in order to diagnose early neonatal sepsis, several parameters have been described by different investigators.

In our study, the sensitivity of Nrbc for detecting sepsis was 35%, its specificity 53.48%, its positive predictive value and its negative predictive value were 23.07% and 67.64% respectively. Our findings were similar with the study done by Tripathi et al (2010)[8]. They stated that activated macrophages release cytokines which play an important role in stimulating Nrbc in absence of hypoxia. She also revealed that Nrbc were significantly increased in early and late neonatal sepsis. Another study which was done by Dulay et al (2008)[9] also stated significant increase in Nrbc with early onset of neonatal sepsis. Mannon et al found that total leukocyte count and differential leukocyte count were not significant in diagnosing neonatal sepsis. Sawankar et al [10] observed that hematological parameters were poor predictors of neonatal sepsis.

Similarly, Setal B et al [11] observed that sensitivity and specificity of platelet count was lowest in diagnosing neonatal sepsis. In contrast, several other studies have successfully established the role of Nrbc in diagnosing neonatal sepsis. They confirmed Nrbc was a more sensitive marker compared to other hematological parameters (Haque KN et al, Khatua SP et al) [7,12,13-15,].

CONCLUSION

In conclusion, the present study revealed that a rise in Nrbc is a more reliable marker than other hematological parameters namely Total WBC count, ESR and toxic granulation in neutrophils. Since rise in Nrbc count is seen in all the culture proven cases, Nrbc can be used as a simple, rapid and cost-effective test in the detection of early neonatal sepsis. It will guide clinicians in instituting early treatment and adopting aggressive treatment whenever applicable, thus reducing the neonatal morbidity and mortality.

REFERENCES:

- Sucilathangam G., Amuthavalli K., Velvizhi G., Ashihabegum M.A., Jeyamurugan T., Palaniappan N. Early diagnostic markers for neonatal sepsis: comparing procalcitonin (pct) and c-reactive protein (crp). *Journal of Clinical and Diagnostic Research* [serial online] 2012 May [cited: 2015 Aug 19]; 6:627-631.
- Narasimha A, Harendrakumar ML. Significance of hematological scoring system (HSS) in early diagnosis of neonatal sepsis. *Indian J Hematol Blood Transfus* 2011;27(1):14-7.
- Sharma M, Goel N, Chaudhary U, Aggarwal R, Arora DR. Bacteraemia in children. *Indian J Pediatr*. 2002;69(12):1029-32.
- Chandna A, Rao MN, Srinivas M, Shyamala S. Rapid Diagnostic Tests in Neonatal Septicemia. *Indian J Pediatr* 1988; 55:947-953.
- Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I Reference values for neutrophilic cells. *J Pediatr* 1979; 95:89-98.
- Aggarwal R, Sakar N, Deorari AK, Paul VK. Sepsis in the newborn. *Indian J Pediatr* 2001; 68:1143-1147.
- Khatua SP, Das AK, Chatterjee BD, Khatua S, Ghose B, Saha A. Neonatal septicemia. *Indian J Pediatr* 1986;53:509-514.
- Tripathi S and Malik GK. Neonatal sepsis: past, present and future; a review article. *Internet Journal of Medical Update* 2010 July; 5(2):45-54. Xanthou. Leucocyte blood picture in ill newborn babies. *Arch Dis Child* 1972; 47:741-743.
- Dulay AT, Buhimschi IA, Zhao G, Luo G, Razeq SA, Rosenberg VA, et al. Nucleated red blood cells are a direct response to mediators of inflammation in newborns with early onset neonatal sepsis. *Am J Obstet Gynecol* 2008; 198:426.e1-426.e9.
- Swarnkar K, Swarnkar M. A Study Of Early Onset Neonatal Sepsis With Special Reference To Sepsis Screening Parameters In A Tertiary Care Centre Of Rural India. *The Internet Journal of Infectious Diseases* 2012; 10(1)
- Chauhan Setal B, Vaghasia Viren, Chauhan Bimal B.C-reactive protein (crp) in early diagnosis of Neonatal septicaemia *NATIONAL JOURNAL OF MEDICAL RESEARCH* Volume 2 | Issue 3 | July – Sept 2012; 276-78.
- Haque KN. Neonatal Sepsis in the Very Low Birth Weight Preterm Infants: Part 1: review of Pathophysiology. *Journal of Medical Sciences* 2010; 3(1):1-10.
- Salafia CM, Ghidini A, Pezzullo JC, Rosenkrantz TS. Early neonatal nucleated erythrocyte counts in preterm deliveries: clinical and pathologic correlations. *J Soc Gynecol Investig*. 1997;4:138-43.
- Mishra UK, Jacobs SE, Doyle LW, Garland SM. Newer approaches to the diagnosis of early onset neonatal sepsis. *Arch Dis Child Fetal Neonatal Ed*. 2006;91:F208-12.
- Antonette t. Dulay, md, irina a. Buhimschi, md, guomao zhao, bs, guoyang lu, md, sonya abdel-razeq, md, michael cackovic, md, victor a. Rosenberg, md, christian m. Pettker, md, stephen thung, md, mert o. Bahtiyar, md, vineet bhandari, md, and catalin s. Buhimschi, MD. Basic science: Obstetrics Nucleated Red Blood cells are a direct Response to mediators of Inflammation in Newborns with early onset Neonatal sepsis. *Am J Obstet Gynecol*. 2008 Apr; 198(4): 426.e1-426.e9.