



STUDY OF NUCLEATED RBC AS AN EARLY MARKER IN NEONATAL SEPSIS

Paediatrics

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ABSTRACT

Introduction: The most common cause of neonatal mortality in developing countries is neonatal sepsis, the diagnosis of which depends on blood culture, which has low sensitivity and takes time. Demonstration of elevated nRBC levels in neonatal sepsis might help in the early diagnosis of sepsis and hence immediate management of sepsis. **Objective:** To measure the nucleated RBC count in blood samples of neonates with clinical features of sepsis or with the risk factors of sepsis and to analyze whether it can serve as an early marker for neonatal sepsis. **Materials And Methods:** This was a hospital-based prospective study done in neonates who were admitted in MMIMSR, Mullana and its associated hospital with risk factors or clinical features of sepsis. 54 neonates who were admitted in NICU MMIMSR, Mullana were studied. After getting informed consent, the maternal details and examination findings were recorded and a blood samples were taken for sepsis screen, blood culture and peripheral smear for nRBC. **Result:** The sensitivity of nRBC for detecting proven sepsis was 77.42%, its specificity 91.30%, its positive predictive value was 92.31% and its negative predictive value was 75%. **Conclusion:** nucleated RBC is a simple and cost-effective test for early diagnosis of neonatal sepsis. It will help clinicians in early diagnosis and treatment, reducing neonatal morbidity and mortality.

KEYWORDS

neonatal sepsis, nRBC, Early marker

INTRODUCTION

Neonatal sepsis is the most common cause of neonatal mortality in developing countries. ¹ The Millennium Development Goal for child survival cannot be achieved without substantial reductions in infant mortality. Neonatal deaths continue to be a topic of interest in the field of global health and account for forty percentage of all deaths in children under the age of five. ²

The diagnosis will likely be delayed because neonates frequently present with clinical signs and symptoms that are vague and nonspecific. Investigations, including absolute neutrophil count (ANC), immature/total neutrophil ratio (I/T ratio), white blood cell count (WBC) and C-reactive protein (CRP) levels, are necessary for diagnosis. ³

Early diagnosis of neonatal sepsis, which continues to be a major diagnostic challenge in neonatology, reveals the need for dependable and timely diagnostic markers to diagnose sepsis risk during the early phases of sepsis to provide effective antibiotic management towards the organisms that are causing the infection. In cases of neonatal sepsis, there is an abnormally high number of nucleated RBCs in the peripheral blood. The demonstration of increased nRBC levels in neonatal sepsis might be helpful in the early diagnosis of neonatal sepsis, which would allow us to manage the condition appropriately.

OBJECTIVE:

To study the correlation of nRBC with neonatal sepsis and whether nRBC can serve as an early marker in neonatal sepsis.

MATERIAL AND METHODS

Place Of Study

The study was conducted in Department of Paediatrics at MMIMSR and its associated hospital, Mullana, Ambala.

Sample Size

54 neonates were enrolled in the study.

Study Design

Hospital-based Prospective study

Duration

One and a half year

Inclusion Criteria

All term neonates admitted in MMIMSR, Mullana and its associated

hospital with risk factors of sepsis or clinical features of sepsis were included in the study.

Exclusion Criteria

Gestational diabetes mellitus
Intra-uterine growth retardation
Maternal pre-eclampsia or eclampsia
Hemolytic anaemia
Birth asphyxia
Maternal smoking
Preterm and post-term

The study group divided into the following 3 groups based on the clinical findings and investigations.

1. Culture-positive sepsis – Neonates with positive blood culture.
2. Clinical sepsis – Neonates with strong clinical features, a positive sepsis screen but a negative blood culture.
3. No sepsis – Neonates with negative blood culture and a sepsis screen. They were presented with associated risk factors or features of sepsis. On further evaluation, they were found to be suffering from other disorders like Transient tachypnea of newborn, Hyaline membrane disease and hypoglycemia.

Statistical Analysis

All the statistical methods were performed through SPSS for windows version 20, p value of <0.05 was considered statistically significant.

RESULTS:

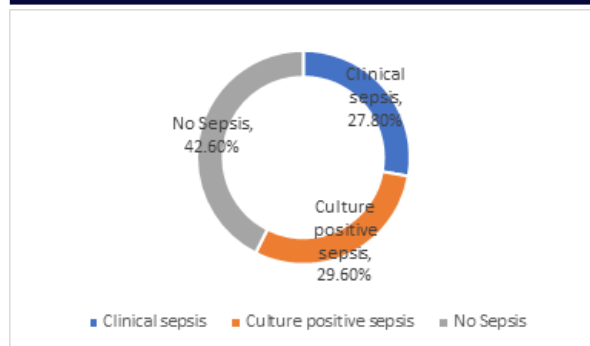
Table 1: Distribution Of Neonates Based On The Final Diagnosis

		Frequency	Percent
FINAL DIAGNOSIS	Clinical sepsis	15	27.8%
	Culture positive sepsis	16	29.6%
	No Sepsis	23	42.6%
	Total	54	100.0%

Final diagnosis showed clinical sepsis [27.8%], culture positive sepsis [29.6%] and suspected sepsis [42.6%].

Table 2: Distribution Of Neonates Based On The nRBC/100WBC

	Sepsis		Total
	Proven sepsis	No sepsis	
nRBC/100WBC >10	24	2	26
<10	7	21	28
Total	31	23	54



Graph 1: Distribution Of Neonates Based On The Final Diagnosis

Culture-positive sepsis and clinical sepsis are considered as proven sepsis cases. >10 nRBC/100WBC considered as significant. The sensitivity of nRBC for detecting proven sepsis was 77.42%, its specificity 91.30%, its positive predictive value was 92.31% and its negative predictive value was 75%.

Table 3: Distribution Of Neonates Based On The Hemoglobin Levels And Final Diagnosis

HB	Mean	SD	95% CI for Mean		Anova	P Value
			Lower Bound	Upper Bound		
Clinical sepsis	11.60	3.45	9.69	13.51	22.95	0.001
Culture positive sepsis	13.73	3.71	11.75	15.71		
No Sepsis	17.59	0.83	17.23	17.95		
Total	14.78	3.73	13.76	15.80		

There is a statistical association between hemoglobin levels and diagnosis.

Table 4: Distribution Of Neonates Based On The Platelet Count And Final Diagnosis

Platelet	Mean	SD	95% CI for Mean		Anova	P Value
			Lower Bound	Upper Bound		
Clinical sepsis	147580.00	90784.00	97305.50	197854.50	12.53	0.001
Culture positive sepsis	130308.75	125485.13	63442.44	197175.06		
No Sepsis	263443.48	56957.04	238813.40	288073.55		
Total	191811.85	109098.91	162033.58	221590.12		

There is a statistical association between platelet count and diagnosis

Table 5: Distribution Of Neonates Based On The qCRP And Final Diagnosis

qCRP	Mean	SD	95% CI for Mean		Anova	P Value
			Lower Bound	Upper Bound		
Clinical sepsis	13.00	6.939	9.16	16.84	11.15	0.001
Culture positive sepsis	32.82	34.695	14.33	51.31		
No Sepsis	3.39	2.169	2.45	4.33		
Total	14.78	22.600	8.61	20.95		

There is a statistical association between qCRP and diagnosis

There is a statistical association between nRBC/100WBC and diagnosis

Table 6: Distribution Of Neonates Based On The nRBC/100WBC And Final Diagnosis

nRBC/100WBC	Mean	SD	95% CI for Mean		Anova	P Value
			Lower Bound	Upper Bound		
Clinical sepsis	12.13	4.406	9.69	14.57	102.86	0.001
Culture positive sepsis	15.31	5.712	12.27	18.36		
No Sepsis	3.13	3.597	1.58	4.69		
Total	9.24	7.031	7.32	11.16		

DISCUSSION

HB

In this study, there is a statistical association between hemoglobin levels and sepsis. In Muthukumaran N et al.,⁴ hemoglobin values are statistically significant between the sepsis babies (10.46 + 2.12) and not proven sepsis group (13.21 + 1.04).

TLC

In this study, there is no statistical association between TLC levels and sepsis. In Muthukumaran N et al.,⁴ there was not much statistically significant difference as TLC in sepsis babies. (8425 + 5627 vs 6756 + 1481).

In Abhishek MG et al.,⁵ total WBC count was normal in 10 neonates out of 14 proven sepsis cases.

PLATELET

In this study, there is a statistical association between platelet count and sepsis. In Muthukumaran N et al.,⁴ there was much statistically significant difference as thrombocytopenia in sepsis babies. (181000 + 85761 vs 332000 + 91101).

micro ESR

In this study, among clinical sepsis neonates, micro ESR was <15 mm in 60% and >15 mm in 40%. Among Culture positive sepsis neonates, micro ESR was <15 mm in 37.5% and >15 mm in 62.5%. Among Suspected Sepsis neonates, micro ESR was <15 mm in 87% and >15 mm in 13%. The association between them was found to be statistically not significant.

In this study, In Abhishek MG et al.,⁵ raised ESR value and Toxic granulation in neutrophils were seen in 2 neonates and 4 neonates among proven sepsis cases.

NRBC/100WBC

Sepsis is an inflammatory reaction that places the body under stress. In a number of studies, selective erythroid hyperplasia was observed in the bone marrow by administering interleukin-6 to adult animals after 12 hours (during this period, this event could not have been caused by the production of EPO). Similarly, an increased NRBC count associated with the elevated production of interleukins 3, 6 and 12 has been reported in critically-ill patients. There is therefore, a direct and positive correlation between the increased production of interleukin-6 (an inflammatory mediator) and a rise in NRBC count.⁶

This study has a statistical association between NRBC/100WBC and sepsis. In this study, Sensitivity of NRBC for detecting proven sepsis was 77.42%, its specificity 91.30%, its positive predictive value was 92.31% and its negative predictive value was 75%. In Muthukumaran N et al.,⁴ there was also statistically significant difference in increase of NRBCs in sepsis group of babies (13.08 + 5.26 vs 4.89 + 4.3). The sensitivity of NRBC in identifying sepsis was 81.96%, its specificity was 61.11%, positive predictive value was 70.42% and negative predictive value was 75%.

The mean value of NRBCs in culture positive sepsis was 13.69, in sepsis screen positive sepsis was 12.38 and 4.87 in no sepsis group of babies. In a previous study done, 47 babies out of 56 babies with proven sepsis had a NRBC score of $>10/100$ WBCs accounting to about 83.9%. In Muthukumaran study sensitivity in identifying sepsis was 81.96%, its specificity was 61.11%, positive predictive value was 70.42% and negative predictive value was 75%.⁴

In Ahirrao M et al.,⁷ Out of the all haematological parameters studied,

Nrbcs count had highest 82.14%, association in culture positive sepsis as compared to others like total Wbc count WBCs and Immature PMN 78.5%, toxic granules 75%, degenerative changes 64.28% and platelet count 75%. Nrbcs counted on peripheral smears of neonates by Nrbcs per 100 white blood cells wbc. NRBCs counted in neonates with proven sepsis were 23, probable sepsis were 30 and clinical were 29. The infant's NRBC count was directly correlated with infection status. Nucleated red cells (Nrbcs) are counted as white blood cells. For this reason, the obtained wbc count is actually corrected by counting number of nrbcs /100 leucocytes while performing peripheral blood smear. NRBC count shows sensitivity, specificity, and positive and negative predictive values for the diagnosis of neonatal sepsis 78.57%, 89.13%, 68.75%, and 93.18% respectively.

Dulay et al.⁸ conducted that inflammation alone plays an important role in increasing Nrbcs. Boskabadi et al.⁹ showed a strong correlation between elevated Nrbcs more than 7 per 100 WBCs and infant mortality rate. They also proved that Nrbcs count was more sensitive and specific than other haematological parameters like I/T ratio and CRP. Many other authors like Cremer M¹⁰ and Baschat AA¹¹, Shah BA¹² and Desai S¹³ and Abhishek MG have evaluated usefulness of Nrbcs in early diagnosis of neonatal sepsis and predicting poor outcome in ill infants.

In Abhishek MG et al.,⁵ 3 neonates shows more than 30 NRBCs/100 WBC out of 14 proven sepsis cases. 2 Cases showed 20-29 Nrbcs/100 WBC among 14 cases of proven sepsis. Significant rise of Nrbcs count was seen in 6 neonates among total 14 proven sepsis neonates. 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%).

CONCLUSION

- Measurement of nRBC is a simple test, easily accessible, cost effective and cause no harm to the patient.
- Measurement of nRBC can be an early marker for diagnosis of neonatal sepsis.
- nRBC count is significant in proven sepsis, which is >10 nRBC/100 WBC.
- nRBC measurement was found to be significant with p value <0.05.
- Sensitivity of nRBC for detecting proven sepsis was 77.42%, its specificity 91.30%, its positive predictive value was 92.31% and its negative predictive value was 75%.

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