

**CLINICAL STUDY OF PERINATAL ASPHYXIA AND ITS SHORTTERM OUTCOME WITH  
RELATION TO NUCLEATED RBC COUNT IN VENOUS BLOOD OF TERM NEONATES**

**\*<sup>1</sup>S.Sonia Rosalind Martina, <sup>2</sup>S.Saravanan and <sup>3</sup>M.Venkatadesikalu**

<sup>1</sup>Post Graduate, Department of Paediatrics, RMMCH, Chidambaram-608002, Tamilnadu, India.

<sup>2</sup>Associate Professor, Department of Paediatrics, RMMCH, Chidambaram-608002, Tamilnadu, India.

<sup>3</sup>Professor, Department of Paediatrics, RMMCH, Chidambaram-608002, Tamilnadu, India

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**ABSTRACT**

**Background and objectives:** Birth asphyxia & subsequently developing hypoxic ischemic encephalopathy is a major cause of morbidity and mortality in India. Study was undertaken to evaluate the association between NRBC per 100WBC & birth asphyxia with respect to its severity & short term prognosis. **Materials and Methods:** A prospective (case-control) study was conducted between January 2015 and July 2016 in the Neonatal Intensive Care Unit, Department of Paediatrics, Rajah Muthiah Medical College & Hospital. Venous blood collected from 50 term asphyxiated neonates comprising cases & 50 healthy neonates comprising controls constituted the material for study. Levels of NRBC/100 WBC were determined from both the groups & compared. **Result:** The NRBC/100 WBC count in the blood of newborns in the cases was  $16.76 \pm 11.46$ ; whereas the corresponding value in the control was  $3.78 \pm 2.79$ . The majority of cases had NRBC between 10-19/100 WBC, whereas 98% of controls had NRBC count of 0-9/100 WBC. There is negative correlation between Apgar score & NRBC values. There is statistically significant positive correlation between HIE stage & NRBC values that is NRBC increases with severity of birth asphyxia. **Conclusions:** The NRBC/100 WBC in peripheral venous blood collected is a simple marker for assessment of severity and early outcomes in perinatal asphyxia. Early NRBC count in venous blood is a simple & cost effective baseline diagnostic tool for determining birth asphyxia.

**Keywords** Diagnosis; hypoxic ischemic encephalopathy; nucleated red blood cells (NRBC); perinatal asphyxia.

**1. INTRODUCTION**

Birth asphyxia-hypoxic ischemic insult has been incriminated as one of the most important causes of perinatal mortality. National neonatal-perinatal database suggests that perinatal asphyxia contributes to 20% neonatal deaths in India. Perinatal asphyxia of moderate grade is defined as slow, gasping breathing or the Apgar score of 4-6 and severe asphyxia as no breathing or the Apgar score of 0-3 at 1 min of life (NNPD, 2005).

The World Health Organization defines birth asphyxia as "failure to initiate and sustain breathing at birth" with the Apgar score of <7 at 1 min of life (WHO, 1997).

*\*Corresponding author: Dr. S.Sonia Rosalind Martina, Post Graduate,  
Department of Paediatrics, RMMCH, Chidambaram-608002,  
Tamilnadu, India.*

In developing countries, intrapartum hypoxic-ischemic injuries appear to be more common, resulting in a huge burden of disabilities (Al-Aifry et al., 1990; Boo, 1991; Airede, 1991).

Approximately 8% of the total global pediatric mortalities (age <5 years) are due to birth asphyxia making it a serious problem in developing countries where the conditions are bad in terms of awareness as well as infrastructure (Lawn et al., 2005).

Globally, hypoxia of the newborn (birth asphyxia) or the fetus ("fresh stillbirth") is estimated to account for 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year (Lawn et al., 2005). Majority of asphyxia insults occur in the antepartum or intrapartum periods as a result of placental insufficiency.

The American Academy of Pediatrics has proposed the term perinatal asphyxia should be reserved to describe an infant who manifests with all of the following features:

1. Umbilical cord arterial pH less than 7;
2. Apgar score of 0 to 3 for longer than 5 minutes;
3. Neonatal neurologic manifestations (seizures, coma, or hypotonia); and
4. Multisystem organ dysfunction (cardiovascular, gastrointestinal, hematologic, pulmonary, or renal system).

Thus hypoxia or asphyxia should be labeled as a cause of disability and handicap only when the neonate demonstrates the four perinatal findings listed above and in whom other possible causes of neurologic damage have been excluded. In the absence of such evidence, subsequent neurologic deficiencies cannot be ascribed to perinatal asphyxia or hypoxia.

Detection of nucleated red blood cells (NRBCs) in cord blood venous blood allows early prediction of development and severity of birth asphyxia-hypoxic ischemic insult as this parameter is related to neurodevelopment.

NRBCs are primarily produced in the fetal bone marrow in response to erythropoietin and are stored in the marrow as reticulocytes and mature erythrocytes. They are normally seen in the blood of neonates. The levels of NRBCs per 100 white blood cells (WBCs) correlates with acute as well antepartum asphyxia and can be used as a reliable index of birth asphyxia and early neonatal outcome.

Count of NRBCs per 100 WBCs is a simple marker for presence and assessment of severity of asphyxia as it is an early outcome and has a direct correlation with increases stress and infection.

NRBC count is also a useful tool for prediction of brain damage and the expected course in hypoxic induced encephalopathy patients.

## 2.METHODOLOGY

A prospective case control study was conducted in NICU, RMMCH. A total of 100 newborns were enrolled after consent from parents, 50 were cases with birth asphyxia who met the inclusion criteria of Apgar score <3/10 at 1 minute and controls were with Apgar score >7/10 at 1 minute. Preterm babies, babies with downs syndrome, TORCH, sepsis & Rh incompatibility with hemolysis were excluded. 2ml of venous blood collected within 6 hours of birth and used for making peripheral smears with Leishman stain and complete blood counts. Number of NRBC were counted per 100WBC in peripheral smear and were reported.

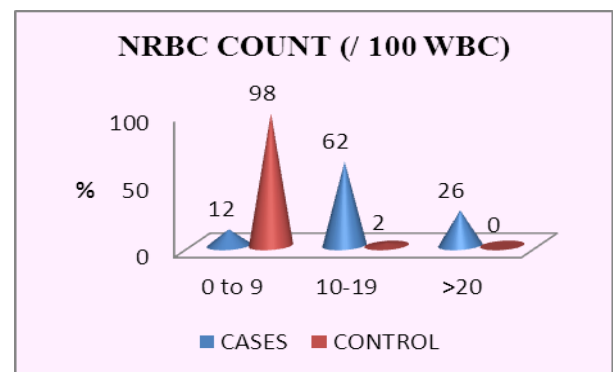
## 3.RESULTS

There is no statistical significant difference in the age, parity status, gestational age of mother, birth weight and mode of delivery between cases and control newborns. The Apgar score at different intervals are comparatively less in cases than in controls. The monocytes and NRBC count are significantly higher in cases than in controls. The majority of cases have NRBC count between 10-19 per 100 WBC whereas 98% of controls have NRBC count of 0-9 per 100 WBC. There is negative correlation between Apgar score and NRBC values. There is statistically significant positive correlation is observed between HIE stage and NRBC values.

That is, when HIE stage is higher, NRBC values is also higher and vice versa. There is statistically positive correlation between NRBC with time of onset of direct breastfeeds, NICU stay, reflex recovery, cry/sucking/activity and hospital stay.

Distribution of NRBC

NRBC Count (Per 100 WBC)	Cases		Control		'P' value
	No.	%	No.	%	
0-9	6	12	49	98	0.001
10-19	31	62	1	2	
≥ 20	13	26	-	-	
Total	50	100	50	100	



## Association of Apgar Score and NRBC count

There is negative correlation between Apgar score and NRBC values. That is when Apgar score is more, the NRBC value is less and vice-versa. But the 'p' value is insignificant (P > 0.05). Pearson's correlation coefficient is used to study the relationship of two variables.

APGAR Score	APGAR 1 Minute		APGAR 5 Minute		No.	NRBC Count	No.	NRBC Count
	Cases	Control	Cases	Control				
0-3	44	8	-	-	6	23 ± 9.84	-	-
4-6	6	14.67 ± 5.01	19	4.26 ± 3.48 ±	38	16.03 ± 15.17	-	-
7-10	-	-	31	1.75	6	± 6.40	50	3.78 ± 2.79

## Difference in NRBC Count with Reference to Stages of HIE

HIE Stage	No.	NRBC Count
HIE Stage 1	19	Mean ± S.D. 10.00 ± 3.40
HIE Stage 2	24	20.83 ± 14.01
HIE Stage 3	7	21.14 ± 7.20
	50	'F' value 'P' value 6.55 0.003

## 4.DISCUSSION

In the present study, attempt has been made to evaluate the relation of venous blood NRBC/100WBC in predicting perinatal asphyxia and its immediate outcome. The NRBC/100WBC count in control and case group was 3.78±2.79 and 16.76±11.46 respectively this correlates with the study done by Gupta et al<sup>9</sup> in cord blood. They found

NRBC of  $10.34 \pm 3.87$  in case group &  $5.7 \pm 2.33$  in control group many different studies all over the world have revealed increased NRBC/100WBC in umbilical cord blood following perinatal asphyxia.

Also, in the present study, we found higher NRBC/100WBC with higher degree of HIE,  $10 \pm 3.40$  in HIE stage 1,  $20.83 \pm 14.01$  in stage 2, and  $21.14 \pm 7.20$  in stage 3 with p value of 0.003 which is significant. This correlates with the study done by Hermansen, (2001), Sikarwar and Gupta, (2011); Phelan et al (1998); Philip and Tito, (1989) who found that NRBC increases with increase in stages of HIE.

Our study also revealed increased NRBC/100WBC count with low Apgar scores many authors like Hanlon-Lundberg and Kirby, (1999), Boskabadi et al., (2010); Saracoglu et al., (2010) and Lundberg et al<sup>15</sup> had reported similar findings in their studies.

## 5. CONCLUSION

Assessment of clinically diagnosed perinatal asphyxia cases with parameters like cord blood pH, blood gas study is not easy in rural settings with limited population. The NRBC count can be easily done in the laboratory. Thus NRBC count parameter can serve as simple and cost effective test in early diagnosis of perinatal asphyxia and in instituting early treatment, thus reducing neonatal morbidity & mortality.

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