

## Original Research Article

# Outcome in the small for gestational age neonates in their early neonatal period in relation with the cord blood nucleated RBC's

T. Prashanth Reddy, Ramesh Chittam\*, Sravan Kumar T., Sindhura K., Sanjeev Chetty

Department of Pediatrics, Navodaya Medical College and Hospital, Raichur, Karnataka, India

**Received:** 26 July 2017

**Revised:** 30 August 2017

**Accepted:** 07 September 2017

### \*Correspondence:

Dr. Ramesh Chittam,

E-mail: [drramesh.navodaya@gmail.com](mailto:drramesh.navodaya@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** NRBCs are physiologically found only in the peripheral blood of the fetus and neonates. Under all other conditions, NRBC is an indicator of pathology, either increase in erythroid activity or damage to the bone marrow has been suggested that the presence of elevated NRBC in the umbilical cord blood is a sign of fetal hypoxia.<sup>1-12</sup> Elevated NRBC is a sign of fetal hypoxia in newborns of mothers with preeclampsia even with well controlled hypertension.

**Methods:** The study period is 1 year from November 2015 to October 2016 on Term SGA babies delivered in Navodaya Medical College Hospital and Research Centre. Inclusion criteria all term SGA and healthy term AGA Newborns. Exclusion criteria were mothers with the following condition: maternal diabetes mellitus, hypertension, preeclampsia, chorioamnionitis and babies with the following conditions meconium stained amniotic fluid, congenital anomalies, twin-to-twin transfusion, severe anemia, cyanotic heart disease.

**Results:** The mean gestational age among control and study group was 18.96 and 19.08 respectively. Low APGAR score ( $\leq 5$ ) was seen in 3 cases in the study group. No newborn in control group had low APGAR. Out of 50 babies included in this study, 24 babies were delivered by LSCS and 26 babies by normal vaginal delivery. the NRBC count was found to be significantly higher in the SGA babies group as compared to the AGA group and this was statistically significant [ $p, 0.005$ ].

**Conclusions:** My study showed that NRBC count was higher in SGA babies than term AGA babies but there was no correlation of NRBC count with the outcome in SGA babies.

**Keywords:** AGA, APGAR score, NRBC's, SGA

### INTRODUCTION

NRBC represents the immature stages of erythrocytes, commonly found in the peripheral blood of newborns at birth. The association between chronic intrauterine hypoxia and increased erythropoietin levels has been established.

In peripheral blood, elevated erythropoietin is reflected as increased NRBC counts. NRBCs are physiologically

found only in the peripheral blood of the fetus and neonates. Under all other conditions, NRBC is an indicator of pathology, either increase in erythroid activity or damage to the bone marrow structure.<sup>1</sup> It has been suggested that the presence of elevated NRBC in the umbilical cord blood is a sign of fetal hypoxia.<sup>1-12</sup> It is affected by factors such as prematurity, preeclampsia, fetal growth restriction, isoimmunization, maternal tobacco use, maternal diabetes mellitus and chorioamnionitis.<sup>1</sup> Elevated NRBC is a sign of fetal

hypoxia in newborns of mothers with preeclampsia even with well controlled hypertension. Hence the purpose of this study was to determine the relationship of cord blood NRBCs with early neonatal outcome (first 7 post-natal days) as well as levels of NRBC in cord blood of SGA neonates. In term babies elevated NRBC is found to be related to perinatal brain damage, neonatal seizures and encephalopathy.<sup>13-16</sup> Preterm babies with higher counts of NRBC are found to have higher incidence of intraventricular haemorrhage, cerebral white matter injury, retinopathy of prematurity and necrotising enterocolitis.<sup>17-20</sup> It is also proved to be an early marker of brain damage.<sup>1</sup>

The purpose of this study was to find out the levels of NRBCs in the cord blood of term SGA neonates as well as to determine the relationship of cord blood NRBCs with early neonatal outcome (first 7 post-natal days).

**METHODS**

The study will be conducted over a period of 1 year from November 2015 to October 2016 on Term SGA babies delivered in Navodaya Medical College Hospital and Research Centre.

Basic data of mothers like age, parity, anemia, diabetics, PIH, Fetal presentation was collected. Also, natal risk factors like prolonged second stage, mode of delivery and presence of meconium stained fluid was collected. Babies were examined soon after birth and data recorded on a proforma. Gestational age was determined by Modified Ballard’s score. Newborns were classified as SGA’s using the graph adapted from Battaglia and Lubchenco. The outcome of these babies during the first postnatal week was monitored and data recorded.

**Inclusion criteria**

All Term SGA and Healthy Term AGA Newborns

**Exclusion criteria**

- Mothers with the following condition: maternal diabetes mellitus, hypertension, preeclampsia, chorioamnionitis,
- Babies with the following conditions: meconium stained amniotic fluid, congenital anomalies, twin-to-

twin transfusion, severe anemia, cyanotic heart disease.

**RESULTS**

The following observations were made after the completion of the study.

In the Table 1 the Gestational age of babies is compared between the two groups.

**Table 1: Gestational age of the newborns.**

Gestational age [weeks]	Min	Max	Mean	SD	P value
Control	19	20	19.92	0.42	0.0857
Study	19	20	19.16	0.45	

The mean gestational age among control and study group was 19.92 and 19.16 respectively. No significant difference was found among control and study group in regarding gestational age.

In the Table 2 the APGAR score at 1 minute is compared between the two groups. Low APGAR score ( $\leq 5$ ) was seen in 1 case in the study group. No newborn in Control group had Low APGAR. This difference was not statistically significant.

**Table 2: APGAR score at 1 minute.**

APGAR score	Control		Study	
	No.	%	No.	%
<_5	0	00	01	03
6-10	25	50	23	47
Total	25		24	

In the Table 3 the APGAR score at 5 minutes is compared between the two groups. In this study, no cases of low APGAR scores ( $\leq 5$ ) at 5 min.

**Table 3: APGAR score at 5 minutes.**

APGAR score	Control		Study	
	No.	%	No.	%
<5	0	00	0	00
6-10	25	50	25	50
Total	25		25	

**Table 4: Association of NRBC count with mode of delivery.**

Mode of delivery	Control			Study			P value
	No.	Mean NRBCS	SD	No.	Mean	SD	
LSCS	12	3.35	0.96	12	5.63	1.09	0.00005
NVD	13	2.84	1.57	13	4.16	1.605	0.0021
Total	25			25			

In the Table 4 the NRBC count is compared with mode of delivery. Out of 50 babies included in this study, 24 babies were delivered by LSCS and 26 babies by normal vaginal delivery.

Table 5 shows the range of the NRBC count.

**Table 5: NRBCs' range.**

NRBCS	Control		Study		P value
	No.	%	No.	%	
0-5	10	19	02	05	0.00005
6-10	14	29	10	20	
11-15	01	02	12	25	

The incidence of elevated NRBCS [ $>10$ NRBC/100WBCS] was statistically more in the study group [P=0.005].

Irrespective of the mode of delivery, the NRBC count was found to be significantly higher in the SGA babies group as compared to the AGA group and this was statistically significant [p=0.005].

**Table 6: Complications.**

Cause of admission	Control		Study	
	No.	%	No.	%
EOS	01	02	01	03
Hypoglycemia	00	00	02	04
Respiratory distress	00	00	00	00
Hyperbilirubinemia	00	01	03	09
Resuscitation	00	00	02	04
Observation	00	00	02	04
Mother side	23	47	14	28

Table 6 shows the complications. There are more complications associated in the study group than in the control group.

In the Table 7 the NRBC count is correlated with the complications in SGA babies.

Incidence of favorable neonatal outcome are more in the control group than in the study group. There was no correlation of elevated NRBCS with these conditions in both groups.

**Table 9: Following table is comparing the NRBC and mode of delivery.**

Study	No	Mode of delivery (no)		NRBC/100 WBC (mean)		P value
		LSCS	NVD	LSCS	NVD	
Present study	25	12	13	5.5	4.23	0.00005
Victoria K et al	36.5	22.5	14	37.8	5.45	0.0015

The data regarding the elevated NRBC counts and various neonatal morbidities are well known but the data

**Table 7: Correlation SGA babies.**

Complications	N	Range	Mean
		NRBC/100 WBC	NRBC/100 WBC
EOS	03	8-11	9.6
Hypoglycemia	05	5-13	9.4
Hyperbilirubenemia	09	2-14	6.8
NICU stay	22	2-14	9.5

In the Table 8 the NRBC count is correlated with the complications in early neonatal. The incidence of elevated NRBCS [ $>10$  NRBC/100WBC] was statistically more in the study group [P,0.005]. The complications were also more in the study group as compared to the control group.

**Table 8: Correlation of NRBCs with the outcome in early neonatal period.**

Outcome	Control		Study	
	No.	%	No.	%
Normal	23	42	14	28
Complications	01	03	11	22
Death	00	00	00	00
	$>10$	$<10$	$>10$	$<10$
NRBC/100WBC	1	0	05	06

**DISCUSSION**

Nucleated red blood cells (NRBCs) are seen in the blood of newborns, but in small numbers. They are primarily produced in the fetal bone marrow in response to erythropoietin. Up to 8 NRBC/100 WBCs are normal and values above 10 NRBC/WBC are considered to be elevated. Common causes of increased nucleated red blood cells include prematurity, chronic intrauterine hypoxia, anaemia and maternal diabetes, from acute stress mediated release from the marrow stores, and from postnatal hypoxia. In contrast, plasma erythropoietin is a good measure of tissue oxygenation and increase only when physiological compensatory mechanism does not prevent tissue hypoxia. There was no correlation between maternal age and NRBC count and there were no similar studies for comparison. there was no correlation between parity and NRBC count.

regarding the levels of NRBC count in term SGA babies are scarce. So, in this study we have tried to find out the

levels of NRBC in term SGA neonates and its correlation with the outcome in early neonatal period.

From the Table 9, it can be found that present study is comparable with Victoria K et al.<sup>21</sup>

The following observations could be made out.

- Gestational age was higher in present study
- Maternal age was lower which could be explained by social factors like early marriage, maternal under nutrition or low pre-pregnancy weight resulting in growth restriction in our setup.
- The incidence of elevated NRBC's was significantly more in neonates delivered by caesarean section in our study (P=0.0001\*). Similar results were reported in previous study by Minior VK.<sup>21</sup> This relation between NRBC and mode of delivery was found to be significant (P=0.003\*).
- The exact effects of labour and delivery on the NRBC count are unknown at the present time. In our study, labour and vaginal delivery was not found to be associated with and elevation of NRBC count and in fact, neonates delivered by caesarean section had significantly higher NRBC counts. Thus, in the AGA as well as growth restricted neonate, elevated NRBC's reflects a chronic process rather than acute events related to mode of delivery.

## CONCLUSION

This study was done to know the utility of neonatal nucleated red blood cells (NRBC) count as an independent predictor of short term perinatal outcome in term small for gestational age (SGA) neonates. My study showed that NRBC count was higher in SGA babies than term AGA babies but there was no correlation of NRBC count with the outcome in SGA babies.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Hermansen MC. Nucleated red blood cells in the fetus and newborn. Arch Dis Child Fetal Neonatal Ed. 2001;84(3):F211-5.
2. D'Souza SW, Black P, MacFarlane T, Jennison RF, Richards B. Haematological values in cord blood in relation to fetal hypoxia. Br J Obstet Gynecol. 1981;88(2):129-32.
3. Naeye RL, Localio AR. Determining the time before birth when ischemia and hypoxemia initiated cerebral palsy. Obstet Gynecol. 1995;86(5):713-9.
4. Soothill PW, Nicolaides KH, Campbell S. Prenatal asphyxia, hyperlacticaemia, hypoglycaemia, and erythroblastosis in growth retarded fetuses. Br Med J (Clin Res Ed). 1987;294(6579):1051-3
5. Thilaganathan B, Athanasiou S, Ozmen S, Creighton S, Watson NR, Nicolaides KH. Umbilical cord blood erythroblast count as an index of intrauterine hypoxia. Arch Dis Child Fetal Neonatal Ed. 1994;70(3):F192-4.
6. Korst LM, Phelan JP, Ahn MO, Martin GI. Nucleated red blood cells: an update on the marker for fetal asphyxia. Am J Obstet Gynecol. 1996;175(4 Pt 1):843-6.
7. Boskabadi H, Maamouri G, Sadeghian MH, Ghayour-Mobarhan M, Heidarzade M, Shakeri MT, et al. Early diagnosis of perinatal asphyxia by nucleated red blood cell count: a case-control study. Arch Iran Med. 2010;13(4):275-81.
8. Gea Y, Araujo O, Silva LV. Clinical value of lactate measurement and nucleated red blood cell counts in the placental segment of the umbilical vein of premature newborns for diagnosis of hypoxia-ischemia. J Pediatr (Rio J). 2007;83(2):186-90
9. Hanlon-Lundberg KM, Kirby RS. Nucleated red blood cells as a marker of acidemia in term neonates. Am J Obstet Gynecol. 1999;181(1):196-201.
10. Low JA. Intrapartum fetal asphyxia: definition, diagnosis, and classification. Am J Obstet Gynecol. 1997;176(5):957-9.
11. Papa D, Jyotsna GP, Ashok BB. Cord blood nucleated red blood cell count -a marker of fetal asphyxia. J Obstet Gynecol India. 2008;58(1):45-8.
12. Phelan JP, Korst LM, Ahn MO, Martin GI. Neonatal nucleated red blood cell and lymphocyte counts in fetal brain injury. Obstet Gynecol. 1998;91(4):485-9.
13. Buonocore G, Perrone S, Gioia D, Gatti MG, Massafra C, Agosta R, et al. Nucleated red blood cell count at birth as an index of perinatal brain damage. Am J Obstet Gynecol. 1999;181(6):1500-5.
14. Blackwell SC, Refuerzo JS, Wolfe HM, Hassan SS, Berry SM, Sokol RJ et al. The relationship between nucleated red blood cell counts and early-onset neonatal seizures. Am J Obstet Gynecol. 2000;182(6):1452-7.
15. Ghosh B, Mittal S, Kumar S, Dadhwal V. Prediction of perinatal asphyxia with nucleated red blood cells in cord blood of newborns. Int J Gynecol Obstet. 2003;81(3):267-71.
16. Haiju Z, Suyuan H, Xiufang F, Lu Y, Sun R. The combined detection of umbilical cord nucleated red blood cells and lactate: early prediction of neonatal hypoxic ischemic encephalopathy. J Perinat Med. 2008;36(3):240-7.
17. Green DW, Hendon B, Mimouni FB. Nucleated erythrocytes and intraventricular hemorrhage in preterm neonates. Pediatrics. 1995;96(3 Pt 1):475-8.
18. Silva AM, Smith RN, Lehmann CU, Johnson EA, Holcroft CJ, Graham EM. Neonatal nucleated red blood cells and the prediction of cerebral white matter injury in preterm infants. Obstet Gynecol. 2006;107(3):550-6.

19. Lubetzky R, Stolovitch C, Dollberg S, Mimouni FB, Salomon M, Mandel D. Nucleated red blood cells in preterm infants with retinopathy of prematurity. *Pediatrics.* 2005;116(5):e619-22.
20. Mandel D, Lubetzky R, Mimouni FB, Cohen S, Littner Y, Deutsch V et al. Nucleated red blood cells in preterm infants who have necrotizing enterocolitis. *J Pediatr.* 2004;144(5):653-5.
21. Minior VK, Bernstein PS, Divon MY. Nucleated red blood cells in growth-restricted fetuses: associations

with short-term neonatal outcome. *Fetal Diagn Ther.* 2000;15:165-9.

**Cite this article as:** Reddy TP, Chittam R, Kumar TS, Sindhura K, Chetty S. Outcome in the small for gestational age neonates in their early neonatal period in relation with the cord blood nucleated RBC's. *Int J Contemp Pediatr* 2017;4:1940-4.