

Cord blood nucleated red blood cell count – A marker of fetal asphyxia

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Abstract:

Background: Perinatal asphyxia is a serious problem and is a common cause of neonatal mortality and morbidity. Various predictors have been used to predict perinatal asphyxia but correlation between the clinical and biochemical markers have been poor. Nucleated red blood cell count of cord blood has been found as a possible marker of perinatal asphyxia.

Aim of study: To assess nucleated RBC count as marker of perinatal asphyxia.

Methods: This prospective case control study was conducted in Lalla-Ded hospital GMC Srinagar from Mar 2019-Mar 2020. We studied 200 patients with 100 each in case and control group. Cord blood sample was assessed for pH, base excess and nucleated RBC count in cases and controls. The results were compared.

Results: The mean NRBC count of cases was 23.3 ± 10.1 and it was 12.5 ± 4.7 in control group. The difference was statistically significant. Also NRBC count correlated with non-reassuring fetal heart rate pattern, meconium stained liquor, low 1min and 5 min Apgar. NICU admission was significantly high in babies with high NRBC count with significant mortality and morbidity.

Conclusion: NRBC count can be used as a marker to confirm perinatal asphyxia. The test is simple, quick, accurate and effective to diagnose and start treatment to prevent long term sequelae.

Key words: Cord blood, Hypoxia, nucleated red blood cells, perinatal asphyxia.

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I. Introduction

Perinatal asphyxia is a condition of impaired blood gas exchange that, if persists, leads to progressive hypoxemia and hypercapnia with a metabolic acidosis.

Essential characteristics defined jointly by American academy of pediatrics and the American college of obstetrics and Gynecologists should be present.

1. Profound metabolic or mixed acidosis on umbilical cord arterial blood sample
2. Persistence of an Apgar score of 0-3 for more than 5 min
3. Neurological manifestations in immediate neonatal period which include seizure, hypotonia, coma or hypoxic-ischemic encephalopathy.

Reflex activated by asphyxia consists of shunting of blood from skin and splanchnic areas to the heart, adrenals, and brain to protect them from hypoxic injury.¹ perinatal asphyxia remains a significant cause of perinatal morbidity and mortality the world over, and is known to complicate 5-10% of all deliveries.²

Various parameters to define perinatal asphyxia are Apgar score, umbilical arterial academia, intrapartum electronic fetal monitoring, scalp PH measurement and presence of meconium in amniotic fluid. However no single marker has shown of perinatal asphyxia has shown good predictive efficacy and a combination of various indices can help in early diagnosis of perinatal asphyxia.³

Considering the hematopoietic response to hypoxia in utero, the elevated count of nucleated red blood cells was investigated as marker of hypoxia.⁴ Recent publications have shown a significant association between nucleated red blood cell count and adverse perinatal outcome such as low Apgar scores and pH values, fetal growth restriction, perinatal brain damage, and early onset seizures.⁵⁻⁸

Erythropoietin stimulated due to hypoxia, is increased in cord blood, in itself, is a marker of fetal hypoxia.⁹ Acute increase in nucleated red blood cell counts may be secondary to mobilization of endogenous cytokines such as IL-6 which is markedly increased in response to hypoxia.¹⁰

Aims and objectives

To study the cord blood nucleated RBC count in asphyxiated and non-asphyxiated fetuses at birth
 To find out the correlation between nucleated RBC count, fetal acidosis and the clinical markers of asphyxia.

II. Materials And Methods

This prospective comparative study was conducted in the department of Obstetrics and Gynecology GMC Srinagar.

Inclusion criteria were Primigravida, singleton pregnancy, 37-40 weeks, Rh +ve cases. 100 cases were taken in study group and 100 in control group. For the cases two or more of the following criteria were chosen.

Thick meconium stained amniotic fluid.

Non reassuring fetal heart rate pattern

Apgar score ≤ 6 at 5 minute of birth

A detailed record of obstetric, menstrual, past, medical or surgical history was taken. A detailed examination was done.

From all the subjects, immediately after delivery, a 10-15 cm segment of cord was isolated between two clamps. Umbilical arterial blood was drawn from cord into heparinized syringe for estimation of pH. A second sample was taken in an EDTA coated bottle for making peripheral blood smear for nucleated RBC count against WBCs until 100 WBCs were counted.

Relationship between NRBCs and pH was assessed. The correlation between meconium stained amniotic fluid, non-reassuring fetal heart pattern, low Apgar score and NRBCs was also analyzed. Infants were followed to 8 weeks of age.

Data was expressed as mean and percentage. The characteristics of cases and controls were compared by student t test, Mannwhitney U-test, chi-square analysis and analysis of variance.

III. Observations

Table 1: Maternal characteristics

	Cases	Controls	P value
Mean age \pm SD	27.5 \pm 4.2	26.9 \pm 4.6	0.406
Mean gestational age	38.4 \pm 1.2	38.4 \pm 1.1	0.839
Haemoglobin(grams)	10 \pm 1.7	9.8 \pm 1.7	0.390

Table 2: Distribution as per route of delivery

Mode of delivery	Cases (%)	Controls (%)	P value
Vaginal	52	65	0.063(NS)
LsCS	48	35	

Table 3: Distribution of risk factors in studied population

		Cases	Controls	P value
Meconium	+++	51	0	0.000
	++	43	0	
	clear	6	100	
Fetal heart rate pattern	Reassuring	23	100	0.000
	Non Reassuring	77	0	
Apgar score at 5 min	>6	25	100	0.000
	≤ 6	75	0	
Number of risk factors	0	0	100	0.000
	2	54	0	
	3	46	0	

Table 4: Distribution of birth weight and gender

	cases	controls	P value
Birth weight	2.93 \pm 0.48	3.04 \pm 0.49	0.119
Gender of babies			
Males	48	53	0.481
Females	52	47	

Table 5: Correlation between umbilical artery pH, base excess, and cord blood nucleated RBC count/100 WBCs in cases and controls

	cases	controls	P value
Umbilical artery pH	6.945 \pm 0.088	7.227 \pm 0.578	<0.0001
Base excess	-13.7 \pm 4.1	-3.7 \pm 3.7	<0.001
NRBC count	23.3 \pm 10.1	12.5 \pm 4.7	<0.001

As obvious from above table 5, a significant correlation was seen between NRBC count, low umbilical artery pH and base excess

Table 6; Correlation between NRBC count/100 WBCs and 1 minute Apgar score in study population

APGAR SCORE AT 1 MIN	N=200	min	max	Mean±SD	P value
≤6	94	5	40	23.5±10.1	<0.001
>6	106	6	31	12.9±5.4	

Table 6 shows Nucleated RBC count was significantly increased in babies with low Apgar (23.5±10.1) and babies with good Apgar(12.9±5.4)(p<0.001)

Table 7; Correlation between NRBC count/100 WBCs and 5 minute Apgar score in study population

Apgar score	number	min	max	Mean±SD	P value
≤6	75	7	40	24.0	0.000
>6	125	5	40	14.2	

Table 8: Correlation between NRBC count/100 WBCs and fetal heart rate pattern

Fetal heart rate pattern	N=200	Min	max	Mean±SD	P value
Reassuring	123	5	40	14.4	0.000
Non Reassuring	77	6	40	23.6	

Table 8 shows that Nucleated RBC count is significantly increased in babies with non- reassuring fetal heart rate pattern(23.6 vs 14.4)

Table 9: Cord blood NRBC count/100WBCs in relation with umbilical artery base excess in study population

Base excess	N=200	min	max	Mean±SD	P value
<-7	113	5	40	21.5±10.3	<0.001
≥-7	87	5	37	13.3±6	

Table 10: Incidence of NICU admission in cases and controls

NICU admission	Cases(100)	Controls(100)	P value
Yes	45	2	0.000
No	55	98	

Nicu admission was significantly high in cases as compared to controls. Nucleated RBC count was higher in babies with NICU admission(p<0.001).

Table 11: Cord blood NRBC count/100WBCs in relation with NiCU admission

NICU admission	n	Min	Max	Mean±SD	P value
Yes	45	8	40	29.5	<0.001
No	55	6	31	18.3	

Table 12: Neonatal outcome in asphyxiated group

Neonatal outcome	n	%
Surviving	95	95.0
Died	5	5.0
HIE		
Yes	21	21.0
No	79	79.0
HIE grade		
Mild	10	47.6
Moderate	7	33.3
Severe	4	19.0

5% of asphyxiated babies died and in surviving 21% developed hypoxic ischaemic encephalopathy and in those 19% had severe grade of HIE. There was a non- significant difference between various grades of HIE.

Table 13:Nucleated RBC count/100 WBCs in various grades of HIE

HIE grade	n	min	max	Mean±SD	P value
Mild	10	10	39	26.2±10.3	0.107(NS)
Moderate	7	26	38	33.0±4.4	
Severe	4	26	40	35.8±6.6	

IV. Discussion:

Various studies have suggested that elevated umbilical cord NRBC counts are associated with either acute and chronic fetal hypoxia. Present study was done to evaluate the same.

In our study max number of patients was in the age group of 25-34yrs with a mean of 27.5 ± 4.2 . Similar age group patients were studied by B. Ghosh et al.¹¹

The mean gestational age was 38.4 ± 1.2 and 38.4 ± 1.1 respectively. Dasari Papa et al¹² studied mean gestational age of 38.95 ± 0.69 and 39.25 ± 1.06 respectively.

In our study 52% of cases and 65% of controls delivered vaginally whereas 48% cases and 35% controls delivered by LSCS.

While assessing markers of asphyxia, it was observed 94% of cases had meconium, 77% had non reassuring fetal heart rate pattern and 75% of cases had Apgar score <6 at 5 min of birth. The respective proportion of cases in the study by Dasari Papa et al were 79%, 90% and 90%.

In our study mean umbilical arterial pH in cases was 6.945 ± 0.088 whereas in controls it was 7.22 ± 0.578 . While assessing the relationship of between cord blood nucleated Red blood cells and umbilical artery pH, it was observed that the mean NRBC count /100WBC in asphyxiated group was 23.3 ± 10.1 and non asphyxiated group it was 12.5 ± 4.7 . In a study by B Ghosh et al¹¹ the mean cord blood NRBC count/100 WBC in asphyxiated group was 16.5 ± 6.4 and in non asphyxiated it was 8.6 ± 7.01 .

In our study an inverse relationship was found between the decreasing base excess and nucleated RBC count. The mean NRBC count was 21.5 ± 10.3 in neonates with umbilical arterial base excess <-7mEq/L, and 13.3 ± 6 in newborns with base excess >-7. Similar relationship was observed in the study by Hanlon-Lundberg et al⁵.

The mean NRBC count/100 WBCs was higher in subjects having meconium stained amniotic fluid (23.3 ± 10) than in those who had clear liquor (13 ± 6.0) and this was statistically significant.

In a study by ROYA Faraji et al¹³ the mean NRBC/100 WBC in subjects having meconium stained liquor was 8.6 ± 6.54 compared to 3.88 ± 3.92 in controls having clear liquor.

Apgar score was devised as a quickly evaluating the status of the neonate. In our study the mean NRBC count/100wbc was 23.5 ± 1 in neonates with Apgar score <6 at 1 min and 12.9 ± 5.4 in neonates having Apgar score >6 at 1 min.

In the study by B Ghosh et al³² the correlation coefficient between NRBC count/100WBCs and Apgar score at 1 min was -0.50. In the study by Dasari Papa et al⁴⁷ the mean NRBC count was 36.23 ± 10.01 in neonates with Apgar score at 5 min <6 and 13.04 ± 6.42 in neonates with Apgar score at 5 min >6 (p=0.026).

While assessing the relation between cord blood NRBC/100WBC and non reassuring fetal heart pattern, our study established a statistically significant correlation, the mean counts were higher in non reassuring fetal heart rate pattern than those in reassuring FHR pattern (23.6 ± 10.4 vs 14.4 ± 7) (p<0.001)

Neonates cared for in the neonatal intensive care unit had higher nucleated RBC count than did those who recovered either with their mothers or in the regular neonatal nursery. The incidence of NICU admission in our study was 45% in cases and 2% in controls. The mean NRBC count in neonates admitted in NICU was 29.5 ± 9.3 whereas in the rest of the cases it was 18.3 ± 7.6 (p,0.001). In the study by Dasari Papa et al⁴⁷ the incidence of NICU admission was 57.69% in cases and the mean NRBC count was much higher in these neonates as compared to those who were cared in regular nursery (p<0.005).

Cord blood NRBC count correlated well with fetal acidosis. As umbilical artery pH and base excess decrease, nucleated red blood cell counts increase. Elevated NRBC counts are also associated with lower Apgar scores, meconium and admission to the special care nursery.

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Footnotes:

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Conflict of interest: Nil

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