

Prediction of Fetal Asphyxia by Cord Blood Nucleated Red Blood Cell Counts

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Abstract:

Introduction: Birth asphyxia is a combination of hypoxia and hypoperfusion of the neonate during the intra-partum period leading to long term complications. Since blood gas analysis is not commonly available, search is on for a surrogate marker of fetal hypoxia which has high accuracy and at the same time is easy to measure and does not require specialised equipment. **Materials and Methods:** This prospective comparative study was conducted at tertiary care hospital in Rajasthan in 50 cases and 50 controls. Women with two or more of the parameters (Meconium staining of amniotic fluid, non-reassuring fetal heart rate patterns, Apgar score ≤ 6 at 5 mins after birth and admission to NICU within 24hrs after birth) were included in the study group while women with none of these parameters were included in control group. Umbilical arterial pH and cord blood NRBC levels were measured at birth. **Results:** NRBC count in study group was 18.40(SD3.33) and in control group was 9.00(SD3.21). Significant association of elevated NRBC count was found with meconium staining of amniotic fluid, low Apgar scores, abnormal fetal heart rate patterns, admission to NICU within 24 hrs of birth and maternal tobacco use. **Conclusion:** NRBC count is a marker that can potentially be used for diagnosis of fetal hypoxia even in peripheral centres.

Keywords: Meconium, umbilical, Apgar, fetal, hypoxia.

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I. Introduction

Birth asphyxia is a combination of hypoxia and hypoperfusion of the neonate during the intra-partum period leading to long term complications. To clarify the role of intra-partum events in causing permanent neurological injury, the American College of Obstetricians and Gynecologists developed a precise definition of birth asphyxia that includes the presence of all three: profound acidosis, persistently low Apgar scores and neurological sequelae/multiorgan dysfunction.¹

Since blood gas analysis is not commonly available, especially in limited resource settings, several other markers are used as surrogate markers of fetal hypoxia. These include meconium staining of amniotic fluid, abnormal Cardiotocograph and severity of neonatal encephalopathy. However, these markers have poor correlation with fetal acidosis. Hence, search is on for a surrogate marker of fetal hypoxia which has high accuracy and at the same time, is easy to measure and does not require specialised equipment.

Measurement of cord blood nucleated RBCs is one such marker which has shown much promise as a future marker of fetal acidosis and fetal hypoxia. This study aims to find the correlation between Nucleated RBC count, fetal acidosis and clinical markers of asphyxia.

II. Materials and Methods

This prospective comparative study was conducted at tertiary care hospital in Rajasthan in 50 cases and 50 controls. Antenatal women attending the labour and delivery room were enrolled for the study divided into cases and controls based on clinical criteria, after written informed consent. The clinical parameters studied were: Meconium staining of amniotic fluid, non-reassuring fetal heart rate patterns, Apgar score ≤ 6 at 5 mins after birth and admission to NICU within 24hrs after birth. Women with two or more of the above parameters were included in the study group while women with none of these parameters were included in control group. Socio-demographic data was collected for all the participants and labour was rigorously monitored, cord blood

sample was collected for umbilical artery pH and for cord blood nucleated RBCs. Babies were examined at birth by paediatrician and followed for 24 hrs after delivery. Sample for umbilical artery pH was collected from umbilical artery from an isolated, double clamped segment of the cord on placental side in a heparinised syringe and sent immediately for blood gas analysis.

Sample for cord blood nucleated RBCs was collected from umbilical vein after delivery of the fetus from an isolated, double clamped segment of cord and transferred to an EDTA coated vial. Thin smear of the blood was made and stained with leishman's stain and examined under 100x magnification.

III. Results

The study and control groups were similar with regard to various socio-demographic factors (Table 1). The mean NRBC count was 18.4(SD3.33) in the study group compared to 9.00(SD3.31) in the control group. Average number of NRBCs in women with Apgar ≤ 6 at 1 min was 15.54(SD5.78) whereas in group with Apgar scores >6 at 1 min, average NRBC number was 9.78(SD2.97) ($p < 0.01$). In neonate with 5 min Apgar score ≤ 6 , NRBC count was 17.74(SD4.84) whereas in neonate with Apgar score >6 , count was 11.22(SD4.47), with a p-value < 0.001 . In neonates who had passed meconium intra-partum, mean NRBC count was 16.82(SD4.57) while neonates who had not passed meconium had a mean NRBC count of 10.45(SD4.94), the difference having a p-value of < 0.001 . Among neonates who needed admission in NICU within 24 hrs of birth had mean NRBC count of 17.35(SD5.35) while neonates who remained healthy had mean NRBC count of 11.55(SD4.77). The difference was highly significant with p-value < 0.001 . Table 2 shows variation of NRBC levels with umbilical artery pH. Highest NRBC values were found in the pH group ≤ 6.9 , with mean NRBC count of 19.44(SD5.4). Lowest values of NRBC were in the pH group ≥ 7.4 with mean NRBC level of 3.33(SD1.00). Foetuses with abnormal fetal heart rate patterns had a mean NRBC count of 16.65(SD5.14) while foetuses with normal fetal heart rate patterns had mean NRBC count of 9.79(SD3.79). This difference was highly significant with p-value of < 0.001 . Cord blood NRBC levels were compared between the modes of delivery, foetuses delivered by caesarean had mean count of 14.56(SD5.34) while vaginally delivered foetuses had a mean count of 12.90(SD5.95), these values are not significantly different. Exposure to tobacco during pregnancy was studied as a parameter affecting NRBC levels. Fetuses exposed to tobacco in-utero had mean NRBC count of 17.00 (SD5.32) compared to 13.29(SD5.64) in non-exposed foetuses. This difference was highly significant with p-value < 0.001 . Age was studied as a parameter possibly affecting NRBC levels but was not found to affect it significantly.

IV. Discussion

As early as 1967, Fox H studied nucleated RBCs in fetal vessels of placenta and suggested that NRBCs increase in response to asphyxial event². Hanlon Lundberg confirmed that term neonates with academia had higher nucleated RBC counts than non-acidotic neonates³. Dasari P et al reported mean NRBC count of 25.65 in acidotic group compared to 12.33 in non-acidotic group⁴. Apgar score is a well established surrogate marker of fetal hypoxia. We found significant correlation of Apgar scores at 1 and 5 mins after birth with NRBC count. Hanlon Lundberg³ and Ghosh et al⁵ found significant association between Apgar scores and NRBC counts. We found that elevated NRBC counts have better correlation with fetal acidosis than presence of meconium in amniotic fluid. M Spencer, in 2000, studied cord blood and early neonatal NRBCs and found it to be a better than non-reassuring CTG, presence of meconium or low 5-min Apgar score for predicting fetal hypoxia⁶.

We found significant association of neonatal ICU admission with cord blood NRBC count. These findings indicate that NRBC count in cord blood is an independent predictor of neonatal outcome and could have additional value as an indicator of early neonatal course and neonatal morbidity. Ghosh et al⁵ also found that cord blood nucleated RBCs can be used as a reliable predictor of early neonatal outcome. The mean umbilical arterial pH was significantly more in study group compared to control group. Spencer MK⁶ and B Ghosh⁵ had findings comparable to our study. When association of cord blood nucleated RBC count was studied with pH values of umbilical artery, an inverse linear association was found. Neonates with pH < 6.9 had maximum number of NRBCs while neonates with pH > 7.4 had least number of NRBCs. Halon- Lundberg et al³ also reported that umbilical blood pH data demonstrates trend towards inverse proportionality with data on NRBC count per 100 WBCs.

We found that abnormal fetal heart rate patterns are significantly associated with elevation of NRBC counts irrespective of other factors. Phelan et al⁷ reported highest NRBC counts in foetuses with non-reactive fetal heart rate patterns. Ferber et al⁸ found significant difference in NRBC counts between etuses with normal and abnormal fetal heart rate patterns.

We found significant association of absence of accelerations within 1 hour before birth with elevation of NRBC levels. Leveno et al⁹ and Krebs et al¹⁰ have also documented an association between lack of FHR accelerations and adverse perinatal outcome. Mode of delivery was not found to be associated with NRBC count, a finding consistent with previous reports by Kathleen M³ and Hanlon Lundberg.

Passive or active tobacco use was found to be associated with increased NRBC counts in cord blood. This could be because smoking increases carboxyhemoglobin in blood and fetal carboxyhemoglobin levels are even higher. Nicotine causes a reduction in utero-placental blood flow. These factors cause relative intra-uterine hypoxia resulting in increased NRBC counts. Dollberg S¹¹, in 2001, also reported passive smoking as a factor causing increased NRBC counts.

Our study did not demonstrate gestational age as a factor affecting NRBC counts. This is in contradiction to findings by Ronald Axt who found that NRBC counts are higher in post-term neonates when compared with term neonates¹².

V. Conclusion

Nucleated RBC count is a specific and sensitive marker of fetal hypoxia and is significantly associated with surrogate markers of fetal hypoxia like meconium staining of amniotic fluid, low Apgar score, abnormal fetal heart rate patterns and admission in NICU. NRBC count is a marker that can potentially be used for diagnosis of fetal hypoxia even in peripheral centres.

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Table 1

Socio-demographic Factors			
		Study group	Control Group
Age(Mean)		24±4.19 yrs	24.02±2.82 yrs
Education	Literate	0.8	0.84
	Illiterate	0.2	0.16
Socio-economic status	Class 1	0.04	0.04
	Class 2	0.28	0.38
	class 3	0.46	0.43
	class 4	0.12	0.08
	class 5	0.1	0.1
Residence	Urban	0.82	0.82
	Rural	0.18	0.18
Gestational Age(mean)		37(SD1.06)	38.26(SD1.02)

Table 2

Variation of NRBC count with pH	
pH	Mean NRBC±SD
≤6.9	19.44(SD5.4)
7.00-7.09	16.95(SD4.85)
7.10-7.19	10.2(SD4.43)
7.20-7.29	9.62(SD2.83)
7.30-7.39	7.02(SD3.74)
≥7.4	3.33(SD2.00)

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