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Original Research Article

Correlation of nucleated red blood cell count with neonatal intensive care unit admission

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ABSTRACT

Background: Perinatal asphyxia should be diagnosed, when baby goes on to develop hypoxic ischemic encephalopathy which has shown to be much more reliable indicator of long term handicap than any other perinatal markers like non reassuring FHR, Apgar score, meconium stained amniotic fluid and blood acid base status of fetus. Since NRBC is related to hematopoietic response to hypoxia it predicts the chance of neurological sequelae and NICU admission. The aim of our study to analyze the significant relationship of NRBC count and NICU admission.
Methods: This was a retrospective comparative study conducted in department of OBG, Patna medical college and Hospital between December 2013 to November 2015 in tertiary care health centre. Umbilical cord blood samples were collected from 100 newborns with asphyxia at birth out of which 56 were admitted in NICU taken as study group and rest 44 asphyxiated babies were not admitted in NICU were taken as control group. NRBC per 100 WBC was counted in Cord blood sample from all babies.
Results: This shows that average count of NRBC/100 WBC in the study with NICU admission was 27.37±7.25. Average count in the study group with no NICU admission was 23.93±6.04. The difference was statistically significant ($p<0.05$).
Conclusions: This study concludes that NRBC count correlate well with fetal asphyxia and finally NICU admission. Early detection leads to decrease neurological morbidity and mortality among survivors.

Keywords: Fetal heart rate, Neonatal intensive care unit, Umbilical cord blood, White blood cell

INTRODUCTION

There is increasing evidence that hypoxic ischemic injury of the neonate might not be related to labor but might occur during pregnancy. For example, clinical or biochemical indicators of severe fetal asphyxia are found in only about 10% to 20% of cerebral palsy cases. Therefore, assessment of additional markers of antenatal intrauterine hypoxemia is a relevant task.[1-4] WHO estimates that globally between 4 to 9 million newborn suffers birth asphyxia each year which leads to 1.2 million deaths and about the same number of infants who develop severe disability. Perinatal asphyxia should be diagnosed, when baby goes on to develop hypoxic ischemic encephalopathy which has shown to be much more reliable indicator of long term handicap than any other perinatal markers like non reassuring FHR, Apgar score, meconium stained amniotic fluid and blood acid base status of fetus. Since NRBC is related to hematopoietic response to hypoxia it predicts the chance of neurological sequelae and NICU (neonatal intensive care unit) admission.

METHODS

This was a retrospective study which establishes relationship between cord blood NRBC count and NICU admission in a tertiary level health care centre. Cord

blood were collected from 100 newborn with asphyxia at birth out of which 56 were admitted in NICU taken as study group and rest 44 asphyxiated babies were not admitted in NICU taken as control group. NRBC per 100 WBC was counted in cord blood sample from all babies. Informed consent was obtained for every patient. Patients in both case and control group were selected from labour room, patient. These were the patients who were having singleton pregnancy and were in labour between 37 to 42 weeks of gestation. All patients who had associated with acute and chronic hypoxia were excluded from this study. These factors may influence hematopoiesis so their presence may give false positive results.

Inclusion criteria for current study were presence of two or more of following criteria; thick meconium stained amniotic fluid, non-reassuring fetal heart rate pattern and low Apgar score ≤6 at 5 minutes of birth. From all the subjects, cord bloods were collected immediately after clamping and cutting the umbilical cord. Sample was taken in an EDTA coated bottle for the purpose of making blood smear. Prepared slide was examined under high power of microscope and number of NRBC was counted against the number of WBC until 100 WBC were counted. Statistical analysis was done using SPSS (software statistical package for social science) and Chi square test.

RESULTS

In this study, out of 100 babies in the asphyxiated group, 56 were admitted in NICU. These were the neonates who had significant neonatal morbidity in the form of severe birth asphyxia, seizures or hypoxic encephalopathy. Rest 44 babies in the control group didn't have significant morbidity. In the neonates who were admitted in the NICU, the mean NRBC count per 100 WBC in the cord blood was 27.37±7.25, where as in the neonates of the control group, who were not admitted in the NICU, the mean NRBC count in the cord blood at the time of birth was 23.93±6.04. The difference in the NRBC count was statistically significant. NICU admission is shown in (Table 1).

Table 1: NICU admission in asphyxiated babies.

NICU Admission	Number of asphyxiated babies n=100	Mean NRBC count
Yes	56	27.37±7.25
No	44	23.93±6.04

Mean NRBC count/100 WBC in the group with NICU admission was 27.37±7.25 and in the group with no admission it was 23.93±6.04. NRBC count in both study and control group is shown in (Table 2). Average NRBC count/100 WBC in babies with NICU admission was 27.37±7.25. Average NRBC count/100 WBC in babies with no NICU admission was 23.93±6.04. Relationship of NRBC count with study and control group is shown in (Figure 1).

Table 2: NRBC count in both study and control group.

NRBC/100 WBC	Babies admitted in NICU (study group)	Babies not admitted in NICU (control group)
0-9	0	0
10-19	7	6
20-29	33	32
30-39	11	5
40-49	5	1
Mean	27.37±7.25	23.93±6.04

p<0.05

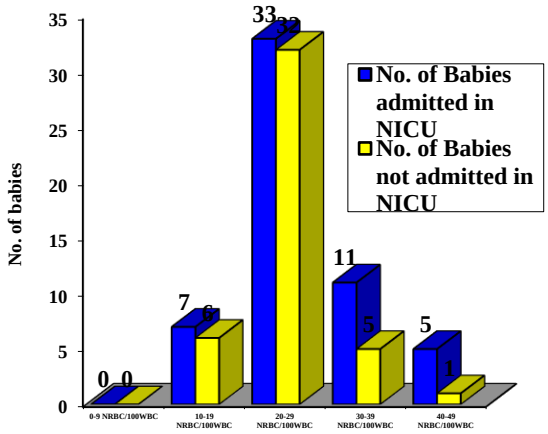

Figure 1: Correlation of NRBC and NICU admissions among patients of study and control group.

DISCUSSION

Nucleated RBC or normoblast are immature cell that were first described in 1871 to be present in neonatal blood.[5] Until the sixth and seventh week of gestation, practically all fetal red blood cells are nucleated; by the twelfth week of gestation, NRBC count declines and is uncommon to find in the circulation of term newborn.[6] Most evidence in human subjects suggests that the time interval between the erythropoietin rise and the peak NRBC count is at least 24 to 48 hrs and declines after 7 days. The number of NRBCs circulating in the blood of a healthy, full-term infant is variable but normally does not exceed 8 or 9 NRBCs per100 WBCs.[7] In a previous study we reported comparable NRBC counts in healthy, full-term infants and slightly higher counts in post-term infants.[8] NRBC are produced in the fetal bone marrow primarily in response to erythropoietin and are stored in marrow as precursors of reticulocytes and mature erythrocytes. Various types of stimulus's leads to increase in the number of circulating NRBC due to their enhanced erythropoietic activity or a sudden release from

the marrow storage pool due to injury to sinusoidal endothelium in beds subjected to ischemia. Previously it was thought that hypoxic ischemic injury of the neonate was caused by intrapartum asphyxia. In addition, in only 10% to 20% of cases of cerebral palsy has an association with clinical or biochemical markers of fetal asphyxia been observe.[1-4] A major challenge of modern perinatal medicine in the future will be to reduce long term neurologic impairment of the neonate. So, the need for alternative markers of antenatal chronic fetal hypoxia is an essential and relevant task.[9] Fetal erythropoiesis is primarily determined by cycle of the hypoxia-erythropoietin-NRBC precursors.[10] Korst et al reported distinct NRBC patterns in relation to the timing of fetal injury in neurologically impaired neonates.[11] They found higher NRBC counts in cases of suspected injury before admission to the hospital than in cases of hypoxic injury occur during birth process. Korst et al in their study also mentioned that the clearance of the NRBC from the circulation may be of help of prognosticating the outcome of these asphyxiated neonates in the study by Phelan et al in 1996 which was done to establish relationship between NRBC and HIE and long term neurologic impairment, it was found that the mean NRBC count in the study group was 34.5±68.3 and in the control group, was 3.4±3.0. The difference was statistically significant.[12] In an animal model, release of reticulocytes after hypoxia was not seen until the second or third day after the hypoxic stimulus.[13] Given this observation, elevated count of NRBC counts should be found in the cord blood of the neonate only if the hypoxic episode occurs prior to the beginning of labor. So, high NRBC counts after acute Intrapartum hypoxia are not probable in postpartum cord blood but might occur during the neonatal period. This is in accordance with our previous work, which did not show any relation between mode or duration of delivery and NRBCs in uncomplicated full and post-term pregnancies.[8] The association of increased erythropoietin levels in fetal plasma with intrauterine growth restriction has been reported previously.[14] Elevated NRBC counts associated with higher resistance indices in fetal vessels have been previously documented by Groenenberg et al.[15] Recently, this finding was confirmed by Bernstein et al and Baschat et al.[16,17] In the study by Dasari Papa et al of JIPMER said that there was no neonatal morbidity or mortality in the control group. The average NRBC count in the NICU admission group was 29.80±10.90 and in the 'not admitted' group it was 20.00±5.26. p value was 0.006, which was statistically significant. Their result is consistent with the present study results.[18] In the study by Lundberg et al conducted between August 1996 to Febrary 1997, neonates with higher NRBC count were more likely to be admitted to NICU.[19] Giuseppe Buonocore et al studied NRBC as an index of perinatal brain damage. They also found that NRBC was helpful in predicting neuro developmental outcome. It not only reflects an adaptive response of infants to perinatal distress but also, is predictive of an increased risk of brain damage.[20] Thus we can see that in the present study, as well as in the previous studies NRBC count in the neonates admitted to NICU due to morbidity from birth asphyxia was significantly higher than the neonates not admitted in NICU. This means that NRBC count correlates well with the neonatal morbidity due to birth asphyxia leading to NICU admissions.

CONCLUSION

The clinical diagnosis of perinatal asphyxia is based on several criteria, the two important ones being evidence of cardio respiratory and neurological depression and evidence of acute hypoxic compromise with acidosis (defined as an arterial blood pH of less than 7.1). From this study, it can be concluded that NRBC count correlates well with fetal acidosis in asphyxiated neonates and finally NICU admission and this is a simple bed side test, the sample being obtained non invasively from an otherwise discarded specimen and analyzed by personnel or equipment easily available in most hospital laboratories.

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

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