

Original Research Article

Role of Nucleated Red Blood Cells in Chronic Intra uterine Fetal Hypoxia

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Abstract: Background and Aims: In India there is 26 million births annually and that this represents 20% of all global live births (UNICEF, 2009). There are also over one million neonatal deaths per year in India due to birth asphyxia. This is 25% of the total global burden of neonatal deaths. The overall neonatal mortality rate in India is 44/1000 live births (Korst, L. M. *et al.*, 1996). NRBC (Nucleated RBC) has emerged as a marker for chronic intra uterine fetal hypoxia. Our study aimed to find the normative value of NRBC in healthy term newborns and evaluate role of Nucleated RBC as a marker for chronic intra uterine fetal hypoxia. **Methods:** A Prospective study conducted in Children and women tertiary care Hospital over a period of 12 months. 180 live born infants who met the inclusion criteria were evaluated. The cases divided into two groups: group C includes (100) normal newborns, group A (30) newborns of chronic birth asphyxia. Blood samples from umbilical cord were collected immediately after delivery and examined for PCV, Platelet count, WBC count & differential count, NRBC (per 100 WBC) , Blood film. **Result:** The mean value of NRBC per 100 white blood cells in a healthy, term, singleton neonate was (2.43 ± 2.34) and a significant increased number of NRBC in cord blood of chronic intra uterine hypoxia & the mean value of nucleated red blood cell was observed (18.5 ± 7.32) . **Conclusion:** It was concluded that in infants with chronic intra uterine hypoxia NRBC per 100 WBC count in cord blood can be regarded as a good indicator for fetuses prone to such chronic hypoxia.

Keywords: Birth asphyxia, Erythropoiesis, Nucleated RBC.

INTRODUCTION:

The erythroblasts or normoblast or nucleated red blood cells (NRBC) is an immature form of the red blood cells a precursor of reticulocytes. The NRBC test was first developed to correct the white blood cells (WBC) count in new born when the later was done with a coulter counter to eliminate NRBCs a source of error with the automated WBCS count (Ingall, D. *et al.*, 2001).

The first investigations as to presence of NRBC in the blood of newborn infants are accredited to Neuman in 1871 (Green, D.W. *et al.*, 1995). Loss, Geiss Lee and Gapha in 1895 concluded that normoblasts did not occur in the blood of newborn infants and that their presence therefore, must be considered as pathological sign. The presence of higher NRBC count indicates pathology, it was found in prematurity and in pathologic conditions such as erythroblastosis fetalis, congenital heart diseases and still birth (1), Another reports of increased of NRBC in states of active erythropoiesis resulting from such events as intrauterine

hypoxia (Green, D.W. *et al.*, 1995), early gestation ,hemolysis and fetal blood loss (Iversen, P.O. 1997; Ruth, V. *et al.*, 1990).

Recently elevated NRBCs counts have been associated with long-term neurological impairment (Hanlon-Lundberg, K. M., & Kirby, R. S. 1999) and with more admission to neonatal intensive care units.

METHODS:

A current study was conducted in Children and women tertiary care Hospital, over a period of 12 months, 180 live born infants with following inclusion criteria

- Singleton.
- Term pregnancy (gestational age >37 wk and <42wk) by last menstrual period and I or early ultrasound (<20 wk gestational age) ended with uneventful vaginal delivery or elective caesarian section.

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- Normal intra partum history (no maternal illness).
- Normal antepartum events.
- Clear amniotic fluid.
- Apgar score at 1 and 5 minute more than 6.
- No neonatal disorder .
- Normal neurological evaluation at discharge
- For all cases mother age ranged between (18-40) years, Parity between (1-4), positive blood group, with no history of diabetes, hypertension, ante partum hemorrhage, blood disease, smoking, alcohol or drug use, were evaluated. Cord bloods specimens of (130) term newborn were examined for nucleated red blood cell (NRBC) per 100 WBC. The cases divided into two groups: group C includes (100) normal newborns, group A (30) newborns of chronic birth asphyxia.

The cases categorized in to two groups:

Group C: Normal Newborns

Consisted of (140) Samples of healthy newborns; from these samples only (100) samples were fulfilled all general criteria while the reminders (40) samples were discarded.

Group A: Newborns with Birth asphyxia

Consist of (40) Samples of newborns with birth asphyxia. Only (30) Samples were fulfilled all general criteria while the reminders (10) samples were discarded.

Blood samples from umbilical cord were collected immediately after delivery the blood sample examined for PCV ,Platelet count , WBC count & differential count, NRBC (per 100 WBC) , Blood film. Data was analyzed by using Student t test. A p value of <0.0001 is considered as significant.

RESULTS:

Table.1 Dermographic Data of Study Population

TOTAL CASES (n=130)	NUMBER	MEAN	PERCENTAGE
Gestational age (weeks)	130	38.2	
Birth weight (gms)	130	3555	
Gravidity	130	28.3	
Primigravida	22		17
Multigravida	108		83
LSCS	25		20
NVD	105		80.7
Male	66		50.7
Female	64		49.3

Group C:

The mean value NRBC per I100 WBC of group I population (n=100) is (2.43), SD (0.235) range 0-12 (table 2) the mean gestational age is (38.92) and mean weight is (3725)

The mean nucleated red blood cell NRBC in healthy newborn population is expected to range between 4.3to 5 as shown in table.

Table.2 Group C

Group C (n=100)	MIN	MAX	MEAN	SD	SE
NRBC(Nucleated RBC) per 1000 WBC	0	12	2.430	2.349	0.235
GESTATIONAL AGE IN WEEKS	37	41	38.92	0.691	6.917
Wt in grams	2600	4000	3725	0.217	2.176
PCV	31.0	67.0	45.20	7.822	5

The result of one sample t test of group one control was highly significant (p=<0.0001).

Group A:-

The mean value of NRBC per I100 WBC count of group II (n=30) Newborns with Birth asphyxia is (18.5) SD (7.323). ... (Table 3) the mean gestational age is (38.92) wk and means weight is (3385) gm

Table.3 Description of Group A

GROUP A (n=30)	MIN	MAX	MEAN	SD	SE
NRBC / 1000 WBC	10	33	18.5	7.32	1.34
Gestational age (weeks)	37	39	37.4	0.56	0.10
weight (gms)	2600	4000	3385	0.38	6.88

The result of one sample t test of group A infant of diabetic mothers was highly significant (p=<0.0001).

The result of a comparison between two means of group C and group A shows that the difference was highly significant (p < 0.0001) as in table 4.

Table. 4 Independent Samples “T” Test

	N	MEAN	SD	STANDARD ERROR MEAN	P VALUE
GROUP C	100	2.4300	2.3495	0.23495	0.0001
GROUP A	30	18.500	7.3285	1.33799	0.0001

The mean value of NRBC per 100 WBC in normal newborns (group C) is (2.43). It was found that there is significant increase in mean of NRBC in the group A (chronic birth asphyxia) which is (18.5, p< 0.0001). It was concluded that in infants with chronic intra uterine hypoxia which result from decreased oxygen delivery to fetus & this lead to stimulating the erythropoietin hormone and this presumed to increase the number of NRBC & RBC in peripheral circulation to overcome the intra uterine hypoxia, so NRBC per

100 WBC count in cord blood can be regarded as a good indicator for fetuses prone to such chronic hypoxia

DISCUSSION:

It was concluded that in infants with chronic intra uterine hypoxia which result from decreased oxygen delivery to fetus & this lead to stimulating the erythropoietin hormone and this presumed to increase the number of NRBC & RBC in peripheral circulation to overcome the intra uterine hypoxia, so NRBC per 100 WBC count in cord blood can be regarded as a good indicator for fetuses prone to such chronic hypoxia.

The hematopoietic system responds to hypoxia by increasing erythropoietin which increases erythroid production, and releasing less mature forms (10), the only known stimulus for erythropoietin is tissue hypoxia, which has been well documented in both human fetal & animal models.

In cord blood of human infants, increase levels have been reported in conditions associated with intra-uterine hypoxia .Other studies found a significant association between fetal EPO and erythroblast count (Maier, R. *et al.*, 1993).Fetal hypoxemia most likely because increased placenta oxygen consumption and decrease oxygen delivery to fetus and within hour's fetal hypoxia stimulates erythropoietin secretion which lead to production of NRBC and increase RBC mass to overcome the intra uterine hypoxia.

Nucleated red blood cells are rarely found in concentrations higher than 10 per 100 WBC in peripheral blood of healthy term newborn infants (Martin, R.J. *et al.*, 2011).

This study reported an association between increased nucleated red blood cells in peripheral blood of neonates and intra uterine hypoxemia

Group C: 100 Normal newborns with body weight >2500gm & >37 WK (G.A). The mean NRBC is (2.43), compared with other studies reporting normative NRBC data from cord blood, our studies reporting normative results which was relatively accepted compared with other studies.

Group A: 30 infant of birth asphyxia, body weight >2500gm, full term.

There was significantly increased NRBC in the cord blood at delivery, mean NRBC is (18.5, $p < 0.0001$) this result is with agreement with previous studies, which found that the NRBC count of newborns with birth asphyxia were considerably higher at birth. .

It is presumed that the increased numbers of NRBC in the peripheral blood reflect increased hematopoiesis or premature release of these cells in response to increased erythropoietin (20) which associated with intra uterine hypoxia. It has been further postulated that appearance of NRBC peripheral blood indicates extramedullary (mostly hepatic) hematopoiesis (Niroumanesh, S., & Mohebi, M. 2009).

CONCLUSION:

- The mean value of nucleated red blood cell (NRBC) per 100 white blood cells in a healthy, term, singleton neonate was (2.43 ± 2.34) .
- A significant increased number of NRBC in cord blood of infant of chronic intrauterine hypoxia & the mean value of nucleated red blood cell was (18.5 ± 7.32) .

Therefore our study concludes that in infants with chronic intra uterine hypoxia (Nucleated RBC) NRBC per 100 WBC count in cord blood can be regarded as a good indicator for fetuses prone to such chronic hypoxia.

Recommendations:

An increased NRBC count can be considered as a potentially useful indicator in detecting chronic intra uterine hypoxia and this could be useful factor for determine further management and admission to neonatal intensive unit .NRBC count could be put in scoring system including the Doppler ultrasonography of umbilical vessels and placental histopathology for determining a normal growth. More advance studies for emphasizing the theory of hematopoietic shifting using the humeral and other regulating factor are recommended. NRBC count is easy test to apply since the cord blood specimen can be analyzed by equipment readily available in most hospital laboratories.

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