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*RESEARCH ARTICLE*

# TO EVALUATE CORRELATION OF NUCLEATED RBCS AND PERINATAL ASPHYXIA IN BABIES.

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*Abstract*



## Introduction:-

Perinatal asphyxia is a major cause of mortality and morbidity among neonates.Birth asphyxia is defined as the failure to establish spontaneous respiration by the end of one minute. Clinical assessment of perinatal asphyxia is done using APGAR scoring. Birth asphyxia is indicated by an APGAR SCORE of 0-6[1]. Other than low APGAR score, Perinatal asphyxia can be assessed by a combination of parameters like fetal distress, meconium stained liquor, umblical cord pH and clinical features of HIE[2]

APGAR stands for:
A- Appearance
P- Pulse
G- Grimace
A- Activity
R- Respiration
Asphyxia can occur before birth, during birth and after birth.

There are various factors which may lead to perinatal asphyxia which include:

**Maternal factors:-**
Pregnancy induced hypertension, eclampsia, maternal cardiopulmonary disease, maternal diabetes, maternal vascular disease

**Placental factors:-**
Abnormal placentation, abruptio placentae

**Umblical cord accidents:-**
Prolapse, Entanglement

**Fetal factors:-**
Hydrops, severe cardiac insufficiency

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**Neonatal factors:-**
Cyanotic congenital heart disease, pulmonary disease as in meconium aspiration

**Hypoxia and ischaemia, in a perinatal asphyxiated babies, leads to multiorgan damage Affecting:-**
**CNS:-** Hypoxic Ischaemic Encephalopathy, intracranial haemorrhage

**Respiratory system:-** respiratory distress, persistent pulmonary hypertension

**CVS:-**Hypotension, myocardial damage

**Gastrointestinal system:-**NecrotizingEnterocolitis, gastritis and stress ulceration

**Metabolic abnormalities:-** Hypoglycemia, Hypocalcemia and Hyponatremia

**Renal system:-** Acute Tubular Necrosis

Although nucleated red blood cells (nRBCs) are rarely found circulating in older children, they are commonly seen in the blood of newborns. They are primarily produced in the fetal bone marrow in response to erythropoietin and are stored in the marrow as precursors to reticulocytes and mature erythrocytes. Many acute and chronic stimuli cause increase in the number of circulating nRBCs from either increased erythropoietic activity or a sudden release from the marrow storage pools. There are various pathological processes associated with increased production and release of nRBCs. Common causes of increased nucleated red blood cells include prematurity, increased erythropoiesis from chronic hypoxia, anaemia, and maternal diabetes, from acute stress mediated release from the marrow stores, and from postnatal hypoxia. Extreme increases may occasionally be idiopathic.[3]Fetal erythropoiesis is regulated by growth factors produced by the fetus. Erythropoietin does not cross the placenta. Erythropoietin is a glycoprotein that binds to specific receptors on the surface of erythroid precursors and stimulates their differentiation and clonal maturation into mature erythrocytes. Erythropoietin gene expression is regulated by an oxygen sensing mechanism. Two factors, hepatic nuclear factor 4 and hypoxia inducible factor 1 ( HIF 1), exhibit transcriptional activation for erythropoietin and other hypoxia inducible genes [4]

A study indicates that HIF promotes erythropoiesis at multiple levels and coordinates cell type-specific hypoxia responses. These include renal and hepatic erythropoietin synthesis, enhanced iron uptake and utilization, as well as changes in the bone marrow microenvironment that facilitate erythroid progenitor maturation and proliferation.[5]

Hence,In an asphyxiated baby, hypoxia leads to exaggerated erythropoiesis by stimulating erythropoietin which in turn results in release of immature RBCs into fetal circulation. Peripheral blood film may reveal the presence of nucleated RBCs which may be taken as amarker of perinatal asphyxia , and the levels of nucleated RBCs may be correlated with the severity of perinatal asphyxia.[3,6,7]

**Aims And Objectives:-**
1. To study the correlation of nucleated RBCs and perinatal asphyxia.
2. To study the correlation of no. of nucleated RBCs in peripheral blood film and severity of asphyxia.

## Material and Methods:-

A prospective study was conducted in NICU of Department of Paediatrics, Government Medical College and Rajindra Hospital, Patiala. 100 newborns born with perinatal asphyxia were the subjects of study. The study was conducted for a duration of 6 months. Detailed history of mother was taken and examination of baby was done along with collection of samples for the purpose of study.

After resuscitation of the babies, babies were shifted in NICU. Detailed information of babies and antenatal history of disease and drugs of mothers were recorded on a predesigned pretested proforma. Blood samples of babies were collected for complete blood count, blood urea, serum creatinine, serum electrolytes. Peripheral blood film was made and was analysed in the department of haematopathology. Nucleated RBCs were seen and counted as compared to 100 WBCs. Data so obtained was analysed for the purpose of study.

## Results:-

30(30%) mothers had history of meconium stained liquor, 16(16%) had Pregnancy induced hypertension, 12(12%) had eclampsia, 6(6%) had polyhydramnios, 4(4%) had antepartum haemorrhage , 24(24%) had prolonged labour.

**Table 1:-**Correlation with gestation

| Gestation | Number of asphyxiated babies born Total number(n)=100 | % of the asphyxiated babies |
|---|---|---|
| <37 wks | 48 | 48 |
| 37-40 wks | 46 | 46 |
| >40 wks | 06 | 06 |

Wks: Weeks

**Table 2:-**Correlation with severity of Birth Asphyxia

| Severity of Birth Asphyxia | Number of babies (n=100) | % of babies %=100% |
|---|---|---|
| Mild (APGAR -5,6,7) | 12 | 12 |
| Moderate (APGAR- 3,4) | 52 | 52 |
| Severe (APGAR-1,2) | 36 | 36 |

**Table 3:-**Correlation of nRBCs in peripheral blood film with % of asphyxiated babies

| Number of nRBCs | % of babies with asphyxia as per nRBCs Total number (n)=100 | % of asphyxiated babies |
|---|---|---|
| Rare | 40 | 40 |
| Absent | 31 | 31 |
| 5-15 | 25 | 25 |
| >15 | 04 | 04 |

**nRBCs:** Nucleated RBCs; nRBCs were counted per 100 WBCs

**Table 4:-** Correlation of babies with severity of asphyxia

| Severity of asphyxia | Number of nRBCs | Number of babies (% of babies) |
|---|---|---|
| Moderate | 5-15 | 25(48%) |
| Severe | >15 | 04(12%) |

## Discussion:-

There are various parameters which depict the presence of birth asphyxia in babies like fetal scalp pH monitoring and presence of acceleration /deceleration of fetal heart rate. The presence of nucleated RBCs in peripheral blood smear may be used as a parameter to predict the presence of birth asphyxia in babies born in rural hospitals or in the hospitals where the above mentioned investigations could not be done due to non availability. So the presence of nucleated RBCs in the peripheral blood smear can be taken as a significant, easily available and cost effective parameter to depict the presence of birth asphyxia which may also be correlated with the severity of birth asphyxia.
In this study, a significant number of nucleated RBCs are found in peripheral blood smear of asphyxiated babies which can be correlated with its severity.

When categorized according to gestation, 48(48%) babies were of <37 wks of gestation, 46 (46%) babies were of 37-40 wks of gestation and 06 (06%) babies were of >40wks of gestation.

On APGAR Scoring, 36(36%) babies suffered from severe birth asphyxia, 52(52%) suffered from moderate birth asphyxia and 12(12%) babies suffered from mild birth asphyxia.

It was found that, 48% of moderately asphyxiated babies had 5-15 nRBCs and 12% of severely asphyxiated babies had >15 nRBCs in their peripheral blood film.

Due to presence of varying degrees of birth asphyxia all of these babies were admitted in NICU following birth. Comparing their final outcome,62% babies were discharged satisfactorily, 10% were referred, while 10% left against medical advice due to increased duration of stay. Mortality rate among these babies was 18%.

Out of need for easier, faster and better accessible tools to identify degree of perinatal asphyxia early on following birth, there have been various studies to find such diagnostic methods. Of these, studies of peripheral blood films of cord blood have yielded significant results.

Boskabadi et al, conducted a prospective study in 2006 and found in their study,a considerable increase in NRBC count for asphyxiated neonates which was predictive of short-term outcome.[6]In a similar study by Ferns et al, it was reported that the rate of erythropoiesis was related to the degree of asphyxia[8]. Hanlon Lundberg and Kirby evaluated the relation between the severity of asphyxia and increased NRBCs by comparing cord NRBCs with cord pH and Apgar scores. The NRBC counts increased with progressive increases in cord acidosis and with progressive decreases in the Apgar scores.[9]

According to a study on neonatal cord blood samples, increased nRBC counts were seen with acute and subacute asphyxia, the magnitude of the increase was a function of the severity and duration of the asphyxia. However, there was a large overlap between the nRBC values found after acute, subacute, and chronic asphyxia; asphyxia of any duration does not always cause an increased nRBC count, and extreme increases may be found without asphyxia.[3]
A study investigated the variations of nucleated red blood cell (NRBC) counts in acute and chronic fetal hypoxia and examined if it could be possible to establish a cutoff value for the number of NRBCs for prediction of fetal acidosis. They prospectively studied 77 pregnant women grouped as acute, chronic fetal distress and controls. They found that the mean NRBC counts in chronic fetal distress group was higher than acute fetal distress. NRBC counts were found to be correlated with umbilical cord pH. Thus, the duration and the severity of fetal asphyxia may be predicted by the number of NRBCs per leukocyte.[10]

## Conclusion:-

Many studies were conducted on umbilical cord blood and concluded the presence of significant number of nucleated RBCs in cord bloodof asphyxiated babies. This study was done on the venous blood of asphyxiated newborns which also shows that peripheral blood smear of these newborns have significant number of nucleated RBCs which may also be correlated with its severity.

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