Study of nucleated RBC count as a marker of severity of perinatal asphyxia in newborns - a case control study

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Abstract

Introduction: This study was done to estimate the nucleated red blood cell count (NRBCs) in normal and asphyxiated babies and find their correlation with severity of birth asphyxia. Materials and Methods: About 50 normal newborns as control and 50 newborns with perinatal asphyxia as cases were considered. At birth 2 mL of venous blood was collected in both cases and control groups. nRBC count per 100 white blood cells (WBC) was done at admission. Clinical assessments in terms of neurologic status at birth, 24 hours after birth and every day thereafter till discharge/death was done. Cord blood nRBC/100 WBC was correlated with stages of HIE during hospital stay. Neonates were monitored for adverse outcome such as tone abnormalities, feeding difficulty, refractory seizures and death. Controls were followed up in the same manner. Results: Among 50 cases, 24 had no hypoxic ischaemic encephalopathy (HIE), 17 had stage 1 HIE, 6 had stage 2 and 3 newborns had stage 3 HIE. The mean APGAR score in cases was 5.34 ± 1.19 whereas for the control group it was 8.12 ± 0.77 with p value of 0.001 which is statistically significant. The mean nRBC in newborns with APGAR score of 3, 4, 5, 6 were 35.5, 19.9, 20.6 and 12 respectively. The low APGAR scores showed high nRBCs. Mean nRBCs for HIE stage 1, 2, 3 was 19.1, 31.0, and 54.3 respectively. High nRBC count correlated with increasing severity of birth asphyxia. Conclusion: nRBC count is an easy, simple and a reliable test to assess the severity of birth asphyxia in resource poor settings.

Key words: Perinatal asphyxia nucleated RBC, APGAR score.

Introduction

Perinatal asphyxia (derived from the Greek word α-σφυξις meaning born without an evident pulse) is one of the most important causes of fetal distress [1]. According to WHO estimates, around 3% of approximately 120 million infants born every year in developing countries develop birth asphyxia [2]. In India, between 250,000-350,000 infants die each year due to birth asphyxia 2.

Asphyxia may occur in utero, at birth or in the postnatal period. World Health Organization (WHO) 2 has defined perinatal asphyxia as a “failure to initiate and sustain breathing at birth”. Data from National Neonatal Perinatal database 3 suggests that perinatal asphyxia contributes to almost 20% of neonatal deaths in India 3 and defines moderate asphyxia as slow gasping breathing or an APGAR score of 4 - 6 at 1 min of age, and severe asphyxia was defined as no breathing or an APGAR score of 0-3 at 1 minute of age [3]. Perinatal asphyxia is a major cause of acute mortality and chronic neurologic disability amongst survivors and is a complication that occurs between 2-10% of deliveries [4]. Perinatal asphyxia results in hypoxic injury to various organs including kidneys, lungs and liver but the most serious effects are seen on the central nervous system [1,5]. Hypoxic ischemic encephalopathy (HIE) refers to the CNS dysfunction associated with perinatal asphyxia. Classification of HIE (Stage I, Stage II and Stage III) in term neonates was proposed by Sarnat and Sarnat[6]. No single parameter can define perinatal asphyxia, rather a combination of parameters like fetal distress, meconium-stained liquor, low APGAR score, umbilical cord blood pH and clinical features of hypoxic ischemic encephalopathy (HIE) can predict it 4. Recent studies on hematological variations in
asphyxiated neonates as a predictor of neonatal asphyxia have suggested that number of nucleated red blood cells (NRBCs) in cord blood of asphyxiated neonates help in identifying birth asphyxia [4]. The hypoxic event induces a compensatory response in the form of exaggerated erythropoesis, resulting in the release of immature red blood cells into the fetal circulation. The levels of nRBC may be correlated with the presence of perinatal asphyxia 7. The number of nRBC/100 white blood cells (WBC) is quite variable but is rarely >104. The instances, where number of nRBCs exceed>10/100 WBC are prematurity, ABO or Rh incompatibility, maternal diabetes, intrauterine growth retardation [8], acute asphyxia, congenital infection, cyanotic heart disease, pre-eclampsia, maternal smoking, and chorio-amnionitis. Considering the hematopoietic response to hypoxia in utero, the elevated NRBC/100 WBC count is being hailed as the marker for not only perinatal asphyxia but also to predict the chances of the neonates developing neurological sequelae [4].

Objectives of the study- The aim of the study was to estimate the nucleated red blood cell count (NRBCs) in normal and asphyxiated babies and its correlation with severity of birth asphyxia and immediate outcome of such babies.

Materials and Methods

Study design: Case control clinical study.

Study center: Dr. B R Ambedkar Medical College and Hospital.

Sample Size: Sample size was based on inclusion and exclusion criteria. 50 normal newborns as control and 50 newborns with perinatal asphyxia as cases were included in the study.

Statistical analysis was done using SSPS version 20 software. ' t ' test of significance was used to compare mean APGAR scores.

Inclusion Criteria

Cases -Term newborns (>37 weeks to 42 weeks of gestation) with perinatal asphyxia2
1) APGAR score < 7 at 5 minutes of life.
2) Thick, meconium stained amniotic fluid and respiratory depression, hypotoniaorbrady cardia.

Results

The present study was done to find the correlation of severity of birth asphyxia with nucleated RBCs. About 50 normal newborns and 50 newborns with low APGAR score<7 at 5 min of life were included in the study. Among 50 cases, 24 had no HIE, 17 had stage 1 HIE, 6 had stage 2 and 3 newborns had stage 3 HIE.
Table-1: Distribution of neonates according to APGAR score at 5 minutes.

| Group     | N  | Median | Mean ± SD | p-value |
|-----------|----|--------|-----------|---------|
| Cases     | 50 | 5      | 5.34 ± 1.19 | 0.001 * |
| Control   | 50 | 8      | 8.12 ± 0.77 |         |
| Total     | 100| 7      | 6.73± 1.72  |         |

p value is statistically significant.

This table indicates distribution of neonates based on APGAR score at 5 min for study and control group. The mean APGAR score in cases was 5.34 ±1.19 whereas for the control group it was 8.12 ± 0.77 with p value of 0.001 which is statistically significant.

Table-2: Correlation of APGAR score at 5 minute and mean nRBC count.

| Apgar Score at 5min | N  | MeannRBC ± SD |
|---------------------|----|----------------|
| 3                   | 4  | 35.5 ± 18.0    |
| 4                   | 7  | 19.9 ± 11.1    |
| 5                   | 17 | 20.6 ± 12.4    |
| 6                   | 12 | 12.0 ± 12.3    |
| 7                   | 22 | 7.0 ± 1.9      |
| 8                   | 20 | 7.6 ± 1.7      |
| 9                   | 18 | 7.6 ± 2.2      |
| Total               | 100| 12.2 ± 10.6    |

Table 2 indicates correlation of APGAR score at 5 min and nRBC count. The mean nRBC count in newborns with APGAR score of 3, 4, 5, 6 were 35.5, 19.9, 20.6 and 12 respectively. Babies with low APGAR scores had high nRBCs.

Table-3: Distribution of nRBCs according to HIE stages.

| HIE Stage | N  | Mean ± SD |
|-----------|----|-----------|
| No        | 24 | 6.9 ± 1.7 |
| stage1    | 17 | 19.1 ± 5.3|
| stage2    | 6  | 31.0 ± 8.7|
| stage3    | 3  | 54.3 ± 4.7|
| Total     | 50 | 16.8 ± 13.4|

This table shows distribution of nRBCs according to the stages of HIE. Mean NRBCs for HIE stage 1, 2, 3 was 19.1, 31.0, and 54.3 respectively.

Table-4: Distribution of neonates according to nRBCs

| nRBC     | CasesN (%) | ControlN (%) | Total |
|----------|------------|--------------|-------|
| <=10     | 24 (48)    | 48 (96)      | 72    |
| 11-20    | 12 (24)    | 2 (4)        | 14    |
| 21-30    | 7 (14)     | 0 (0)        | 7     |
| >30      | 7 (14)     | 0 (0)        | 7     |
| Total    | 50 (100)   | 50 (100)     | 100   |

This table shows the distribution of neonates according to nucleated RBCs. It was found that 96% of neonates in control group had nRBC count of <10/ 100 WBCs which is normal, whereas only 48% of cases had normal nRBC count. The remaining 52% of neonates among cases has nRBCs> 10 / 100 WBCs which is considered significant.
Discussion

Perinatal asphyxia is a major cause of acute mortality and chronic neurologic disability amongst survivors [4]. Perinatal asphyxia results in hypoxic injury to various organs including kidneys, lungs and liver but the most serious effects are seen on the central nervous system 6. No single parameter can define perinatal asphyxia, rather a combination of parameters like fetal distress, meconium-stained liquor, low APGAR score, umbilical cord blood pH and clinical features of hypoxic ischemic encephalopathy (HIE) can predict it [4]. Recent studies have suggested that number of nucleated red blood cells (NRBCs) in cord blood of asphyxiated neonates help in identifying birth asphyxia 4,14. The levels of nRBC may be correlated with the presence of perinatal asphyxia [7].

The number of nRBC/100 white blood cells (WBC) is quite variable but is rarely > 10/100 WBCs [4]. Considering the hematopoietic response to hypoxia in utero the elevated nRBC/100 WBC count is being hailed as the marker for perinatal asphyxia and also to predict the chances of the neonates developing neurological sequelae 4. It can be used as a prognostic marker to anticipate neonatal complications of severe birth asphyxia and to manage them effectively.

In our present study, the mean APGAR score at 5 minutes for cases was 5.34±1.19 as compared to controls which was 8.12±0.77, with the p value of 0.001. This was comparable to the study done by Mohanty et al [11] and Tae Hwan Kil et al [12].

Our study showed significant correlation between APGAR score at 5 minutes and nucleated RBC count as shown in table 2. The APGAR scores were inversely proportional to nRBC count. This was comparable to the study done by Ganta S.J et al [9] and Colacoa et al [14].

The present study showed a strong correlation between the NRBCs and severity of birth asphyxia. The mean nRBC count was 19.1 in stage 1 HIE, 31 in stage 2 HIE and 54.3 in stage 3 HIE. Other studies have observed lower number of cord blood nRBCs in severe birth asphyxia compared to our study [9,10,13,17].

Meena P et al [15], in their study compared mean nucleated RBC count in neonates with and without birth asphyxia. A statistically significant negative correlation of nRBC count was found with severity of birth asphyxia.

Mohanty et al [11], in their study showed mean nRBC of 15.8 in stage 1 HIE, 46.5 in stage 2 HIE and 77.1 in stage 3 HIE. This was comparable to our study except that mean nRBC in stage 3 HIE was higher.

Study conducted by Hermansen M.C et al [16], has concluded that an increase in nRBC counts are seen with acute and subacute asphyxia, the magnitude of the increase is a function of the severity and duration of asphyxia.

Hereby our study strongly supports that nRBC count is an easy, simple and a reliable test for severity of birth asphyxia.

Limitations of the study: Correlation of nRBC with blood gas analysis was not done in our study. nRBCs were not correlated with complications of birth asphyxia.

What this study adds to the existing knowledge?

Combination of parameters such as fetal distress, low APGAR scores, cord blood pH and many others are used to predict severity of birth asphyxia.

But our study suggest that nRBC count can be used as an early and an alternative marker to predict the severity of birth asphyxia.

Conclusion

nRBC count is an easy, simple and a reliable marker for severity of birth asphyxia in a resource poor settings where facilities for ABG, cord pH analysis are not easily available.

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