International Journal of Contemporary Pediatrics
Koreti S et al. Int J Contemp Pediatr. 2017 May;4(3):1041-1045
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20171724

Original Research Article

Simple and feasible blood markers-as predictors of perinatal asphyxia

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Received: 11 March 2017
Accepted: 07 April 2017

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ABSTRACT

Background: The objective of this research work was to study the hematological parameters as predictors of perinatal asphyxia and to assess their correlation with severity. Setting: Postnatal Wards, Kamla Raja Hospital and SNCU, Department of Pediatrics, Kamla Raja Hospital, Gajra Raja Medical College, Gwalior. Design: A prospective case control study. Participants :100 cases and 100 controls enrolled based on the selection criteria, on day 1 of life.
Methods: New born on day 1, who fits the selection criteria was enrolled. Birth details, relevant perinatal history, findings on physical examination and systemic signs were recorded on a predesigned proforma. Staging was done and new born classified as HIE stage I, II or III. Cord blood samples were collected and results analysed.
Results: This study included 100 cases and 100 controls. Presence of maternal illness and birth history were found to have significance (p value <0.001) when compared between cases and controls. Number of nucleated RBCs/100 WBCs were found to be 6±1.93 in HIE-I; 9.5±4.8 in HIE-II and 16.45±6.6 in HIE-III as compared to 5.9±3.6 among the controls. The results are found to be significant (p value <0.001). Mean value of hemoglobin found among the controls was 16±2.5. This was 17.4±2.18 in HIE-I; 17.45±1.8 in HIE-II and 15.5±3.07 in HIE-III. The results are significant on comparison between cases and controls and among cases (p value <0.015, <0.001 respectively). Mean value of hematocrit among the controls was 49.24±7.98. This was 52.5±6.57 in HIE-I;52.56±5.46 in HIE-II and 47.6±5.8 in HIE-III. The difference was significant (p value <0.001) when comparison was done among the cases. Value of total leucocyte count (TLC) among the controls was 14.14±4.15; 14.06±6.8 in HIE-I;15.8±5.6 in HIE-II; 21.14±7.90 in HIE-III. The results were significant (p value <0.001) when comparing cases with controls and cases among themselves. There was no correlation seen with platelet count. Polychromatophilia was found significant (p value <0.001) when compared between cases and controls and among cases themselves.
Conclusions: Hematological parameters are altered in perinatal asphyxia and can be used to predict the severity and outcome.

Keywords: Hypoxic ischaemic encephalopathy, Nucleated RBCs, Polychromatophila, Predictors, Severity

INTRODUCTION

WHO has defined perinatal asphyxia as a "failure to initiate and sustain breathing at birth". Birth asphyxia refers to a condition of hypoximea, hypercapnia and insufficient blood perfusion of new born during labour and birth.

Perinatal asphyxia is one of the significant causes of morbidity and mortality. According to WHO estimates, around 3% of approximately 120 million infants born every year in developing countries, develop birth asphyxia.[1] It is estimated that some 9,00,000 of these newborns die each year.

Globally, hypoxia of the new born (birth asphyxia) or the fetus (fresh stillbirth) is estimated to account for 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year.[1] An estimated 1 million children who survive birth asphyxia live with chronic

neurodevelopmental morbidities, including cerebral palsy, mental retardation, and learning disabilities

From these Statistics, we infer that Birth asphyxia is remaining as a major cause of neonatal deaths. Perinatal asphyxia has an incidence of 1 to 6 per 1,000 live full-term births, and represents the third most common cause of global neonatal death (23%) after preterm birth (28%) and severe infections (26%).

During hypoxia-ischaemia, blood flow is redistributed in order to preserve circulation to the most vital organs-the brain, heart and adrenals. This is at the expense of the kidneys, liver, and gastrointestinal tract, which are therefore vulnerable to hypoxic-ischaemic damage. Multi-organ dysfunction is a natural consequence of this defence mechanism because of the cellular damage inflicted on the non-prioritised organs. Such damage to these and other organs serves as further marker of hypoxia-ischaemia.

Hematopoietic system changes are observed as a complication of asphyxia. Altered biophysical characteristics of blood e.g. changes in the structure and function of erythrocytes, leucocytes and thrombocytes can be caused by asphyxia.[2] Hematologic adaptations in the fetus include short term and long term responses.[3] Acute hypoxia either in utero or during perinatal period causes short term responses like reduction of body temperature, reduction in heart rate, and redistribution of circulation. Chronic hypoxemia involves bone marrow resulting in polycythemia, thrombocytosis and thrombocytopenia.

Polychromatophilia is a condition where there is an abnormally high number of red blood cells found in the bloodstream as a result of being prematurely released from the bone marrow during blood formation. It is usually a sign of bone marrow stress as well as immature red blood cells.

The present study was conducted to evaluate the various hematological changes following asphyxia and also to compare these variables among themselves in their role in assessing the severity of asphyxia. The hematological parameters chosen for the study are; 1. Nucleated RBCs (n-RBCs) 2. Platelet count 3. Total leucocyte count 4. Hemoglobin and 5. Hematocrit

METHODS

The objective of the study was to hematological parameters as predictors of perinatal asphyxia and to assess their correlation with severity. Setting of the study was SNCU, Department of Paediatrics, Post-natal wards, Kamla Raja Hospital, Gajra Raja Medical College, Gwalior. Study design: Prospective Cross sectional study. Sample size: 100 cases 100 control. Duration: One year (July 2015-July 2016). Participants: 100 newborns admitted in sncu on day1 who fulfill the selection criteria are taken as cases. Similarly, 100 newborns (first Post-natal day) of post-natal wards fulfilling the selection criteria, as controls. consent: Informed and written consent is taken from the attender. Material: Thermometer, EDTA vials, heparinised syringes, glass slides, surgical blades and cord clamps.

Inclusion criteria

All full term newborn

- Who need resuscitation on admission
- With distress
- With Meconium Aspiration(non-vigorous)
- With history of Delayed cry

Exclusion criteria

- Preterm neonates
- VLBW
- Blood culture proven sepsis
- Neonates with congenital malformations

A newborn, based on the inclusion and exclusion criteria, was chosen as a case or a control. For enrolment of a case or a control, informed and written consent was taken and details of mother and father's name, address; name and signature of attender bringing the baby; also, the details of the birth, details of any maternal complications like bad obstetric history etc. and examination of the newborn, as mentioned in a preformed proforma were recorded.

Clinical staging done based on Levene staging for HIE and newborns were classified as stage I, II or III. Two blood samples were taken from the umbilical cord of the newborn- for arterial blood gas analysis and for blood parameters used in the study (i.e. n-RBCs, platelet count, total leucocyte count, haemoglobin and hematocrit); both taken in EDTA vials.

Sample for ABGA and blood parameters were sent within the hospital. ABGA was done using blood gas analyser. Blood counts were determined by an automatic analyser using an optical system. Hemoglobin was measured calorimetrically. Peripheral smear was done for nucleated RBCs (n-RBCs) and for manual platelet count. Values obtained were compared with the normal values.

Clinical examination and HIE Staging was done on day 1 and day 3. Correlation was done with all haematological parameters and pH and HIE staging to assess the severity and compared the outcome among case.

Statistical analysis

Normally distributed variables were compared using the unpaired t test whereas Mann-Whitney U test was used for variables not distributed normally. Variables were

analysed using either the chi square test or Fisher's exact test ANOVA was used to evaluate the significance of the differences in severity of HIE among cases.

RESULTS

This study included 23(23%) cases of HIE-I, 46 (46%) cases of HIE-II and 31 (31%) cases of HIE-III.58.0% of cases were associated with maternal illness, Bad obstetric history found in 22%; eclampsia and preeclampsia in 6%; MSL in 13%. This is found to be significant (p value <0.001) when compared between cases and controls and among the case. Birth history of fetal distress (27%), trauma (23%), delayed cry (29%) and assisted ventilation (29%) when compared between the cases and the controls, was found to be significant (p value <0.001).

Among the hematological parameters mean value of n-RBCs/100 WBCs were 10.85±6.39 for cases and 5.91±3.60 for controls. The results were significant (p value <0.001) when cases were compared with the controls. Number of n- RBCs were 6.00±1.93 for HIE-I; 9.50±4.80 for HIE-II and 16.45±6.66 for HIE-III. The result was again found to be significant (p value <0.001 (Table 1).

In this study, it was found that 51.6% of HIE-III; 26% of HIE-II and 17.3% of HIE-I cases showed polychromatophilia as compared to 2% of controls, which is found to be statistically significant (p value <0.001). Polychromatophilia represents the presence of immature cells which is again an indicator of hypoxic-ischaemic event (Table 1).

Table 1: Correlation between blood parameters in perinatal asphyxia.

	Controls	Cases				P value	
		Total	HIE I	HIE II	HIE III	Controls vs cases	Severity in cases
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD		
Nucleated rbcs/ 100 wbcs	5.91 ± 3.60	10.85 ± 6.39	6.00 ± 1.93	9.50 ± 4.80	16.45 ± 6.66	<0.001	<0.001
Hemoglobin	16.00 ± 2.52	16.86 ± 2.48	17.43 ± 2.18	17.45 ± 1.81	15.55 ± 3.07	0.015	0.001
Hematocrit	49.24 ± 7.98	51.01 ± 6.22	52.50 ± 6.57	52.56 ± 5.46	47.62 ± 5.85	0.081	0.001
Platelet count (lacs/mm3)	2.20 ± 0.71	2.17 ± 0.72	2.17 ± 0.63	2.16 ± 0.79	2.19 ± 0.70	0.776	0.986
Tlc (x109/ l)	14.14 ± 4.15	17.06 ± 7.18	14.06 ± 6.81	15.82 ± 5.62	21.14 ± 7.90	0.001	<0.001
Polychromatophilia	02%	24%	8.6%	26%	32.2%	<0.001	0.001

When outcome was compared between the cases, 100% of the HIE-I cases were discharged. Whereas 69.5% cases of HIE-II were discharged and 26.0% cases expired. Two cases were lost as LAMA. 64.5% cases of HIE-III expired and 35.4% got discharged. This was found to be statistically significant (p value <0.003) with poorest outcome seen in HIE-III (Table 2).

Table 2: Correlation between severity and outcome.

Cases (100)	Outcome			P value
	Discharge	LAMA	Death	
HIE-I n (%)	23	00	00	<0.001
HIE-II n (%)	32	02	12	
HIE-III n (%)	11	00	20	

Mean value of hemoglobin for controls is 16.00±2.52 This was 16.86±2.48 among the cases. On comparing the two groups, the result was significant (p value 0.015). The values were 17.43±2.18 for HIE-I; 17.45±1.81 for HIE-II; 15.55±3.07 for HIE-III. When compared among the cases, the result appears more significant (p value 0.001). Mean value of hematocrit for controls was 49.24±7.98. This was 51.01±6.22 for cases.

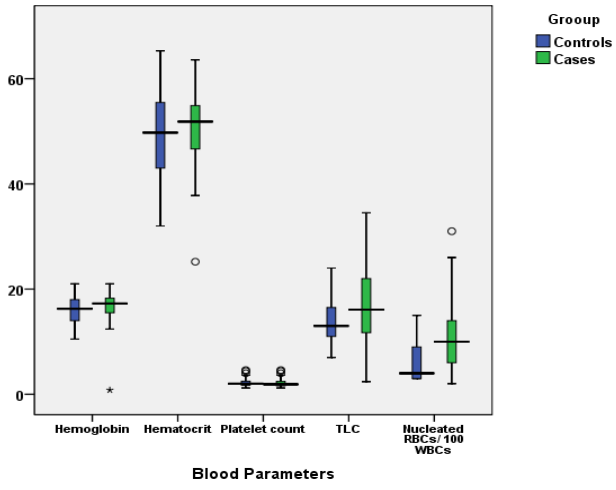

Figure 1: Comparison of hematological parameters among the cases and controls.

No significance (p value 0.081) was found when comparison was done between the two groups. Value of hematocrit was 52.50±6.57 among HIE-I; 52.56±5.46 among HIE-II and 47.62±5.85 among HIE-III. The difference was significant (p value 0.001) on comparing the three.) Mean value of platelet count (lacs/mm^3) among the controls was 2.20±0.71. This was 2.17±0.72 among the cases. It was 2.17±0.63 for HIE-I;2.16±0.79 for HIE-II and 2.19±0.70 for HIE-III. No significant difference was seen on comparing the two groups or between the HIE stages (p value 0.776 ;0.986) (Figure 1, Figure 2).

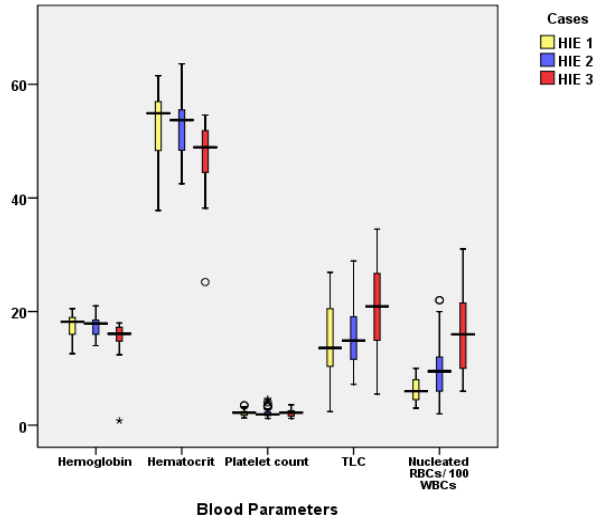

Figure 2: Comparison among various hematological parameters in assessing the severity of asphyxia.

Value of TLC among the controls was found to be 14.14±4.15 and 17.06±7.18 for the cases. There was significant difference found (p value 0.001) when cases were compared with controls. Also, the values were 14.06±6.81 for HIE-I; 15.82±5.62 for HIE-II; 21.14±7.90 for HIE-III. The result was again significant (p value <0.001).

DISCUSSION

This study was done to with the objective to identify the various hematological parameters which are affected in perinatal asphyxia and to compare these parameters, for their role in assessment of severity of asphyxia and outcome.

Among 100 cases, 23% cases were of HIE-I, 46% of HIE-II and 31% of HIE-III. The staging was done based on the Levene staging for HIE. Among the case, 42% were associated with maternal risk factors. Maximum associated risk factor found was the bad obstetric history (BOH) found among 22% of cases followed by meconium stained liquor (MSL) found in 13% of cases followed by pregnancy induced hypertension (PIH)/eclampsia found in 6% of cases and instrument assisted delivery in 19%. Similar results were found in the study done by Ramesh R Pol et al.[4] 35.1% cases were associated with pregnancy induced hypertension 63.2% had in the form of MSL, 8.8% as instrument assisted delivery. Mohammed LH et al noted risk factors in form of PROM (13%), MSL (34%), obstructed labour (19%). Significant neonatal history is found in stage III of HIE. 51.6% HIE-III cases had fetal distress; 58.1% had history of birth trauma, 64.5% had history of delayed cry and 51.6 % needed assisted ventilation. This is highly significant in comparison to stage HIE-II and HIE-I.

n-RBCs are a common observation in the circulating blood of newborn. 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 n-RBCs from either increased erythropoetic activity or a sudden release from the marrow storage pools.[5] The number of n-RBC /100 WBCs is variable but is rarely more than 10 [6-8]. Frequent conditions like prematurity, rhesus sensitization, in which the number of n-RBCs exceeds 10, have been excluded from our study. The presence of n-RBCs in umbilical cord confirms the presence of an asphyxia event during intrauterine development. In the present study, statistically significant difference was found in number of n- RBCs among the three stages of HIE with highest number seen in stage III. Also significant difference was found between cases and controls.Similar observations were made by Phelan et al and Korst et al, Spencor et al in their study of 14 and 78 asphyxiated and non-asphyxiated neonates respectively, found that asphyxiated group had a high n-RBCs count than the control group.[9,10] Buonocore et al in his study concluded that increase in n-RBC count at birth not only reflects a response of the infant to perinatal hypoxia but is also a reliable index of perinatal brain damage.[11]

Similar to the study done by Ramesh R Pol et al, there is significant difference found in the values of hemoglobin between cases and controls.[5] But unlike their study, significant difference was not found in value of hematocrit when compared between cases and controls. Similar to finding in their study, leucocyte count was higher among the cases with highest among the HIE-III cases which may be due to the oxidative stress present during birth.

In this study, no significant difference was found in the platelet count between cases and controls and also when cases were compared among themselves. This is similar to the study done by I. Brucknerova et al and Phelan et al.[12-14]

In our study, polychromatophilia was a significant finding present in 32% of HIE cases as compared to only 2% in controls. This was found to be statistically significant and thus can be used to assess the severity of asphyxia. No such study is done in the past studying the role of polychromatophilia in perinatal asphyxia.

HIE-III cases were associated with maximum mortality (64.5%), HIE-II cases were associated with 26% mortality and 69.5% newborns were discharged. Outcome was worst in stage III.

CONCLUSION

Hematological parameters are the first to get affected in perinatal asphyxia within first hour of delivery, even before other systemic changes occur. They are most simple and feasible prameters to be done. Among the hematological parameters nucleated RBCs and Total leucocyte count are found to be good prognostic indicators of perinatal asphyxia. Polychromatophilia can be used as early diagnostic marker for asphyxia. These parameters are good prognostic indictor of the severity of asphyxia and outcome as well.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. State of World's children, UNICEFF Report: Maternal and Newborn health; 2009.
2. Curtin WM, Shehata BM, Khuder SA, Robinson SB, Brost B. The feasibility of using histologic placental sections to predict new born nucleated red blood cell counts. Obstret Gyaenecol. 2002;100:305-10.
3. Rolfo A, Maconi M, Cardaropoli S, Biolcati M, Danise P, Todros T. Nucleated red blood cells in term fetuses: reference values using anautomated analyzer. Neonatol. 2007;92:205-8.
4. Pol R, Pattar R, Anilraj BC, Yelamali, Badakali A, Int J Curr Med App Sci. 2015;7(2),91-3.
5. Ruth V, Fyhrquist F, Clemons G, Raivio KO. Cord plasma vasopressin, erythropoietin and hypoxanthine as indices of asphyxia at birth. Pediatr Res. 1988;24:490-4.
6. Phelan JP, Ahn MO, Korst LM, Martin GI. Nucleated red blood cells: a marker for fetal asphyxia? Am J Obstet Gynecol.1995;173:1380-4.
7. Green DW, Mimouni F. Nucleated erythrocytes in healthy infants and in infants of diabetic mothers. J Pediatr. 1990;116:129-31.
8. McCarthy JM, Capullari T, Thompson Z, Zhu Y, Spellacy WN. Umbilical cord nucleated red blood cell counts: Normal values and the effect of labour. J Perinatol. 2006;26:89-92.
9. Korst LM, Phelan JP, Ahn MO, Martin GI. Nucleated red blood cells: An update on the marker for fetal asphyxia. Am J Obstet Gynecol.1996;175:843-6.
10. Spencor MK, Khong TY, Mathews BL, MacLennan AH. Hematopoeitic indicators of fetal metabolic acidosis. Aust N Z J Obstet Gynaecol. 2000;40;286-9.
11. Buonocore G, Perrone S, Gioia D, Gatti MG, Massafra C, Agosta R, et al. Nucleated rbcs count at birth as an index of perinatal brain damage. Am J Obstet Gynecol.1999;181:1500-5.
12. Brucknerova L, Benedekova M. Asphyxia of the newborn- the ever topical problem. Biologia. 2000;55(8):23-6.
13. Brucknerova L, Benedekova M, Pechan L, Holoman K, Bielikova E, Kostrova A, et al. Delivery as a physiologic stress and its influence on some parameters of oxidative stress. Neuroendocrinal Lett. 2007;27(2);65-8.
14. Phelan JP, Kirkendall C, KorstL-M, MartinG-I. Nucleated rbcs and platelet count in asphyxiated neonates sufficient to result in permanent neurological impairment. J Mater Fetal Neonatal Med. 2007;20(5):377-80.

Cite this article as: Koreti S, Gupta A. Simple and feasible blood markers-as predictors of perinatal asphyxia. Int J Contemp Pediatr 2017;4:1041-5.