

Role of Haematological Markers in Predicting Short-term Outcome in Neonates with Birth Asphyxia

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ABSTRACT

Introduction: Perinatal asphyxia is a major global cause of neurological morbidity and mortality in neonates. In a developing country with major over population crisis, a large number of deliveries occur in peripheral healthcare facilities and at home by trained and untrained birth attendants in a very minimal infrastructure. In these scenarios, an accurate and reliable marker for birth asphyxia is needed for both diagnostic as well as prognostic evaluation.

Aim: To study neonates with birth asphyxia in terms of Nucleated RBC (NRBC) and Reticulocyte Count in cord blood and/or neonatal venous blood and correlate it with the short-term outcome (up to discharge).

Materials and Methods: A prospective observational study conducted in Neonatal Intensive Care Unit (NICU) in teaching hospital affiliated with medical college with study period of one and a half years involving 125 term neonates with birth asphyxia. Cord blood/peripheral venous blood collected within six hours of birth was used for preparation of peripheral smear for evaluating NRBC count and Reticulocyte count.

Reticulocyte counts more than 7% were considered high/positive and NRBC counts more than 10/100 WBC's were considered high/positive. Duration of NICU stay more than five days was considered significant among asphyxiated babies. Babies less than 37 weeks gestational age or with birth weight less than 1500 g, syndromic babies or with any congenital anomalies were excluded.

Results: Both NRBC counts and Reticulocyte counts were statistically significant with relation to duration of NICU stay. NRBC counts were statistically significant with relation to Hypoxic Ischemic Encephalopathy (HIE) staging, even though Reticulocyte counts were higher in neonates with higher staging of the disease it was statistically not significant. Both NRBC counts and Reticulocyte counts were statistically not significant with relation to neurological outcome at discharge.

Conclusion: It can be concluded that NRBC count and Reticulocyte count are simple markers for assessment of severity and early outcomes of perinatal asphyxia and duration of stay in NICU.

Keywords: Asphyxia Neonatorum, Hypoxia-ischemia, Nucleated erythrocyte count, Reticulocyte Count

INTRODUCTION

Perinatal asphyxia is a serious global cause of acute neonatal mortality and chronic neurologic disability among survivors, and it is a complication that occurs between 2-10% of deliveries [1]. According to World Health Organisation (WHO), birth asphyxia is failure to initiate and sustain breathing immediately after birth [2]. Newborn babies may not breathe at birth due to many causes originating at different periods of the pregnancy.

“The National Neonatal and Perinatal Database (NNPD) defines perinatal asphyxia as Apgar score of <7 at one minute of life. NNPD also defines moderate asphyxia as slow gasping breathing or an Apgar score of 4-6 and severe asphyxia as no breathing or an Apgar score of 0-3 at one minute of life” [3].

India contributes to one-fifth of global live births and more than a quarter of neonatal deaths [4]. The review, which included the data from the Million Death Study from India, found perinatal asphyxia and malformations to be the other two significant causes of neonatal mortality [5]. A recent prospective study by Baqui AH et al., provided data on the timing of cause-specific neonatal deaths: almost all deaths (97.8%) due to asphyxia occur in the first week of life, with 70% of them occurring within the first 24 hours [6].

Previously conducted similar studies were of the smaller sample size, directed towards diagnosis of the asphyxia rather than predicting severity and conducted in a far more well-equipped setting. This study helps in correlation of haematological markers on first day of life to short-term outcome of babies with perinatal

asphyxia, which in turn is helpful for predicting long-term outcomes in a developing nation where large number of deliveries are conducted in a rural setup with minimal resources.

MATERIALS AND METHODS

This was a hospital based prospective observational study, conducted from September 2016 to March 2017, at Shri BM Patil Medical College and Research Centre, Vijayapur. Out of 634 neonates admitted within this period, 125 neonates with birth asphyxia were studied. A total of 117 were excluded for the following reasons: prematurity (n=45), intrauterine growth retardation (n=13), congenital or perinatal infection (n=23), congenital malformation (n=9), mothers' pre-eclampsia (n=13), and maternal diabetes (n=6) and lack of consent (n=8). The study was approved by Institutional Ethics Committee (Approval no: 64/17).

On admission, 2 mL of Cord Blood or Peripheral venous blood were collected and sent to required investigations according to our NICU protocols and required for our study of asphyxia case fulfilling inclusion criteria. Details of the baby like date of birth, sex, gestational age, birth weight, APGAR score at one and five minutes, resuscitation (American Academy of Paediatrics guidelines) and examination details were recorded. Clinical assessments included assessments of the neurologic status daily during the stay, the grade of HIE (Hypoxic Ischemic Encephalopathy) (Stage 1, Stage 2 or Stage 3). The time taken for recovery and duration of hospital stay and neurological examination at discharge which included mental status, pupillary reflexes, response to sound, coordinated suck or swallow, muscle tone of the neonate, moros reflex, asymmetric tonic neck reflex and palmar grasp were also noted. Any deviation of the above parameters was considered neurologically abnormal. Laboratory

assessments included CBC, Nucleate RBC counts, Reticulocyte counts and routine investigations for Birth Asphyxia as per NICU protocol. The blood smears were stained by Leishman stain and manual differential count was done to count Nucleated Red Blood Cells (NRBC), and Reticulocyte count. Number of Nucleated red blood cells (NRBC) was counted per 100 leukocytes in peripheral smears and was reported as 'number of NRBC/100 WBC' and reticulocyte counts were reported in percentage.

STATISTICAL ANALYSIS

All characteristics were summarised descriptively. For continuous variables, the summary statistics of mean, Standard Deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher-Exact test was employed to determine the significance of differences between groups for categorical data. If the p-value was <0.05 , then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analysed using SPSS software v.23.0. and Microsoft office.

RESULTS

Out of 634 neonates admitted to our NICU, 242 neonates had birth asphyxia; 125 neonates with birth asphyxia were included after fulfilling the criteria. Out of 125 neonates, 63.2% were males and 36.8% were females, of birth weight more than 1500 grams with APGAR scores less than 7 at one minute and five minute.

[Table/Fig-1] shows the association of duration of NICU stay with reticulocyte count and NRBC count; that higher the number of reticulocytes and NRBC count, higher is the duration of NICU stay and it is statistically significant.

Parameters		NICU Stay								Total	p-value
		1-2		3-4		5-6		≥7			
		N	%	N	%	N	%	N	%		
NRBC/100WBC	0-10	5	6.5%	31	40.3%	26	33.8%	15	19.5%	77	0.002*
	>10	3	6.3%	8	16.7%	13	27.1%	24	50.0%	48	
Reticulocyte count	0-7	6	6.6%	35	38.5%	24	26.4%	26	28.6%	91	0.030*
	>7	2	5.9%	4	11.8%	15	44.1%	13	38.2%	34	

[Table/Fig-1]: NICU stay studied in relation to NRBC counts and Reticulocyte counts.

* significant at 5% level of significance (p<0.05)

Parameters		HIE Stage						Total	p-value
		1		2		3			
		N	%	N	%	N	%		
NRBC/100WBC	0-10	38	49.4%	26	33.8%	13	16.9%	77	0.004*
	>10	10	20.8%	21	43.8%	17	35.4%	48	
Reticulocyte count	0-7	36	39.6%	33	36.3%	22	24.2%	91	0.869
	>7	12	35.3%	14	41.2%	8	23.5%	34	

[Table/Fig-2]: HIE staging studied in relation to NRBC counts and Reticulocyte counts.

* significant at 5% level of significance (p<0.05)

Parameters		Neurological Status At Discharge				Total	p-value
		ABNORMAL		NORMAL			
		N	%	N	%		
NRBC/100WBC	0-10	9	11.7%	68	88.3%	77	0.096
	>10	11	22.9%	37	77.1%	48	
Reticulocyte Count	0-7	16	17.6%	75	82.4%	91	0.43
	>7	4	11.8%	30	88.2%	34	

[Table/Fig-3]: Neurological outcome studied in relation to NRBC counts and Reticulocyte counts.

[Table/Fig-2] shows the distribution of reticulocyte count and NRBC count with HIE staging. Higher the NRBC counts higher is the HIE staging and it is statistically significant whereas such association is not seen with reticulocyte counts.

[Table/Fig-3] shows the association of neurological status at discharge of babies with reticulocyte counts and nucleated RBC count and it is statistically not significant in both the cases.

DISCUSSION

In our study NRBC counts were significantly higher in neonates with severe birth asphyxia correlated by short-term outcome, higher HIE staging and increase in duration of NICU stay of more than five days which was comparable to a reported similar literature by Boskabadi H et al., where they have compared with short outcome and severity of acidosis [1]. Association of NRBC to birth asphyxia has been observed in other studies but with a smaller sample size and only for diagnostic purposes and not for prognostic purposes [7-12]. NRBC counts and platelet counts were studied and asphyxiated neonates, sufficient to cause neurological impairment had significant results with NRBC as a marker [13].

These studies did not indicate the severity of the asphyxia or did not include duration of stay or neurological outcomes. It remains possible that the outcome of asphyxiated babies could be predicted on first day of admission by correlating the nucleated RBC's and reticulocyte counts with the severity of birth asphyxia and could reflect the long-term outcome.

There is paucity of published studies in the Indian literature related to predicting short-term outcome of birth asphyxia with the help of NRBC counts and specially reticulocyte count as none of the studies have included the simple parameter for assessing severity of asphyxia.

The findings of this study may have clinical implications as in our country, a large number of deliveries occur in peripheral health facilities and at home by trained and untrained birth attendants, reliable recording of well-established markers of birth asphyxia like Apgar scores, intra-natal tocography recording for fetal distress, fetal scalp pH monitoring is often not available. Such babies pose diagnostic dilemmas for treating doctors in tertiary health care centres where these babies are referred. Early and

accurate diagnosis of birth asphyxia is crucial in determining both short-term and long-term prognosis.

LIMITATION

Study involved only term new-borns. Therefore, it cannot be generalised to whole neonatal population. Study followed babies only up to discharge (categorised more than or less than five days). Therefore, the association of nucleated RBC count with long-term neurological outcome can just be correlated with short-term outcome. This study did not correlate NRBC count and reticulocyte counts with pH which is reported to be a reliable marker of perinatal asphyxia. This study was involved in a setup where more than half of the cases were referred from outside delivered hospitals, in which history is not reliable.

CONCLUSION

As Nucleated RBC count and Reticulocyte count show significant correlation in the above study, their interpretation in peripheral venous blood or cord blood is a low cost, simple and easily available test which can be done in any health care facility with minimal infrastructure.

The present study establishes the role of NRBC count as well as Reticulocyte count in peripheral venous blood collected within six hours of birth in diagnosis and prognostication of birth asphyxia. Hence, this simple and reliable test can routinely be included in investigation of all new-borns with suspected birth asphyxia for diagnosis as well as prognosis.

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