

Hypoxia as a Predisposing Factor for the Development of Early Onset Neonatal Thrombocytopenia

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ABSTRACT

Background: Thrombocytopenia in hypoxic neonates admitted in NICU is a morbid condition encountered very commonly. Early-onset thrombocytopenia (<72 h) is most commonly associated with fetomaternal conditions complicated by placental insufficiency and/or fetal hypoxia. Chronic intrauterine hypoxia is the most frequent cause of early-onset thrombocytopenia in preterm neonates. **Aims:** In this study incidence and clinical impact of early thrombocytopenia in hypoxic neonates was investigated. **Setting and Design:** Neonatal intensive care unit of a tertiary level hospital attached to a medical college in Central India. A cross-sectional, observational hospital based study in hypoxic neonates for development of thrombocytopenia. **Materials and Methods:** 603 hypoxic newborns were evaluated for development of thrombocytopenia. 155 (25.07%) developed thrombocytopenia and were the cases. Non thrombocytopenic babies 448 (74.29%) served as controls. The two groups were compared for birth weight, sex ratio, gestational age, severity of asphyxia, platelet counts and mortality rate. **Statistical Analysis:** Descriptive statistics of continuous variable were expressed in mean and SD. *P* value less than or equal to 0.05 were statistically significant. **Results and Conclusions:** We found thrombocytopenia to be associated with male gender, prematurity and low birth weight. Most babies had mild to moderate thrombocytopenia. Mortality was higher in preterm thrombocytopenic babies as compared to term. We suggest screening for thrombocytopenia in all asphyxiated newborns, as hypoxia can lead to neonatal thrombocytopenia.

Key words:

Neonate, birth asphyxia, hypoxia, thrombocytopenia, platelet count

INTRODUCTION

Thrombocytopenia is the most common hematological abnormality encountered in hypoxic neonates admitted in the neonatal intensive care unit (NICU).^[1] But while the disorder is frequently seen; it should not be dismissed without consideration of its significance. As an important component of blood, platelets are intimately involved in both vascular and clotting aspects of hemostasis. Various inherited, congenital and acquired diseases may affect the platelets in the newborn. Thrombocytopenia thus, can be a marker of underlying disease as well as an obvious risk factor for hemorrhage.

Whereas a large number of varied precipitating conditions has been identified, early-onset thrombocytopenia (<72 hours) is most commonly associated with fetomaternal conditions complicated by placental insufficiency and/or fetal hypoxia.^[2,3] Transient destructive thrombocytopenia develops in a large proportion of hypoxic newborns.

Screening of hypoxic neonates for thrombocytopenia might be helpful in early diagnosis, management and prevention of complications of thrombocytopenia.

In this study we aimed to determine the incidence and risk factors of thrombocytopenia in asphyxiated newborns.

MATERIALS AND METHODS

A hospital-based case-control study was carried out. Out of 1338 neonates with different clinical diagnosis admitted in NICU of Kamla Nehru hospital under Department of Pediatrics Medicine, Gandhi Medical College, Bhopal from Nov 2010 to Oct 2011, 603 babies with history of birth asphyxia irrespective of the gestational age constituted the study population. We used the National Neonatology Forum of India definition of asphyxia^[4] for identifying cases. Moderate asphyxia was defined as slow gasping breathing or an apgar score of 4-6 at 1 minute of age and severe birth asphyxia was defined as no breathing or an apgar score of 0-3 at 1 minute of

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10.4103/2249-4847.101693

age. (Reference) All babies with gestational age less than 37 completed weeks and all babies with birth weight of less than 2500 g were considered preterm and low birth weight respectively.

Thrombocytopenia was defined as platelet count less than 150,000/ml. The non-thrombocytopenic hypoxic neonates 448 (74.29%) served as control in our study. All data were collected prospectively.

Assessment of birth asphyxia was based on Apgar score at birth and thrombocytopenia was assessed with the help of a trained pathologist in the ward who assisted in sample collection for platelet count on day 1 and day 3. Platelet count was performed by automated analyzer. The study was approved by the institutional ethical committee.

Procedure

Blood samples of all hypoxic neonates included in the study were obtained from anterior cubital vein at two different times (First sample at the time of admission, second on day 3rd after birth) with all aseptic precautions. Two millimeters of blood withdrawn were collected in EDTA tube. Platelet counts were done on PCE120 automatic analyzer using an optical system for measurement.

Statistics

Descriptive statistics of continuous variables were expressed in mean and SD. *P* value less than or equal to 0.05 was considered statistically significant. SPSS and Epi calculator was used to measure variables statistically.

RESULTS

Out of 603 asphyxiated neonates, included in the study 155 (25%) developed thrombocytopenia. 412 (68.3%) were males. 489 (81%) were term and 114 (19%) were preterms.

Among 489 term asphyxiated neonates, 117 (23.9%) had thrombocytopenia, where as among 114 preterm hypoxic neonates; 38 (33.3%) had thrombocytopenia (*P* value 0.05).

Out of 155 thrombocytopenic asphyxiated neonates, severe birth asphyxia was noted in 105 (67.7%) and low birth weight was seen in 100 (64.51%) as compared to 81 (18.08%) and 100 (64.51%), (*P* value 0.0001) in the 448 non-thrombocytopenic asphyxiated neonates, respectively.

Statistically significant differences in gender distribution, gestational age, Apgar score, and birth weight were noted among the two groups as shown in [Table 1].

Mean platelet count of 155 thrombocytopenic neonates at the time of birth was 83.8 ± 36.13 . A rise in the mean platelet count was noticed on day 3 in this group, whereas the mean platelet count of 448 non-thrombocytopenic neonates was 200.1 ± 23.2 . There was no difference of platelets counts noted on day 3 [Figure 1].

As for the degree of thrombocytopenia, mild thrombocytopenia (platelet count $51-100 \times 10^9/L$) was found in 12.5% of cases, 16.6% of them had moderate thrombocytopenia (platelet count $30-50 \times 10^9/L$), while

Table 1: Showing characteristics and demographic profile of the cases

Factors	Thrombocytopenic asphyxiated babies (n=155) – cases		Nonthrombocytopenic asphyxiated babies (n=448) – controls		Significance
	No	%	No	%	
Sex					Chi-square 17.73
Male	99	63.8	313	69.8	<i>P</i> =0.00*
Female	56	36.1	135	30.1	
Gestational age					Chi-square 0.13
Preterm	38	24.5	76	16.96	<i>P</i> =0.00*
Term	117	75.4	372	83	
Apgar score					Chi-square 6.20
Moderate	50	32.25	367	81.91	<i>P</i> =0.012*
Severe	105	67.74	81	18.08	
Birth weight					Chi-square 6.33
Normal	55	35.48	302	67.41	<i>P</i> =0.01*
Low birth	100	64.51	146	32.58	
Platelet count					<i>P</i> =0.18**
At admission	83.8±36.13		200.11±23.21		<i>P</i> =0.16**
Day 3	100.16±31.26		200.55±17.38		
Mortality rate					<i>P</i> =0.16**
Preterm	16/38	42	17/76	22.36	<i>P</i> =0.16**
Term	30/117	25.6	87/372	23.38	

* = Significant; ** = Non-significant

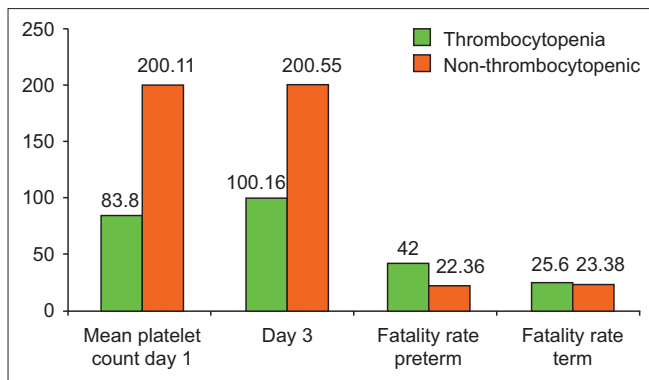


Figure 1: Showing mean platelet count and mortality rate in asphyxiated newborns

severe thrombocytopenia (platelet count $< 30 \times 10^9/L$) was detected in 2.08%.

Mortality rate in thrombocytopenic hypoxic neonates and non-thrombocytopenic hypoxic neonates was 29.67% and 23.2%, respectively. In terms of gestational age, fatality rate was higher (42%) in preterm thrombocytopenic hypoxic neonates as compared to (25.6%) term thrombocytopenic hypoxic neonates [Figure 1].

DISCUSSION

The incidence of thrombocytopenia in the general neonatal population is low. In contrast, thrombocytopenia in the neonatal intensive care unit (NICU) is quite common^[1,2] Asphyxia is a common morbid condition in neonates admitted in NICU and it can cause thrombocytopenia. Roughly one-quarter of all NICU patients and half of all sick preterm neonates develop thrombocytopenia. Neonatal thrombocytopenia occurs more frequently in neonates with history of birth asphyxia than in non-asphyxiated neonates. In our study, neonatal thrombocytopenia developed in quarter of asphyxiated neonates admitted in our NICU. Castle *et al.*^[2] in their study of 807 babies found transient, destructive thrombocytopenia in 22% of infants and birth asphyxia was an important risk factor. Oren *et al.*^[5] also found that hypoxia was present in 20% of thrombocytopenic neonates.

Our study found that neonatal thrombocytopenia was observed more frequently in preterm newborns. Hypoxia is an important aggravating risk factor in preterms for development of thrombocytopenia as compared to non-hypoxic term and preterm neonates. Oren *et al.*^[4] found that among 31 thrombocytopenic preterm infants; 55% had history of birth asphyxia, and severe respiratory distress syndrome before onset of thrombocytopenia.

In our study, 67.7% of thrombocytopenic hypoxic neonates had low Apgar score at 5 minutes. Beiner *et al.*^[6] found that

low 5 min. Apgar scores were significantly associated with neonatal thrombocytopenia in preterm infants, which lead to a significant morbidity.

In our study, males had a higher incidence of asphyxia and thrombocytopenia. A higher male predilection for asphyxia has been noted by Bekedem *et al* and Aly *et al.*^[7,8] Beiner *et al.*^[6] concluded that thrombocytopenic infants had a significantly lower birth weight. In another study conducted by Zacccheaus *et al.*^[9] 13.6% of thrombocytopenic infants were of low birth weight. Hidehiko Maruyana *et al.*^[10] concluded that birth weight and head circumference of the infants with thrombocytopenia were significantly smaller than those infants without thrombocytopenia. In our study also, the majority of thrombocytopenic infants were of low birth weight.

Bruknerova *et al.*^[11] found that there was a decrease in the levels of thrombocytes within 5 days of birth. No such decrease in platelet count was observed in our study.

As regard the severity of thrombocytopenia, Zacccheaus *et al.*^[9] in their study found mild thrombocytopenia in 39.4% of neonates, 12.1% had moderate thrombocytopenia, while severe thrombocytopenia was detected in 1.5% of neonates.

We noted a higher mortality rate in preterm infants with thrombocytopenia as compared to term asphyxiated neonates. Oren *et al.*^[5] concluded that thrombocytopenic preterm neonates had more complications and higher fatality rate (39%) when compared to non-thrombocytopenic preterm neonates ($P < 0.05$).

We conclude that thrombocytopenia is a frequent association with asphyxia and is associated with male gender, prematurity and low birth weight. Screening for development of thrombocytopenia is necessary in hypoxic neonates.

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How to cite this article: Nadkarni J, Patne SK, Kispotta R. Hypoxia as a predisposing factor for the development of early onset neonatal thrombocytopenia. *J Clin Neonatol* 2012;1:131-4.
Source of Support: Nil, **Conflict of Interest:** None declared.

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