

A Study of Platelet Count as a Marker of Severity of Hypoxic Ischemic Encephalopathy

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Abstract: The incidence of hypoxic-ischemic encephalopathy (HIE) is reportedly high in countries with limited resources; It is one of the top 20 leading causes of burden of disease in all age groups (in terms of disability life adjusted years) by the world health organization (WHO) and is the fifth largest cause of death of children younger than 5 years(8%). The purpose of this study was to investigate variations in platelet count in blood associated with HIE and its relation with the severity of HIE. A prospective (case control) study was undertaken between august 2011 and october2013 in the neonatal intensive care unit. The study population was consisted of 50 full term infants with asphyxia (group-1) and 50 healthy new-born (group-2). During the first 48 hrs. of life reduced platelet counts were noted in severely asphyxiated groups (HIE Gr-III) only. During the 2nd time period[(2-7) days] low counts were noted only in HIE Gr-2 categories. Low counts were noted in all three categories during the time periods of (7-14) days. Thrombocytopenia did not found in any cases of control groups. Reduced platelet count is a frequent findings in HIE. During the early period (0-2)days it is related to severity of HIE [found only in HIE Gr-III], but in the later period (3-14) days it may be found in all categories.

Key word: Hypoxic-ischemic encephalopathy, Thrombocytopenia, platelet count.

I. Introduction:

Birth asphyxia is estimated to account for 920,000 neonatal deaths every year and is associated with another 1.1 million intrapartum stillbirths. More than a million children who survive birth asphyxia develop problems such as cerebral palsy, mentalretardation, learning difficulties, and other disabilities.^[1,2] Encephalopathy is a term used to describe central nervous system dysfunction. Neonatal encephalopathy associated with perinatal asphyxia is called hypoxic ischemic encephalopathy (HIE). Multiorgan systems involvement is a hallmark of hypoxic-ischemic encephalopathy.^[3] Apart from brain involvement organ system involved following a hypoxic-ischemic events include the following: heart (43-78%), lungs (71-86%), renal (46-72%), liver (80-85%), hematologic (32-54%). Because the present indices of asphyxia are un helpful in the diagnosis and prediction of the severity of asphyxia, we wished to investigate the relationship between platelet count and the severity of HIE.

II. Materials & Methods:

The study population was consisted of 50 full term infants with asphyxia (group-1) and 50 healthy new-born (group-2). All the new-borns were delivered at our hospital, Dept. of obstetrics& gynaecology, and admitted in NICU of dept. Of Paediatrics, BMCH will be evaluated regarding their eligibility to be included or excluded in the study. The study protocol is approved by Institutional Ethical Committee of the college.

Inclusion criteria:

- 1) Newborn suffering from birth asphyxia and subsequently developing hypoxic ischaemic encephalopathy
- 2) Newborn who fulfill the case definition criteria
- 3) Gestational age (37-40) weeks [assessed GA]
- 4) Birth weight 2.5- 3.5 Kg
- 5) Neonates surviving more than 24 hrs.

Exclusion Criteria:

- 1) Newborn with sepsis, major congenital anomalies, birth trauma
- 2) Any bleeding infant
- 3) Premature infant
- 4) Newborn borns to mothers having major diseases like malariaDM, severe anaemia, pre eclamsia/eclamsia, thyroid disorder, idiopathic purpura, placental disorder like vascular thrombosis, abruptio placenta

- 5) H/o maternal intake of any drugs causing bone marrow suppression/ thrombocytopenia
- 6) Newborn with congenital leukaemia, necrotising enterocolitis, those having exchange transfusion

At first the parents will be interviewed regarding the ante natal history, drug history of mother, family history of perinatal asphyxia etc. New-borns will be examined for any major congenital anomalies, haematological diseases, bleeding manifestations, sepsis or any congenital heart diseases. Then the parents of the new-borns; eligible for the study as per inclusion or exclusion criteria will be briefed about the procedures and the purpose of the study. A written consent will be taken from them regarding this matter. The eligible new-borns will be screened for other conditions mimicking HIE like hypoglycaemia, hypocalcaemia, etc. Then the following factors were noted in each infants: sex, birth weight, gestational age, condition at birth including Apgar scores, respiratory status, sepsis, hyperbilirubinemia, medications, clinical course. The gestational age of all infants were determined by a combinations of LMP and Ballard scoring.

The new-borns whose Apgar score at 5th minutes was 5 or below and arterial blood ph. During birth or a few hours after birth below 7.2, and had the findings of HIE were accepted as having perinatal asphyxia. Patients were recorded according to the HIE staging of the Sarnath and Sarnath.^[4] The blood samples were collected in asphyxiated infants in three different times named as period. The same tests were performed in control infants in three different times after parental consent was obtained. The first period was within 48 hours after birth, the second was between the third and the sixth days after birth, and the third period between the seventh and the fourteenth days after birth. All asphyxiated babies had coagulation work-up including prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen and fibrin degradation products to rule out disseminated intravascular coagulation (DIC). Trans fontanel and abdominal ultrasonographic examination were performed to evaluated intracranial haemorrhage and renal vein thrombosis in the asphyxiated new-borns. The mechanism responsible for the thrombocytopenia was investigated by measuring MPV. The platelet count and MPV was assessed on EDTAant coagulated specimens using a coulter-S+ counter (Coulter STKS, coulter electronics Ltd North well drive, England).

III. Result:

Asphyxiated and control groups were not different for matched features, which includes birth weight and gestational age. However a major difference between the two groups was the Apgar score. **Fig-1** & also table 1 shows the value of platelet counts in different periods and stages of HIE along with the control groups. During the first 48 hrs. of life reduced platelet counts were noted in severely asphyxiated groups (HIE Gr-III) only. During the 2nd time period[(2-7) days low counts were noted only in HIE Gr-2 categories. Low counts were noted in all three categories during the time periods of (7-14) days. Thrombocytopenia did not found in any cases of control groups. However low platelet counts due to perinatal asphyxia was not directly associated with mortality. Thrombocytopenia (platelet count < 150×10⁹ /L) was noted in 12 neonates during first time period, 22 neonates during 2nd time period, and 17 neonates during the 3rd time period.

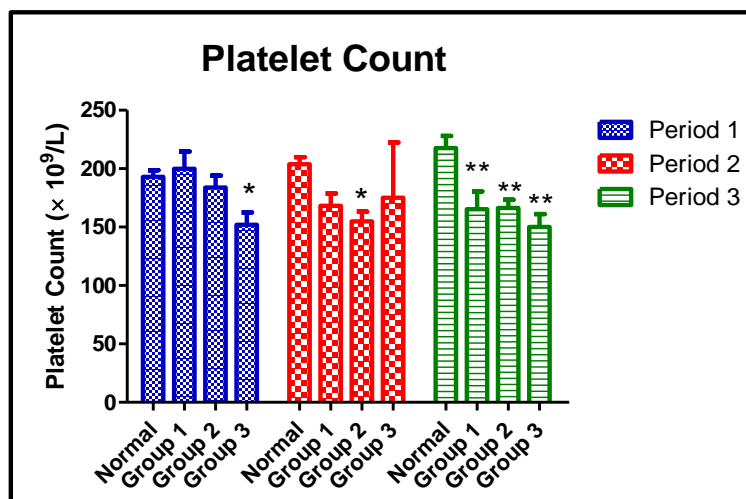


Figure 1: Comparison of platelet count among various stages of HIE and normal control. Values are expressed as mean ± SEM. Statistical analysis (One way Anova; Dunnett compare all vs. control) was performed using Graph Pad Instat Software. *p < 0.05, **p < 0.01 when all the groups compared with normal.

Parameters	Average	SD	SEM
Plat. P1 G1	199.93	63.00	14.84
Plat. P1 G2	183.80	66.41	14.85
Plat. P1 G3	152.06	66.38	19.16
Plat. P2G1	168.20	65.76	15.50
Plat. P2G2	183.80	65.35	14.61
Plat. P2G3	175.05	64.33	18.57
Plat. P1 G1	165.41	63.91	15.06
Plat. P1 G2	166.28	65.58	14.66
Plat.P1 G3	150.13	59.89	17.29

Table 1

IV. Discussion:

Few studies have been performed to find a relationship among platelet count and the grade of hypoxic ischemic encephalopathy. But most of the studies have been carried out in animals.

The present study will be carried out to analyze the hematological parameter and to find out a relationship between this and severity of HIE. These hematological parameters with a cut of value can be a useful marker and may serve as a guide for grading. Moreover these parameters may be used to assess short term prognosis. It will help us in better understanding of the problem and will be helpful in the development of post insult therapy.

Nursen BELET et al.^[5] suggests in their study regarding perinatal asphyxia and thrombocytopenia that the thrombocytopenia ratio in the asphyxiated patients was 25.0% in the first period, 36.8% in the 2nd period and 26.6% in the third time period. They couldn't find any correlation between the severity of HIE and platelet count and also the effect of thrombocytopenia on mortality ratio in perinatal asphyxia.

Sarnat HB et al. commented in their study that birth asphyxia has consistently been associated with evidence of thrombocytopenia and DIC in sick neonates. The clinical observation is supported by animal studies, that directly linked exposure to hypoxia and thrombocytopenia.

Kroost LM et al.^[6] did the study on neonatal platelet count and fetal brain injury. The neonates and platelet counts for each group were as follows: Control: 104 neonates, mean 281 +/- 56, range 154 to 411; I: 60, mean 185 +/- 80, range 28 to 365; II: 34, mean 251 +/- 66, range 100 to 375; and III: 35, mean 267 +/- 93, range 86 to 569. Platelet counts were significantly lower in neonates with encephalopathy (p <0.001). Group I differed statistically from both Groups II and III (p <0.001). These data suggest an association between the FHR pattern, foetal asphyxial brain injury, and the initial platelet count in singleton term neonates.

V. Conclusion:

The study was carried out to analyze the hematological parameter (platelet count) and to find out a relationship between this and severity of HIE, at dept. of pediatrics, Burdwan medical college from Aug-2011 to Oct-2013. It involved 50 cases suffering from birth asphyxia and subsequently developing hypoxic ischemic encephalopathy. The specific objectives of this study is: To evaluate platelet count as a marker of severity of HIE.

The study revealed the following findings: Reduced platelet count is a frequent findings in HIE. During the early period (0-2)days it is related to severity of HIE [found only in HIE Gr-III], but in the later period (3-14) days it may be found in all categories.

Acknowledgements

Author is thankful for the authority of Burdwan Medical College and Hospital, Burdwan, West Bengal, India for providing the facilities of this research work.

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