Effect of Gestational Age, Prematurity and Birth Asphyxia on Platelet Indices in Neonates

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ABSTRACT

Context: Platelet indices are useful markers of platelet maturity and function and can be used for the early diagnosis of thromboembolic disorders. Prematurity, birth asphyxia (BA) and small for gestational age (SGA) babies have been associated with increased risk of hemostatic abnormalities. **Aims:** The aim was to study the platelet indices in prematuriy, SGA, and BA newborns. **Settings and Design:** The type of this study is Prospective study. **Materials and Methods:** Blood samples from 253 newborns were collected in K2EDTA (Becton Dickenson, USA) tubes within 24 h of birth. The following parameters were studied - platelet count, mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW). Data regarding the neonatal physiological status with respect to prematurity, gestational age and BA were collected. Statistical Analysis Used: The statistical analysis was performed on the entire sample used was mean, standard deviation and one-way ANOVA. $P < 0.05$ was considered as significant. **Results:** The average platelet count in preterm, SGA, and BA newborn was significantly lower than the average platelet count in controls. MPV averaged 8.29 fL, 8.16 fL, and 8.35 fL in preterm, SGA and BA neonate, respectively and was significantly increased. PCT was 0.18% in preterm, SGA and in BA. Though, the difference was not statistically significant. PDW was significantly increased in preterm, SGA, and BA newborns when compared with controls. **Conclusions:** MPV, PDW was significantly increased in SGA, premature and BA newborns, which may be due to platelet activation. Platelet indices may provide to be a useful marker of thromboembolic status in newborns.

Key words:
Birth asphyxia, neonates, platelet indices, prematurity, small for gestational age

INTRODUCTION

Platelets in newborn demonstrate several activities, including hemostasis and maintaining integrity of blood vessels. Hemostasis of a neonate is a dynamic system that gradually evolves throughout gestation and early infancy.[1] The newborn physiological status affects the risk for and the presence of acquired hemostatic disorders. Prematurity, birth asphyxia (BA) and small for gestational age (SGA) babies have been associated with hemostatic abnormalities.[2]

Platelets and their activity have an important role in initiating thrombotic events. However the platelet count alone does not give a complete picture of platelet maturity and function. Hence plateletindices such as mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) have been the subject of intensive study in recent years. Platelet size correlates with platelet activity and can be assessed by MPV and PDW. Larger platelets are enzymatically and metabolically more active and have a higher potential thrombotic ability as compared with smaller platelet. MPV and PDW are increased during platelet activation due to platelet swelling and pseudopodia formation. Hence, platelet indices are potential useful markers for the early diagnosis of thromboembolic disorders.

Automated hematology analyzers have made possible to measure several blood cell parameters, including platelet indices precisely and fast. Platelet indices have been studied in many pathological conditions such as diabetes, coronary artery diseases, angina, pulmonary tuberculosis, iron deficiency anemia, but they have not been firmly established in neonates.[3-6] Only few studies have been done to determine the platelet indices in preterm, SGA and BA neonates. The aim of the study was to determine platelet indices in prematuriy, SGA, and BA newborns and to compare it with platelet indices in full term appropriate for gestational age (AGA) without BA neonates.

MATERIALS AND METHODS

The study consisted of 253 newborns whose blood samples were collected in K2 EDTA tubes within 24 h of birth for

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complete blood count. Samples were analyzed in Beckman Coulter Ac.T 5 Diff autoanalyser (Beckman Coulter, USA). The following parameters were studied-platelet count, MPV, PCT, PDW. Samples received after 24 h of birth or with clinically or laboratory confirmed infections were excluded from the study.

Data regarding the neonatal physiological status with respect to prematurity, gestational age and BA were collected. Newborns in gestational age 25-32 weeks and weighing 1000-2150 g and Apgar score of 4-8 points at 1 min were considered preterm. Newborns in gestational age 38-41 weeks, but weighing <10th percentile were considered as SGA. Newborns whose Apgar score at 5th min was <5 and arterial blood pH during birth or a few hours after birth below 7.2 and had the findings of hypoxic ischemic encephalopathy were accepted as having BA. Platelet indices from full term, AGA without BA were taken as controls.

Data distribution in groups was verified with the Kolgomorov–Smirnof or Shapiro–Wilk normality tests. The statistical analysis performed on the entire sample used was mean, standard deviation and one way ANOVA. P <0.05 was considered as significant. Multiple comparison between groups was done using *post-hoc* test least square difference. This study was approved by the Institutional ethics Committee.

RESULTS

Out of 253 newborns, 70 were full term SGA, 43 preterm, 55 full term AGA with BA and 85 full term AGA without any complications were taken as controls. The average platelet count in preterm was 227 × 10^3/μl, in SGA 215 × 10^3/μl, and BA newborn was 219 × 10^3/μl. This was significantly lower than the average platelet count in controls 246 × 10^3/μl. MPV averaged 8.29 ± 0.80 fL in preterm 8.16 ± 0.64 fL in SGA, and 8.35 ± 0.76 fL in BA neonate and was significantly increased when compared with controls 8.02 ± 0.70. PCT was 0.18 ± 0.05% in preterm, 0.18 ± 0.06% in SGA and 0.18 ± 0.70% in BA. PCT was lower when compared with controls 0.19 ± 0.05, though the difference was not statistically significant. PDW was 14.79 ± 4.01 in preterm, 14.10 ± 2.93 in SGA, and 15.05 ± 3.68 in BA newborns. PDW was significantly increased when compared with controls 13.33 ± 2.97.

The values are shown in Table 1 and the line diagram for graphical representation of platelet count, MPV, PCT and PDW is shown in Figures 1-4.

DISCUSSION

Hemostasis of a neonate is a dynamic system that gradually evolves throughout gestation and early infancy. Platelets first appear in the human fetus at 5 weeks after conception and increase in number during fetal life, reaching a mean of 150 × 10^9/L by the end of the first trimester of pregnancy and values within the adult range by 22 weeks of gestation.[1] The MPV averages 7-9 fL for full term neonates. The newborn physiological status affects the risk for and the presence of acquired hemostatic disorders.

Platelet count in preterm babies, is found to be decreased, depending on birth weight and gestational age.[7] The functions of platelet is also found to be related to the gestational age.[8] Hence preterm babies are at risk for hemorrhagic and thrombotic complications which may increase mortality and morbidity in this age group. Prenatal risk factors like pre eclasmpsia in the mother and perinatal risk factors such as maternal morbidity and mortality may also disturb hemostasis and increase hemorrhagic incidents in the newborn.[9] In pre-eclampsia, activation of the coagulation system, fibrinolytic system and platelet may alter the hemostatic

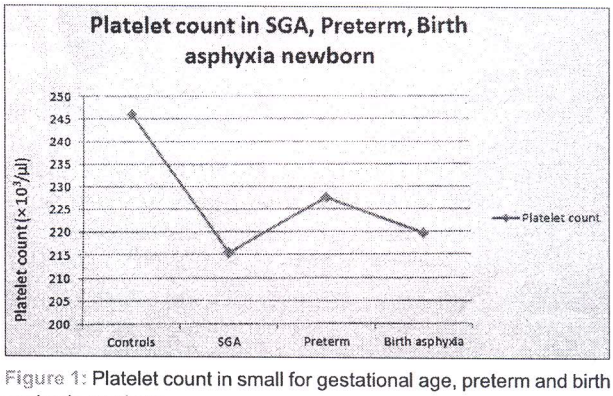

Figure 1: Platelet count in small for gestational age, preterm and birth asphyxia newborn

Table 1: Platelet indices in preterm, SGA and birth asphyxia neonates

Platelet indices	Controls n=85	SGA n=43	Preterm n=70	Birth asphyxia AGA n=55	P value
Platelet count×10^3/μl	246.01±73	215.48±75.43	227.54±64.80	219.58±64.93	0.042
MPV (fL)	8.02±0.70	8.16±0.64	8.29±0.80	8.35±0.76	0.046
PCT (%)	0.19±0.05	0.18±0.05	0.18±0.06	0.18±0.07	0.577
PDW fL	13.33±2.97	14.10±2.93	14.79±4.01	15.05±3.68	0.015

MPV – Mean platelet volume; PCT – Plateletcrit; PDW – Platelet distribution width; SGA – Small for gestational age; AGA – Appropriate for gestational age

balance at birth and predispose to intravascular coagulation.[10]

This study showed that the average number of platelet in preterm, SGA and BA newborns was significantly lower than the average platelet count in the control group. The reduced number of platelet in SGA and preterm neonates maybe the result of impaired thrombopoiesis due to the limited maturity of the organs responsible for this process. Thrombopoiesis in newborns occurs in liver and spleen. Hiett *et al.* found a lower number of hematopoietic progenitor cells in the cord blood of SGA when compared to AGA.[11] This may indicate an impaired process of megakaryopoiesis.

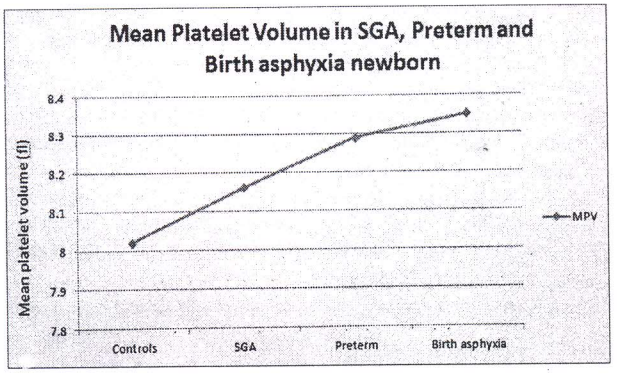

Figure 2: Mean platelet volume in small for gestational age, preterm and birth asphyxia newborn

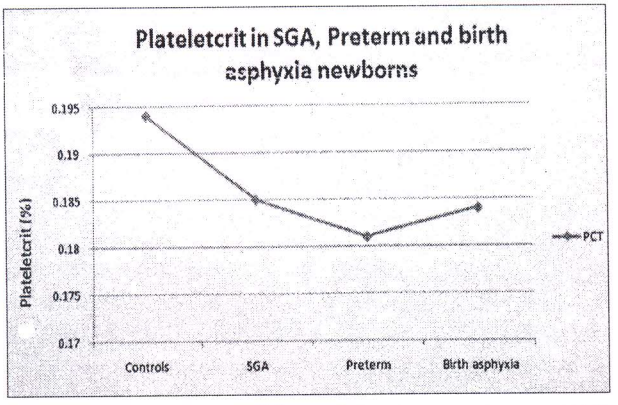

Figure 3: Plateletcrit in small for gestational age, preterm and birth asphyxia newborn

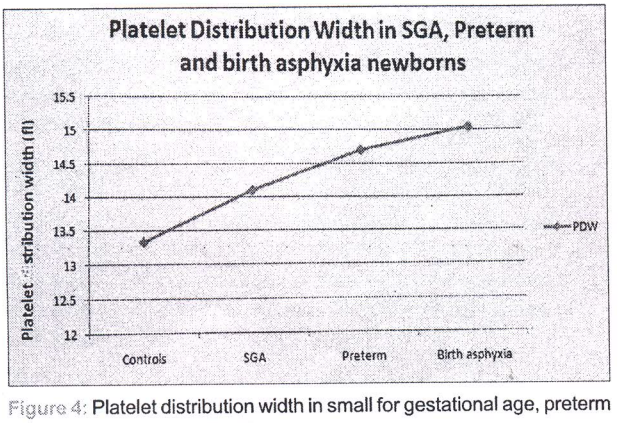

Figure 4: Platelet distribution width in small for gestational age, preterm and birth asphyxia newborn

An important factor in stimulating the formation of platelet is thrombopoietin (TPO). TPO is synthesized in the liver of fetus and newborns. It acts through the c-myeloproliferative leukemia (MPL) receptor present on platelets and megakaryocytes. Its plasma concentration depends on the amount of free receptor c-MPL.[12] When platelet count falls, free circulating plasma TPO stimulatesthrombopoiesis. When platelet count increases, circulating TPO binds to the receptor c-MPL, resulting in decrease of free thrombopietin and inhibits thrombopoiesis. Wasiluk *et al.*found higher levels of TPO in SGA suggesting the role of impaired thrombopoiesis.[13]

Mean platelet volume is the measurement of the average size of the platelet in the blood. PDW reflects the variability in the platelet size and is increased in the presence of platelet anisocytosis. In this study, MPV and PDW was found to be significantly increased when compared with controls. The difference is probably due to the increase in the production of young and activated platelets. The increase in MPV could also be due to an inverse relationship to the platelet count. Similar findings were seen in preterm and SGA neonates by Wasiluk *et al.* as shown in Tables 2 and 3.[14,15] The literature describes several studies that were performed to determine PDW reference ranges, but the results are expressed as percentages probably due to different analyzers being used and thus cannot be compared to results found in this study.[14,16]

Table 2: Comparison of platelet indices in SGA

Platelet indices	Present study	Wasiluk *et al.*
Platelet count×10^3/μl	215.48±75.43	237.60±61.4
MPV (fL)	8.16±0.64	8.25±0.8
PCT (%)	0.18±0.05	0.19±0.049
PDW	14.10±2.93 fL	47.0±10.33%

MPV – Mean platelet volume; PCT – Plateletcrit; PDW – Platelet distribution width; SGA – Small for gestational age

Table 3: Comparison of platelet indices in preterm

Platelet indices	Present study	Wasiluk *et al.*
Platelet count×10^3/μl	227.54±64.80	197±44
MPV (fL)	8.29±0.80	8.02±0.92
PCT (%)	0.18±0.06	0.16±0.04
PDW	14.79±4.01 fL	50.64±10.32%

MPV – Mean platelet volume; PCT – Plateletcrit; PDW – Platelet distribution width

Vagdatli *et al.* showed that simultaneous increase of MPV and PDW is seen during platelet activation.[17] Platelet activation causes morphologic changes of platelets, including both the spherical shape and pseudopodia formation. Platelets with increased number and size of pseudopodia differ in size, possibly affecting PDW. Hence, he concluded PDW to be a more specific marker of platelet activation, since it does not increase during simple platelet swelling.[17]

Very few studies have shown the association of MPV in newborns with BA. Belet *et al.* found that MPV was not elevated in full term non thrombocytopenic newborns with BA, Platelet count was 207.67 ± 12.12 and MPV 7.99 ± 0.16.[18] This could be attributed to the less number of cases included, and also that the samples were collected during 48 h of birth.

Plateletcrit was mildy reduced than controls in present study, though it was not statistically significant. The decrease in PCT could be due to a decrease in platelet count as PCT is directly related to the platelet count. Wasiluk *et al.* however found a statistical association of PCT in SGA and preterm babies.[14,15] This study however did not correlate the platelet indices with adverse neonatal outcome. Further studies are needed to evaluate the platelet indices in the physiological status of newborn to adverse neonatal outcome.

CONCLUSION

Mean platelet volume, PDW and PCT are affected by the physiological status of the newborn. MPV, PDW was significantly increased in SGA, premature and BA newborns, which may be due to platelet activation. Platelet indices may provide to be a useful marker of thromboembolic status in newborns.

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