

Original Research Article

Comparative Study of Platelet Indices between Term, Preterm and Small for Gestational Age Newborns

Prof. Sathyavathi R Alva¹, Dr. Ashwini K.T², Dr. Navya B.N³,¹Prof., Dept. of Pathology, KVG Medical College and Hospital, Sullia, D.K, Karnataka²Postgraduate, Dept. of Pathology, KVG Medical College and Hospital, Sullia, D.K, Karnataka³Associate Prof., Dept. of Pathology, KVG Medical College and Hospital, Sullia, D.K, Karnataka***Corresponding author**

Dr. Navya B. N

Email: navyabn@rediffmail.com

Abstract: Hemostasis in neonate is a dynamic entity which evolves gradually throughout the fetal period and early infancy. Physiological status of newborn affects the hemostasis mechanism. To evaluate the number and morphological parameters of blood platelets in preterm, full term SGA newborns and to compare it with platelet indices of full term appropriate for gestational age neonates. This was a prospective study, blood samples of 90 newborns were collected in K2EDTA tubes within 24h of birth and platelet indices such as platelet count, mean platelet volume, plateletcrit and platelet distribution width were estimated using Mindray Coulter BC3000plus autoanalyser. Data regarding the neonatal physiological status with respect to prematurity, gestational age were collected. The statistical analysis were mean, standard deviation, one way ANOVA test was used to compare differences of hemostatic parameters between SGA, prematurity, full term AGA. Average platelet count of preterm ($206 \times 10^3/\mu\text{L}$) and SGA ($202 \times 10^3/\mu\text{L}$) was low compared with term neonates ($256 \times 10^3/\mu\text{L}$) with a P value <0.0001 . Average plateletcrit was decreased in preterm (0.17%) and SGA (0.19%) as compared with term (0.22%) with a P value <0.0001 . Average Mean platelet volume of preterm (8.4fL) & SGA (8.29fL) was higher compared to term neonates (8.13fL) with a P = 0.008. Average platelet distribution width was significantly increased in preterm (16.46) and SGA (16.19) when compared to term neonates (15.57) with a P = 0.002. Platelet indices may represent easy and early biomarker for identification of thromboembolic status in neonates and thus improves the neonatal outcome.

Keywords: Term, preterm, SGA, newborns, platelet indices

INTRODUCTION

In the neonatal period, there are physiological immunological deficiencies and disorders of the process of hemostasis [1]. Hemostasis in neonate is a dynamic entity which evolves gradually throughout the fetal period and early infancy [2]. Platelets in neonates are necessary for hemostasis, for maintaining blood vessel integrity and phagocytosis. Physiological status of newborn affects the hemostasis mechanism. Prematurity, birth asphyxia and small for gestational age babies (SGA) are associated with hemostatic abnormalities [3, 4].

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 platelet indices 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 [5].

Automated hematology analyzers have made possible to measure 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 [6-9].

Preterm neonates are prone to develop various complications like intraventricular hemorrhage, chronic lung disease. It has been observed that platelet indices can be used to predict the development of above-mentioned complications at an early stage [10, 11]. Only few studies have been conducted to determine the platelet indices in preterm and SGA neonates and hence this study was undertaken to evaluate the number and morphological parameters of blood platelets in preterm, full term SGA newborns and to compare it with platelet indices in full term appropriate for gestational age neonates.

MATERIALS AND METHODS

The present study was a prospective study conducted at central diagnostic laboratory, KVG medical college and hospital from April 2016 to July 2016.

After obtaining informed written consent from parents, the venous blood samples of 90 newborn cases were collected in K2 ethylene diamine tetra acetic acid (EDTA) tubes within 24 hrs of birth. Samples were analyzed using Mindray Coulter BC 3000plus autoanalyser. The following indices: PLT (platelet count), MPV (mean platelet volume), PDW (platelet distribution width), PCT (platelet hematocrit) were studied. Inclusion Criteria were: samples collected within 24hrs of birth from full term appropriate for gestational age, preterm, SGA neonates. Samples collected from neonates after 24hr of birth, clinically or laboratory proven infections and major congenital anomalous newborns, neonates with birth asphyxia were excluded from the study.

Detailed history regarding antenatal checkup in mother, mode of delivery, data regarding the neonatal physiological status with respect to prematurity & gestational age and drugs affecting the functions of platelets administered to mothers within 10 days before delivery were collected. Gestational age was calculated

from the date of last menstrual period, in concordance with New Ballard Score [12].

Newborns in gestational age 25-32 weeks, weighing 1000-2150g with an 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 of gestational age 37-42 weeks, weighing 2500-3900 g with an Apgar score of 8-10 at 1min were considered as full-term AGA neonates.

The statistical analysis performed on the entire sample was mean, standard deviation and one way ANOVA test to compare the differences of hemostatic parameters between SGA, prematurity, full term AGA. *Pvalue* <0.05 was considered as significant.

RESULTS

A total of 90 newborns delivered during the study period were included in the present study, of which 30 were fullterm AGA neonates, 30 were preterm neonates and rests 30 were small for gestational age neonates.

The values of study subject are depicted in table 1. The Average platelet count of preterm (206 x 10³ /μL) and SGA (202x10³/μL) was low compared to term neonates (256x10³/μL) with a P value <0.0001. Plateletcrit was decreased in preterm (0.17%) and SGA (0.19%) as compared to term neonates (0.22%) with a P value<0.0001. Average Mean platelet volume of preterm (8.4fL) & SGA (8.29fL) was higher compared to term neonates (8.13fL) with a P value 0.008. Platelet distribution width was significantly increased in preterm (16.46fL) and SGA (16.19fL) when compared to term neonates (15.57fL) with a P value 0.002.

The graphical representation of average platelet count, plateletcrit, mean platelet volume and platelet distribution width are shown in figures 1- 4.

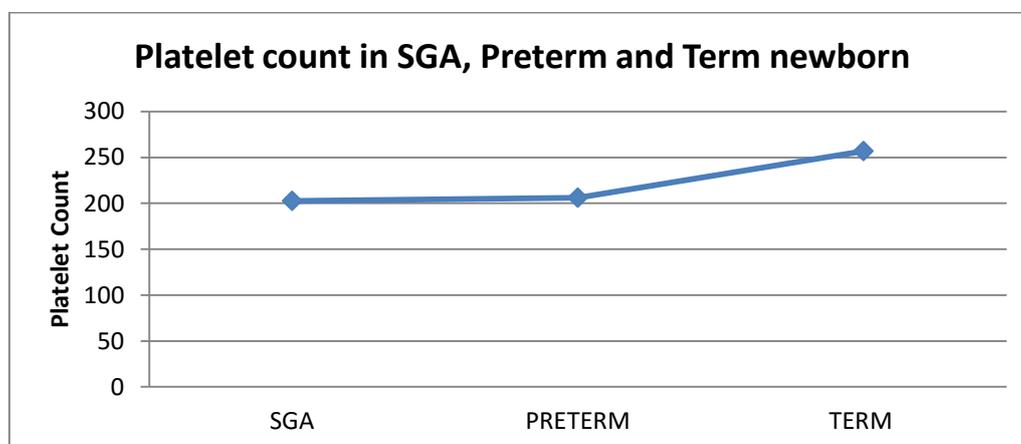


Fig-1: Average platelet count in SGA, preterm, term newborns

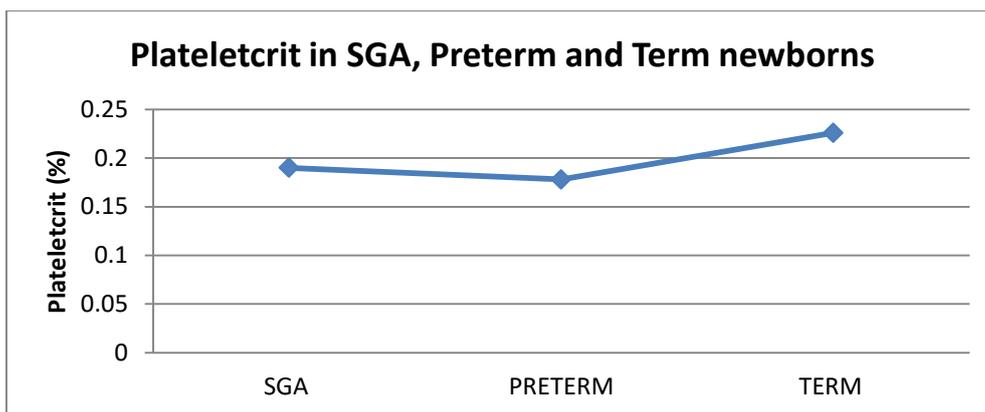


Fig-2: Average Plateletcrit in SGA, preterm, term newborns

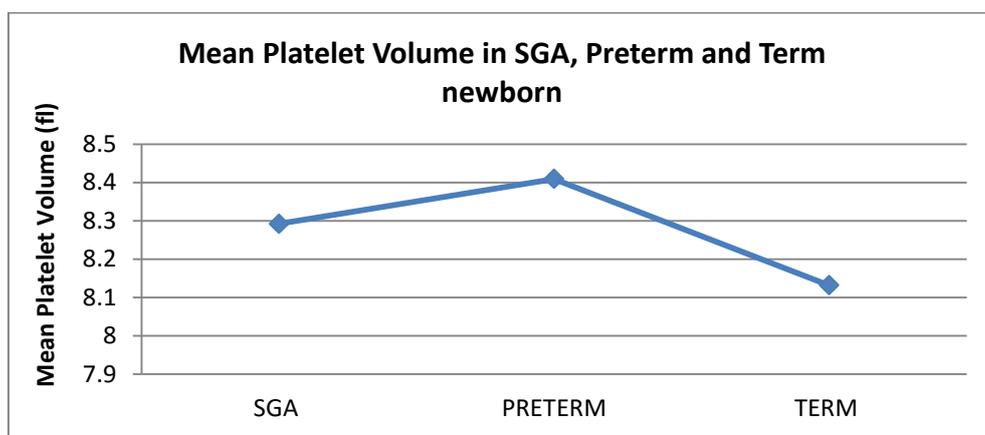


Fig-3: Average mean platelet volume in SGA, preterm, term newborns

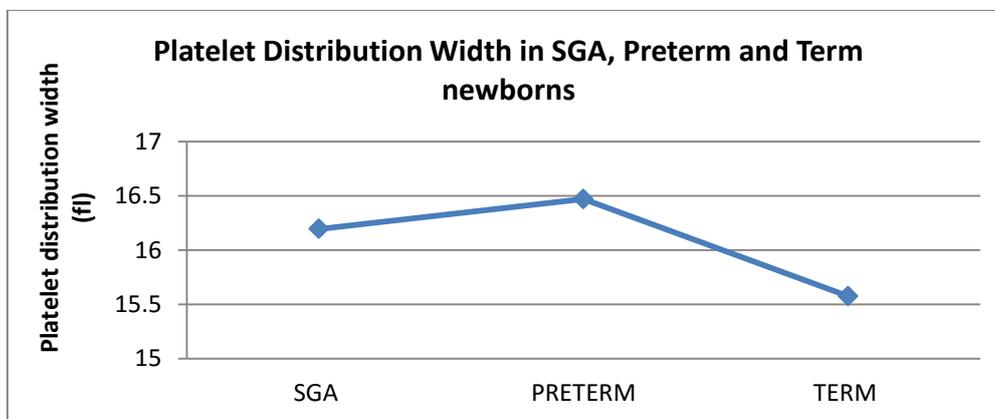


Fig-4: Average Platelet Distribution Width in SGA, preterm, term newborns

Table-1: Platelet indices in term, preterm, SGA neonates

PLATELET INDICES	TERM	PRETERM	SMALL FOR GESTATIONAL AGE	P VALUE
Platelet count x10 ³ /μl	256±37.3	206±24.14	202.56±14.92	P=<0.0001
Plateletcrit (%)	0.22±0.03	0.178±0.02	0.19±0.01	P= <0.0001
Mean platelet volume (n=7- 9fL)	8.13±0.36	8.409±0.59	8.29±0.43	P = 0.008
Platelet distribution width(fL)	15.5±0.74	16.469±1.27	16.19±0.82	P=0.002.

DISCUSSION:

In our present study, it was observed that average platelet count in preterm and SGA neonates was found to be decreased as compared with full term AGA newborns. Hemostasis in neonate is a dynamic entity which evolves gradually throughout the fetal period and early infancy. Platelets first appear in human fetus at the gestational age of 5 weeks after conception, it gradually increases during the fetal life, reaching a mean of $150 \times 10^9/L$ by the end of first trimester and reach the adult value by gestational age of 22 weeks [2].

An important factor in stimulating the formation of platelets is thrombopoietin, whose principal place of synthesis is liver in newborns and fetuses. Thrombopoietin acts through the c-MPL receptor present on platelets, megakaryocytes and precursor cells of megakaryopoiesis, and its plasma concentration depends on the amount of free receptor c-MPL [13]. When the platelet count increases, a significant proportion of circulating TPO binds to the receptor c-MPL, resulting in a decrease of free TPO, and inhibits thrombopoiesis. When the platelet count falls, more freely circulating plasma thrombopoietin stimulates thrombopoiesis. Wasiluk *et al.* found higher levels of TPO in SGA suggesting the role of impaired thrombopoiesis [14].

The functions of platelets are found to be related to the gestational age [4]. Lower platelet counts observed in preterm neonates is mostly due to developmental limitation in the ability to increase megakaryocyte size and placental dysfunction may also be responsible for the alteration of platelet count in newborns at birth [15, 16]. The reduced platelet count and their function in relation to gestational age may result in higher risk of bleeding tendency in preterm neonates [4].

Plateletcrit was reduced in preterm and SGA neonates than term neonates in present study. 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].

Mean platelet volume is the measurement of the average size of the platelet in the blood. Normal range 7-9 fL for full term neonates. 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 in preterm and SGA when compared with term neonates. 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.* and Kannar *et al.* as shown in table 2 and 3.

Vagdatli *et al.* showed that simultaneous increase of MPV and PDW is seen during platelet activation. 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, they concluded PDW to be a more specific marker of platelet activation, since it does not increase during simple platelet swelling. PDW is a more sensitive index for estimation of changes in platelet size [18, 19]. Increase in PDW may be due to negative correlation with gestational age and birth weight [18]. PDW may be useful in detection of conditions like sepsis and platelet consumption at an early stage.²⁰The increase in MPV is seen in conditions like disseminated intravascular coagulation which is associated with platelet activation and consumption.

Table-2: Comparison of platelet indices in SGA:

PLATELET INDICES	PRESENT STUDY	KANNAR <i>et al.</i>	WASILUK <i>et al.</i>
1. Platelet count $\times 10^3/\mu l$	202.56 \pm 14.92	215.48 \pm 75.43	237.60 \pm 61.4
2. Plateletcrit (%)	0.19 \pm 0.01	0.18 \pm 0.05	0.19 \pm 0.049
3. Mean platelet volume (fL)	8.29 \pm 0.43	8.16 \pm 0.64	8.25 \pm 0.8
4. Platelet distribution width	16.19 \pm 0.82fL	14.10 \pm 2.93fL	47.0 \pm 10.33%

Table-3: Comparison of platelet indices in preterm

PLATELET INDICES	PRESENT STUDY	KANNAR <i>et al.</i>	WASILUK <i>et al.</i>
1. Platelet count $\times 10^3/\mu l$	206 \pm 24.14	227.54 \pm 64.80	197 \pm 44
2. Plateletcrit (%)	0.178 \pm 0.02	0.18 \pm 0.06	0.16 \pm 0.04
3. Mean platelet volume (fL)	8.409 \pm 0.59	8.29 \pm 0.80	8.02 \pm 0.92
4. Platelet distribution width	16.469 \pm 1.27fL	14.79 \pm 4.01 fL	50.64 \pm 10.32%

CONCLUSION

The obtained results show that thrombopoiesis in SGA and premature newborns was impaired. Platelet count & plateletcrit was decreased, mean platelet volume & platelet distribution width was significantly increased in SGA and premature newborns due to platelet activation. Platelet indices may represent easy and early biomarker for identification of thromboembolic status in neonates, and thus improves the neonatal outcome.

REFERENCES

1. Maconi M, Rolfo A, Cardaropoli S, Brini M, Danise P. Hematologic values in healthy and small for gestational age newborns. *Laboratory hematology: official publication of the International Society for Laboratory Hematology*. 2004 Dec;11(2):152-6.
2. Sola-Visner M. Platelets in the neonatal period: developmental differences in platelet production, function, and hemostasis and the potential impact of therapies. *ASH Education Program Book*. 2012 Dec 8;2012(1):506-11.
3. Strauss T, Sidlik-Muskatel R, Kenet G. Developmental hemostasis: primary hemostasis and evaluation of platelet function in neonates. *In Seminars in Fetal and Neonatal Medicine* 2011 Dec 31 (Vol. 16, No. 6, pp. 301-304). WB Saunders.
4. Levy-Shraga Y, Maayan-Metzger A, Lubetsky A, Shenkman B, Kuint J, Martinowitz U, Kenet G. Platelet function of newborns as tested by cone and plate (let) analyzer correlates with gestational age. *Acta haematologica*. 2006 Mar 17;115(3-4):152-6.
5. Kannar V, Deepthi A, Kumar ML, Junjgowda K, Mariyappa N. Effect of gestational age, prematurity and birth asphyxia on platelet indices in neonates. *Journal of clinical neonatology*. 2014 Jul 1;3(3):144.
6. Jindal S, Gupta S, Gupta R, Kakkar A, Singh HV, Gupta K, Singh S. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. *Hematology*. 2011 Mar 1;16(2):86-9.
7. Kadikoylu G, Yavasoglu I, Bolaman Z, Senturk T. Platelet parameters in women with iron deficiency anemia. *Journal of the national medical association*. 2006 Mar;98(3):398.
8. Tozkoparan E, Deniz O, Ucar E, Bilgic H, Ekiz K. Changes in platelet count and indices in pulmonary tuberculosis. *Clinical Chemical Laboratory Medicine*. 2007 Aug 1;45(8):1009-13.
9. Chu SG, Becker RC, Berger PB, Bhatt DL, Eikelboom JW, Konkle B, Mohler ER, Reilly MP, Berger JS. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *Journal of Thrombosis and Haemostasis*. 2010 Jan 1;8(1):148-56.
10. Hussein NF, Helaly NS, Ghanya EA, Anisb SK. Relationship between Mean Platelet Volume and Bronchopulmonary Dysplasia and Intraventricular Hemorrhage in Very Low Birth Weight Neonates. *Journal of American Science*. 2012;8(5).
11. Nourripoor S, Tabasizadeh H, Afjehi A, Ghorbani R, Seifhashemi M, Masoudian N. Could mean platelet volume predict developing of bronchopulmonary dysplasia in preterm infants with respiratory distress syndrome?. *Iranian Journal of Neonatology IJN*. 2013 Oct 1;4(3):35-41.
12. Ballard JL, Khoury JC, Wedig KL, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. *The Journal of pediatrics*. 1991 Sep 30;119(3):417-23.
13. Kaushansky K. The molecular mechanisms that control thrombopoiesis. *The Journal of clinical investigation*. 2005 Dec 1;115(12):3339-47.
14. Wasiluk A, Mantur M, Kemonia H, Szczepański M, Jasińska E, Milewski R. Thrombopoiesis in small for gestational age newborns. *Platelets*. 2009 Jan 1;20(7):520-4.
15. Sola-Visner MC, Christensen RD, Hutson AD, Rimsza LM. Megakaryocyte size and concentration in the bone marrow of thrombocytopenic and nonthrombocytopenic neonates. *Pediatric research*. 2007 Apr 1;61(4):479-84.
16. Kush ML, Gortner L, Harman CR, Baschat AA. Sustained hematological consequences in the first week of neonatal life secondary to placental dysfunction. *Early human development*. 2006 Jan 31;82(1):67-72.
17. KA P. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. *Hippokratia*. 2010;1(1):2-32.
18. Patrick CH, Lazarchick J, Stubbs T, Pittard WB. Mean platelet volume and platelet distribution width in the neonate. *Journal of Pediatric Hematology/Oncology*. 1987 Jul 1;9(2):130-2.
19. Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. *Platelets*. 2002 Jan 1;13(5-6):301-6.
20. Patrick CH, Lazarchick J. The effect of bacteremia on automated platelet measurements in neonates. *American journal of clinical pathology*. 1990 Mar 1;93(3):391-4.