Platelet Indices in Neonates: A Comparative Study of Normal and Low Birth Weight Babies

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ABSTRACT

Introduction: Birth weight is an important indicator of perinatal and neonatal outcome. Low birth weight (LBW) babies suffer from many problems in neonatal period and have more morbidity and mortality as compared to normal weight babies. Platelets play an important role in neonatal immunity. Platelet indices of LBW babies are not well understood and may have contributed to morbidities in these babies. This study was conducted to study the platelet indices in LBW babies.

Methods: All inborn LBW babies born in our centre and fulfilling the inclusion criteria were enrolled in the study. Study period was of one and half years (Oct 2015 – Apr 2017). Cord blood sample (2 ml) was collected and platelet indices namely Platelet Count (PC), Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), were assessed. Blood sample was processed with a hospital laboratory based automated analyser. Neonatal morbidities were recorded. Platelet indices were analysed with respect to low birth weight.

Results: The platelet count in LBW babies was lower than the control group. Other indices i.e. PDW and MPV however did not show significant variation between both the groups.

Conclusions: LBW babies had lower platelet counts but other platelet indices were not significantly affected. The results need to be substantiated with further larger studies in the future.

Key words: Low birth weight; newborn; platelet indices

INTRODUCTION

As per World Health Organisation (WHO), low birth weight (LBW) is defined as weight of less than 2500 grams at birth.[1] These include both preterm and term (small for gestational age) babies. Incidence of LBW babies is as high as 28% of all babies born in India (six to eight million) per year.[2]

Weight at birth is an important indicator of any unfavourable perinatal and neonatal outcome. Low birth weight babies suffer from many problems such as birth asphyxia, hypoglycemia, hypothermia, respiratory distress and develop infections very rapidly as compared to normal weight babies.[3] It is observed that LBW is responsible not only for about 50% of perinatal deaths and about 30% of infant deaths but also for early development of adulthood morbidities.[4]

Platelets have important role to play in achieving haemostasis, maintaining blood vessel integrity and for phagocytosis. In newborns, haemostasis is an ongoing process which goes on throughout the foetal period into early childhood.[5] Those neonates who suffer from impaired immunity also have impaired haemostasis.[5] It has been documented in literature that in addition to platelet count (PC), other platelet indices are also useful in predicting the onset of various neonatal morbidities at an earlier stage. Platelet distribution width (PDW) represents the degree of heterogeneity of platelets. The changes in PDW are the results from recruitment of multiple ploidy classes of megakaryocytes during rapid platelet production. An increased proportion of higher ploidy classes increases megakaryocyte heterogeneity. Mean platelet volume (MPV) is also a machine calculated value on routine coulter reports. Increased production of platelets causes increased MPV.[6] It has been documented that thrombocytes also have a vital role to play as a participant in immune responses or as a part of developmental process of thrombosis.[7,8]

Multiple disease process can cause neonatal thrombocytopenia and this can be early onset thrombocytopenia (less than 72 hours) or late onset thrombocytopenia (more than 72 hours).[9] About 17% to 30% of newborns who are in NICU are seen to suffer from thrombocytopenia[10] and although the risk is more in LBW babies, it is greater in the most preterm infants i.e. in those with lesser gestational age.[10,11] This study was an attempt to observe the effect of LBW with regard to clinical profile as well as haematological profile of platelet indices. This study was aimed to compare clinical profile of normal and LBW babies and to compare platelet indices of normal and low birth weight babies.

METHODS

This study was an observational comparative study conducted over a period of one and a half year (October 2015 to April 2017). It was conducted in neonatal division of a tertiary care hospital in North India. Prior ethical approval was taken from institute ethics committee before the start of study. Small for gestational age was defined as weight less than 10th percentile according to gestational age.[2] Period of gestation was calculated from the first day of last menstrual period. All inborn LBW babies except those fulfilling exclusion criteria were enrolled in the study. Babies excluded from study were those having birth asphyxia, born to mothers on non steroid anti inflammatory drugs, specific drugs of antiplatelet action or babies born with major congenital malformations, mothers having TORCH group of infections, infants of HIV positive mothers, mothers having thrombocytopenia of any cause in the last 15 days prior to delivery, mothers having conditions like idiopathic thrombocytopenic purpura, mothers having chorioamnionitis and newborns whose parents did not give consent. Based on an earlier study,[6] assuming 90% power (with level of significance to be 5%), sample size calculated was 35 in each group (i.e. normal birth weight and low birth weight). Considering possible loss of some of the sample size due to various reasons, the number of babies for the study was kept to 45 in each group. Thus a minimum of 90 babies were recruited for this study. An electronic weighing machine, Phoenix Medical Systems (P) Ltd, BWS101, May, 2015, Tamil Nadu, India was used to measure the weight of the newborn. The base of the machine was hard, baby was fully unclothed (diaper also) and the weight was taken preferably before feeds, under all aseptic conditions. Blood was collected after the cutting of the umbilical cord. The primary volume of 0.5 ml was disposed off to keep away from platelet activation. The next part of blood was collected in haematological tubes with

anticoagulant potassium edetate (K$_2$EDTA). PC, MPV and PDW were assessed. Blood sample was analysed with a hospital laboratory based automated haematology analyser- SYSMEX-XP100 (XP series), Japan. Information regarding maternal profile was retrieved from maternal records and entered in the neonatal case sheet. All the neonatal morbidities were noted from the neonatal case records and the data were entered into Microsoft excel worksheet. In this study, data of clinical profile and platelet indices of cord blood of LBW babies were compared with those of normal weight babies. Follow up of these babies was not the part of this study.

Data was presented in frequency, percentage, mean, standard deviation etc. Normality of data was checked and statistical tests were applied accordingly. Student's t test and ANOVA tests were applied for continuous variables having normalised data, whereas Mann Whitney U and Kruskal-Wallis tests for the non-normalised data. Categorical data and proportions were analysed by Chi-square, Fisher exact and Yates correction tests as and wherever applicable. Statistical analysis was performed using SPSS 20.0 statistical program (Chicago, IL, USA). Values of p < 0.05 were considered significant. Descriptive statistics were given as mean and standard deviation (SD) or median: categorical variables were given as values and percentages.

RESULTS

A total of 45 babies with birth weight of < 2500 grams were taken as cases and they were compared with 45 controls (> 2500 grams birth weight). In this study of 90 newborns, gestational age of newborns ranged from 28 weeks to 43 weeks of gestational age, (overall mean ± 2 SD 36.08 weeks ± 3.21 weeks). The mean gestational age of cases was 33.6 weeks (range 28-38 weeks) and that of controls was 37.8 weeks (range 34 to 43 weeks). Birth weight ranged from 906 grams to 4500 grams, (mean ± 2 SD = 2344 ± 749 grams). The mean birth weight of cases was 1.75 kg (range 0.906 – 2.434 kg) while that of controls was 2.94 kg (range 2.52 to 4.5 kg). Sixty one out of 90 newborns were born to primigravida mothers. (Table 1)

Table 1. Demographic profile of study patients

S. No	Profile	Descriptive statistics
1	**Gestation age (weeks)**	
	Range	28 – 43
	Mean ± SD	36.08 ± 3.219
2	**Gender**	
	Male : Female	50 : 40
3	**Birth Weight (Kg)**	
	Range	0.906 – 4.500
	Mean ± SD	2.344 ± 0.749
4	**Parity**	
	Primi : Multi	61 : 29

In our study population, various morbidities of newborns were compared between normal and low birth weight babies. Among cases, 25 (55.6%) had hyperbilirubinemia requiring phototherapy, whereas in control group 19 (42.2 %) had hyperbilirubinemia. Seven (15.6%) newborns among cases had hypoglycemia whereas four (8.9%) newborns had the same morbidity amongst controls. Hypocalcemia was observed among the 13 cases (28.9%) whereas in control group five (11.1%) newborns. Hypothermia was noted in four (8.9%) newborns among cases and three (6.7%) amongst the control group. Among the cases 10 babies had apnea (22.2%), whereas in control group one (2.2%) had apnea. Respiratory distress syndrome was noted in five newborns in this study all of them being low birth weight babies. Pneumonia was diagnosed in 26 newborns, out of which 15 (33.3 %) were among the cases and 11 (24.4%) were among the control groups. Ten newborns in our study developed intraventricular haemorrhage (IVH); all the 10 newborns having IVH were from the case group accounting for 22.2%. In this study, seven out of 90 newborns developed NEC during their stay in NICU; all the newborns who developed this clinical morbidity were from the case group (15.6%) whereas none were noted in the control group. Overall, 20 newborns had meningitis. Among cases 13 (28.9%) newborns had meningitis, in control group seven

Table 2. Profile of neonatal morbidities in study patients

Complications	N	Case	(n-45)	Control	(n-45)	X²	p-value
		F	%	F	%		
Hyperbillirubinemia requiring phototherapy	44	25	55.6	19	42.2	1.601	0.292
Hypoglycaemia	11	7	15.6	4	8.9	0.932	0.522
Hypocalcemia	18	13	28.9	5	11.1	4.444	0.063
Hypothermia	7	4	8.9	3	6.7	0.155	1.000
Apnea	11	10	22.2	1	2.2	8.399	0.007
RDS/HMD	5	5	11.1	0	0.0	3.388	0.066
Pneumonia	26	15	33.3	11	24.4	0.865	0.486
IV hemorrhage	10	10	22.2	0	0.0	11.250	0.001
NEC	7	7	15.6	0	0.0	5.577	0.018
Meningitis	20	13	28.9	7	15.6	2.314	0.204
Sepsis	49	33	73.3%	16	35.6	12.947	0.001

(15.6%) had meningitis. There was no significant difference between the cases and controls in relation to meningitis. Out of 90 babies, sepsis was seen in 49 babies. Thirty three (73.3%) septic babies belonged to low birth weight group, in the control group 16 (35.6%) had sepsis. Overall, among the various neonatal morbidities studied, there were significant differences found in apnea, IVH, NEC, and sepsis among the cases and controls. (Table 2)

In this study, platelet indices were compared between cases and controls. There was no significant difference of various platelet indices (PC, MPV, PDW) between cases and controls (table 3). In our study, 90 newborns were categorised under birth weight < 1000 grams, 1000 - 1499 grams, 1500 - 2499 grams and ≥ 2500 grams. There was a decreasing trend of platelet count was observed with decreasing birth weight, but this was

Table 3. Assessment of platelet indices in both groups

Parameter	Case (n-45)		Control (n-45)		p-value @
	Median	Mean ± SD	Median	Mean ± SD	
Platelet count (lakh/cu mm)	1.80	1.74 ± 0.80413.1	1.90	1.95 ± 0.822274	0.184
PDW (%)	11.5	11.7 ± 2.9	11.1	11.2 ± 2.5	0.383
MPV (fl)	10.0	9.8 ± 1.5	9.8	9.6 ± 2.4	0.617

@ - Mann Whitney

Table 4. Mean distribution of platelet count according to birth weight of neonates

Birth weight	N	Platelet Count Mean ± sd	PDW Mean ± sd	MPV (fl) Mean ± sd
< 1000 grams	3	1.08 ±0.13	10.6 % ±1.8	9.7 ±1.6
1000 – 1499 grams	14	1.58±0.52	12.0 % ±3.3	10.1 ±1.5
1500 – 2499 grams	28	1.90±0.83	11.6 % ±2.9	9.7 ±1.5
≥ 2500 grams	45	1.95±0.82	11.2 % ±2.5	9.6 ±2.4
P value*	0.296	0.701	0.882	

*Kruskal-Wallis Test

not significant statistically (table 4) although there was no significant difference of PDW and MPV between the various birth weight categories.

DISCUSSION

In this study, LBW babies were largely preterm and term small for date babies. In the normal weight group, almost all of them, were > 34 weeks gestational age. Neonates suffered from various morbidities. Morbidities like neonatal jaundice, hypoglycemia, hypocalcaemia, hypothermia were not different statistically in low birth weight babies. It seems in contrast to old literature where LBW has been a risk factor for all these issues. These findings possibly relate to be the result of improved neonatal care in a tertiary care hospital. Morbidities like respiratory distress syndrome (RDS), apnea of prematurity, pneumonia, meningitis and sepsis were more in LBW group, in agreement with earlier studies. There was significantly prolonged stay in NICU and duration of antibiotics use in LBW babies as also the problems of intraventricular-haemorrhage and necrotising enterocolitis, similar to available literature.[12-17]

Platelet indices were analysed in relation to birth weight. In our study (based on birth weight difference), the PC in LBW babies was lower than the control group similar to another Indian study.[18] Other indices i.e. PDW and MPV however did not show significant variation between both the groups. In another study from India, authors have shown a significant difference of PDW in both the groups.[19] Belet et al. also concluded that PC and MPV don't differ significantly in term and preterm babies.[20] A study in India showed that MPV of preterm were higher and PDW was also significantly increased in preterm compared to term neonates.[21] Similarly in a study by Wasiluk et al., the platelet count was lower in pre-terms, PDW and MPV were significantly higher.[22] Thus, there is no general agreement in these studies regarding platelet indices in the neonatal period. Moreover, these other studies, were based on gestational age difference (and not on birth weight difference).

The platelet indices were correlated with various sub-categories of birth weight (ELBW, VLBW, LBW and normal). This study though showed a trend of decrease in PC with decreasing birth weight, which was not found significant on

statistical terms. It is to be considered that although our LBW babies groups, especially preterm babies, had lower platelet counts but did not cause any significant clinical problem of bleeding. All these parameters do reflect the immaturity of thrombopoiesis in newborn preterm infants. The western studies have more babies in extreme preterm and ELBW category. Also, the results may be influenced due to difference in the overall size of study groups.

In our study none of the indices showed any significant difference in normal and LBW babies among the septic neonates. Ahmad MS, and E Guclu et al. had findings of thrombocytopenia in LBW babies, and reported PDW as a uniquely significant parameter suggestive in severe sepsis.[23,24] As the number of patients with sepsis were small in our study, appropriate statistical interpretations would be difficult to comment upon.

CONCLUSIONS

This study was an attempt to observe the effect of LBW with regard to clinical profile as well as haematological profile of platelet indices. In this study we did find similarities with earlier literature with respect to the acute clinical implication of LBW. We did not find any significant impact of birth weight, gestational age and birth weight for gestation on various platelet indices, which is important as India faces a huge problem of LBW and small weight for gestational age. This study had very few babies less than 1000 grams birth weight. So the effect of extreme preemies may not be reflected in our study results. Number of babies with morbidities like RDS and IVH were lesser. The age at which platelet count became 'normal' in babies with low PC at birth, was not studied. The study is a relatively smaller study conducted in a single centre. More such multi-centric extensive studies with larger number of babies are thus recommended.

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