Original Article

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Quick Response Code:

Website: https://journals.lww.com/ijhm

DOI: 10.4103/ijh.ijh_17_24

Thrombocytopenia-related outcome and pattern in preterm neonates hospitalized in neonatology unit: A single-center experience

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Abstract:

BACKGROUNDS: In preterm newborns, thrombocytopenia is one of the most often observed hematologic findings. Most cases of thrombocytopenia are mild to moderate, self-limiting, and have a short duration; nevertheless, in rare cases, it can result in serious complications including pulmonary hemorrhage that lead to death and morbidity.

OBJECTIVES: The objective of this study was to identify the pattern, risk factors, and outcome of thrombocytopenia in preterm neonates hospitalized in a tertiary-level neonatal intensive care unit (NICU).

PATIENTS AND METHODS: All sick preterm neonates who developed thrombocytopenia within the first 28 days of life admitted to the NICU were included. A platelet count was performed at presentation time and as needed after that. Thrombocytopenia-related morbidities (intraventricular hemorrhage, pulmonary hemorrhage, and sepsis), mortality, and risk factors were analyzed concerning severity (mild, moderate, and severe) and age of thrombocytopenia onset (early and late) in preterm neonates.

RESULTS: A total of 100 preterm neonates were admitted to our NICU. Of these, 48% of neonates developed thrombocytopenia. In terms of severity, mild, moderate, and severe thrombocytopenia were present in 62.5%, 37.5%, and 16.7% of newborns, respectively. The prevalent risk factors for late-onset thrombocytopenia (LOT) were necrotizing enterocolitis (NEC) and late-onset sepsis; for early-onset thrombocytopenia, the risk factors were pregnancy-induced hypertension and early-onset sepsis. Neonates with sepsis, severe birth asphyxia, and NEC were significantly associated with severe thrombocytopenia ($P < 0.001$). Thrombocytopenia-related morbidities and mortality were significantly higher among moderate-to-severe thrombocytopenia cases ($P < 0.001$).

CONCLUSIONS: Sepsis was the most common risk factor associated with severe and LOT. Compared to mild/moderate thrombocytopenia, severe thrombocytopenia required more platelet transfusions, was associated with major bleeding manifestations, and had a higher mortality rate. When caring for premature newborns, these issues need to be taken into account.

Keywords:

Low platelets count, mortality, newborn, sepsis, severity

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Submission: 25-02-2024
Revised: 10-04-2024
Accepted: 11-04-2024
Published: 17-05-2024

Introduction

Thrombocytopenia, defined as a platelet count <150,000/μL, is frequently seen hematologic finding in preterm neonates.[1] Thrombocytopenia caused by different conditions in neonates may appear before 72 h of life (early-onset thrombocytopenia [EOT]) and after 72 h (late-onset thrombocytopenia [LOT]).[2] The occurrence of thrombocytopenia among the neonates ranges from 1% to 5%.[3]

How to cite this article: Jain S, Gaur BK, Sharma M, Singh RR. Thrombocytopenia-related outcome and pattern in preterm neonates hospitalized in neonatology unit: A single-center experience. Iraqi J Hematol 2024;13:110-7.

However, thrombocytopenia is present in 22%–35% of neonates admitted to the neonatal intensive care unit (NICU), and it can reach 50% in preterm neonates.[4] Early-onset neonatal thrombocytopenia is commonly associated with maternal disorders, such as pregnancy-induced hypertension (PIH), intrauterine growth restriction (IUGR), gestational diabetes mellitus (GDM), maternal immune thrombocytopenic purpura (ITP), and congenital infection. LOT is usually secondary to severe perinatal asphyxia, fungal sepsis, and necrotizing enterocolitis (NEC).[5] The underlying pathogenesis for thrombocytopenia is increased destruction, sequestration, or decreased production of platelets.[6] If the platelet count is below 50,000/μL, it is classified as severe; if it is between 50,000 and 99,999/μL, it is called moderate; and if it is between 100,000 and 149,999/μL, it is considered mild thrombocytopenia.[7] Thrombocytopenia is generally mild to moderate in severity and resolves without any intervention. Life-threatening bleeding, intraventricular hemorrhage (IVH), or pulmonary hemorrhage may occur in severe thrombocytopenia.[8] Only a small number of studies[9-11] have attempted to determine whether there is a correlation between the risk factors for thrombocytopenia and the onset/degree of thrombocytopenia in preterm neonates. Moreover, a clear correlation between the degree of thrombocytopenia and outcome has not been demonstrated in preterm neonates. It is important to check platelet counts, severity, outcome, and pattern of onset of thrombocytopenia as well as the associated risk factors in the preterm newborns admitted because thrombocytopenia can have serious consequences and is very common among preterm neonates admitted to NICU. Therefore, the purpose of this study was to estimate the occurrence of thrombocytopenia in preterm newborns as well as to identify its pattern, risk factors, and outcomes.

Patients and Methods

Study site
This study was conducted in the NICU at a tertiary care hospital, in North India.

Study design
The design of the study was a descriptive, hospital-based study.

Study period
This study was conducted for 1 year from March 2019 to April 2020.

Ethical consideration
This study was approved by the Clinical Research Committee and the Ethical Committee of our institute. Written informed consent from the parents or legally acceptable caregiver was obtained before enrollment in the study.

Study population
The study population was sick preterm neonates.

Sampling technique
A convenience sampling technique was used.

Sample size
The study population has been calculated with the formula given below:

$$n = Z^2\,\alpha/2\,P\,(100 - P)\,E^2$$

where, $Z^2\,\alpha/2$: Standard normal variate, P: Prevalence rate, E: Error In my Study: $Z^2\,\alpha/2 = 1.96$ at 5% type 1 error $P = 58.7\%$[12] $E = 10\%$ $n = (1.96)^2 \times 58.7\,(100 - 58.7) = 9313.23 = 93.13\,(10)^2\,100 \approx 93$ (minimum sample size). However, given the nature of the study, the sample size was taken to be 100 cases.

Inclusion criteria
All the sick preterm (gestational age <37 weeks)[13] neonates delivered intramurally or extramurally, who had thrombocytopenia or who developed thrombocytopenia within the first 28 days of life while being hospitalized in a NICU, were included in this study.

Exclusion criteria
Maternal history of autoimmune diseases such as ITP and systemic lupus erythematosus and neonates with identifiable syndromes such as Turner syndrome, Noonan syndrome, and Kasabach–Merritt syndrome were excluded.

Methodology
All preterm neonates were divided into three groups based on gestational age: extremely preterm (<28 weeks), very preterm (28–32 weeks), and moderate to late preterm (32–36 weeks).[14] Age, gender, birth weight, gestational age, mode of delivery, history of resuscitation, APGAR score, oxygen saturation, and length of stay were all thoroughly recorded, along with the mother's obstetric history (including any history of hypertension, GDM, premature rupture of membranes, drug use, anemia, and bleeding). Each neonate was given a complete general physical examination by the pro forma, with a focus on any bleeding signs such as ecchymosis, purpuric rashes, petechial rashes, mucosal bleeding, and pulmonary hemorrhage. The neonates' gestational ages were determined using the New Ballard Score.[15] The INTERGROWTH-21st fetal growth standards were used for growth assessment at delivery or admission to identify small for gestational age (SGA).[16] Neonates underwent the following tests:

peripheral smear, complete blood counts (hemoglobin, platelet counts, and total leukocyte counts [TLCs]), sepsis screen parameters (C-reactive protein, TLC, absolute neutrophil count, and immature-to-total neutrophil ratio), prothrombin time, X-ray chest, blood culture and sensitivity, blood sugar, serum electrolytes, arterial blood gas analysis, cranial ultrasonography, liver function testing, and renal function test. For bacterial growth and blood culture, the BACTEC system was employed. All preterm neonates were treated by the standard NICU protocol. Sysmex XN-350 analyzer was used to analyze venous samples for platelet counts, and low platelet counts were further assessed by peripheral blood smear. Platelet counts were used to categorize thrombocytopenia into three different levels: mild (platelet counts between 100 and 149 × 10^9/L), moderate (platelet counts between 50 and 99 × 10^9/L), and severe (platelet counts <50 × 10^9/L). Neonatal thrombocytopenia was further divided into two categories: early-onset (onset within 72 h of life) and late-onset (onset after 72 h of life).[17] Numerous causes, maternal and neonatal risk factors, were evaluated in neonates with thrombocytopenia. The following outcomes related to thrombocytopenia were reported in the pro forma: length of NICU stay, requirement for platelet transfusion, requirement for ventilator support, gastrointestinal (GI) bleeding, mortality, pulmonary, and IVH.

Statistical analysis

Microsoft Excel spreadsheet 2019 and SPSS (Statistical Package for the Social Sciences) software version 25.0 (IBM Corp., Armonk, NY, USA) were used for the statistical analysis. There were categorical variables in the form of percentages and frequencies. The mean and standard deviation were used for analyzing the continuous variables. The Chi-square tests and Fisher's exact tests were used to analyze the categorical variables. $P < 0.05$ was considered statistically significant.

Results

During the study, a total of 100 preterm neonates were admitted to our NICU. Of these, 48 (48%) neonates developed thrombocytopenia. Thirty-five (72.9%) preterm neonates were inborn and 13 (27.1%) were out born. Thirty (62.5%) neonates were male, and 18 (37.5%) were female. Twenty-two (45.8%) newborns were presented in the very early neonatal period (<24 h of life), 24 (50%) in early neonatal periods (1–7 days), and 2 (4.2%) in the late neonatal period (8–28 days). Cesarean delivery was done in 29 (60.4%) neonates and normal delivery in 19 (39.6%) newborns. Based on gestational age, there were 27 (56.2%) late preterm neonates, 19 (39.60%) very preterm neonates, and 2 (4.20%) extremely preterm. Of these, 2 (4.2%) neonates had a birth weight <1000 g (extremely low birth weight), 15 (31.3%) had a birth weight between 1000 and 1499 g (very low birth weight), 28 (58.4%) had a birth weight between 1500 and 2499 g (low birth weight [LBW]), and rest 3 (6.3%) had a birth weight more than 2500 g (normal birth weight). The onset of thrombocytopenia was <72 h (early onset) among 19 (39.6%) neonates and more than 72 h among 29 (60.4%) neonates. Severity wise, 22 (45.8%) neonates had mild thrombocytopenia, 18 (37.5%) had moderate thrombocytopenia, and 8 (16.7%) had severe thrombocytopenia, respectively [Figure 1]. With regard to the clinical manifestations of thrombocytopenia in preterm neonates, 31 (64.5%) neonates had no GI bleeding, 9 (18.7%) had minor bleeding manifestations, and 8 (16.7%) had major bleeding manifestations [Table 1]. The mean value of platelet counts in mild, moderate, and severe thrombocytopenia was 126 ± 12 × 10^9/L, 83 ± 16 × 10^9/L, and 37 ± 09 × 10^9/L, respectively.

Table 1: Demographic characteristics of preterm neonates with thrombocytopenia (*n*=48)

Demographic characteristics	Frequency, *n* (%)
Age of newborns	
Very early neonatal period (<24 h)	22 (45.8)
Early neonatal period (1–7 days)	24 (50)
Late neonatal period (8–28 days)	2 (4.2)
Gender	
Male	30 (62.5)
Female	18 (37.5)
Type of cases	
Inborn	35 (72.9)
Out born	13 (27.1)
Mode of delivery	
NVD	19 (41)
LSCS	29 (60.4)
Gestational age	
32–36 weeks (late preterm)	27 (56.2)
28–32 weeks (very preterm)	19 (39.6)
<28 weeks (extremely preterm)	2 (4.2)
Birth weight (g)	
<1000 (ELBW)	2 (4.2)
1000–1499 (VLBW)	15 (31.3)
1500–2499 (LBW)	28 (58.4)
>2500 (NBW)	3 (6.1)
Onset of thrombocytopenia	
Within 72 h of birth	19 (39.6)
After 72 h of birth	29 (69.4)
Degree of thrombocytopenia	
Mild	22 (45.8)
Moderate	18 (37.5)
Severe	8 (16.7)
Clinical manifestations of thrombocytopenia	
No bleeding manifestations	31 (64.5)
Minor bleeding manifestations	9 (18.7)
Major GI bleeding and IVH	8 (16.7)

LBW=Low birth weight, NBW=Normal birth weight, GI=Gastrointestinal, IVH=Intraventricular hemorrhage, NVD=Normal vaginal delivery, LSCS=Lower-segment cesarean section, ELBW=Extremely LBW, VLBW=Very LBW

The neonatal risk factors for thrombocytopenia in preterm neonates included early-onset sepsis (EOS) (14.6%), late-onset sepsis (LOS) (29.1%), severe birth asphyxia (11.9%), NEC (11%), respiratory distress syndrome (8.6%), and SGA (6%). However, EOS ($P < 0.001$), LOS ($P < 0.001$), NEC ($P = 0.039$), LBW ($P < 0.001$), severe birth asphyxia ($P = 0.013$), and respiratory distress syndrome (RDS) ($P < 0.001$) were significantly associated with moderate-to-severe thrombocytopenia [Table 2].

Maternal risk factors for thrombocytopenia in preterm newborns were prolonged rupture of membranes (PROM) (27.1%), PIH (16.7%), anemia (8.3%), oligohydramnios (4.2%), and drug use (2.1%). However, the following maternal risk factors are significantly

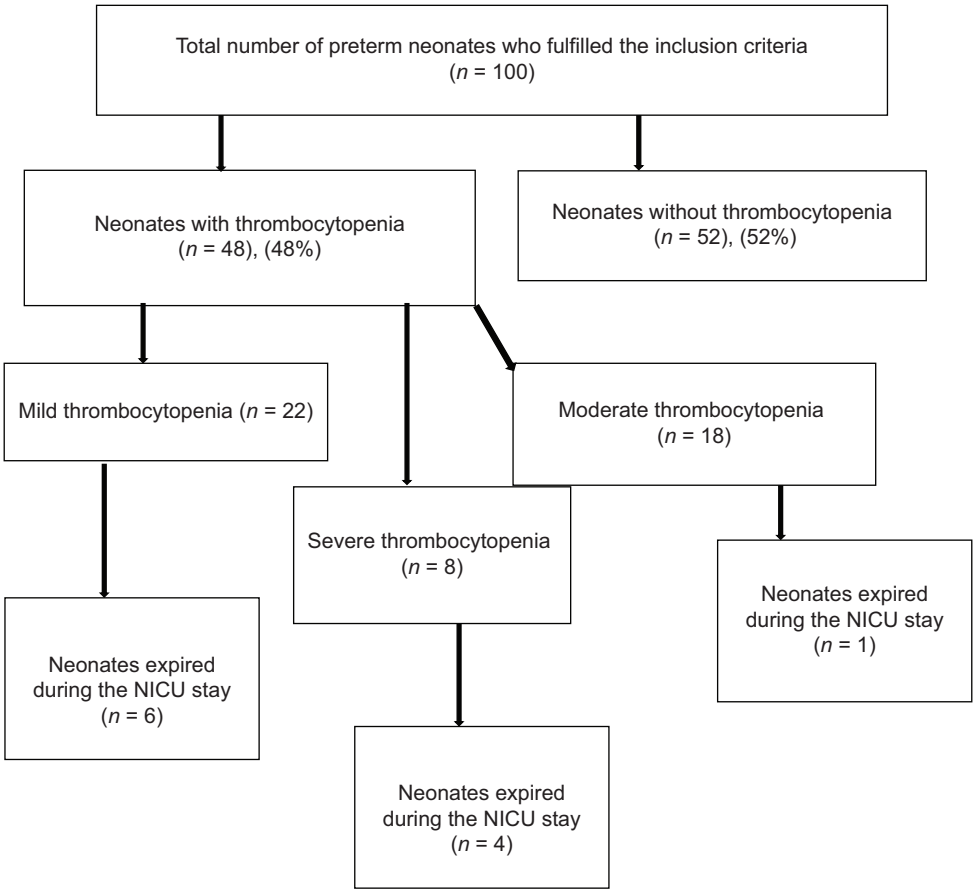

Figure 1: Flow diagram of the distribution of preterm neonates enrolled in the study. NICU: Neonatal intensive care unit

Table 2: Correlation between maternal risk factors and severity of thrombocytopenia

Maternal risk factors	Severity of thrombocytopenia			χ^2	*P*
	Mild (100,000–149,999/µL), *n* (%)	Moderate (50,000–99,999/µL), *n* (%)	Severe (<50,000/µL), *n* (%)		
Oligohydramnios	1 (4.5)	0	1 (12.5)	6.656	0.084
PIH	5 (22.7)	3 (16.7)	1 (12.5)	4.682	0.197
Anemia (hemoglobin <13 g)	2 (9.1)	1 (5.6)	1 (12.5)	11.376	0.010
Maternal drug intake	5 (22.7)	0	0	6.857	0.047
PROM	6 (27.3)	4 (22.2)	3 (37.5)	2.047	0.563
GDM	0	1 (5.6)	0	7.396	0.286
Place of delivery					
Home	3 (13.6)	2 (11.1)	0	14.291	0.112
Hospital	19 (86.4)	16 (88.9)	8 (93.1)		
Mode of delivery					
LSCS	12 (54.5)	12 (66.7)	6 (75.0)	6.951	0.043
NVD	10 (45.5)	6 (33.3)	2 (25.0)		

PROM=Prolonged rupture of membranes, GDM=Gestational diabetes mellitus, NVD=Normal vaginal delivery, LSCS=Lower-segment cesarean section, PIH=Pregnancy-induced hypertension

associated with the severity of thrombocytopenia in preterm newborns: anemia (P = 0.010), drug use (P = 0.047), PROM (P = 0.034), and delivery mode (P = 0.43) [Table 3].

Similarly, there were statistically significant differences between the severity of thrombocytopenia (mild vs. moderate vs. severe) and neonatal risk factors such as EOS (P < 0.001), LOS (P = 0.001), RDS (P < 0.001), LBW (P = 0.001), MAS (P = 0.090), severe birth asphyxia (P = 0.013), and NEC (P = 0.039) [Table 4]. However, there were statistically significant differences in the onset of thrombocytopenia and neonatal risk factors, such as EOS (P = 0.005), LOS (P = 0.001), SGA (P = 0.044), and severe birth asphyxia (P = 0.034) [Table 5].

Table 6 illustrates the thrombocytopenia-related morbidities and mortality and its correlation with the severity of thrombocytopenia in preterm neonates: the IVH (n = 11/13), pulmonary hemorrhage (n = 6/7), requirement for mechanical ventilator support (n = 24/17), and platelets transfusion (n = 21/25) were significantly more common in cases of moderate-to-severe thrombocytopenia

Table 3: Correlation between maternal risk factors and age of thrombocytopenia onset

Maternal risk factors	Age of thrombocytopenia onset		Total, *n* (%)	χ^2	*P*
	Early onset, *n* (%)	Late onset, *n* (%)			
Oligohydramnios	1 (5.6)	1 (3.6)	2 (4.3)	0.104	0.747
PIH	5 (27.8)	4 (14.3)	9 (19.6)	1.267	0.260
Anemia	0	4 (14.3)	4 (8.7)	2.816	0.093
Maternal drug intake	3 (16.7)	2 (7.1)	5 (10.9)	1.026	0.311
PROM	6 (33.3)	6 (21.4)	12 (26.1)	0.805	0.370
GDM	17 (94.4)	28 (100.0)	45 (97.8)	1.590	0.207
Place of delivery					
Home	0	4 (14.3)	4 (8.7)	4.221	0.121
Hospital	18 (100.0)	24 (85.7)	41 (89.1)		
Mode of delivery					
LSCS	14 (77.8)	15 (53.6)	29 (63.0)	2.755	0.097
NVD	4 (22.2)	13 (46.4)	17 (37.0)		

PROM=Prolonged rupture of membranes, GDM=Gestational diabetes mellitus, NVD=Normal vaginal delivery, LSCS=Lower-segment cesarean section, PIH=Pregnancy-induced hypertension

Table 4: Correlation between neonatal risk factors and severity of thrombocytopenia (*n*=48)

Neonatal risk factors	Severity of thrombocytopenia			χ^2	*P*
	Mild, *n* (%)	Moderate, *n* (%)	Severe, *n* (%)		
LBW neonate	5 (22.7)	0	0	17.024	0.001
RDS	1 (4.5)	6 (33.3)	2 (25.0)	20.487	<0.001
MAS	3 (13.6)	1 (5.6)	1 (12.5)	6.484	0.090
Severe birth asphyxia	0	1 (5.6)	2 (22.2)	10.840	0.013*
EOS	5 (21.7)	1 (5.6)	1 (11.1)	21.582	<0.001
LOS	5 (21.7)	7 (38.9)	2 (22.2)	11.478	0.001
NEC	0	2 (11.1)	1 (11.1)	8.362	0.039*
SGA	1 (4.3)	1 (5.6)	0	3.012	0.390

*Birth asphyxia significantly associated with severity of thrombocytopenia. LBW=Low birth weight, RDS=Respiratory distress syndrome, MAS=Meconium aspiration syndrome, EOS=Early-onset sepsis, LOS=Late-onset sepsis, NEC=Necrotizing enterocolitis, SGA=Small for gestational age

Table 5: Correlation between neonatal risk factors and the onset of thrombocytopenia

Neonatal risk factors	Age of thrombocytopenia onset		Total	χ^2	*P*
	EOH, *n* (%)	LOT, *n* (%)			
LBW	5 (26.3)	0	5 (10.4)	2.548	0.110
RDS	3 (15.8)	6 (20.7)	9 (18.8)	0.181	0.671
MAS	1 (5.3)	4 (13.7)	4 (8.3)	0.895	0.344
Severe birth asphyxia	0	3 (10.4)	3 (6.3)	4.493	0.034
EOS	6 (31.6)	1 (3.4)	7 (14.6)	5.852	0.005
LOS	1 (5.3)	13 (44.8)	13 (27.1)	9.857	0.001
NEC	0	3 (10.3)	3 (6.3)	2.097	0.148
SGA	2 (10.5)	0	2 (4.2)	3.185	0.044

LBW=Low birth weight, RDS=Respiratory distress syndrome, MAS=Meconium aspiration syndrome, EOS=Early-onset sepsis, LOS=Late-onset sepsis, NEC=Necrotizing enterocolitis, SGA=Small for gestational age, EOH=Early-onset thrombocytopenia, LOT=Late-onset thrombocytopenia

Table 6: Thrombocytopenia-related morbidities and mortality and its correlation with the severity of thrombocytopenia in preterm neonates (*n*=48)

Outcome variables	Severity of thrombocytopenia			Total	χ^2	*P*
	Mild, *n* (%)	Moderate, *n* (%)	Severe, *n* (%)			
IVH	2 (8.7)	7 (38.9)	4 (44.4)	13	26.383	<0.001
Pulmonary hemorrhage	1 (4.3)	2 (11.1)	4 (44.4)	7	23.863	<0.001
GI bleed	8 (34.8)	17 (94.4)	8 (88.9)	33	64.212	<0.001
Platelet transfusion needed	4 (18.2)	13 (72.2)	8 (100.0)	25	8.362	0.039
Need of MV support	7 (31.8)	9 (50.0)	8 (100.0)	24	15.997	0.001
Inhospital mortality	1 (4.3)	6 (33.3)	4 (44.4)	11	26.673	<0.001
Duration of hospital stay	4.34±2.04	7.12±2.55	9.23±2.92			0.001

IVH=Intraventricular hemorrhage, GI=Gastrointestinal, MV=Mechanical ventilator

than in cases of mild thrombocytopenia ($P < 0.001$). Furthermore, mortality was high in cases with moderate-to-severe thrombocytopenia (11 cases out of a total of 10 cases died) compared to only one case with mild thrombocytopenia who died ($P < 0.001$) [Table 6].

Discussion

A common hematologic finding encountered in preterm neonates is thrombocytopenia, and it can contribute to high mortality. Only a few prospective studies have been done in India to date to ascertain the frequency, severity, pattern, outcome, and risk factors for thrombocytopenia, particularly in preterm newborns.

In this study, thrombocytopenia occurred in 48% of preterm neonates. It was in line with the results of studies by Goyal *et al*.[9] and Beiner *et al*.,[10] which reported that 33% and 31% of preterm neonates were thrombocytopenic, respectively. At least one episode of thrombocytopenia was observed in 94 (8.9%) newborns in a different study conducted by Bonifacio *et al*.[11] On the other hand, 58.2%, 66.7%, and 70.5% of preterm newborns, respectively, developed thrombocytopenia according to Sharma and Thapar,[18] Khetavath *et al*.,[19] and Gupta *et al*.[20] Christensen *et al*.[21] reported that thrombocytopenia was 85% common among neonates weighing ≤800 g.

The male-to-female ratio was 1.76:1 in this study, which is almost the same as Goyal *et al*.[9] who discovered that 59.5% of newborns were male and 49.5% were female (male:female ratio 1.62:1). Male neonates displayed greater thrombocytopenia than female neonates in studies by Sharma and Thapar[18] and Khetavath *et al*.,[19] where the male: female ratio was 2:1 and 4.5:1, respectively.

There were 39.6% of cases of EOT and 60.4% cases of LOT. Almost similar results were reported by Bonifacio *et al*.,[11] in which 31 (33%) had EOT and 63 (76%) had LOT. Our findings were indistinct in contrast to the findings of Goyal *et al*.,[9] Sharma and Thapar,[18] and Khetavath *et al*.,[19] which reported EOT as 62.5%, 51%, and 66.6% and LOT as 37.5%, 49%, and 33.4%, respectively. The pattern of thrombocytopenia can also aid in determining the alternative diagnosis.

In this study, the percentages of neonates with mild, moderate, and severe thrombocytopenia were 45.8%, 37.5%, and 16.7%, respectively. This was comparable to the study by Christensen *et al*.,[21] which revealed that 9% of neonates had severe thrombocytopenia, while 38% of those with moderate thrombocytopenia and 77% of those with mild thrombocytopenia. On the other hand, Sharma and Thapar[18] observed that mild, moderate, and severe thrombocytopenia, respectively, were present in 16.4%, 37.4%, and 47.2% of newborns. In contrast to our findings, Bonifacio *et al*.[11] reported mild, moderate, and severe thrombocytopenia in 12.8%, 36.2%, and 51% of preterm newborns, respectively. Another study by Khetavath *et al*.[19] reported that 41.6%, 33.3%, and 25% of preterm neonates developed mild, moderate, and severe thrombocytopenia, respectively. Goyal *et al*.[9] reported that 24 (42.8%) had mild thrombocytopenia, 20 (35.7%) had moderate thrombocytopenia, and 12 (21.4%) had severe thrombocytopenia. Chaurasiya and Chhabra[22] reported that the percentage of severe thrombocytopenia in preterm infants was about 1.5 times higher than in term infants (8.3% vs. 4.5%).

PIH was the most common maternal risk factor (16.7%), followed by PROM (27.1%), oligohydramnios (4.2%), anemia (8.3%), and GDM (2.1%). This was similar to the research done by Goyal *et al*.,[9] which showed that 8.9% had PIH and only 4.3% had a history of GDM. Christensen *et al*.[21] found that neonates born to women with PIH developed thrombocytopenia in 76/208 (36.5%) cases. In contrast, 46% of mothers in research of a similar nature by Bhat and Cherian[23] had PIH, and 32% had GDM. Severe thrombocytopenia has been linked with all these maternal risk factors. The correlation of severe thrombocytopenia with PROM and maternal anemia was statistically significant ($P < 0.05$). A correlation between PROM and neonatal thrombocytopenia has

been reported in a study performed by Sharma and Thapar[18] and Beiner *et al*.[10] In this study, the maternal risk factors did not show any significant difference between EOT and LOT ($P > 0.05$). This contrasted with the study of Khetavath *et al*.,[19] which showed that the most common maternal factors were hypertension and diabetes that caused EOT.

This study found that 10.4% of newborns had LBW, 18.8% had RDS, 10.4% had meconium aspiration syndrome, 6.3% had birth asphyxia, 14.6% had early-onset neonatal sepsis, 29.2% had late-onset neonatal sepsis, 6.3% had NEC, and 4.2% had SGA. The studies by Sharma and Thapar[18] and Goyal *et al*.[9] were complementary to our own because they revealed that sepsis affected 63.6% and 23.2% of newborns, respectively. On the other hand, according to data provided by Gupta *et al*.,[20] 19% of newborns in the SGA group and 24% of thrombocytopenic neonates had birth asphyxia. According to Sharma *et al*.,[18] 77.7% of newborns in the SGA category, 71.4% had perinatal asphyxia, and 63.6% of neonates had sepsis. Similar to our findings, studies by Gupta *et al*.[20] and Nandyal *et al*.[24] found an association between severe thrombocytopenia and birth hypoxia. This study demonstrated a significant association between thrombocytopenia and SGA neonates. Both Beiner *et al*.[10] and Bonifacio *et al*.[11] reported similar findings.

In this study, we found statistically significant correlations between the severity of thrombocytopenia and the length of hospital stay. This may be explained by the increased mortality rate in the severe thrombocytopenia group as the neonates died early in the course of illness. Similar results were reported by Ree IM *et al*.[25] who found the duration of stay to be positively related to the severity of thrombocytopenia.

Mortality, IVH, GI bleeding, platelet transfusion, ventilator support, and pulmonary hemorrhage were significantly higher among patients with severe thrombocytopenia ($P < 0.001$). Pulmonary hemorrhage, GI bleeding, and IVH were reported in 14.6%, 68.8%, and 27.1%, respectively, among neonates with thrombocytopenia. However, a clear correlation between neonatal thrombocytopenia and IVH was found in the study by Beiner *et al*.[10] and Mehta *et al*.[26] In this study, the mortality rate of neonatal thrombocytopenic neonates was 22.9%. This is higher than the study by Sharma and Thapar,[18] in which mortality was only 14.5%.

Conclusions

We concluded that preterm neonates have a high frequency of thrombocytopenia. The most common risk factors associated with thrombocytopenia were sepsis, PIH, NEC, and birth asphyxia. Most episodes are mild to moderate and without apparent complications, and resolve spontaneously. Major bleeding manifestations generally develop in severe thrombocytopenic neonates. Most importantly, in premature newborns, severe thrombocytopenia may be used as a prognostic indicator. Identification of risk factors and severity is crucial for a better approach to thrombocytopenia in premature neonates.

Strength and limitation

This study has appreciable strengths. This is one of the few prospective studies that focused on preterm neonates. A small negative was the study's single-canter design. We advise conducting larger multicentric trials to assess the pattern, risk factors, and thrombocytopenia-related outcome in low-birth-weight and preterm neonates.

Author's contribution details

The conception and design of the study by SJ and BKG. RSR and BKG were involved in data collection and analysis. MS was involved in statistical analysis of data. All authors assisted in the drafting and analysis of the results and final approval.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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