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Frequency of Thrombocytopenia in Newborn with Birth Asphyxia

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ABSTRACT

Background: Thrombocytopenia is a frequent hematologic perturbation in term neonates with birth asphyxia that may cause life-threatening hemorrhagic complications. Establishing risk factors among the mother and the neonate facilitates early diagnosis and treatment, particularly in settings that are short of resources where early intervention may be life-saving. **Objective:** To determine the frequency of thrombocytopenia in newborn with birth asphyxia. **Study Design:** Descriptive cross-sectional study. **Duration and Place of Study:** The study was conducted from August 2024 to January 2025 at the Department of Pediatric Medicine, Combined Military Hospital, Rawalakot. **Methodology:** A total of 93 neonates with birth asphyxia, aged 1–25 days and with gestational age between 37 and 41 weeks, were included using non-probability consecutive sampling. Thrombocytopenia was defined as a platelet count below 150×10^9/L. Clinical and demographic data were collected, including maternal conditions such as hypertension, diabetes, thrombocytopenia, mode of delivery, and antenatal care adequacy. Neonatal factors included gender, gestational age, birth weight, Apgar score, and clinical features of hypoxic-ischemic encephalopathy. **Results:** The mean age of neonates was 14.27 ± 7.47 days, with a mean gestational age of 39.01 ± 0.91 weeks and platelet count of 201.55 ± 107.77 $\times 10^9$/L. Thrombocytopenia was observed in 45.2% of cases. Significant associations were found with maternal hypertension ($p<0.001$), maternal thrombocytopenia ($p=0.021$), prolonged labor ($p=0.014$), and adequacy of antenatal care ($p=0.001$). **Conclusion:** Thrombocytopenia has a common association with birth asphyxia. Maternal hypertension, thrombocytopenia, and prolonged labor are strong risk factors.

INTRODUCTION

Thrombocytopenia is a frequent hematologic finding in babies presenting with birth asphyxia.[1] Birth asphyxia or gas exchange impairment leading to hypoxia and hypercapnia in the perinatal period stimulates a series of metabolic and cellular aberrations.[2] An outcome of the hypoxic insult is an suppression of the bone marrow with potential for decreased platelet generation.[3] A second effect is the systemic stress response and consequent systemic inflammation due to asphyxia, leading to an increase in platelet consumption and destruction with consequent exacerbation of thrombocytopenia.[4]

Neonates with birth asphyxia are predisposed to disseminated intravascular coagulation (DIC), a phenomenon where widespread coagulation cascade activation leads to the formation of microthrombi with consumption of platelets and clotting factors.[5] The consumptive coagulopathy also further augments the extent of thrombocytopenia in such neonates.[6] Apart from this, hypoxic endothelial injury may also activate coagulometric pathways by causing platelet aggregation and adhesion, further decreasing circulating platelet levels.[7] The mutual interaction between coagulopathic abnormalities and thrombocytopenia makes affected neonates highly vulnerable to hemorrhagic complications such as intracranial or gastrointestinal hemorrhage.[8]

Clinically, the severity of thrombocytopenia in newborns presenting with birth asphyxia is generally reflective of the severity of the hypoxic insult.[9] Moderate to severe perinatal asphyxia is more likely to result with severe thrombocytopenia requiring vigilant monitoring and potential intervention.[10] Serial complete blood counts and coagulation profiles are requisite to establish the trend in platelet counts as well as for the early detection of coagulopathy emerging.[11] Supportive management includes adequate oxygenation and perfusion with correction of metabolic abnormalities, as well as the employment of platelet transfusions in patients with severe thrombocytopenia or active hemorrhage.[12]

Earlier recognition and correct management of thrombocytopenia in neonates with birth asphyxia are crucial to prevent adverse outcomes.[13] Because such a hematologic finding may occur or worsen during the early days of life, watchful monitoring during this period is warranted.[14] Thrombocytopenia may also serve as a prognostic indicator for severity of disease as well as risk

for secondary sequelae such as hypoxic-ischemic encephalopathy.[15] Thus, a multidisciplinary management by neonatologists, hematologists, and intensive care unit personnel is essential for optimal management for such high-risk newborns.

Kadhum et al. (2017) documented a prevalence of thrombocytopenia in 40.74% of neonates diagnosed with birth asphyxia, highlighting a significant hematological complication associated with perinatal hypoxia.[16]

It was necessary to conduct this study in Azad Kashmir due to the non-availability of local data and the unsatisfactory accessibility of high-quality neonatal facilities. It was crucial to diagnose thrombocytopenia early in new-born with birth asphyxia so as to intervene in a timely fashion and obtain better clinical outcomes. The study contributed to the local burden ascertainment of the disease and furthered the development of regionally relevant management guidelines in an effort to improve neonatal survival.

METHODOLOGY

It was a descriptive cross-sectional study, carried out between August 2024 to January 2025 in the Department of Pediatric Medicine, Combined Military Hospital, Rawalakot. A total of 93 neonates were enrolled. The sample size was adjusted using the WHO sample size calculator. The assumption of the frequency of thrombocytopenia in neonates with birth asphyxia was 40.74,[16] with a confidence level of 95% and 10% margin of error. Non-probability consecutive sampling was used to select participants.

Newborns eligible for the study had a gestational age between 37 and 41 weeks, determined using the first day of the mother's last menstrual period. Birth asphyxia was identified in neonates with an Apgar score less than 7 at five minutes after birth or clinical findings consistent with moderate to severe hypoxic-ischemic encephalopathy (HIE). Moderate HIE was defined by lethargy, reduced muscle tone, weak Moro and suck reflexes, seizures, and a duration of symptoms lasting 2 to 14 days. Severe HIE presented as stupor or coma, absent reflexes, prolonged seizures, and signs of raised intracranial pressure persisting for several weeks. Neonates were excluded if their mothers had a history of antiepileptic drug use during pregnancy, as such medications are known to affect platelet levels, or if there was clinical suspicion of hematologic disorders such as leukemia, thrombotic thrombocytopenic purpura, or hypersplenism.

Once ethical approval was secured from the relevant institutional review board, written informed consent was obtained from parents or legal guardians. Each neonate underwent a detailed evaluation, and relevant clinical information was documented, including gender, gestational age, birth weight, and maternal factors such as platelet count, history of diabetes or hypertension during pregnancy, mode of delivery, and adequacy of antenatal care. Antenatal care was considered inadequate if the mother had fewer than four documented visits during pregnancy. Prolonged rupture of membranes was defined as leakage of amniotic fluid for more than 18 hours before delivery, and prolonged labor was noted when the total duration of labor exceeded 24 hours, as recorded in obstetric charts.

Blood samples were drawn from all enrolled neonates using standard aseptic techniques. Platelet counts were measured in a certified laboratory. A platelet concentration below 150×10^9 per liter was categorized as thrombocytopenia.

All data were entered and analyzed using SPSS version 25. The Shapiro-Wilk test was used to assess the normality of distribution for continuous variables. Mean and standard deviation or median with interquartile range were reported as appropriate for variables such as gestational age, birth weight, Apgar score, and platelet count. Categorical variables including gender, maternal medical conditions, mode of delivery, adequacy of antenatal visits, prolonged membrane rupture, and prolonged labor were expressed as frequencies and percentages. To control for confounding factors, stratification was performed for variables such as gestational age, birth weight, maternal conditions, and delivery characteristics. Post-stratification chi-square testing was applied, with a p-value ≤0.05 considered statistically significant.

RESULTS

The mean age of participants was 14.27±7.47 days, with a mean gestational age of 39.01±0.91 weeks and birth weight of 2.46±0.38 kg. The cohort had a mean Apgar score of 5.16±0.73 and platelet count of 201.55±107.77 $\times 10^9$/L. Female infants comprised the majority at 73.1% (n=68) compared to males at 26.9% (n=25). Regarding maternal factors, 31.2% (n=29) had irregular antenatal care, 15.1% (n=14) experienced premature rupture of membranes, and 25.8% (n=24) had prolonged labor. Maternal complications included thrombocytopenia in 8.6% (n=8), diabetes in 15.1% (n=14), and hypertension in 23.7% (n=22). Delivery was predominantly by cesarean section in 52.7% (n=49) versus vaginal delivery in 47.3% (n=44) cases (as shown in Table-I).

Table I

Patient Demographics

Demographics	Mean ± SD
Age (days)	14.27±7.47
Gestational Age (weeks)	39.01±0.91
Birth Weight (kg)	2.46±0.38
Apgar Score	5.16±0.73
Platelet Count ($\times 10^9$/L)	201.55±107.77
Gender	
Male n (%)	25 (26.9%)
Female n (%)	68 (73.1%)
Irregular ANC	
Yes n (%)	29 (31.2%)
No n (%)	64 (68.8%)
PROM	
Yes n (%)	14 (15.1%)
No n (%)	79 (84.9%)
Prolonged Labour	
Yes n (%)	24 (25.8%)
No n (%)	69 (74.2%)
Maternal Thrombocytopenia	
Yes n (%)	8 (8.6%)
No n (%)	85 (91.4%)
Mode of Delivery	
Vaginal n (%)	44 (47.3%)
C-section n (%)	49 (52.7%)
Maternal Diabetes	

Yes n (%)	14 (15.1%)
No n (%)	79 (84.9%)
Maternal Hypertension	
Yes n (%)	22 (23.7%)
No n (%)	71 (76.3%)

The frequency of thrombocytopenia among newborns with birth asphyxia was substantial, affecting 42 infants (45.20%) while 51 infants (54.80%) maintained normal platelet counts (as shown in Table-II).

Table II

Frequency of Thrombocytopenia in Newborn with Birth Asphyxia

Thrombocytopenia	Frequency	% age
Yes	42	45.20%
No	51	54.80%

Age stratification showed that among infants ≤15 days, 20 (40.0%) developed thrombocytopenia while 30 (60.0%) did not, compared to infants >15 days where 22 (51.2%) developed thrombocytopenia and 21 (48.8%) did not, yielding no significant difference (p=0.281). Gender analysis demonstrated similar thrombocytopenia rates between males [11 (44.0%) affected, 14 (56.0%) unaffected] and females [31 (45.6%) affected, 37 (54.4%) unaffected] with p=0.891. Gestational age comparison showed infants ≤39 weeks had 20 (40.8%) with thrombocytopenia and 29 (59.2%) without, while those >39 weeks had equal distribution of 22 (50.0%) each for affected and unaffected groups (p=0.374). Birth weight analysis revealed a notable trend where infants ≤2 kg showed higher thrombocytopenia rates at 6 (75.0%) versus 2 (25.0%) unaffected, compared to those >2 kg with 36 (42.4%) affected and 49 (57.6%) unaffected, though this did not reach statistical significance (p=0.134). Irregular antenatal care demonstrated a paradoxically protective effect, with only 6 (20.7%) of irregularly monitored pregnancies resulting in neonatal thrombocytopenia compared to 23 (79.3%) without thrombocytopenia, while regular antenatal care was associated with higher thrombocytopenia rates of 36 (56.3%) affected versus 28 (43.8%) unaffected (p=0.001). Premature rupture of membranes showed no significant association, with 6 (42.9%) affected and 8 (57.1%) unaffected in the PROM group, compared to 36 (45.6%) affected and 43 (54.4%) unaffected in the non-PROM group (p=0.851). Prolonged labor significantly increased thrombocytopenia risk, affecting 16 (66.7%) with only 8 (33.3%) unaffected, contrasting with normal labor duration where 26 (37.7%) were affected and 43 (62.3%) were unaffected (p=0.014). Maternal thrombocytopenia showed strong correlation with neonatal outcomes, present in 7 (87.5%) of affected newborns with only 1 (12.5%) unaffected, compared to mothers without thrombocytopenia where 35 (41.2%) newborns were affected and 50 (58.8%) were unaffected (p=0.021). Mode of delivery showed no significant difference, with vaginal delivery resulting in 20 (45.5%) affected and 24 (54.5%) unaffected, while cesarean section resulted in 22 (44.9%) affected and 27 (55.1%) unaffected (p=0.957). Maternal diabetes demonstrated no significant association, affecting 7 (50.0%) with equal numbers unaffected, compared to non-diabetic mothers where 35 (44.3%) were affected and 44 (55.7%) were unaffected (p=0.693). Most significantly, maternal hypertension showed the strongest association with neonatal thrombocytopenia, affecting 20 (90.9%) of infants born to hypertensive mothers with only 2 (9.1%) unaffected, compared to normotensive mothers where 22 (31.0%) were affected and 49 (69.0%) were unaffected (p<0.001) (as shown in Table-III).

Table III

Association of Thrombocytopenia with Demographic Factors

Demographic Factors		Thrombocytopenia		p-value
		Yes n(%)	No n(%)	
Age (days)	≤15	20 (40.0%)	30 (60.0%)	0.281
	>15	22 (51.2%)	21 (48.8%)	
Gender	Male	11 (44.0%)	14 (56.0%)	0.891
	Female	31 (45.6%)	37 (54.4%)	
Gestational Age (weeks)	≤39	20 (40.8%)	29 (59.2%)	0.374
	>39	22 (50.0%)	22 (50.0%)	
Birth Weight (kg)	≤2	6 (75.0%)	2 (25.0%)	0.134*
	>2	36 (42.4%)	49 (57.6%)	
Irregular ANC	Yes	6 (20.7%)	23 (79.3%)	0.001
	No	36 (56.3%)	28 (43.8%)	
PROM	Yes	6 (42.9%)	8 (57.1%)	0.851
	No	36 (45.6%)	43 (54.4%)	
Prolonged Labour	Yes	16 (66.7%)	8 (33.3%)	0.014*
	No	26 (37.7%)	43 (62.3%)	
Maternal Thrombocytopenia	Yes	7 (87.5%)	1 (12.5%)	0.021*
	No	35 (41.2%)	50 (58.8%)	
Mode of Delivery	Vaginal	20 (45.5%)	24 (54.5%)	0.957
	C-section	22 (44.9%)	27 (55.1%)	
Maternal Diabetes	Yes	7 (50.0%)	7 (50.0%)	0.693
	No	35 (44.3%)	44 (55.7%)	
Maternal Hypertension	Yes	20 (90.9%)	2 (9.1%)	<0.001*
	No	22 (31.0%)	49 (69.0%)	

***Fischer Exact Test**

DISCUSSION

Present study reveals that thrombocytopenia is a common hematologic complication of birth asphyxia in the newborn, being present in nearly half (45.2%) of the population studied. The finding upholds the pathophysiologic notion that perinatal asphyxia triggers a series of events that culminate in the formation of platelet dysfunction as well as consumption. Activation of the coagulation system as well as disseminated intravascular coagulation, by the hypoxic-ischemic injury in the birth asphyxia process, causes excessive platelet consumption and decreased production by virtue of suppression of the bone marrow by the hypoxemia.

Most prominent in this study was the strong correlation of maternal hypertension with neonatal thrombocytopenia, with 90.9% of offspring born of hypertensive mothers having decreased platelet counts. Both the strong correlation as well as direct pathogenesis can be accounted for by the placental pathology inherent in the uterine hypertensive disorders, secondary to chronic uteroplacental insufficiency, fetal hypoxia, as well as fetal coagulation system activation. Hypertensive disorders are likewise frequent concomitants of endothelial damage as well as microangiopathic alterations that may directly affect fetal platelet synthesis in addition to fetal platelet survival. The strong correlation with maternal thrombocytopenia (87.5% of thrombocytopenic mothers having thrombocytopenic offspring) supports a direct maternal-fetal transmissible process, secondary to antiplatelet antibodies that traverse

the placoderm or shared pathophysiologic processes affecting maternal as well as fetal hematopoiesis.

Prolonged labour was also an important risk factor that emerged, with two-thirds of the thrombocytopenic infants developing thrombocytopenia. Prolonged labour increases the risk of fetal acidosis and hypoxia, directly impairing platelet function and causing consumption coagulopathy. Mechanical tension and repeated uterine contractions in the prolonged labour process might compromise uteroplacental blood flow, further aggravating fetal hypoxemic states. Interestingly, the apparently protective factor of irregular antenatal care must be interpreted with caution, because the outcome might represent selection bias or confounding factors rather than an actual protective factor, possibly implicating that mothers with regular care had complicated antenatal courses that deserved closer follow-up because of inherent high-risk states.

Our study results revealed a thrombocytopenia frequency of 45.20% among newborns with birth asphyxia, which aligns closely with several published studies while showing notable variations with others. This finding demonstrates remarkable consistency with Masood A, et al. [17] who reported 41.5% prevalence in neonates born to mothers with pregnancy-induced hypertension, and Tirupathi K, et al. [18] who found thrombocytopenia in a broader population of admitted neonates. However, our results contrast with higher prevalences reported by Gebreselassie HA, et al. [19] at 55.8% in surgical neonates and Kausar M, et al. [20] at 68.24% in culture-proven sepsis cases, suggesting that the underlying pathophysiology and severity of clinical conditions significantly influence thrombocytopenia rates.

The strong association betweenmaternal hypertension and neonatal thrombocytopenia in our study (90.9% vs 31.0%, p<0.001) corroborates findings by Masood A, et al. [17] who specifically studied pregnancy-induced hypertension, and Sodha N, et al. [21] who identified maternal hypertension in 22.4% of cases with preeclampsia affecting 7.6%. Similarly, Tirupathi K, et al. [18] reported PIH in 13.5% of thrombocytopenic neonates. The consistent association across multiple studies suggests that maternal hypertensive disorders create a shared pathophysiological pathway leading to neonatal platelet dysfunction, possibly through placental insufficiency, inflammatory mediators, or direct maternal antibody transfer.

Our finding of maternal thrombocytopenia strongly correlating with neonatal outcomes (87.5% vs 41.2%, p=0.021) represents a novel observation not extensively documented in the reviewed literature, highlighting the importance of maternal platelet assessment in predicting neonatal complications. The significant association with prolonged labor (66.7% vs 37.7%, p=0.014) aligns with the mechanical and hypoxic stress factors identified by Samad N, et al. [22] who demonstrated that birth asphyxia leads to multi-organ dysfunction and pronounced thrombocytopenia, with platelet counts dropping significantly compared to non-asphyxiated controls.

Interestingly, our study revealed a paradoxical protective effect of irregular antenatal care (20.7% thrombocytopenia rate vs 56.3% with regular care, p=0.001), which contrasts with conventional expectations and warrants further investigation. This finding diverges from established literature patterns where adequate prenatal care typically correlates with improved outcomes. The demographic distribution in our study showed female predominance (73.1%), which differs from several studies including Aslam A, et al. [23] who reported 69% female participation, Gebreselassie HA, et al. [19] with 56.2% male predominance, and Tirupathi K, et al. [18] with 56% males, suggesting that gender distribution may vary based on study selection criteria and regional factors.

The absence of significant associations with gestational age, birth weight (despite a notable trend at ≤2 kg), and mode of delivery in our study contrasts with Aslam A, et al. [23] who found significant correlations with low birth-weight and pre-term birth, and Tirupathi K, et al. [18] who identified 62.5% low birth-weight association. Sodha N, et al. [21] reported 70% preterm infants and 55.2% with IUGR, while Gebreselassie HA, et al. [19] found 78.6% term infants, indicating that the relationship between these factors and thrombocytopenia may depend on the specific population studied and underlying pathological processes.

The mean platelet count in our asphyxiated population (201.55±107.77 $\times 10^9$/L) shows considerable overlap with normal ranges, yet the substantial proportion developing thrombocytopenia reflects the dynamic nature of platelet changes following birth asphyxia, as demonstrated by Samad N, et al. [22] who showed dramatic reductions in platelet counts alongside elevated liver enzymes and other markers of multi-organ dysfunction. This temporal relationship between asphyxia severity and platelet consumption may explain why some studies report higher thrombocytopenia rates, particularly when examining more critically ill populations like those studied by Kausar M, et al. [20] in septic neonates or Gebreselassie HA, et al. [19] in surgical cases where prolonged hospitalization and multiple interventions compound the risk factors

These findings together draw attention to the multifactorial etiology of neonatal thrombocytopenia following birth asphyxia, whereby maternal, labor, and neonatal factors impinge on platelet homeostasis. The observation of recognizable high-risk maternal factors, most notable of which are hypertension and maternal thrombocytopenia, presents the clinical community with promising predictive signs of early identification of the at-risk neonate. These findings contribute further to the burgeoning base of evidence supporting the use of targeted surveillance policies and may inform the derivation of risk stratification guidelines for asphyxiated newborns managed in the settings of neonatal intensive care units.

Some of the limitations of the present study need to be acknowledged. It was a single-center study at a single tertiary care center, therefore, restricting generalizability of findings to other clinical settings where clinical practices are different and the populations may be different. Its moderately sized participant group of 93, with limited statistical power, may be less likely to identify some of the less common maternal and peripartum risk factors. Its cross-sectional design also precludes us from

being able to determine temporal relations, as well as causality, between risk factor exposures and development of thrombocytopenia. It also did not offer long-term follow-up to ascertain clinical outcomes and recovery patterns of the involved neonates, whose data would be informative to appreciate the prognostic significance of the severity of thrombocytopenia in this group.

CONCLUSION

In this study, we determined thrombocytopenia to be a relevant complication in neonates with birth asphyxia, present in nearly half of the population studied. Maternal hypertension was shown to be the strongest predictor of neonatal thrombocytopenia, with maternal thrombocytopenia and protraction of labor in second and third place respectively, highlighting the very necessity of careful maternal evaluation and monitoring during gestation and delivery. These findings emphasize the fact that certain maternal diseases produce predisposition to platelet malfunction in the neonate, and that prompt identification of high-risk gestations may permit directed surveillance as well as prompt intervention.

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