

## Study of Thrombocytopenia in Neonatal Intensive Care Unit

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### Abstract

**Background:** Neonatal thrombocytopenia (platelet count less than  $150 \times 10^9 /L$ ) is one of the commonest haematological abnormality encountered in neonatal intensive care unit (NICU). Though thrombocytopenia is so prevalent it is often overlooked assuming that it will resolve spontaneously. However, if it is not detected and managed properly can result in devastating complications. The present study highlights the pattern, prevalence, severity and possible causes of neonatal thrombocytopenia encountered in our hospital. **Method:** A prospective observational study was conducted on sick neonates admitted to NICU with different clinical problems and were evaluated for pattern and severity of thrombocytopenia as per the blood samples analysed. **Results:** Out of 426 consecutive neonates admitted to NICU, 276 developed thrombocytopenia with a high prevalence of 65.1 %. 38.7% had early onset and 61.3% had late onset thrombocytopenia. The most common cause of neonatal thrombocytopenia was prematurity (36.9%) followed by neonatal sepsis (26.1%). Mild and moderate thrombocytopenia was found in 22.5% and 27.8 % of the neonates, while severe was more common accounting for 49.7% of cases. **Conclusion:** Neonatal thrombocytopenia is common in NICU and it could be used as a prognostic marker for multiple diseases. As its clinical course and outcome depend on etiology, an appropriate diagnostic workup is essential for early diagnosis and better management

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### Introduction

Thrombocytopenia is the commonest haematological abnormality encountered in neonatal intensive care unit (NICU), the incidence of which varies greatly, depending upon the studied population<sup>(1,2)</sup> Healthy foetuses and neonates at gestational ages  $\geq 22$  weeks have platelet counts within the normal range for adults ( $150-450 \times 10^9 /L$ ).<sup>2,3</sup> Neonatal thrombocytopenia is defined as a platelet count less than  $150 \times 10^9 /L$  regardless of gestational age.<sup>(2,3,4)</sup> However, platelet counts in the range of  $100-150 \times 10^9 /L$  is somewhat more common among healthy neonates.<sup>2</sup>

Thrombocytopenia exists in 1–5% of newborns at birth and severe thrombocytopenia occurs in 0.1–0.5%.<sup>5</sup> Thrombocytopenia is present in 22 to 35% of all newborns admitted to NICU and in up to 50% of those admitted to NICUs who need intensive care.<sup>2,4,5</sup> The majority of neonates will have mild or moderate thrombocytopenia and about 20% of neonates have severe thrombocytopenia (a  $< 50 \times 10^9 /L$ ).<sup>2</sup>

The important causes of thrombocytopenia in neonates are infections, birth asphyxia, preterm, intrauterine growth retardation, hyperbilirubinemia, respiratory distress syndrome, meconium aspiration syndrome and low birth weight. Apart from platelet counts, bleeding manifestations depend on underlying ailments.<sup>1,6,7</sup> Early onset neonatal thrombocytopenia

occurs commonly in NICU population regardless of gestational age with a benign course and a predictable outcome.<sup>5,8</sup> Late onset thrombocytopenia is typically more severe than early onset disease.<sup>9</sup>

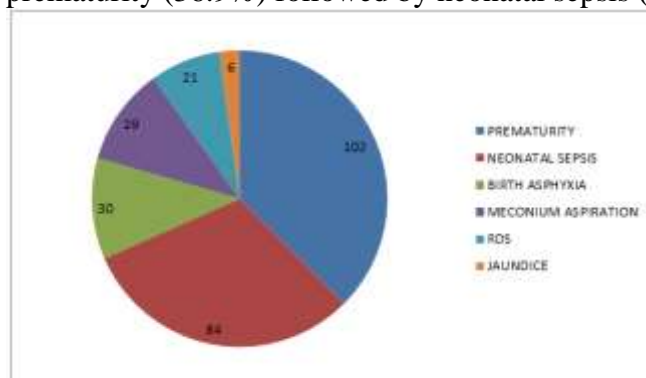
Detection of thrombocytopenia is a useful initial assessment for sick neonates and it is considered as one of the complication of the disease process, but in some cases thrombocytopenia is detected accidentally.<sup>10</sup> Though thrombocytopenia is so prevalent it is often ignored in the assumption that it will resolve spontaneously. However if it is not detected and managed properly can result in devastating complications. The present study aim to highlight the pattern, prevalence, severity and possible causes of neonatal thrombocytopenia encountered in our hospital.

### Material and Methods

A prospective observational study was conducted at NICU of Rainbow Hospital, Panipat for a period of 6 months (JAN – JUNE 2023). Neonates from 1 to 28 days of age admitted to NICU with different clinical problems were evaluated for platelet count and counts less than  $150 \times 10^9 /L$  were included in this study. Venous EDTA samples were sent to hematology laboratory and analysed by automated hematology analyser (HORIBA ABX). Platelet counts were done on the day of admission, 1st day, 3rd day and thereafter every 72 hours till counts became normal. Low platelet counts were cross verified by peripheral blood smear study. Data was collected from hematology laboratory records and analysed. Neonates were categorized depending on presentation, time of onset of thrombocytopenia, presence of risk factor, etiology and severity. Pattern of onset of thrombocytopenia was classified as early if it developed <72 hours of birth and late if it presented after 72 hours. Severity of thrombocytopenia was graded as mild if counts were in the range of 100 to  $150 \times 10^9 /L$ , moderate if count was  $>50 \times 10^9 /L$  to  $<100 \times 10^9 /L$  and severe if  $<50 \times 10^9 /L$ . Neonatal sepsis was confirmed by blood culture. Platelet serology was not done due to lack of facility for testing. Neonates born to mothers with idiopathic thrombocytopenic purpura and neonates with congenital anomalies were excluded from the study. Data analyzed was expressed in terms of numbers and percentage. Ethical clearance was obtained from institutional ethical committee.

### Results

Out of 426 consecutive neonatal admissions to NICU of our hospital 276 neonates were found to have thrombocytopenia due to various etiological factors as per the blood samples analysed. The overall prevalence of neonatal thrombocytopenia was 64.7%. The etiological profile is shown in figure I. The most common causes of neonatal thrombocytopenia were prematurity (36.9%) followed by neonatal sepsis (26.1%) and Birth asphyxia (10.8%).



**Figure 1: Various etiological factors of neonatal thrombocytopenia**

**Table I: Pattern of onset of neonatal thrombocytopenia**

<b>Etiology</b>	<b>Number of early onset</b>	<b>Number of late onset</b>
Prematurity	64	38
NEONATAL SEPSIS	16	68
BIRTH ASPHYXIA	08	22
MECONIUM ASPIRATION	13	16
RDS	03	18
JAUNDICE	02	04
IUGR	01	03
<b>TOTAL</b>	<b>107</b>	<b>169</b>

Out of 276 neonatal thrombocytopenia cases, 107 (38.7%) developed early onset thrombocytopenia and 169 (61.3 %) had late onset thrombocytopenia (Table I).

**Table II: Grading of neonatal thrombocytopenia according to severity**

<b>Etiology</b>	<b>Mild</b>	<b>Moderate</b>	<b>Severe</b>
PREMATURITY	19(18.6%)	27(26.4%)	56(55%)
NEONATAL SEPSIS	15(17.8%)	20(23.8%)	49(58.4%)
MECONIUM ASPIRATION	11(38%)	10(34.5%)	08(27.5%)
BIRTH ASPHYXIA	04(13.4%)	08(26.6%)	18(60%)
RDS	07(33.4%)	09(42.8%)	05(23.8%)
JAUNDICE	03(50%)	02(33.3%)	01(66.7%)
IUGR	03(75%)	01(25%)	00
<b>TOTAL</b>	<b>62</b>	<b>77</b>	<b>137</b>

Prevalence of prematurity was high (23%) in early thrombocytopenic group and prevalence of sepsis was high (24%) in late thrombocytopenic group. Septicemia, birth asphyxia and respiratory distress syndrome were significantly associated with late onset and severe thrombocytopenia. Prematurity was associated with early onset and severe thrombocytopenia. Mild and moderate thrombocytopenia was found in 30.7 % of neonate and 23.3%, while severe thrombocytopenia was seen in 48 % of cases. Severe thrombocytopenia was predominantly observed in neonates with prematurity (%), neonatal sepsis (54.1 %), meconium aspiration syndrome (66.6%) and birth asphyxia (60%) (Table II).

### **Discussion**

Thrombocytopenia is the one of the most common hematological abnormality seen in the NICU but may be missed if not specifically looked for.<sup>1</sup> Several studies have reported thrombocytopenia in 22 to 35% in all the neonates admitted to NICU.<sup>1</sup> Despite of its high prevalence, several basic patho-physiologic questions regarding neonatal thrombocytopenia remain unsolved.<sup>1</sup>

Clinically, thrombocytopenic neonates may vary from asymptomatic to mild oozing from venepuncture site to severe single organ hemorrhage (pulmonary, gastrointestinal, intraventricular) to disseminated intravascular coagulation.

**Table III: Comparison of prevalence of neonatal thrombocytopenia.**

Studies of neonatal thrombocytopenia in NICUs	Prevalence of neonatal thrombocytopenia
This study	64.7 %
Gupta et al 1	70.5 %
Aman et al <sup>6</sup> 25% 4 28.5% 17.9%	24.1 %
Jeremiah et al <sup>12</sup>	53 %
Patil et al <sup>13</sup>	25.45 %
Wong et al <sup>10</sup>	25 %
Eslami Z et al	28.5 %
Khalessi et al <sup>14</sup>	17.9 %
Ghamdi et al <sup>8</sup>	14 %

It is evident from table III that there is high prevalence (64.7%) of neonatal thrombocytopenia in our study which is in concordance with the study done by Gupta et al (70.5%).<sup>1</sup> The higher prevalence of neonatal thrombocytopenia in the present study signifies the importance of platelet studies in the neonates and could be attributed to the factors like the study place, which is a referral centre and to the higher proportion of neonatal prematurity and septicemia in NICU admissions.

**Table IV: Comparison of pattern of neonatal thrombocytopenia.**

Studies of neonatal thrombocytopenia in NICUs	Percentage of Early onset thrombocytopenia	Percentage of Late onset thrombocytopenia
Present studies	38.7	61.3
Khalessi et al <sup>14</sup>	67.7	32.3
Ghamdi et al <sup>8</sup>	77	23
Jeremiah et al <sup>12</sup>	84.8	15.2
Eslami Z et al <sup>4</sup>	75.3	24.7

**Table V: Comparison of severity of neonatal thrombocytopenia.**

Studies of neonatal thrombocytopenia in NICUs	Mild	Moderate	Severe
Present studies	22.5%	27.8 %	49.7 %
Gupta et al 1	84.4%	13%	2.6%
Ghamdi et al <sup>8</sup>	60%	20%	20%
Jeremiah et al <sup>12</sup>	39.4%	12.1%	1.5%
Khalessi et al <sup>14</sup>	43.5%	26.8%	29.7%

### Etiological profile

Etiological profile of our study showed prematurity (36.9%) as the most common cause of neonatal thrombocytopenia followed by neonatal sepsis (26.1%). Gupta et al and Khalessi et al found sepsis to be the most common cause of neonatal thrombocytopenia with a proportion of 42% and 24.1% respectively.<sup>1,14</sup> According to Jeremiah et al, birth asphyxia (33.3%) followed by jaundice (19.7%) were the most common etiologies.<sup>12</sup> Eslami Z et al recorded neonatal sepsis and intra uterine growth retardation as important causes of thrombocytopenia.<sup>4</sup>

In the present study, late onset neonatal thrombocytopenia was more common (56.5%) in contrast to other studies where early onset neonatal thrombocytopenic pattern was predominant (Table IV). The proportion of severe thrombocytopenia was higher in our study, where as other studies showed predominance of mild thrombocytopenia. This once again is the reflection of higher contribution of prematurity and septicemia (Table V).

Fetomaternal and neonatal conditions result in neonatal thrombocytopenia.<sup>5</sup> Mechanisms underlying thrombocytopenia in neonates include increased platelet consumption as seen in sepsis, decreased production, hypersplenism or combination of these. It has been hypothesized that relative decrease in platelet production might contribute to most cases of thrombocytopenia because of specifically smaller, less mature megakaryocytes and low thrombopoietin levels in neonates.<sup>3</sup> Newer classification based on the timing of onset of thrombocytopenia (early vs late) appear more useful and important for planning diagnostic investigations and subsequent management of neonatal thrombocytopenia though overlap between the two patterns is common. According to Modanlou et al, thrombocytopenia was frequently associated with bacterial sepsis in neonates and rapid appearance of thrombocytopenia long before the confirmation with positive blood culture made the test valuable adjunct to the management of septic neonates.<sup>7</sup> In our study also thrombocytopenia appeared before the culture positivity. Gupta et al observed an overall mortality of 33% in babies with thrombocytopenia despite >90% of these cases having received blood transfusion.<sup>1</sup> Eslami Z et al found no relation between occurrence of thrombocytopenia and gender.

Most episodes of thrombocytopenia resolve spontaneously without any clinical sequelae. When platelet count normalizes, no further evaluation is required. The clinical features and outcome of thrombocytopenia were not evaluated in this study which is the major limitation of the study. Though the main stay of specific therapy of neonatal thrombocytopenia is platelet transfusion, there are no safe guidelines for defining the optimum dose of platelets to administer or when to administer.<sup>2</sup> Knowing the importance of life threatening events among the thrombocytopenic newborns, it is best to keep the risk factors in mind to prevent the future complications of thrombocytopenia.

### **Conclusion**

Neonatal thrombocytopenia is a common clinical problem and is a prognostic marker of many disease conditions in neonates. The leading causes of neonatal thrombocytopenia include prematurity, sepsis, meconium aspiration syndrome, birth asphyxia, respiratory distress syndrome, hyperbilirubinemia and intra-uterine growth retardation among which prematurity and sepsis contribute to significant number of severe thrombocytopenic group. As the prevalence of neonatal thrombocytopenia is high, it is important to look for platelet count, severity, degree and pattern of onset of thrombocytopenia in each and every case of neonate admitted to NICU, which will help the clinician in diagnosis, planning investigations and aid in appropriate management. As even in apparently low risk babies, the prevalence, morbidity and mortality associated with neonatal thrombocytopenia is high and the clinical course and outcome of thrombocytopenia depend on etiology, an appropriate workup is essential to avoid complications.

### **References**

1. Gupta A, Mathai SS and Kanitkar M. Incidence of thrombocytopenia in neonatal intensive care unit. Medical journal armed forces India. July 2011; 67(3): 234-6.
2. Roberts I, Stanworth S, Murray NA. Thrombocytopenia in neonates. Blood Review. 2008; 22:173-86.

3. Sola-Visner M, Saxonhouse MA and Brown RE. Neonatal thrombocytopenia: what we do and don't know. *Early Human Development*. 2008; 84: 499-506.
4. Eslami Z, Lookzadeh MH, Noorishadkam M, Hashemi A, Ghilian R and Phir Dehghan A. Thrombocytopenia and associated factors in neonates admitted to NICU during years 2010-2011. *Iran J Ped Hematol Oncol*. 2013; 3(1):205-15.
5. Roberts I, Murray NA. Neonatal thrombocytopenia: causes and management. *Arch Dis Child Fetal Neonatal Ed*. 2003; 88: 359-64.
6. Aman I, Hassan KA and Ahmad TM. The study of thrombocytopenia in sick neonates. *J Coll Physicians Surg Pak*. May 2004; 14(5): 282-5.
7. Modanloud HD, Ortiz O and Gluck L. Thrombocytopenia in neonatal sepsis: Time relationship between clinical signs, detection of thrombocytopenia and positive blood culture. *Pediatric Research*. 1977; 11: 503.
8. Ghamdi AM, Umran KA and Buali WA. A practical approach to assessment of neonatal thrombocytopenia in NICU. *Journal of Neonatal-Perinatal Medicine*. 2008; 1(3): 175-80.
9. Holzhaur S and Zieger B. Diagnosis and management of neonatal thrombocytopenia. *Seminar in fetal and neonatal medicine*. 2011; 16: 305-10.
10. Wong W and Glader B. Approach to newborn who has thrombocytopenia. *NeoReviews*. 2004; 5(10): 444-9.
11. Bonifacio L, Petrova A, Nanjundaswamy S, Mehta R et al. Thrombocytopenia related neonatal outcomes in preterms. *Indian Journal of Pediatrics*. 2007;74:269-74.
12. Jeremiah ZA and Oburu JE. Pattern and prevalence of neonatal thrombocytopenia in Port Hartcourt, Nigeria. *Pathology and laboratory medicine international*. April 2010; 2:27-31.
13. Patil S, Mangshetty R and Patil B. Outcome of neonates with thrombocytopenia. *Journal of Evolution of Medical and Dental Sciences*. 2014; 3(17): 4533-38.
14. Khalessi N, Khosravi N, Sanni S. The prevalence and risk factors for neonatal thrombocytopenia among newborns admitted to intensive care unit of Aliasghar children's hospital. *Iranian journal of blood and cancer*. 2013; 5(2): 41-5.