MEDICAL CHANNEL

Original Article

FREQUENCY AND PATTERN OF THROMBOCYTOPENIA IN NEONATES ADMITTED IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To determine the frequency and pattern of thrombocytopenia in neonates admitted in the NICU of a tertiary care hospital.

Place of Study: The study was carried out in the NICU of the National Institute of Child Health from January 1, 2012 to June 30, 2012

Study Design: It was a cross sectional study.

Subjects: Neonates aged from 0 to 28 days of either sex, irrespective of birth weight and gestational age admitted in the NICU were included. Newborns with congenital malformations were excluded.

Methods: The subjects were enrolled after informed consent.2 ml. of venous blood was collected from each neonate with 24 gauge butterfly needle or disposable needle. Counting was done manually in a Neubaur chamber and the results were expressed as platelets per 10^9per litre. By a haematologist. Thrombocytopenia was classified as mild (100,000 to 150,000 per ml.). moderate (50,000 to 100,000 per ml.) and severe (less than 50,000 per ml.) The data was collected on a predesigned proforma and analyzed using SPSS version 15.

Results: A total of 150 newborns were studied. Their mean age was 12.84 +/ -7.6 days.63 (42%) were male and and 87 (58%) were female. The mean gestational age was 37.2 +/- 3.5 weeks and mean weight was 2.4 +/- 1.5 Kg. The frequency of thrombocytopenia was 40 (26.7%). 23 (57.5%) had mild thrombocytopenia , 13 (32.5%) had moderate thrombocytopenia and 4 (10%)had severe thrombocytopenia. Thrombocytopenia was there in 48.3% of neonates 0 to 6 days age, 12.2% in 7 to 28 days age, (P<0.001) . 31.7% of thrombocytopenic neonates were male and 23% were female.

33.8% thrombocytopenic neonates were preterm (<37 weeks gestation) and 21.2% were term (P= 0.05). 24.4% were low birth weight (Less than 2.5 Kg.) compared to 30% who were of normal birth weight (P= 0.28).

Conclusion: The frequency of thrombocytopenia was 26.7%. Birth asphyxia, neonatal jaundice and neonatal sepsis was found in 32.5%, 20% and 17.5% respectively.

Key Words: Neonatal thrombocytopenia, birth asphyxia , neonatal jaundice, neonatal sepsis.

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INTRODUCTION

Neonatal thrombocytopenia is a common haematological abnormality. By the end of the first trimester of pregnancy, the fetal platelet count reaches a level of approximately $150x10^9$/L. Thus, platelet count of < $150x10^9$/L is defined as thrombocytopenia in neonates regardless of gestational and clinical condition.[1] However, the clinical significance of platelet counts between 100-$150x10^9$/L is unclear and may not suggest an increased risk of bleeding. Platelet production and turnover in neonates is similar to that of older children and adults. The platelet life span is 7-10 days.[2]

According to the severity, thrombocytopenia was classified as mild (100,000-150,000/mcL), moderate (50,000-100,000/mcL) and severe (less than 50,000/mcL).[3] Neonatal thrombocytopenia may occur as early onset or late onset. Early onset thrombocytopenia is a mild moderate, self-limiting and requires no treatment. Late onset thrombocytopenia is often severe, prolonged and will require treatment with platelet transfusions.[4] The reported incidence of thrombocytopenia among the neonates admitted to Neonatal Intensive Care Unit (NICU) is high and varies between 22-35%. Aman I et al.[5] in their study reported that the frequency of neonatal thrombocytopenia is 24.1%. Intra ventricular hemorrhage is a major form of bleeding and is a leading cause of death and disability in very preterm neonates.[6,7] Many preterm neonates receive platelet transfusion, to treat bleeding, or prophylactically to decrease the risk of hemorrhage.[8]

The pattern of neonatal thrombocytopenia includes birth asphyxia (33.3%); neonatal jaundice (19.7%); neonatal sepsis (16.7%) and low birth weight (13.6%).

Therefore, this study was planned to document the magnitude and pattern of neonatal thrombocytopenia, so that strategies may be made to avoid the morbidity and mortality associated with severe thrombocytopenia

OPERATIONAL DEFINITIONS

Neonatal Thrombocytopenia: It was labeled if the platelet count <$150x10^9$/L.

Early onset thrombocytopenia: It was labeled if the thrombocytopenia occurs within first 72 hours of life.

Late onset thrombocytopenia: It was labeled if the thrombocytopenia occur at any age after 72 hours after birth till 28 days of life.

Severity of thrombocytopenia:

- Mild thrombocytopenia (100,000-150,000/mcL)
- Moderate thrombocytopenia (50,000-100,000/mcL)
- Severe thrombocytopenia (less than 50,000/mcL).

Preterm: A baby before completing 37 weeks of gestation.

Birth asphyxia; Neonates who have APGAR score of <7

Neonatal Jaundice: When serum bilirubin level is in the phototherapy / exchange transfusion range according to weight and age of the body.

Low birth weight: It is defined as birth weight <2.5kg.

METHODOLOGY

Study Design: Cross Sectional Study.

Setting: This Study was carried out in the Department of Neonatology (NICU) of National Institute of Child Health, Karachi.

Duration of Study: From January 1, 2012 to June 30, 2012

Sample Size: Taking confidence level (1-á) of 95%, anticipated population proportion (P) of low birth weight of 13.6% and absolute precision (d) of 5.5% the sample size is calculated as (n) 150.

Sample Technique: Non-probability Purposive sampling

Sample Selection:

Inclusion criteria:

- Neonates (0-28) days of life admitted in the neonatal ward.
- All neonates of either sex (Male & Female).
- Irrespective of gestational age

Exclusion Criteria:

- Neonates who are visiting well baby clinic (OPD) clinic for routine check-up.
- Neonates with congenital malformation.

Data Collection Procedure:

Neonates admitted in neonatal ward and fulfilling the inclusion criteria were selected for this study. Informed consent was taken from the parents. Two milliliters of venous blood sample was collected from each neonate carefully with 24 gauze butterfly needle or disposable needle to allow free flow of blood. Ethylene diamine tetra acetic acid (EDTA) was used as an anticoagulant and sample was kept on roller mixer for constant mixing until platelet count was performed by automated cell counter using (Sysmex Kx-21 and Sysmex XT 2000i). Manual Neubaeur counting chamber was used for counting and results were expressed as platelet $x10^9$/L by a hematologist. Severity was classified as mild, moderate and severe as per operational definition.

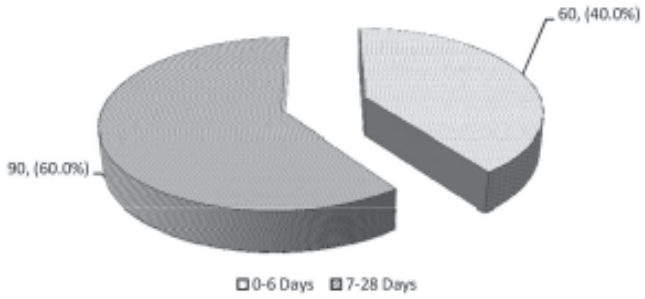
Data including age of the baby, gender, weight, gestational age at birth, platelet count and pattern including, birth weight and blood culture report was recorded in a predesigned Proforma.

Data Analysis Procedure:

The collected data was entered and analyzed using descriptive statistic by SPSS version 15. Categorical variables like gender, thrombocytopenia and pattern like birth asphyxia, neonatal jaundice, neonatal sepsis and low birth weight were presented as frequencies and percentage. Numerical variables like gestational age at birth, birth weight, age of the baby and platelet count level were expressed as man ± Standard Deviation (SD).

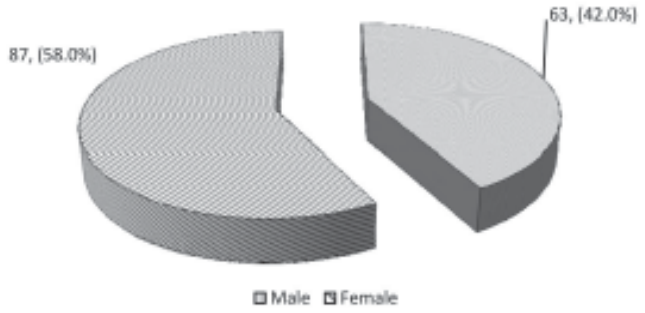
Stratification was done with regards to age of baby, gender, gestational age at the time of delivery and birth weight to see the effect of these on outcome through Chi square test

FIGURE 1:
AGE DISTRIBUTION
(n=150)



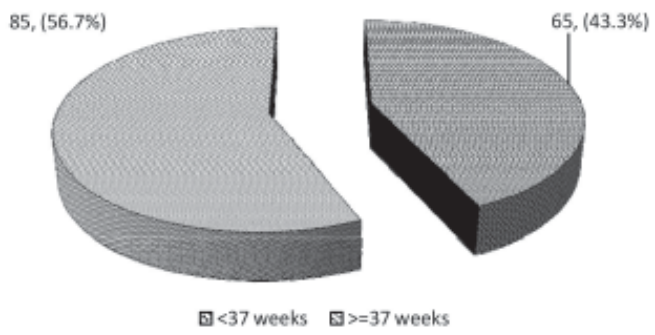
Mean age: 12.84±7.6 days

FIGURE 2:
SEX DISTRIBUTION
(n=150)



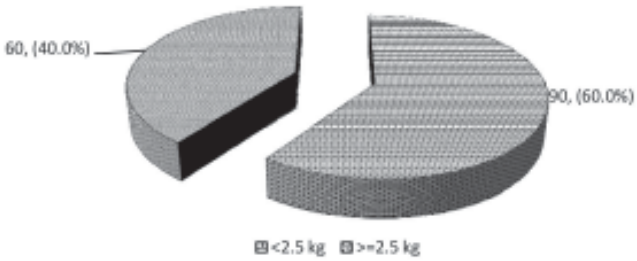
Female to male ratio: 1.4:1

FIGURE 3:
DISTRIBUTION OF GESTATIONAL AGE
(n=150)



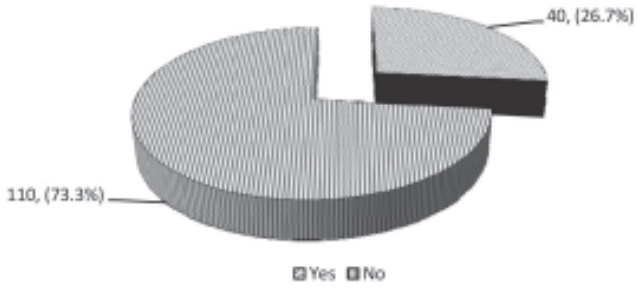
Mean gestational age: 37.2±3.5 weeks

FIGURE 4
DISTRIBUTION OF BIRTH WEIGHT
(n=150)



Mean weight: 2.4±1.5 kg

FIGURE 5
FREQUENCY OF THROMBOCYTOPENIA
(n=150)



Mean platelets count: 145±58.5 x10^9/L

FIGURE 6
SEVERITY OF THROMBOCYTOPENIA
(n=40)

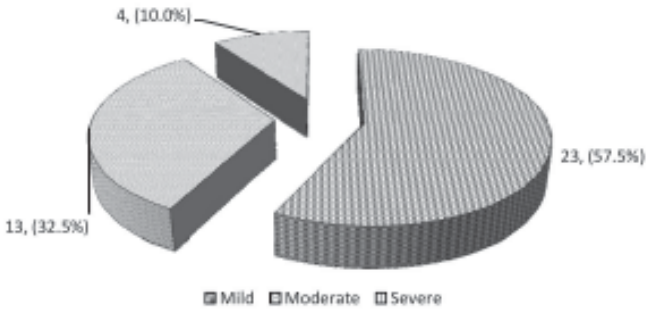


FIGURE 7
FREQUENCY OF APGAR SCORE <7
(n=150)

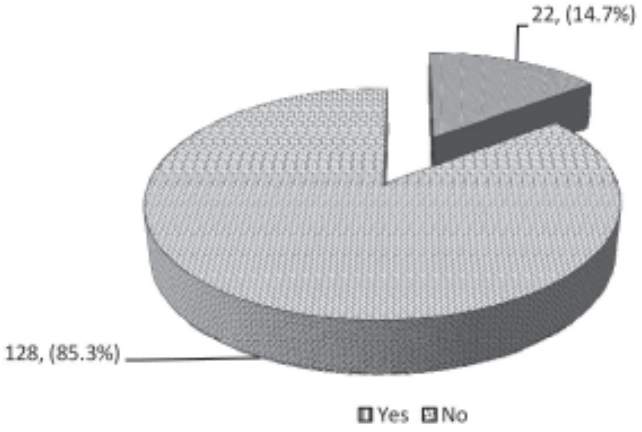
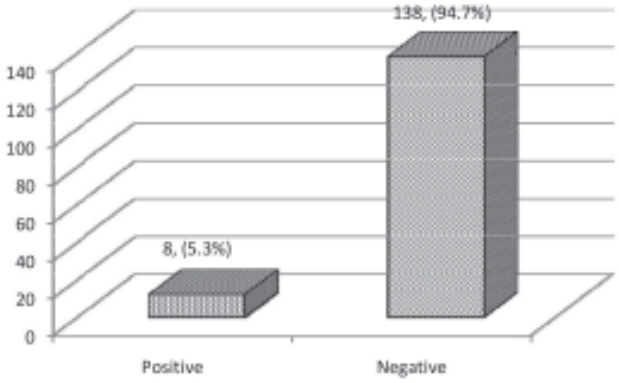


FIGURE 8
FREQUENCY OF BLOOD CULTURES
(n=150)



and p-value of <0.05 was considered significant.

STRATIFIED ANALYSIS:

Stratified analysis of outcome was done, based on age, sex, gestational age and weight

RESULTS

A total of 150 neonates were enrolled in this study during study period. The mean age of enrolled participants was 12.84±7.6 days (Figure 1).

Of 150 enrolled participants, 63 (42%) were male and 87 (58%) were female with male to female ratio of 1:1.4 (Figure 2). Mean gestational age was 37.2±3.5 weeks (Figure 3) and mean weight of newborn was 2.4±1.5 kg (Figure 4).

The frequency of thrombocytopenia in newborns was 40 (26.7%) cases (Figure 5). Of 40 patients of thrombocytopenia, 23 (57.5%) had mild thrombocytopenia, 13 (32.5%) had moderate and 4 (10%) had severe thrombocytopenia (Figure 6).

A total of 22 (14.7%) newborns had APGAR score of <7 (Figure 7) and 8 (5.3%) had positive blood culture (Figure 8)

Of 40 newborns with thrombocytopenia, 32.5% had birth asphyxia, 20% neonatal jaundice, 17.5% neonatal sepsis and 12.5% had low birth weight (Figure 8).

DISCUSSION

THROMBOCYTOPENIA

Thrombocytopenia is defined as a platelet count of less than 150,000 regardless of gestational age[9], and this definition is consistent for neonates, children and adults[10]. Two large studies report the occurrence of thrombocytopenia in all newborns to range from 0.7 to 0.9%, with these studies differing in whether infants of mothers with known thrombocytopenia were included and what value was used to define thrombocytopenia (100,000 versus 150,000)[11,12]. Among sick neonates, there is a much higher incidence of thrombocytopenia, reported at 18 to 35% among admissions to neonatal intensive care units.[13]

If an infant, child or adult is thrombocytopenic, it is due to one or more of the following mechanisms: decreased platelet production, increased platelet destruction, or platelet sequestration[14]. When evaluating an infant with thrombocytopenic purpura without coagulation abnormalities, the following factors regarding the infant should be considered: presence or absence of hepatosplenomegaly, congenital anomalies, and/or signs of sepsis. The mother should be evaluated for platelet count and appearance of her blood smear, history of hematologic and infectious diseases, complete drug history, and evidence of transmissible infection. The family should also be evaluated for presence of parental consanguinity and/or hematologic disease in family members[15].

Both alloimmune and autoimmune thrombocytopenia are a result of extravascular platelet destruction by antiplatelet antibodies. IgG antiplatelet antibodies are produced in the mother and cross the placenta and coat the infant's platelets. These are then removed from the circulation within a few hours.[16]

Disseminated intravascular coagulation occurs when an underlying disease process is complicated by increased tissue factor activity, cytokine release, and excess thrombin production. This is in addition to other abnormalities of various clotting factors.[17] Coagulation activation can be triggered by acidosis, poor perfusion, or endotoxins.[18]

Perinatal hypoxia has been associated with severe and prolonged thrombocytopenia and disseminated intravascular coagulation.

TABLE 1
FREQUENCY OF CAUSES OF THROMBOCYTOPENIA
(n=40)

Causes	Frequency	Percentage
Birth Asphyxia	13	32.5
Neonatal Jaundice	8	20.0
Neonatal sepsis	7	17.5
Low birth weight	5	12.5

TABLE 2
STRATIFICATION OF THROMBOCYTOPENIA BY AGE

Thrombocytopenia	Age		Total
	0-6 days	**7-28 days**	
Yes	29 (48.3%)	11 (12.2%)	40
No	31 (51.7%)	79 (87.8%)	110
Total	60	90	150

P-value: <0.001

TABLE 3
STRATIFICATION OF THROMBOCYTOPENIA BY SEX

Thrombocytopenia	Sex		Total
	Male	**Female**	
Yes	20 (31.7%)	20 (23%)	40
No	43 (68.3%)	67 (77%)	110
Total	63	87	150

P-value: 0.15

TABLE 4:
STRATIFICATION THROMBOCYTOPENIA BY GESTATIONAL AGE

Thrombocytopenia	Gestational age		Total
	<37 weeks	**≥37 weeks**	
Yes	22 (33.8%)	18 (21.2%)	40
No	43 (66.2%)	67 (78.8%)	110
Total	65	85	150

P-value: 0.05

TABLE 5:
STRATIFICATION THROMBOCYTOPENIA BY BIRTH WEIGHT

Thrombocytopenia	Weight		Total
	<2.5 kg	**≥2.5 kg**	
Yes	22 (24.4%)	18 (30%)	40
No	68 (75.6%)	42 (70%)	110
Total	90	60	150

P-value: 0.28

The prevalence of thrombocytopenia in neonates is ranges from 1–5%.[19] In neonates admitted to neonatal intensive care units, thrombocytopenia was observed 22–35% of all admissions, with the rate increasing as gestational age decreases.[28, 20, 21, 22.] The majority of neonates have mild or moderate thrombocytopenia. However, 5–10% have severe thrombocytopenia at birth (platelets <50 x 109/L) and require urgent investigation and prompt treatment.[22] Thrombocytopenia which presents after the first 3 days of life is due to sepsis in >80% of cases.[28] By contrast, sepsis is an uncommon cause of early neonatal thrombocytopenia, in the first 3 days of life.

The most frequent cause of early-onset thrombocytopenia is birth asphyxia [29, 22] This form of thrombocytopenia is usually mild or moderate and it is self-limiting, resolving within 10 days in the majority of cases.[29, 22] The mechanism of thrombocytopenia is reduced megakaryopoies.[28, 29] In this study, the frequency of neonatal thrombocytopenia was 26.7%, of which 57.5% had mild, 32.5% moderate and 10% severe thrombocytopenia. Similarly Aman et al reported the that 24.1% neonates had thrombocytopenia.[5] The prevalence of neonatal thrombocytopenia in this study therefore seems high when compared with studies from other places.[24, 25] The major mechanism underlying neonatal thrombocytopenia, has been attributed to impaired platelet production, while increased platelet consumption and/or sequestration accounts for the remainder of cases.[26]

In this study, birth asphyxia (APGAR score <7) was seen as the most common provisional diagnosis, accounting for 32.5% cases. Similarly, Jeremiah ZA et al reported 33.3% of neonatal thrombocytopenia attributed to birth asphyxia.[3] This is due to hypoxic injury to fetal megakaryocytes, which cause the progenitor cell to be driven toward the erythroid series at the expense of leucocytes and platelets[25]. The second most common diagnosis among the neonates in this study was neonatal jaundice, accounting for 20% cases, followed by neonatal sepsis (17.5%) and 12.5% due to low birth weight. Jaundice may also have been due to sepsis in some neonates, but their blood culture was negative. More than 80% of neonates with proven infections become thrombocytopenic. These infections may be bacterial, fungal, or viral.[25] By the time bacterial infection is diagnosed, 25% of neonates will already have low platelet counts. By the next 36–48 hours, virtually all will be thrombocytopenic.[26] The average duration of bacterial infection-mediated thrombocytopenia has been reported to be 6 days[27].

Bacterial sepsis also causes thrombocytopenia by disseminated intravascular coagulation (DIC), immune-mediated destruction, platelet aggregation due to bacterial products adhering to platelet membrane and decreased platelet production.[24] Viral infections in the perinatal period cause severe thrombocytopenia as a result of sialic acid loss from platelet membranes due to viral neuraminidase, intravascular platelet aggregation, and decreased production from the degeneration of megakaryocytes.[24, 25] Neonatal sepsis may contribute largely to the cause of severe thrombocytopenia in this region.[27]

CONCLUSION

In this study, the overall frequency of neonatal thrombocytopenia was found to be 40 (26.7%).More than 57.5% had mild thrombocytopenia, 13 (32.5%) had moderate and 4 (10%) had severe thrombocytopenia. Regarding the underlying causes of thrombocytopenia, 32.5% had birth asphyxia, 20% neonatal jaundice, 17.5% neonatal sepsis and 12.5% had low birth weight Thrombocytopenia was more common in neonates of <7 days (48.3%), in males (31.7%) , in neonates of<37 weeks gestation than in normal birth weight (30%).

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PROFORMA

Date……. Hospital Reg. No:…… S.No:…….

B/O.———————————-

Age of baby:……..(hour/days)

Gender: Male ( ) Female ( )

Gestational Age:……

Admission birth weight…….(kg)

APGAR Score <7 Yes ( ) No ( )

Pattern:.

A…Birth asphyxia Yes ( ) No ( )

B…Neonatal Jaundice Yes ( ) No ( )

C…Neonatal sepsis Yes ( ) No ( )

D…Low Birth weight Yes ( ) No ( )

Labs:

Platelet count:

Thrombocytopenia Yes ( ) No ( )

Blood C/S_____ Positive ( ) Negative ( )

PROFORMA

Date……. Hospital Reg. No:…… S.No:…….

B/O.———————————-

Age of baby:……..(hour/days)

Gender: Male ( ) Female ( )

Gestational Age:……

Admission birth weight…….(kg)

APGAR Score <7 Yes ( ) No ( )

Pattern:.

A…Birth asphyxia Yes ( ) No ( )

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C…Neonatal sepsis Yes ( ) No ( )

D…Low Birth weight Yes ( ) No ( )

Labs:

Platelet count:

Thrombocytopenia Yes ( ) No ( )

Blood C/S_____ Positive ( ) Negative ( )