Original Article

Etiology and Outcome of Thrombocytopenia in Sick Neonates

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ABSTRACT

Objective: Enlist risk factors of thrombocytopenia in sick neonates and determine the outcome in sick neonates with thrombocytopenia in relation to risk factors.

Study Design: Descriptive multi center case series study

Place and Duration of Study: This study was conducted at the Pediatric Ward Teaching Hospital, D.G.Khan and Pediatric Unit-I, Nishtar Hospital, Multan from June 2019 to November 2019,

Materials and Methods: A total of 100 sick neonates with thrombocytopenia were included in the study. Neonates with different risk factors like neonatal sepsis, birth asphyxia, prematurity,RDS, NEC and (jaundice, infant of diabetic mother) were evaluated and were included in the study

Results: Among 100 cases with thrombocytopenia (platelets count< 150,000/ul) were included in this study. Out of 100 cases, 35(35%) were found to have early-onset thrombocytopenia and 65 cases (65%) were found to have late-onset thrombocytopenia. 23(67.4%) were with early-onset sepsis and 20 cases (46.5%) were late-onset sepsis. Out of 100 cases, 17(17%) cases were of birth asphyxia, 11 cases were of prematurity with gestational age <37 weeks and birth weight<2.5 kg, 6 cases of prematurity (54.5%) were with hemorrhagic skin manifestation and remaining were with occult mild thrombocytopenia. 20 cases of RDS with thrombocytopenia, 5 cases of NEC with thrombocytopenia and 4 cases with mild thrombocytopenia. The common manifestations in thrombocytopenic cases were petechiae and bruises followed by gastrointestinal hemorrhage.

Conclusion: The leading causes of thrombocytopenia in sick neonates are sepsis, asphyxia, prematurity, RDS,NEC. Apart from the platelets counts the bleeding manifestations also depend upon underlying ailments.

Key Words: Neonatal Sepsis, Neonatal mortality, Thrombocytopenia and other basic investigations.

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INTRODUCTION

Platelets are non-nucleated cellular fragments in blood and play an important role in homeostasis[1]. The life span of platelets in 10-14 days. Normal platelet count in a newborn is 150,000-450,000/ul[1,2,3]. Thrombocytopenia is defined as platelet count less than 150,000/ul[1,2]. Thrombocytopenia is classified into mild, moderate and severe form[3,4] . Mild thrombocytopenia (100,00-150,000/ul) is associated with risk of bleeding. Moderate thrombocytopenia (50,000-100,000/ul) can cause spontaneous bleeding but usually doesn't cause serious bleeding. Severe thrombocytopenia (platelets less than 50,000) can cause spontaneous serious bleeding[3,4](ertheroblastosis fetalis)[1,3,6,7]. Most episodes are mild to moderate and resolve spontaneously[3].

Thrombocytopenia presenting after 72 hrs of life is usually secondary to sepsis, necrotizing enterocolitis, hemolytic uremic syndrome, disseminated intravascular coagulation and associated with more severe and prolonged bleeding[1,3,6,7].

Depending on the stage of the disease, common presentations are[3] pain in 66%, weight loss in 59%, jaundice in 51% and right upper quadrant mass in 40% patients (mostly the tumor is discovered). Thrombocytopenia is seen in 1-2% of healthy term babies but is more common in preterm babies[5] . Ten to twenty percent of babies develop neurodevelopment problems due to intracranial hemorrhage (ICH). Neonatal autoimmune thrombocytopenia occurs in about 10% of the cases and risk of ICH in these babies is 1%.

Neonatal thrombocytopenia presenting in first 72 hrs of life is usually due to placental insufficiency, small for gestational age, acidosis, early-onset neonatal sepsis, congenital infections, autoimmune (idiopathic thrombocytopenic purpra), drugs and iso-immune (neonatal allo-immume). A total of hundred sick neonates with thrombocytopenia admitted with

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different problems were selected. Neonates with different risks factors were evaluated which were of neonatal sepsis, birth asphyxia & prematurity.

Thrombocytopenia is frequent in neonates and not diagnosed due to no manifestations of clinical symptoms[5]. Neonatal thrombocytopenia is a common clinical problem in Neonatal Intensive care unit (NICU). Thrombocytopenia is a significant cause of morbidity and mortality in the sick preterm and full-term babies. Multiple mechanisms can cause or contribute to the development of thrombocytopenia, including decreased platelets production, increased platelets removal from the circulation and sequestration of platelets in spleen[6]. Thrombocytopenia is an important cause of active bleeding in sick neonates. Prognosis of thrombocytopenia depends upon the cause, severity and duration of thrombocytopenia with the overall mortality rate of 40% [6]. Early detection and proper management of thrombocytopenia reduces the frequency of morbidity and mortality. With the help of this study we shall be able to determine the more common and fatal causes of thrombocytopenia in neonates and to target the preventive strategies towards more common and dangerous causes of thrombocytopenia like RDS, NEC and others (jaundice, infant of diabetic mother).

MATERIALS AND METHODS

This descriptive case series study was conducted for a period of 6 months In both cases mild hrombocytopenia resolved spontaneously without any complications.

The most common manifestations in thrombocytopenic infants were petechiae and bruises followed by gastrointestinal hemorrhages (malena, chocolate color aspirate and mucosal bleeding). Out of 43 cases of sepsis, only 30 cases (69.7%) had bleeding manifestation and 4 had bleeding due to DIC. Out of 17 cases of birth asphyxia, 7 cases (41.1%) had bleeding manifestations. Out of 31 cases of prematurity, 20 cases had RDS and 11 cases (55.0%) of which had bleeding manifestations, two of which due to DIC. Out of 31 cases of prematurity, 11 cases had mild to moderate thrombocytopenia, 6 cases (54.5%) had common cause of thrombocytopenia (43%). On the basis of clinical symptoms, signs and various laboratory tests, 43 cases out of 100 were found to have sepsis with thrombocytopenia. Sepsis was divided into early-onset sepsis (age <7 days) and late-onset sepsis (age>7 days).

Out of 100 cases, 2 cases of Rh incompatibility were studied. They developed mild thrombocytopenia after exchange transfusion. Mild thrombocytopenia detected in 2 cases of infant of diabetic mother admitted in NICU hadsk in manifestation (petechial hemorrhage).

RESULTS

A total 100 cases of sick neonates with thrombocytopenia were studied. Early-onset thrombocytopenia was seen in 35% of sick neonatespresenting with different risk factors during first 72 hours of life (<3 days of life). Late-onset thrombocytopenia was seen in 65% of the sick neonates who developed thrombocytopenia after 72 hours of life (>3 days of life), as shown in Table-I.

Out of 100 cases 32 sick neonates (32%) were with mild thrombocytopenia, 46 sick neonates (46%) were with moderate thrombocytopenia and 22 sick neonates (22%) were with severe thrombocytopenia as shown in table 2. At the time of admission out of 100 sick neonates, 35 sick neonates had age of <3 days and 65 sick neonates had age of >3 days, minimum age was 1 day and maximum age was 25 days (mean age 7.22$\pm$3.51). Both gender were included in the study, 58 were males and 42 were females. Minimum weight was 1.2 kg and maximum weight was 4.50 kg. Mean weight was 2.46 $\pm$ 0.84 kg.

The neonatal sepsis was the most common risk factor in this region.

All cases of necrotizing enterocolitis had bleeding manifestations either due to thrombocytopenia or due to DIC, the exact mechanism is not clear. Thus out of 100 patients with thrombocytopenia, 59 patients (59%) had bleeding manifestations, whereas 41 patients (41%) had occult thrombocytopenia with no clinical manifestations.

Table No. I: Onset of thrombocytopenia (n= 100)

Onset of thrombocytopenia	No of cases	% age
Early on set thrombo-cytopenia Age>3 days	35	35%
Late onset thrombocytopenia	65	65%

Table No.2: Severity of thrombocytopenia (N=100)

Platelets count	No of cases	Percentage
Mild	32	32%
Moderate	46	46%
Severe	22	22%

Table No.3: Risk Factor of Thrombocytopenia (N=100)

Risk Factors	No. of cases	Percentage
Sepsis	43	43%
Birth asphyxia	17	17%
RDS	20	20%
NEC	05	05%
Preterm	11	11%
IDM	02	02%
Jaundice	02	02%
Total	100	100%

RDS= respiratory distress syndrome NEC= Necrotizing Enterocolitis

IDM= Infant of diabetic mother.

A total number of 100 sick neonates with thrombocytopenia, 35 sick neonates were with early-

onset and 65 sick neonates with late-onset thrombocytopenia. Out of 100 cases, 68 neonates (68%) survived. The recovered neonates were clinically and vitally stable, taking and tolerating orally and platelets count > 150,000/ul. A total of 30 cases with different risk factors with thrombocytopenia recovered.

Table No.4: Onset of sepsis in neonates (N=43)

Onset	No.of cases	Pt with sepsis	Percentage
Early sepsis	43	23	53.5%
Late sepsis	43	20	46.5%

Table No.5: Mortality rate with sepsis(N=43)

Onset	No.of cases	Pt with sepsis	Percentage
Early sepsis	23	10	43.4%
Late sepsis	20	07	35.0%

Table No. 6: Hemorrhagic Manifestation in Thrombo-Cytopenia INFANTS (N=100)

Risk of factor	No.of cases	Hem	%age
SEPSIS	43	30	69.76%
ASPHYXIA	17	07	41.17%
RDS	20	11	55.00%
NEC	05	05	100.0%
PRETERM	11	06	54.54%
IDM	02	00	00%
JAUNDICE	02	00	00%

DISCUSSION

In Pakistan, the neonatal mortality is 40 per thousand live births. Neonatal thrombocytopenia is an important contributor in infant mortality rate. Neonatal thrombocytopenia is life threatening condition and is associated with predisposing risk factors like sepsis, birth asphyxia, RDS, NEC and prematurity and contributes in increasing the frequency of thrombocytopenic sick neonates than the neonates without thrombocytopenia. Thrombocytopenia developed in 22-35% of all neonates admitted to NICU and 50% of those who required intensive care. Early diagnosis and appropriate use of antimicrobial therapy (in sepsis, NEC) with other supportive measures and platelet infusion can reverse this situation. Even a slight delay in the treatment may cause high morbidity and mortality.

In literature, similar studies as of my have been reported with variable incidence of thrombocytopenia. In a prospective study of 807 by Castle and colleagues, 22% incidence of thrombocytopenia has been reported[13]. In another study, the incidence was founded to 20-40% of all the admissions to NICU. According to D-George, the incidence of thrombocytopenia ranges as high as 1% or more for a healthy term infant to 22% of the newborns admitted to NICU. In my study, the neonatal sepsis was the most common cause of thrombocytopenia. Out of 100 cases, 43 cases with sepsis, 17 cases with birth asphyxia, 20 cases with RDS, 5 cases with NEC, 11 cases of prematurity and 2 cases of jaundice and IDM of each having mild, moderate to severe thrombocytopenia. These result are comparable with the study conducted by Tahir Masood Ahmad and colleagues at Jinnah Hospital, Lahore from September 1997 to February 1998[5]. The platelet counts were found to be low in 40.78% of the total cases of sepsis. These figures are quite comparable to a study conducted in NICU of Jinnah hospital, Lahore in 1998 on the usefulness of laboratory predictors in early diagnosis of neonatal sepsis. In this study the thrombocytopenia was found in 50% of the cases of sepsis. While another study showed the incidence of thrombocytopenia to be 62.5% in proved cases of sepsis. This shows that infection is the leading cause of thrombocytopenia in infants and children. In most of the cases, the thrombocytopenia is attributed to either megakaryocytic suppression, increased peripheral consumption or due to destruction such as aggregation, lysis and DIC.

Neonatal asphyxia has also an association with thrombocytopenia. In asphyxia, the widespread damage to the vascular endothelium and increased utilization of the platelets are the likely explanations of thrombocytopenia. However, according to Castle and his colleagues, the precise pathogenic mechanism for thrombocytopenia of sick neonates in the newborn period remains unclear. In my study, preterms (11%) with no other complications had mild thrombocytopenia. Gladder and Buchanan in 1976 suggested that the platelets counts in term and preterm infants are the same as in older children having a range of 150,000-400,000/mm. In my study, the majority of patients with prematurity had complications like respiratory distress syndrome and necrotizing enterocolitis, with moderate to severe thrombocytopenia. Exchange transfusion to prevent kernicterus in hyperbilirubinemic states is also seen as the cause of thrombocytopenia. This complication was also documented in a study of 203 exchange transfusions performed, in 143 infants the complications after the exchange transfusion were bradycardia, apnea, thrombocytopenia, hypoglycemia and hyponatremia. In a study conducted by Castle V and Andrew M et al observed the severity of thrombocytopenia in infants, and found out that there was mild thrombocytopenia in 42%, moderate in 38% and severe in 20%[8]. In my study approximately same results are observed (mild 32%, moderate 46% and severe 22%).

Considering the manifestations of thrombocytopenia in our study, most of the cases with low platelet count had petechiae and bruises and some of the infants had GIT hemorrhage. It has been seen that hemorrhagic problems do not occur in all the cases of

thrombocytopenia. Regarding the outcome in relation to the risk factors causing thrombocytopenia in sick neonates, no data is available in term of improved/ recovered. Several studies show that mortality is more in thrombocytopenic sick neonates than non-thrombocytopenic sick neonates. Outcome in relation to risk factors also depends on the severity of the disease and age of the sick neonates. Sepsis is leading cause of morbidity and mortality among other risk factors. The exact cause of death is not clear either infant died due to the disease, its complications or due to thrombocytopenia.

CONCLUSION

Thrombocytopenia is not an uncommon finding in the sick neonates under various circumstances. The leading cause of thrombocytopenia in sick neonates is bacterial septicemia. Low platelet counts can occur in any condition leading to hypoxia, acidosis, tissue necrosis and endothelial injury as it happens in respiratory distress syndrome, perinatal asphyxia and necrotizing enterocolitis.

Author's Contribution:

Concept & Design of Study:	Shakeel Ahmad
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