A Cross-Sectional Observational Study on Neonatal Thrombocytopenia in a Teaching Hospital in Telangana

Rajesh Khanna Pulmamidi[1], Ramya Madhuri Yendamuri[2]

[1]Department of Paediatrics, MediCiti Institute of Medical Sciences, Medchal, Telangana, India. [2]Department of Paediatrics, Gandhi Medical College, Secunderabad, Telangana, India.

ABSTRACT

BACKGROUND

Neonatal thrombocytopenia is one of the most common haematological abnormalities in neonates occurring in 1 to 2 % of healthy term neonates. Various risk factors like sepsis, prematurity, and birth asphyxia are known to be associated with this condition. Maternal factors also predispose to this condition. Early detection and appropriate management is of utmost importance to prevent complications. The aim of the study is to evaluate the predisposing factors for neonatal thrombocytopenia in a teaching hospital.

METHODS

This was a cross sectional observational study done in the Department of Peadiatrics, MediCiti Institute of Medical Sciences, Medchal, Telangana, for a duration of one year i.e., from January 2019 to December 2019. A total of 60 neonates with thrombocytopenia were studied for onset of thrombocytopenia, severity based on platelet counts, aetiology and for contributing maternal factors.

RESULTS

Early onset thrombocytopenia (< 3 days of age) was seen in 46.6 % (28 / 60) and late onset thrombocytopenia (3 - 28 days) in 53.3 % (32 / 60). The most common cause for neonatal thrombocytopenia was neonatal sepsis 30 % (10 / 60), followed by birth asphyxia. Common maternal predisposing factors were pregnancy-induced hypertension and pregnancy-induced diabetes mellitus.

CONCLUSIONS

Neonatal thrombocytopenia is one of the most common clinical problems in neonates. It can be of early or late onset type and has fetal and maternal predisposing factors. Neonatal sepsis is one of the most common cause for neonatal thrombocytopenia followed by birth asphyxia which is a preventable cause. Early diagnosis and thorough evaluation are needed to prevent complications.

KEYWORDS

Neonatal Thrombocytopenia, Neonatal Sepsis

Corresponding Author:
Dr. Ramya Madhuri Yendamuri,
Assistant Professor,
Department of Paediatrics,
Gandhi Medical College,
Secunderabad, Telangana, India.
E-mail: y.ramya14@gmail.com

DOI: 10.18410/jebmh/2021/65

How to Cite This Article:
Pulmamidi RK, Yendamuri RM. A Cross-sectional observational study on neonatal thrombocytopenia in a teaching hospital in Telangana. J Evid Based Med Healthc 2021;8(05):337-341. DOI: 10.18410/jebmh/2021/65

Submission 19-09-2020,
Peer Review 26-09-2020,
Acceptance 19-11-2020,
Published 08-02-2021.

BACKGROUND

Thrombocytopenia is seen in 22 - 35 % of all babies admitted to neonatal intensive care units (NICUs) and in up to 50 % of those admitted to NICUs who require intensive care. About 20 % of cases with thrombocytopeniaa are severe in nature and have an increased risk of haemorrhage. Haemorrhages are more common in preterm babies.[1,2,3]

Almost 1 - 5 % of newborns may have thrombocytopenia at birth. However, more severe thrombocytopenia usually occurs in only 0.1 - 0.5 % of cases.[4,5]

The term early onset thrombocytopenia is used when thrombocytopenia occurs within 72 hours after birth. It is seen in babies whose mothers had history of hypertension (pregnancy induced hypertension / PIH preeclampsia, eclampsia), maternal diabetes mellitus, insufficiency of placenta, various congenital infections, hypoxia in the perinatal period and immune mediated platelet destruction. Severe infection, perinatal asphyxia and disseminated intravascular coagulation (DIC) usually are associated with marked thrombocytopenia.[6,7,8]

The thrombocytopenia that is seen in preterm and intrauterine growth restricted (IUGR) newborns resolves spontaneously within ten days and is self-limited.[9]

The term late onset thrombocytopenia is used when thrombocytopenia occurs after 72 hours of birth. The most common predisposing factors are sepsis and necrotizing enterocolitis. It may also be caused by congenital infections of toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex (TORCH) group; medications and metabolic disorders. This type of thrombocytopenia is often severe. It has the risk of intraventricular haemorrhage and often necessitates platelet transfusion. It is somewhat prolonged and takes several weeks to recover.[10]

We wanted to study the predisposing factors for neonatal thrombocytopenia in a teaching hospital.

METHODS

This was a prospective, cross-sectional, observational study, conducted in the Department of Paediatrics at MediCiti Institute of Medical Sciences, Medchal, Telangana, over a period of one year from January 2019 to December 2019. There were no ethical issues involved in the study. Informed consent forms were obtained from mothers of the neonates with thrombocytopenia. A total of 60 cases of neonatal thrombocytopenia were included in the study.

A proforma was prepared for collection of neonatal data that included neonatal age, gender, gestational age, birth weight, weight on admission, 5-minute Apgar score, the time of passing meconium, reason for hospitalisation, blood group and direct coombs test (in relevant cases), time of initiation of breast feeding and frequency of breast feeding.

The proforma also contained information for collection of maternal data like antenatal history, antenatal registration, maternal age, parity, history of pregnancy-induced hypertension, bad obstetric history, premature rupture of membranes > 18 hours, diabetes mellitus, anaemia and human immunodeficiency virus (HIV) / hepatitis B surface antigen (HBsAg) status of mother, type of delivery, blood group with Rhesus (Rh) factor of mother.

The following investigations were done for all the neonates included in the study.

- Complete blood count
- Peripheral smear examination
- Platelet count
- Serum bilirubin levels

Grading of Thrombocytopenia

Reduced platelet count was classified as mild, moderate and severe thrombocytopenia.
Mild thrombocytopenia: 1 - < 1.5 lakh / µL
Moderate thrombocytopenia: 50,000 to < 1 lakh / µL
Severe thrombocytopenia: < 50,000 / µL

The pattern of onset of neonatal thrombocytopenia was classified as early onset if it developed < 72 hours of birth and late onset if presented after 72 hours. Platelet counts were repeated every 24 hours in babies with severe thrombocytopenia and every 48 hours in those with moderate thrombocytopenia. Total white blood count (WBC) count and differential leukocyte count was assessed in detail and features suggestive of sepsis were looked for. Micro erythrocyte sedimentation rate (ESR) and C reactive protein were done in all patients. If any two of the above mentioned were positive then the neonate was labeled as having septicemia. Maternal and neonatal risk factors were analysed with respect to severity of thrombocytopenia. The data was noted in Microsoft excel sheets for statistical analysis

RESULTS

A total of 60 cases of neonatal thrombocytopenia was studied. In the present study, 58.3 % (35 / 60) were males and 41.6 % (25 / 60) were females. In the present study, early onset thrombocytopenia (< 3 days of age) was seen in 46.6 % (28 / 60) and late onset thrombocytopenia (3 - 28 days) in 53.3 % (32 / 60) cases. In the present study, most of the cases 46.6 % (28 / 60) were of moderate thrombocytopenia.

In the present study, most common cause for neonatal thrombocytopenia was neonatal sepsis 30 % (10 / 60) followed by birth asphyxia which was seen in 18.3 % (11 / 60) cases.

In the present study, 46.6 % (28 / 60) presented with early and 53.3 % (32 / 60) presented with late onset thrombocytopenia respectively.

Gender Distribution	No. of Cases	Percentage (%)
Males	35	58.3 %
Females	25	41.6 %
Total	60	100 %

Table 1. Gender Distribution

Onset of Thrombocytopenia	No. of Cases	Percentage (%)
Early onset thrombocytopenia	28	46.6 %
Late onset thrombocytopenia	32	53.3 %
Total	60	100 %

Table 2. Onset of Thrombocytopenia

Grading of Neonatal Thrombocytopenia	No. of Cases	Percentage (%)
Mild thrombocytopenia (100,000 - 150,000 / cu mm)	12	20 %
Moderate thrombocytopenia (50,000 - 100,000 / cu mm)	28	46.6 %
Severe thrombocytopenia (less than 50,000 / cu mm)	20	33.3 %
Total	**60**	**100 %**

Table 3. Grading of Neonatal Thrombocytopenia

Etiology	No. of Cases	Percentage (%)
Prematurity	10	16.6 %
Neonatal sepsis	18	30 %
Meconium aspiration syndrome	04	6.6 %
Birth asphyxia	11	18.3 %
Respiratory distress syndrome	05	8.3 %
Jaundice	08	13.3 %
Intrauterine growth retardation	02	3.3 %
Metabolic syndrome	02	3.3 %
Total	**60**	**100 %**

Table 4. Aetiological Distribution

	Early Onset (N = 28)			Late Onset (N = 32)		
Aetiology	**Mild**	**Moderate**	**Severe**	**Mild**	**Moderate**	**Severe**
Prematurity (10)	01	03	01	01	02	02
Neonatal sepsis (18)	01	02	01	02	05	07
Meconium aspiration syndrome (4)	01	01	01	01		
Birth asphyxia (11)	01	06	01	-	01	02
Respiratory distress syndrome (5)	01	02	01	-		01
Jaundice (8)	-	02	-	02	02	02
Intrauterine growth retardation (2)	-	02	-	-	-	
Metabolic syndrome (2)	-	-	-	01	-	01
Total	**05 (8.3 %)**	**18 (30 %)**	**05 (8.3 %)**	**07 (11.6 %)**	**10 (16.6 %)**	**15 (25 %)**

Table 5. Aetiological Distribution Based on The Time of Onset of Thrombocytopenia

Maternal Factors	No. of Cases	Percentage (%)
PIH	35	58.3 %
Diabetes mellitus	10	16.6 %
PIH + diabetes	10	16.6 %
Eclampsia.	05	8.3 %
Total	**60**	**100 %**

Table 6. Maternal Factors

PIH: Pregnancy-induced hypertension.

Neonates	No. of Cases	Percentage (%)
Preterm	10	16.6 %
Term	50	83.3 %
Total	**60**	**100 %**

Table 7. Distribution of Thrombocytopenia Based on Gestation

In the present study, PIH and diabetes mellitus were the most common maternal findings. Thrombocytopenia was more commonly seen in term new-borns than in preterm births.

DISCUSSION

In our study, we had a sample size of 60 cases of neonatal thrombocytopenia as a result of various aetiological factors. Tirupathi K et al.[8] in a similar study evaluated 200 newborns with thrombocytopenia and Nandyal et al.[9] in their study had 99 neonates with thrombocytopenia.

In our study, there were 58.3 % (35 / 60) males and 41.6 % (25 / 60) female babies. Similar findings were observed by Tirupathi K et al.[8] where there were 112 (56 %) male babies and 88 (44 %) female newborns. Eslami Z et al.[10] observed 34 (40 %) male and 51 (60 %) female babies with thrombocytopenia. Our findings can be compared with the above studies.

Comparing the gestational age, in the present study, thrombocytopenia was present in 50 (83.3 %) of term neonates and in 10 (83.3 %) of preterm neonates. Our findings are contrary to that of Eslami Z et al.[10] where thrombocytopenia was present in 56 (65.9 %) of preterm and 29 (34.1 %) of term neonates.

The onset of thrombocytopenia is very important and depends upon the aetiology. In the present study, 46.6 % (28 / 60) cases presented with early onset thrombocytopenia and 53.3 % (32 / 60) cases presented with late onset thrombocytopenia. In the study by Eslami Z et al.[10] 64 (75.3 %) patients had early onset and 21 (24.7 %) cases had late onset of thrombocytopenia. In a similar study by Sharma A et al.[11] early onset thrombocytopenia (< 3 days of age) was seen in 51 % and late onset thrombocytopenia (3 - 28 days) was encountered in 49 % cases.

Grading of thrombocytopenia is important as it has treatment implications and also more the severity, more the chances of complications and mortality. In the present study, mild thrombocytopenia was observed in 20 % (12 / 60) neonates, moderate thrombocytopenia in 46.6 % (28 / 60) and severe thrombocytopenia in 33.3 % (20 / 60) cases.

In the study by Sharma A et al.,[11] mild thrombocytopenia was observed in 16.4 % neonates, moderate and severe thrombocytopenia was seen in 36.4 % and 47.5 % cases respectively.

Nandyal et al.[9] observed relatively less number of cases with mild and moderate thrombocytopenia and found them in 17.1 % of neonates each, while severe thrombocytopenia was seen in 65.6 % of cases. In Eslami Z et al. study[10] 42 (49.4 %) of patients had mild and 40 (47.1 %) had moderate and 3 (3.5 %) of the neonates had severe thrombocytopenia.

The aetiology can be varied for neonatal thrombocytopenia. In the present study, most common cause for neonatal thrombocytopenia was neonatal sepsis and was seen in 30 % (10 / 60) cases. Next common cause was birth asphyxia which was seen in 18.3 % (11 / 60) cases and 16.6 % (10 / 60) had prematurity. Meconium aspiration syndrome was seen in 6.6 % (04 / 60) cases. Respiratory distress syndrome was seen in 8.3 % cases, intrauterine growth restriction was seen in 3.3 % cases and metabolic syndrome was seen in 3.3 % cases. Our observations could be compared well with findings of Tirupathi K et al study.[8] where sepsis was the most common cause of neonatal thrombocytopenia and was found in 48.5 % babies. Birth asphyxia was present in 20 %, RDS (respiratory distress syndrome) in 7 %, neonatal hyperbilirubinemia in 19.5 % and meconium aspiration syndrome in 5 % cases. Sepsis was associated with severe neonatal thrombocytopenia and it was statistically significant in their study. In the study by Eslami Z et al.[10] in the early onset thrombocytopenia patients, 28.8 % of neonates had sepsis, 23.1 % IUGR, 17.3 % asphyxia, 3.8 % IUGR and sepsis, 9.6 % IUGR and asphyxia, 1.9 % sepsis and asphyxia, and 1.9 % had ABO

incompatibility. None of them had necrotizing enterocolitis (NEC) and 13.5 % had other aetiology. In the late onset group of patients, 40 % had sepsis, 15 % IUGR, 5 % asphyxia, 10 % ABO incompatibility, 10 % NEC, and 20 % had other aetiology.

Nandyal et al.[9] in their study observed the most common causes of neonatal thrombocytopenia as prematurity (38.3 %) followed by neonatal sepsis (22.2 %) and respiratory distress syndrome (14.1 %). Why thrombocytopenia occurs in neonatal sepsis is not clearly understood but it is thought that the sepsis leads to endothelial damage which in turn activates the reticuloendothelial system and hastens the clearing or removal of platelets. As platelets are consumed at a faster rate than production, it eventually leads to thrombocytopenia.

Maternal risk factors predisposing to neonatal thrombocytopenia are well known. In the present study, among maternal risk factors 58.3 % (35 / 60) of mothers had hypertension, 16.6 % (10 / 60) had diabetes mellitus, 16.6 % (10 / 60) had both hypertension and diabetes mellitus and 8.3 % (05 / 60) had eclampsia. These observations were consistent with findings of Tirupathi K et al. study[8] where pregnancy induced hypertension was the commonest associated maternal risk factor. In their study, 27 (13.5 %) neonates had PIH as a maternal risk factor followed by preterm prelabour rupture of membranes (PROM) in 15 (7.5 %) cases, anaemia in 11 (5.5 %) neonates, oligohydramnios in 8 (4 %) and eclampsia in 6 (3 %) cases. In the study by Eslami Z et al.[10] in the mild thrombocytopenia group of neonates; 46.7 % of mothers had hypertension, 33.3 % had diabetes mellitus, 13.3 % had hypertension & diabetes mellitus and 6.7 % had eclampsia. In neonates with moderate thrombocytopenia; 60 % of mothers had hypertension, 20 % had diabetes mellitus, 10 % had hypertension and diabetes and 10 % had eclampsia. In neonates with severe thrombocytopenia; 66.7 % of mothers had diabetes and 33.3 % had immune mediated thrombocytopenia / idiopathic thrombocytopenic purpura (ITP).

The pathogenesis for neonatal thrombocytopenia in preeclampsia is not well understood. Robert and Murray proposed that preeclampsia and the accompanying fetal hypoxia directly depress the bone marrow megakaryopoiesis and platelet production.[12]

Castle et al. have reported that the thrombocytopenia could be due to combination of impaired megakaryopoiesis and accentuated platelet activation mediated through cytokines, thrombopoietin and interleukin-6.[13]

Ree et al.[14] in their study concluded that thrombocytopenia is independently associated with maternal hypertension, intravascular thrombosis and gram-negative sepsis. Thrombocytopenia in neonatal sepsis has an increased risk of mortality by four-fold and when the sepsis is gram negative type then the risk of mortality increases by six-fold.

CONCLUSIONS

Neonatal thrombocytopenia is one of the most common clinical problems in neonates. It can be of early or late onset type and has fetal and maternal predisposing factors. Neonatal sepsis is one of the most common cause for neonatal thrombocytopenia followed by birth asphyxia which is a preventable cause. Early diagnosis and thorough evaluation are needed to prevent complications.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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