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Causes, Severity and Outcome of Neonatal Thrombocytopenia in Hi-Tech Medical College and Hospital, Bhubaneswar

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Abstract:-

Background: Thrombocytopenia (platelet count<1,50,000cells/cu.mm) is the most challenging haematological disorder in Neonatal Intensive Care Units(NICU).1 to 5% is the prevalence of thrombocytopenia in neonatesand it is in higher side neonates admitted to NICUs (18 to 35%). It should not be ignored without consideration of its causes. Multiple diseases can cause neonatal thrombocytopenia like sepsis, birth asphyxia, prematurity, IUGR(intra-uterine growth retardation), NNHB (hyperbilirubinemia), RDS(respiratory distress syndrome),MAS(meconium aspiration syndrome) and LBW(low birthweight).

Objective: The objective were to study the causes, severity and outcome of thrombocytopenia in neonates admitted to Neonatal Intensive Care Unit in Hi-Tech Medical College and hospital,Bhubaneswar.

Method: Prospective randomized controlled trial was done in NICU at Hi-Tech Medical College and Hospital, Bhubaneswar from September 2019 to August 2021. 100 neonates with or developed neonatal thrombocytopenia were involved during study.

Result: In this study, out of 100 neonates with thrombocytopenia- 46%(mild thrombocytopenia), 35%(moderate thrombocytopenia) and 19%(severe thrombocytopenia). 51% had(<72hr)early onset neonatal thrombocytopenia and 49% had(>72hr)late onsetneonatal thrombocytopenia. Anaemia was the most common risk factor found in mother. Sepsis was found to be commonest cause of thrombocytopenia in neonates. Apnea was the most common symptom. Sepsis, Respiratory Distress Syndrome (RDS) and Necrotising Enterocolitis(NEC) were the cause of mortality.Sepsis was thecommonest cause of death followed by RDS and NEC.

Conclusion: In neonates, thrombocytopenia is a treatable condition. It shouid identify the neonates at risk and initiate platelet therapy or IVIG to prevent bleeding in neonates and morbidity. The commonest maternal risk factors wereAnaemia and Premature ruptureof membrane(PROM). Hence, close monitoring needed if a baby born to mother with additional risk factor.

Keyword:- *Neonatal Thrombocytopenia, Sepsis, Maternal Anemia, Respiratory Distress Syndrome.*

I. INTRODUCTION

The most common haematological problems in Neonatal intensive care units (NICUs) is thrombocytopenia (platelet count <1,50,000cells/cumm).).1 to 5% is the prevalence of thrombocytopenia in neonatesand it is in higher side neonates admitted to Neonatal Intensive Care units(18 to 35%)[1] It is more common in ELBW baby(<1000 gms birth weight) orGA <36 weeks(preterm) or sick neonates in NICUs.1 In contrast, Severe thrombocytopenia (platelet count <50,000cells/cumm) occurring in less than 3/1000 term infants i.e. only 2% of normal neonates.[2]Thrombocytopenia in neonates can be classified as early onset(<72hours) and late onset(>72 hours) neonatal thrombocytopenia.[3]Sepsis, birth asphyxia(BA), prematurity, intra-uterine growth retardation(IUGR), hyperbilirubinemia(NNHB), respiratory distress syndrome(RDS), meconium aspiration syndrome(MAS) and low birth weight(LBW) are the important causes of thrombocytopenia in neonates. Bleeding in neonates depend on underlying causes apart from total platelet count.[4] Platelets are small anuclear cellular fragments which formed from megakaryocytes progenitor cells and then released to blood stream[5.] There aremany studies have shown that by 2nd trimester of pregnancy, the average fetal platelet count is above 150,000cells/cumm and remain constant then represents thrombocytopenia. Neonatal thrombocytopenia are classified into mild NT(>1,00,000cells/cumm and <1.50,000cells/cumm), moderate NT (>50,000cells/cumm) and severe NT (<50,000 cells/cumm).[1,2]

II. METHODS

This prospective study covered,100 neonates with or developed neonatal thrombocytopenia randomly selected in the Neonatal intensive care unit (NICU) at Hi-Tech Medical College and Hospital, Bhubaneswar from September 2019 to August 2020. At admission, the parents or guardian were informed about the study, A detailed history of mother, obstetric and neonatal history with a focus on history of bleeding and its type in the new born or the mother was obtained. Maternal risk factor like age of mother, parity, pregnancy induced hypertension , any chronic disorder (ITP, SLE, chronicinfection, malignancy), intake of any drugs during pregnancy(NSAID, Quinine, Heparin); Perinatal risk factor like number of birth order,IVF,GA in weeks, birth weight (SGA,IUGR, Placental vascular abnormalities),APGAR score at1,5and 10min; Neonatal

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factor like gender, onset of sepsis, NEC, Ventricular haemorrhage, TORC Hinfection, Birth asphyxia, IEM, Hemolytic disease of Newborn(HDN),chromosomal abnormalities, myeloproliferative disorder, neonatal alloimmune thrombocytopenia and mortality data were collected.

All the neonates were advised for blood investigations like Comlete Blood Count, peripheral blood smear and sepsis screening. Peripheral smear study were repeated withLow platelet count neonates.The difference between platelet counts at onset and recovery was measured. The time to onset of thrombocytopenia and duration of recovery was measured.

Platelet counts were repeated, neonates with severe thrombocytopenia every 24 hourly and neonates with moderate thrombocytopenia in every 48 hourly. Prothrombin Time and aPTT were also collected. Other investigations like culture of urine, chest X-ray, neuro imaging and CT scan of brain were done whenever needed.

The data were collected with consent of parents and enterd in a case proforma sheet.Students t-test,chi square test was used for statistical analysis. Statistical analysis was done by SPSS software and 'P' value less than 0.05 was considered as significant.

III. RESULT

The study was conducted on 100 neonates with thrombocytopenia admitted in the NICU of Hi-Tech Medical College and Hospital, Bhubaneswar and subjects were divided into 3 categories based on their platelet counts.(Table 1)

Categories	Severity	N=100	Percentage
Category 1	Mild thrombocytopenia (1-<1.5 lac cells/cumm)	46 neonates	46%
Category 2	Moderatethrmbocytopenia (50,000-<1 lac cells/cumm)	35 neonates	35%
Category 3	Severe thrombocytopenia(<50,000cells/cumm)	19 neonates	19%

Table 1: Distribution of neonates based on severity of thrombocytopenia

Anaemia was the most common maternal risk factor which was present in 48 neonates(48%) followed by PROM in 30neonates (30%), PIH in 19 neonates (19%), oligohydramniosin 2 neonates (2%) and eclampsia in 2 (2%) neonates.Severe neonatal thrombocytopenia was found to be associated with anaemia and statisticaly significant having p value less than 0.05(Table 2).

Nearly 51neonates (51%) had early onset neonatal thrombocytopenia and 49 neonates(49%) had late onset neonatal thrombocytopenia.

Maternal factor		Category 1	Category 2	Category 3	Total	X^2 value	P value
PIH	Yes	09	09	01	19	3.3644	0.1859
	No	37	26	18	81		
Eclampsia	Yes	0	2	0	2		
	No	46	33	19	98		
PROM	Yes	11	10	9	30	3.574	0.1673
	No	35	25	10	70		
Anemia	Yes	26	11	11	48	5.9944	<0.05
	No	20	24	8	52		
Oligohydrominos	Yes	1	1	0	2		
	No	45	34	19	98		

Table 2: Distribution of babies according to maternal risk factors

53 neonates(53%) were found neonatal thrombocytopenia due to sepsis which is most common cause of thrombocytopenia in neonates. Respiratory distress (RDS) in 15 neonates (15%), Birth asphyxia(BA) was present in 11neonates (11%) , Meconium aspiration Syndrome(MAS) in 10 (10%) neonates, neonatal hyperbilirubinemia(NNHB) in 6 (6%) neonates and Necrotising Enterocolitis (NEC) in 5 (5%)neonates. Severe neonatal thrombocytopenia was significantly associated with sepsis in NICU and P valueaws 0.0001. 36neonates (67.92%) had late onset thrombocytopenia andP value was 0.00003(statistically significant)out of 53 babies with sepsis(Table 3).

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Etiology		Category 1	Category 2	Category 3	Total	X^2 Value	P value
Sepsis	Yes	14	24	15	53	17.94	0.0001
	No	32	11	4	47		
Birth Asphyxia	Yes	7	3	1	11	1.6853	0.4305
	No	39	32	18	89		
RDS	Yes	13	2	0	15		
	No	33	33	19	85		
Neonatal Hyperbilirubinemia	Yes	4	1	1	6	1.223	0.5422
	No	42	34	18	94		
MAS	Yes	7	3	0	10		
	No	49	32	19	90		
NEC	Yes	01	02	02	05	2.03	0.361
	No	45	33	17	95		

Table 3: Distribution of babies according to their Etiology

Apnoea was the commonest symptom of thrombocytopenia in 28neonates (28%) followed by lethargy in 24neonates (24%), difficulty in feeding in 23neonates (23%) and Seizure in 20 (20%) neonates. All the above symptoms were mostly found in moderate to severe neonatal thrombocytopenia. Severe thrombocytopenia (47.37%)categorywas associated with high mortality as compared to two other categories and statistically it wasinsignificant (p value 0.2286). Late onset neonatal thrombocytopenia (40.82%)category was associated with high mortality as compared to early onset neonatal thrombocytopenia (27.45%)category which was statistically insignificant. Death occurred in NICU was 34 neonates due to sepsis in 23neonates (67.64%) which was significantly high followed by Necrotisingenterocolitis (8.82%) in 3neonates, Respiratory distress syndrome (8.82%) in 3 neonates, Meconium aspiration syndrome (5.88%) in 2 neonates, birth asphyxia(5.88%) in 2neonates and NNHB (2.9%) in one neonate. Mortality was significantly high due to sepsis (Table 4).

Etiology	**Number of cases**	**Number of Deaths**	**Percentage**
Sepsis	53 neonates	23 neonates	67.64%
Birth Asphyxia(BA)	11 neonates	2 neonates	5.88%
Respiratory Distress syndrome(RDS)	15 neonates	3 neonates	8.82%
Neonatal Hyper bilirubinemia(NNHB)	6 neonates	1 neonates	2.9%
Meconium Aspiration Syndrome(MAS)	10 neonates	2 neonates	5.88%
Necrotising Enterocolitis(NEC)	5 neonates	3 neonates	8.82%

Table 4: Correlation of Etilogy and Outcome

IV. DISCUSSION

Neonatal thrombocytopenia (platelet count <1.5 cells/cumm) is the common haematological disorder encountered in NICU. It should be detect and managed properly to prevent neonatal complications.

The severity of neonatal thrombocytopenia in this study was 46% in mild,35% in moderate and 19% in severe . The studies conducted by Ghamdi AM et al, and KhalessiN et al had similar result.[7,8] The prevalence of moderate and sever thrombocytopenia was high in this study due to higher proportion of septicemic neonates in the NICU of Hitech Medical college which is a tertiary care centre.

Anaemia was the most common maternal risk factor in this study. 48% mother had anaemia which associated with moderate to severe neonatal thrombocytopenia. Other maternal risk factors were PROM(30%), PIH(19%), oligohydramnios(2%) and eclampsia(2%) and were associated with severe thrombocytopenia. Severe neonatal thrombocytopenia was associated with anaemia and statistically it was significant (P value <0.05) among all maternal risk factors. Associationof anaemia with thrombocytopeniahas been documented by a study ofTirupath K et al. Early onset neonatal sepsis were associated with PROMwhich leads to neonatal thrombocytopenia.[14]

The commonest cause of neonatal thrombocytopenia was sepsis among neonatal risk factor(53% neonates). Similar studies conducted byGupta A et al, andBasil M et al, sepsis was associated with neonatal thrombocytopenia.[3,16]Thrombocytopenia due to sepsis occurred by both decreased production and increased destruction of platelets and results in severe thrombocytopenia in neonates.

Respiratory Distress Syndrome(RDS) was present in 15% neonates, birth asphyxia(BA) was in 11%,Meconium Aspiration Syndrome(MAS) in 10% and neonatal hyper bilirubinemia(NNHB) in 6% neonates. Mild to moderate thrombocytopenia was associated with Birth asphyxia and similar studies was conducted byGupta A et al, andNandyal SS et al.[3,4]

Late onset thrombocytopenia associated with sepsis and Early onset neonatal thrombocytopeniawas associated withbirth asphyxia in this study.

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The overall mortality was 34% among the thrombocytopenic neonates in this study.Mortality was high(40.82%)in this study and significantly higher in late onset neonatal thrombocytopenia group but it was not significantstatistically.

Death occurred in NICU was 34 neonates due to sepsis in 23neonates (67.64%) which was significantly high followed by Necrotisingenterocolit is (8.82%) in 3neonates, Respiratory distress syndrome (8.82%) in 3 neonates, Meconium aspiration syndrome (5.88%) in 2 neonates, birth asphyxia(5.88%) in 2neonates and NNHB (2.9%) in one neonate. Mortality was significantly high due to sepsis.

V. CONCLUSION

In neonates, thrombocytopenia is a treatable condition. It should identify neonates at risk and initiate platelet therapy or IVIG to prevent severe bleeding and morbidity. Moderate to severe type of neonatal thrombocytopenia was present in the NICU. Neonates having Late onset neonatal thrombocytopenia was more common than early onset neonatal thrombocytopenia.Preterm neonates had severe thrombocytopenia whereas term neonates had moderate thrombocytopenia.Low birth weight(LBW) neonates were more prone to severe thrombocytopenia than term babies. The commonest maternal risk factors wereanaemia and PROM . Hence, we recommendedforclose monitoring, if a baby born to mother with additional risk factor for thrombocytopenia.

The common factors associated with thrombocytopenia in neonates were neonatal Sepsis and Respiratory distress syndrome. Sepsis was associated with late onset neonatal thrombocytopenia and RDS was associated with early onset neonatal thrombocytopenia. Apnea was the most common symptom. Cutaneous bleeding (petechiae/purpura) was the most common sign.High mortality in neonates was associated with severe neonatal thrombocytopenia and in neonates with early onset neonatal thrombocytopenia. Sepsis and birth asphyxia(BA) was the common etiology of hrombocytopenia in neonates.

In NICUs for sick neonates, severe thrombocytopenia can be used as a prognostic indicator. But more studies are required for causes, severity and outcome in neonatal thrombocytopenia with similar results.

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