Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

"INCIDENCE AND CLINICO ETIOLOICAL PROFILE OF THROMBOCYTOPENIA IN NEONATES IN TERITARY HOSPITAL GGH,GUNTUR".

Dr.B.Ramesh Kumar, DrShaik Karimulla, Dr.P.Brahmaiah, Dr.A.Deepak Kumar, Dr.K Vanibai, Dr.K. Prudhvi Krishna, Dr.K Swetha, Dr.Sk Haroon Rasheed Shaik

Associate's Profesor Of Pediatrics Guntur Medical College, Guntur,
Assistant Professor , Guntur Medical College , Guntur,
Assistant Professor , Government Medical College, Eluru,
Associate Professor Of Pediatrics, Government Medical College , Eluru,
Asst professor of pediatrics GMC GUNTUR,
Asst professor of pediatrics GMC GUNTUR,
Asst professor of pediatrics GMC GUNTUR.
Junior Resident In Pediatrics, Guntur Medical College, Guntur

ABSTRACT ;Thrombocytopenia is a common problem in NICU .there are so many causes of thrombocytopenias , in this study we are evaluating clinical and etilogies of thrombocytopenias. The incidence of thrombocytopenia in this study was 43%.In our study, out of the 28 cases of early onset thrombocytopenia, the leading cause was culture proven sepsis seen in 43.9 % of cases followed by 31.8 % cases having birth asphyxia , 15.15% of cases were born to mothers having preeclampsia and 9 % of cases were IUGR neonates.Out of the 15 cases of late onset thrombocytopenia , 62.2% of cases were having c sepsis and 26.6 %of cases having meconium aspiration syndrome , 8% cases having birth asphyxia and 0% cases having Rh incompatibility.Maternal risk factors like pregnancy induced hypertension and maternal

Keywords: Thrombocytopenia, Neonates,Preterm,Sepsis.

Review of literature

Schematically, there are four main processes involved in the production of thrombopoietic factors, **a**) primarily thrombopoietin [Tpo], **b)** the proliferation of megakaryocyte (MK) progenitors, **c)** the differentiation and maturation of MKs through a specific process of endomitosis and cytoplasmic changes, and **d)** the production and release of platelets into the circulation.

Despite the fact that thrombocytopenic newborns often have lower Tpo concentrations than adults with same mechanisms of thrombocytopenia, healthy fullterm and preterm neonates have higher Tpo concentrations in response to thrombopoietic stimulation than healthy adults.Numerous studies have demonstrated that MK progenitors multiply more rapidly in fo etuses and newborns than in adults.

Causes of thrombocytopenia

IMPARIED PLATELET PRODUCTION,

CONSUMPTION AND SEQUESTRATION OF PLATELETS

COMBINED MECHANISMS

IMPARIED PLATELET PRODUCTION

According to studies, decreased platelet generation is the main cause behind newborn thrombocytopenia. 75% of the time, low platelet counts are either present at birth or start to show up within the first 72 hours of life4. Only a small percentage of these patients suffer from immunological conditions or coagulopathies that lead to thrombocytopenia. Preterm neonates delivered during pregnancies complicated by placental insufficiency and/or foetal hypoxia, such as those involving maternal pre- eclampsia and foetal intrauterine growth restriction, make up the majority of the remaining patients.. Megakaryocytes and their precursor and progenitor cells are significantly decreased at birth in neonates with this early-onset thrombocytopenia, and as a result, levels of the megakaryocytopoietic cytokine thrombopoietin are raised. Megakaryocytopoiesis and platelet formation are also hampered. Tpo levels in neonates are lower in thrombocytopenic neonates than in children or adults, especially in tiny for gestational age newborns. In comparison to those of children or adults, they produce colonies with more megakaryocytes and may be more responsive to Tpo stimulation. Neonatal megakaryocytes are smaller and have decreased ploidy, yet they still have mature-looking cytoplasm5. Finally, the Tpo action prevents neonatal megakaryocyte polyploidization. Due to the higher proliferative capacity of their megakaryocyte progenitors, neonates maintain normal platelet levels.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

CONSUMPTION AND SEQUESTRATION OF PLATELETSAbout 25–35% of newborn thrombocytopenias are caused by increased platelet consumption and/or sequestration. The transmission of maternal platelet alloantibodies and autoantibodies through the placenta causes 15-20% of neonatal thrombocytopenias to be present at delivery.
An additional 10-15% of cases—almost invariably in babies who are extremely ill and frequently in conjunction with infection and prenatal asphyxia—are attributable to intravascular coagulation. Another example of newborn thrombocytopenias primarily brought on by platelet consumption is thrombosis or platelet activation/immobilization at sites of inflammation, such as the gut during necrotizing enterocolitis (NEC) or in haemangiomas. Additionally, there is proof that ill neonates experience little platelet sequestration in the spleen

CONSUMPTION AND SEQUESTRATION OF PLATELETS
About 25–35% of newborn thrombocytopenias are caused by increased platelet consumption and/or sequestration. The transmission of maternal platelet alloantibodies and autoantibodies through the placenta causes 15-20% of neonatal thrombocytopenias to be present at delivery.
An additional 10-15% of cases—almost invariably in babies who are extremely ill and frequently in conjunction with infection and prenatal asphyxia—are attributable to intravascular coagulation. Another example of newborn thrombocytopenias primarily brought on by platelet consumption is thrombosis or platelet activation/immobilization at sites of inflammation, such as the gut during necrotizing enterocolitis (NEC) or in haemangiomas. Additionally, there is proof that ill neonates experience little platelet sequestration in the spleen.

COMBINED MECHANISMS
Placental insufficiency, which can occur in newborns born to mothers who have foetalgrowth restriction (FGR) or diabetes during pregnancy, as well as in those who have pregnancy induced hypertension/preeclampsia, is the most common cause of mild to moderate, early onset thrombocytopenia in a well-appearing neonate8. In fact, it is likely that the majority of newborns who develop thrombocytopenia do so because their unfavourable foetal environment impairs megakaryocytopoiesis at birth, and that the baby is predisposed for thrombocytopenia to get worse when exposed to concurrent neonatal platelet consumptive "stress." Additionally, the typical course of thrombocytopenia in sepsisand NEC (fast onset, rapid progression, sluggish recovery over five to seven days) shows that Platelet consumption (rapid initiation phase), followed by poor platelet synthesis (delayed recovery phase), are likely the combined factors that lead to it.
PLATELET COUNT AND RISK OF BLEEDING
However, this range of platelet count comes from a limited number of small sample studies of healthy newborns. A study from Circulating platelets have a typical volume between 7 and 9 fL and are around 1/5th the diameter of a red blood cell. With a half-life of 7 to 10 days, platelets only remain in the circulation for a very little period of time. Their major job is to protect the vascular endothelium from damage and to limit bleeding after small-vessel injury by forming tiny aggregates or plugs in the microcirculation. When platelets are insufficient in number or function, bleeding tends to occur. In babies and young children, a typical platelet count is thought to range between 150,000 to 450,000/mcL. The lower limit of platelet ranges from neonates at various gestational ages during their first 90 days after birth was reported by 18 hospitals in the United States using data from more than 47,000 neonates as 123,000/mm3 in late preterm and term neonates and 104,000/mm3 in infants born at less than 32 weeks' gestation6. A platelet count below 150,000/mm3 should always be read in the context of the clinical circumstances, regardless of whether it is considered abnormal. The quantity of platelets in the bloodstream directly relates to bleeding propensity. Platelet levels between 20,000 and 100,000/mm3 are associated with a minimum or mild risk of bleeding, whereas platelet counts below 20,000/mm3 are associated with a significant risk of bleeding. The relationship between platelet count and bleeding in neonates has not been demonstrated. Clinicians should take action based on this platelet count to stop bleeding in the NICU since the trauma and stress of childbirth can, albeit infrequently, cause intracranial or internal bleeding. For premature newborns, this threshold seems to be higher. Preterm newborns will frequently have platelet transfusions when their platelet count is 50,000/mm37. However, there is limited proof that this strategy will stop intracranial bleeding (ICH).It is necessary to conduct prospective research to determine the safest and most economical threshold for transfusing premature newborns. Mucocutaneous haemorrhage occurs when there is moderate to severe thrombocytopenia. Low platelet counts are characterised by petechiae, bruising, or bleeding from the mucous membranes. In the neonate, thrombocytopenia may also result in intraventricular haemorrhage or cerebral bleeding

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

Approach to thrombocytopenia

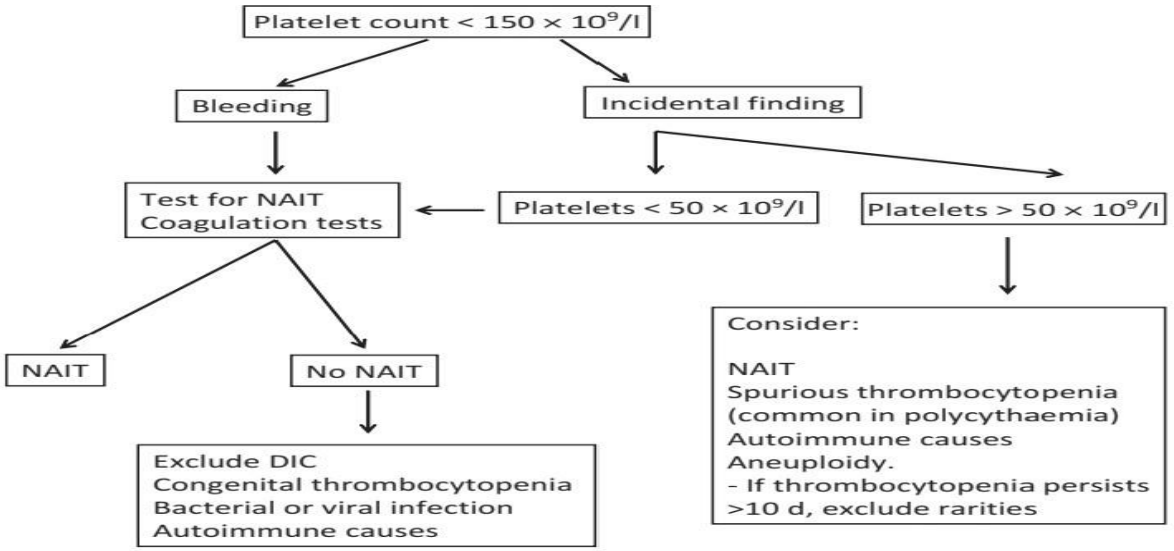

Fig 2. Diagnostic algorithm for investigation of term neonates with thrombocytopenia. NAIT, neonatal alloimmune thrombocytopenia; DIC, disseminated intravascular coagulation.

It may be congental or acquired , may be early onset sepsis or lte onset of sepsis, it may be coagulopathy or immune thrombocytopenia or non immune thrombocytopenia .to evaluate and identify the cause we have to follow the algorhythm.

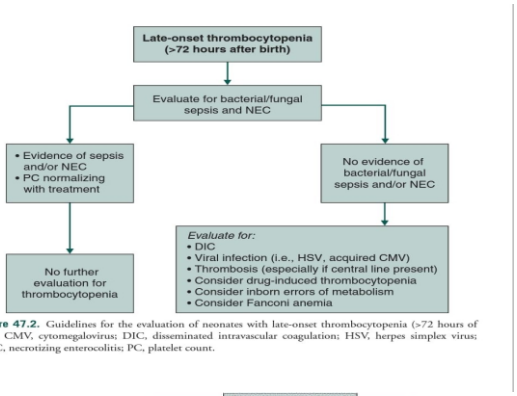

Figure 47.2. Guidelines for the evaluation of neonates with late-onset thrombocytopenia (>72 hours of life). CMV, cytomegalovirus; DIC, disseminated intravascular coagulation; HSV, herpes simplex virus; NEC, necrotizing enterocolitis; PC, platelet count.

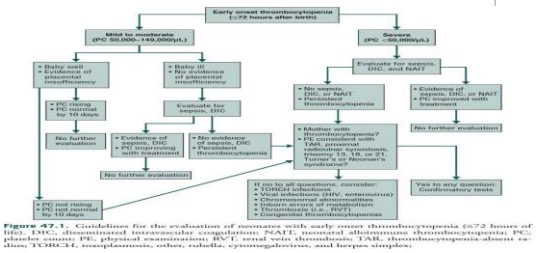

Figure 47.1. Guidelines for the evaluation of neonates with early-onset thrombocytopenia (≤72 hours of life). DIC, disseminated intravascular coagulation; NAIT, neonatal alloimmune thrombocytopenia; PC, platelet count; PE, physical examination; RVT, renal vein thrombosis; TAR, thrombocytopenia-absent radius; TORCH, toxoplasmosis, other, rubella, cytomegalovirus, and herpes simplex.

Management

Patelet transffusion is the main stay of treatment if counts less than 50000 irrespective of gestational age and bleeding manifaestations ,dose being 10-15ml of platelt cocentrate and utmost care to be taken to not to develop transfusion induced infections and development of TRALI nd also measures were taken not to develop GVHD by minimising the number of transfusions. but if the new born have bleeding manufestations we can transfuse platelets , VitK, FFP as and when required . and also we can give hemopoeitic growth factors ,TPo, IL-11 though it is given rarely.

Matrilas & methods .

In this study sample size calculated as per the incidence of of thrombocytopenia ,2 x (p) x (1 – p) C2

SS = Sample Size Z = Z-value

(e.g., 1.96 for a 95 percent confidence level) P = prevalence in the population

C = Confidence interval, expressed as decimal (e.g., .05 = +/- 5 percentage points) N =100

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

Inclusion criteria

Neonates which were admitted on day one of life to NICU of Government General Hospital ,Guntur.

Exclusion criteria

Neonates that succumbed to death within 72 hours of admission.

Neonates who got discharged before 72 hours of admission.Sampling method

Simple random sampling. type of the study,Prospective explorative hospital based study.

METHODOLOGY

WE CONVINIENTLY classify the new borns in to 2 categories 1high risk.2.low risk

High risk

The newborns in this group included those with suspected or proven sepsis (proven on culture), significant birth asphyxia (Apgar score 0-3 at 1 minute of life), intrauterine growth restriction (IUGR) (10th centile for GA), extreme low birth weight (ELBW) (birth weight 1000 g), and newborns whose mothers had a known condition that caused thrombocytopenia (Rh isoimmunization)

Low risk

Babies with low birth weight (LBW) (babies weighing between 1,500 and 2,500 g), babies with moderate birth asphyxia (Apgar scores 4- 6 at 1 minute of life), preterms with a primary diagnosis of respiratory distress syndrome, babies with meconium aspiration syndrome without significant birth asphyxia or IUGR, and neonates weighing more than 1,000 g but less than 1,500 g.

Collection of Blood Samples.blood sample is collected from the babies on day 1 and whenever symptomatic and day 3 in EDTA sample and sent it for analysis.

STATISTICAL METHODS

Descriptive statistics , Contigency table analysis and Chi square test were used for statistical analysis and p value <0.05 was taken as statistically significant using SPSS software version 20.0

RESULTS

In this study , 100 neonates admitted to our NICU were studied and the study results were analysed with appropriate statistical methods and compared with previous studies.

Table 1Distribution according to gestational age and gender

Gestational Age	Male	Female	Total
28-32	9 (45%)	11(55%)	20
33-36	13 (59.1%)	9 (40.9%)	22
>37	30 (51.7%)	28 (48.3%)	58
Total	52 (52%)	48 (48%)	100
Chi square value= 0.838 P value= 0.658			

Table 2 Incidence and severity of thrombocytopenia

SEVERITY	Frequency	Percent
No thrombocytopenia	0	0
MILD	85	85.0
MODERATE	7	7.0
SEVERE	8	8.0
Total	100	100.0
Chi square value= 29.58 P value= <0.001		

Table 3 Onset of thrombocytopenia in the study according to

ONSET	Frequency	Percent
Early	28	28.0
Late	15	15.0
NO	57	57.0
Total	100	100.0
Chi square value= 0.838 **P value= 0.157**		

Table 4Severity of thrombocytopenia gestational age

Gestational Age	MILD	MODERATE	SEVERE	Total
28-32	10 (50%)	3 (15%)	7 (35%)	20
33-36	19 (86.4%)	2 (9.1%)	1 (4.5%)	22
>37	56 (96.6%)	2 (3.4%)	0 (0%)	58
Total	85 (85%)	7 (7%)	8 (8%)	100

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

Chi square value= 30.002 P value= <0.001

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

Table5 Distribution of thrombocytopenia and thrombocytopenia in relation to its severity according to weight

Birth Weight Kg	Mild	Moderate	Severe	Total
<0.9	0 (0%)	0 (0%)	1(100%)	1
1-1.49	40 (93%)	3 (7%)	0 (0%)	43
1.5-2.49	5 (38.5%)	2 (15.4%)	6 (46.2%)	13
>2.5	40 (93%)	2 (4.7%)	1 (2.3%)	43
Total	85 (85%)	7 (7%)	8 (8%)	100
Chi square value= 45.9 P value= <0.001**				

Table 6 Incidence and severity of maternal PIH

PIH	Mild	Moderate	Severe	Total
Yes	10 (66.7%)	0	5 (33.3%)	15
No	75 (88.2%)	7 (8.2%)	3 (3.5%)	85
Total	85 (85%)	7 (7%)	8 (8%)	100
Chi square value= 16.09 P value= <0.001**				

Table no 7: birth asphyxia – stages of hypoxiaic isvhemia encephalopathy and neonatal thrombocytopenia

	Mild	*Moderate*	*Severe*	*Total*
No birth Asphyxia	*72 (83.7%)*	*6 (7%)*	*8 (9.3%)*	*86*
HIE I	*9 (100%)*	*0*	*0*	*9*
HIE II	*3 (75%)*	*1 (25%)*	*0*	*4*
HIE III	*1 (100%)*	*0*	*0*	*1 (100%)*
Total	85 (85%)	7 (7%)	8 (8%)	*100*
Chi square value= 16.09 *P value= <0.001***				

Table 8 Respiratory distress syndrome and neonatal thrombocytopenia.

Respiratory distress syndrome	*Mild*	*Moderate*	*Severe*	*Total*
Present	*17 (65.4%)*	*2 (7.7%)*	*7 (26.9%)*	*26*
Absent	*68 (91.9%)*	*5 (6.8%)*	*1 (1.4%)*	*74*
Total	85 (85%)	7 (7%)	8 (8%)	*100*
Chi square value= 17.34 *P value= <0.001*				

Table 9 Gestational age and culture positive sepsis.

Gestational Age (weeks)	*No growth*	*Klebsiella Sps*	*CONS*	*Citrobacter Sps*	*Candida albicans*	*E coli*	*Total*	
28- 32	*11 (55%)*	*4 (20%)*	*3 (15%)*	*1 (5%)*	*0*	*1(5%)*	*20*	
33- 36	*18 (81.8%)*	*0*	*0*	*0*	*2 (9.1%)*	*2(9%)*	*22*	
>37	*56 (96.5%)*	*1 (1.7%)*	*0*	*0*	*0*	*1(1.7%)*	*58*	
Total	*85 (85%)*	*5 (5%)*	*3 (3%)*	*1 (1%)*	*2 (2%)*	*4 (4%)*	*100*	
Chi square value= 48.42 *value= <0.001***								

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

Table10 Culture positive sepsis and neonatal thrombocytopenia

Blood culture	*Mild*	*Moderate*	*Severe*	*Total*
Positive	*2 (13.3%)*	*6 (4%)*	*7 (46.6%)*	*15*
Negative	*83 (97.6%)*	*1 (1.1%)*	*1 (1.1%)*	*85*
Total	85 (85%)	7 (7%)	8 (8%)	*100*
Chi square value= 71.09				
*value= <0.001***				

Table 11 Distribution of thrombocytopenia and its severity in low and high risk and its severity

Risk	*Mild*	*Moderate*	*Severe*	*Total*
High	*0*	*5 (38.5%)*	*8 (61.5%)*	*13*
Low	*85 (97.7%)*	*2 (2.3%)*	*0*	*87*
Total	85 (85%)	7 (7%)	8 (8%)	*100*
Chi square value= 87.6				
*P value= <0.001***				

DISCUSSION

Thrombocytopenia is one of the most common haematological abnormalities seen in the NICU but can be missed if not specifically looked for. Several studies have reported thrombocytopenia in 22–35% in all infants admitted to the neonatal intensive care unit . The basic mechanisms include decreased platelet production , increased consumption and sequestration and combined mechanisms.In our study a total of 100 neonates admitted to the NICU selected randomly ,meeting the criteria were included. Neonates were divided in two risk groups- high risk and low risk depending upon the presentation, maternal history and any antenatal/perinatal events. Platelet counts were done on the first, third and fifth day of admission and thereafter every 72 hours till counts were normal. The incidence of thrombocytopenia was studied along with the clinico-etiological profile. The clinical course and outcome of newborns with severe thrombocytopenia was also studied. The incidence of thrombocytopenia in this study was 43%.Severe thrombocytopenia was seen in 8%of thrombocytopenic babies and Mild thrombocytopenia was seen in 85% of thrombocytopenic neonates and moderate thrombocytopenia was seen in 7%. The study done by Gupta A et al (2011) had the incidence of thrombocytopenia of 70.5%. Severe thrombocytopenia accounted for 34.4% of cases while mild to moderate thrombocytopenia accounted for in 66.5% cases. In the study conducted by Zaccheaus et al (2010) the overall prevalence of neonatal thrombocytopenia was 53.0%. Mild thrombocytopenia was found in 39.4%of the neonates, 12.1% had moderate thrombocytopenia , while severe thrombocytopenia was detected in 1.5% of the neonates. In the study conducted by Bonifacio(2007) , they found thrombocytopenia (67%) of cases and was mild in 12.8 %, moderate in 36.2 % and severe in 51 % of the cases.The results of our study were comparable to the other studies Incidence and severity of thrombocytopenia in different studies Thrombocytopenia Mild ModerateSevere

Maternal PIH and neonatal thrombocytopenia In our study total of 15(15%) cases have maternal risk factor as PIH out of which 10(66.7%) cases have mild thrombocytopenia and 5 (33.3%)cases have severe thrombocytopenia and the difference being statistically significant (p <0.001) In study done by Bhat R et all (2008), they had 36.1% prevalence of thrombocytopenia in neonates born to mother having PIH. Out of which 20.6% was severe.In study conducted by Sivakumar S et al (2006),

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

thrombocytopenia was in 22% of 64cases of neonates born to mothers with PIH and 9 % were severe. P<0.02. Maternal PIH and neonatal thrombocytopenia in various studies. Thrombocytopenia severe p-value in maternal PIHthrombocytopenia
We had a higher incidence of thrombocytopenia in neonates born to mothers with PIH when compared to the other studies.
Birth asphyxia and neonatal thrombocytopenia
In our study we had 28% of patients with birth asphyxia had thrombocytopenia of which 0% had severe thrombocytopenia .
In the study conducted by Christensen RD et al (2015), thrombocytopenia was seen in 31 % of neonates with asphyxia.

In study conducted by Nadkarni J (2012) , 25.07% of neonates with asphyxia developed thrombocytopenia, out of which 67.7% had severe birth asphyxia(p<0.0001). Mild thrombocytopenia was seen in 12.5 %, moderate in 16.6% and severe in 2.08%.65 Birth asphyxia and neonatal thrombocytopenia in various studies Thrombocytopenia severe p-value thrombocytopenia Our study 28%
In our study incidence of thrombocytopenia in Asphyxiated newborns is nearly same as previous studies
Neonatal sepsis and thrombocytopenia
In our study we had a total of 15culture positive sepsis cases. Out of which 100% of cases having thrombocytopenia which was significant (p<0.001) Neonatal sepsis and thrombocytopenia in other studies Culture positive mild moderate severe total p-value
Sepsis Our study 13.3% 40% 46.7% 100% p<0.001 Charoo B A et al 27 % 20% 12.5% 59.5% Organism specific response to thrombocytopenia In neonates having culture proven sepsis, 25%grew Klebsiella pneumonia, 15%grew coagulase negative staphylococcus , 9.1% of cases had candida albicans, 5% grew citrobacter sps and 15.7% of neonates having E. coli sepsis.
In a similar study conducted by Charoo B A et al (2009) showed 62.5% having Klebsiella sepsis, CONS in 10.5% of cases 3 % cases of having fungal growth and the rest having mixed growth in blood culture. In our study incidence of thrombocytopenia was highest in neonates with klebsiella and fungal sepsis. In the study conducted by Charoo B A et al,103 fungal sepsis had the highest incidence of thrombocytopenia . Organism specific response to thrombocytopenia
0Necrotising enterocolitis and thrombocytopenia
In our study , all cases of necrotizing enterocolitis had thrombocytopenia out of which 12.5% had mild thrombocytopenia , 25 % had moderate thrombocytopenia and 62.5% had severe thrombocytopenia which was significant(p <0.001) In study conducted by Charoo B A et al , in neonates with NEC , 5 % had mild thrombocytopenia , 47 % had moderate thrombocytopenia , 35 % had severe thrombocytopenia and rest did not have thrombocytopenia (p<0.001). The association between necrotizing enterocolitis and thrombocytopenia is known and our study re- emphasizes the same.
Prematurity and neonatal thrombocytopenia
Out of 44 preterms included in our study , 44 % had thrombocytopenia and 18.1% having severe thrombocytopenia and the incidence and severity of thrombocytopenia increasing with decreasing gestational age.Neonatal patients with severe and moderate thrombocytopenia usually hadlower gestational ages and birth weights, according to a 2007 study by Bonafacio L.The development of NEC and sepsis, particularly that brought on by a Candida infection, were linked to serious thrombocytopenic events. Lower gestational age wassignificantly related with the development of IVH, but not with the severity or age at
which thrombocytopenia first appeared.
Intrauterine growth retardation and neonatal thrombocytopenia

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

In our study 62 % of neonates with intrauterine growth retardation have 68thrombocytopenia, out of these thrombocytopenic neonates , 18.18 % have severethrombocytopenia. There is no significant difference in the severity of thrombocytopenia and intra uterine growth restricted neonates .In study conducted by Maruyama H (2008), shows significant increase in theincidence of thrombocytopenia in IUGR neonates. (p<0.0001Respiratory distress syndrome and neonatal thrombocytopenia

In our study 26%of neonates with RDS had thrombocytopenia , out of which 26.9% had severe thrombocytopenia which was significant (p<0.001)In a earlier study conducted by Kohelet D , severity of RDS was correlated to the platelet counts and they demonstrated statistically that decreased oxygenation exerted a unique influence on the change in platelet counts in the early neonatal days.Neonatal thrombocytopenia and bleeding manifestations In our study 50% of patient having severe thrombocytopenia had bleeding manifestations in the form of gasrointestinal hemorrhage in 75%and intraventricular hemorrhage in 25% .In the study conducted by Stanworth S et al (2012) , found bleeding manifestations in 13 % of cases with severe thrombocytopenia with 53% of

them having IVH,26 % having pulmonary bleeding and 11 % having renal involvement.

Platelet transfusion and Outcome in severe thrombocytopenia

In our study 11 cases are transfused with platelets out of which 6 (54.4%)expired and 5 (45.5%)survived.

Etiological profile of neonatal thrombocytopenia

Early onset thrombocytopenia

In our study out of the 28 cases of early onset thrombocytopenia, sepsis was seen in 28.5%% of cases , followed by 21.4%% cases having birth asphyxia .21.4%of cases were born to mothers having PIH and and 10.7%of cases were IUGR neonates.

Late onset thrombocytopenia

In our study out of the 15 cases of late onset thrombocytopenia , 46.6%of cases had culture proven sepsis , cases having NEC and and of cases having meconium aspiration syndrome , 6.6%cases having birth asphyxia and cases having Rh incompatibility.In both groups , sepsis has been found to be the main risk factor for the development of thrombocytopenia with preterms significantly affected more than term neonates . (p<0.02) Several other studies by Sola et al96 , Roberts M et al97 , also have similar results

In the study conducted by Gupta et al , aetiological profile of thrombocytopenia included 34 % of cases with sepsis, 21.01 % of birth asphyxia , 20.2 % of extremely low birth weight infants , 17.39 % born to preeclamptic mothers and 13.7 % were intrauterine growth retarded.In our study , incidence of thrombocytopenia was higher in the high risk group (78.9%)which included neonates with culture proven sepsis ,IUGR , extremely low 70birth weight babies, severe birth asphyxia, maternal thrombocytopenia, when compared to the low risk group(21.1%) which statistically significant (p<0.001).Newborns with Rh isoimmunisation did not have statistically significant difference. We did not have neonates with congenital thrombocytopenic syndromes in our study.

Similar study done by Gupta A et al showed the overall incidence of thrombocytopenia was 70.5% (182/258). This was 93.7% (134/143) of the high-risk group and 41.7% (48/115) of the low-risk group . P < 0.05. Of all cases of thrombocytopenia 72% were late onset thrombocytopenia.

BIBLIOGRAPHY

1. Subarna Chakravorty, Neil Murray, Irene Robert Early human development 81 (1), 35-41, 2005

2. Liu ZJ, Italiano J, Ferrer-Marin F, et al. Developmental differences in megakaryocytopoiesis are associated with up-regulated TPO signaling through

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

mTOR and elevated GATA-1 levels in neonatal megakaryocytes, Blood, 2011, vol. 117 15(pg. 4106-4117)
3. Blumenau D, Lordier L, Di Stefano A, Chang Y, Raslova H, Debili N, Vainchenker W (2009) Regulation of megakaryocyte maturation and platelet formation. J Thromb Haemost 7(Suppl 1):227–234
4. Castle V, Andrew M, Kelton J, et al. Frequency and mechanism of neonatal thrombocytopenia. J Pediatr1986;108:749–55.
5. Murray NA, Roberts IAG. Circulating megakaryocytes and their progenitors in early thrombocytopenia in preterm neonates. Pediatr Res1996;40:112–19
6. SF Fustolo-Gunnink, K Fijnvandraat, H Putter, et al. Dynamic prediction of bleeding risk in thrombocytopenic preterm neonatesHaematologica, 104 (10) (2019), p. 208595
7. Strauss R, Wehler M, Mehler K, Kreutzer D, Koebnick C, Hahn EG: Thrombocytopenia in patients in the medical intensive care unit: bleeding prevalence, transfusion requirements, and outcome. Crit Care Med. 2002, 30: 1765-1771. 10.1097/00003246-200208000-00015
8. J Nadkarni, SK Patne, R Kispotta – Journal of clinical neonatology, 2012
9. Nandyal SS, Shashikala P, Sahgal V. Study of thrombocytopenia in neonatal intensive care unit. Indian J Pathol Oncol. 2016
10. Arnold, D.M., Smith, J.W. & Kelton, J.G. (2008) Diagnosis and management of neonatal alloimmune thrombocytopenia.Transfusion Medicine Reviews, 22, 255–267.
11. Bussel, J. (2009) Diagnosis and management of the fetus and neonate with alloimmune thrombocytopenia. Journal of Thrombosis and Haemostasis, 7(Suppl. 1), 253–257.
12. Bussel, J.B., Berkowitz, R.L., McFarland, J.G., Lynch, L. & Chitkara, U. (1988) Antenatal treatment of neonatal alloimmune thrombocytopenia. New England Journal of Medicine, 319, 1374–1378.13. Bussel, J.B., Berkowitz, R.L. & McFarland, J.G. (1997b) Maternal IVIG in neonatal alloimmune thrombocytopenia. British Journal of Haematology, 98, 493–494.
14. Bussel J, McFarland J, Berkowitz R. Antenatal management of fetal alloimmune and autoimmune thrombocytopenia. Transfus Med Rev 1990; 2: 49-62
15. Grosbois B, Le Gall E, Picaud JC, Poulain P, Bergeron C, Jacomy D, Grall JY, Leblay R. Traitement de la thrombopénie néonatale auto-immune par les immunoglobulines intraveineuses à fortes doses [Treatment of autoimmune neonatal thrombocytopenia with high-dose intravenous immunoglobulins]. Ann Med Interne (Paris). 1990;141(2):111-4. French. PMID: 2191612.
16. Autosomal dominant macrothrombocytopenia in Italy is most frequently a type of heterozygous Bernard-Soulier syndrome.Savoia A, Balduini CL, Savino M, Noris P, Del Vecchio M, Perrotta S, Belletti S, Poggi , Iolascon A Blood. 2001;97(5):1330.
17. A novel primary human immunodeficiency due to deficiency in the WASP interacting protein WIP. Lanzi G, Moratto D, Vairo D, Masneri S, Delmonte O, Paganini T, Parolini S, Tabellini G, Mazza C, Savoldi G, Montin D, Martino S, Tovo P, Pessach IM, Massaad MJ, Ramesh N, Porta F, Plebani A, Notarangelo LD, Geha RS, Giliani SJ Exp Med. 2012 Jan;209(1):29-34. Epub 2012 Jan 9.
18. X-linked thrombocytopenia (XLT) due to WAS mutations: clinical characteristics, long-term outcome, and treatment options. Albert MH, Bittner TC, Nonoyama S, Notarangelo LD, Burns S, Imai K, Espanol T, Fasth A, Pellier I, Strauss G, Morio T, Gathmann B, Noordzij JG, Fillat C, Hoenig M, Nathrath M, Meindl A, Pagel P, Wintergerst U, Fischer A, Thrasher AJ, Belohradsky BH, Ochs HD Blood. 2010;115(16):3231. Epub 2010 Feb 19
19. Fanconi anemia.Soulier J Hematology Am Soc Hematol Educ Program. 2011;2011:492-7.
20. GeneReviews: Thrombocytopenia Absent Radius syndrome http://www.ncbi.nlm.nih.gov/books/NBK23758/

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

21. Congenital amegakaryocytic thrombocytopenia: a retrospective clinical analysis of 20 patients.King S, Germeshausen M, Strauss G, Welte K, Ballmaier M Br J Haematol. 2005;131(5):636.
22. Kasabach-Merritt phenomenon Kasabach-Merritt phenomenon: a single centre experience.Ryan C, Price V, John P, Mahant S, Baruchel S, Brandão L, Blanchette V, Pope E, Weinstein MEur J Haematol. 2010 Feb;84(2):97-104. Epub 2009 Nov 03.
23. Disseminated intravascular coagulation in term and preterm neonates. Veldman A, Fischer D, Nold MF, Wong FY Semin Thromb Hemost. 2010;36(4):419
24. Nadkarni J, Patne SK, Kispotta R. Hypoxia as a predisposing factor for the development of early onset neonatal thrombocytopenia. Journal of clinical neonatology. 2012 Jul 1;1(3):131.
25. Arif SH, Ahmad I, Ali SM, Khan HM. Thrombocytopenia and bacterial sepsis in neonates. Indian Journal of Hematology and Blood Transfusion. 2012 Sep;28(3):147-51.
26. Ahmad MS, Waheed A. Platelet counts, MPV and PDW in culture proven and probable neonatal sepsis and association of platelet counts with mortality rate. J Coll Physicians Surg Pak. 2014 May 1;24(5):340-4.
27. Maheshwari A, Corbin LL, Schelonka RL. Neonatal Necrotizing Enterocolitis. Res Rep Neonatol. 2011;1:39-53
28. Patel CC. Hematologic abnormalities in acute necrotizing enterocolitis. Pediatr Clin North Am. 1977 Aug;24(3):579-84.
29. Tighe P, Rimsza LM, Christensen RD, Lew J, Sola MC. Severe thrombocytopenia in a neonate with congenital HIV infection. The Journal of pediatrics. 2005 Mar 1;146(3):408-13.
30. Sola-Visner M, Sallmon H, Brown R. New insights into the mechanisms of nonimmune thrombocytopenia in neonates. InSeminars in perinatology 2009 Feb 1 (Vol. 33, No. 1, pp. 43-51). WB Saunders.
31. Aslam M, Anderson JL, Guglietti D, Cardwell D. CMV-induced neonatal thrombocytopenia: a case report and review of the literature. American journal of perinatology. 2007 Aug;24(07):429-34.
32. Nogalski MT, Collins-McMillen D, Yurochko AD. Overview of human cytomegalovirus pathogenesis. InHuman cytomegaloviruses 2014 (pp. 15-28). Humana Press, Totowa, NJ.
33. Lake AM, Lauer BA, Clark JC, Wesenberg RL, McIntosh K. Enterovirus infections in neonates. The Journal of pediatrics. 1976 Nov 1;89(5):787-91.
34. Emmons RV, Reid DM, Cohen RL, Meng G , Young NS , Dunbar CE et al. Human thrombopoietin levels are high when thrombocytopenia is due to megakaryocyte deficiency and low when due to increased platelet destruction. Blood. 1996;87:4068–71.
35. Peck-Radosavljevic M, Wichlas M, Zacherl J, Steigler G, Stohlawetz P , Kreil A et al. Thrombopoietin induces rapid resolution of thrombocytopenia after orthotropic liver transplantation through increased platelet production. Blood. 2000;95:795–801.
36. Murray NA, Roberts IA. Circulating megakaryocytes and their progenitors (BFU-MK and CFU-MK) in term and pre-term neonates. Br J Haematol. 1995;89:41–6.
37. Saxonhouse MA, Christensen RD, Walker DM, Hutson AD , Sola MC et al. The concentration of circulating megakaryocyte progenitors in preterm neonates is a function of post-conceptional age. Early Hum Dev. 2004;78:119–24.
38. Ault KA, Rinder HM, Mitchell J, Carmody MB, Vary CP, Hilman RS . The significance of platelets with increased RNA content (reticulated platelets). A measure of the rate of thrombopoiesis. Am J Clin Pathol. 1992;98:637–46.
39. Saxonhouse MA, Sola MC, Pastos KM, Ignatz ME, Hutson AD, Christenson RD et. Al. Reticulated platelet percentages in term and preterm neonates. J Pediatr Hematol Oncol. 2004;26:797–802.
40. Kurata Y , Hayashi S, Kiyoi T, Kosugi S, Kashiwagi H, Honda S et al. Diagnostic value of tests for reticulated platelets, plasma glycocalicin, and thrombopoietin levels

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

for discriminating between hyperdestructive and hypoplastic thrombocytopenia. Am J Clin Pathol. 2001;115:656–64.
41. Baer VL, Lambert DK, Henry E, Snow GL, Christensen RD. Red blood cell transfusion of preterm neonates with a Grade 1 intraventricular hemorrhage is associated with extension to a Grade 3 or 4 hemorrhage. Transfusion. 2011;51(9):1933-1939.
42. Stanworth SJ, Clarke P, Watts T, Ballard S, Choo L, Morris T, et al. Prospective, observational study of outcomes in neonates with severe thrombocytopenia. Pediatrics. 2009;124(5):e826-e834.
43. Muthukumar P, Venkatesh V, Curley A, Kahan BC, Ballard S, Choo L et al. Severe thrombocytopenia and patterns of bleeding in neonates: Results from a prospective observational study and implications for use of platelet transfusions. Transfus Med. 2012 ;22(5):338-43
44. Andrew M, Vegh P, Caco VC, et al. A randomized, controlled trial of platelet transfusions in thrombocytopenic premature infants. J Pediatr 1993;123:285– 91.
45. Cremer M, Solar-Visner MC, Roll S, et al. Platelet transfusions in neonates: practices in the United States vary significantly from those in Austria, Germany, and Switzerland. Transfusion 2011;51(12):2634–2641.
46. Curley A. Platelet transfusion in the preterm infant: Results of the PlaNet-2/MATISSE Study. Transfus Clin Biol. 2019;26(3, Suppl):S24.
47. Albert TSE, Meng G, Simms P, et al. Thrombopoietin in the thrombocytopenic term and preterm newborn. Pediatrics 2000;105:1286–91.
48. Watts TL, Murray NA, Roberts IAG. Thrombopoietin in term and preterm babies with and without thrombocytopenia [abstract]. Blood 1997;90:141a.
49. Chang M, Williams A, Ishizawa L, et al. Endogenous interleukin-11 (IL-11) expression is increased and prophylactic use of exogenous IL-11 enhances platelet recovery and improves survival during thrombocytopenia associated with experimental group B sepsis in neonatal rats. Blood Cells Mol Dis 1996;22:57–67.
50. Claud E, Jackson M, Jilling T, et al. Interleukin-11 diminishes intestinal injury in a rat model of necrotizing enterocolitis [abstract]. Pediatr Res 2000;47:163