Thrombocytopenia Vs Thrombocytosis as a Predictor of Outcome in Neonatal Sepsis

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ABSTRACT

The objective of this study is to determine the incidence of thrombocytopenia and thrombocytosis in neonatal sepsis in NICU and to study them as a predictor of outcome in neonatal sepsis. This study was carried out in Neonatal Intensive Care Unit (NICU), Department of Pediatrics, M.L.B Medical College, Jhansi on 70 newborns admitted as neonatal sepsis in SNCU. The study showed that normal platelet count is observed in 26(37.1%) patients .Thrombocytopenia was found in 41(58.5%) cases out of total 70 cases of sepsis. Mild thrombocytopenia was seen in 8 (11.4%) cases, moderate in 18(25.7%) and severe thrombocytopenia in 15 (21.4%) cases in the study group. It is also observed that the neonatal sepsis is more common in babies having birth weight <2500gms (74.2%) as compared to babies with a birth weight ≥ 2500gms. Thrombocytosis was seen in only 3(4.28%) patients. The thrombocytopenia was more commonly seen in culture proven cases of neonatal sepsis. Also thrombocytopenia is more common in preterm neonates and in low birth weight babies. It can be concluded that the neonatal sepsis is more common in preterm babies (<37wks) than the term babies (≥37wks) and more commonly occurs in babies having birth weight <2500gms as compared to babies with a birth weight ≥ 2500gms. Thrombocytopenia was more in culture proven cases of neonatal sepsis and in low birth babies and with gestational age <37 wks. Also Thrombocytopenia was more commonly observed than thrombocytosis in cases of neonatal sepsis with complications.

KEY WORDS: thrombocytopenia, thrombocytosi, sepsis

INTRODUCTION:

Neonatal sepsis is a common cause of morbidity and mortality in newborns throughout the world, currently causing about 1.6 million deaths annually in developing countries. (WHO Health Bulletin 2012). Thrombocytopenia in newborns is a result of increased platelet consumption (infections, thrombosis, immune-mediated) or decreased platelet production. In many neonates, particularly sick preterm infants, both impaired megakaryopoiesis and accelerated platelet destruction may occur simultaneously. Neonatal platelet counts of 100 to 150 $\times 10^3$ /mm3 represent mild thrombocytopenia, platelet counts of 50 to 100 $\times 10^3$ /mm3 are considered /moderate thrombocytopenia, and levels less than 50 $\times 10^3$ /mm3 are categorized as severe thrombocytopenia [1]. Thrombocytosis is defined as platelet count >5 lakh/mm3[2].

MATERIALS AND METHODS:

This is a prospective observational study conducted from January 2016-January 2017. A total of 100 cases of neonatal sepsis, admitted in the NICU of MLB Medical College, in the Department of Pediatrics, Jhansi, were enrolled in this study. Out of them, 70 patients having symptoms and signs of sepsis formed the case group.

Inclusion Criteria: All neonates with either of following clinical features of sepsis like: Refusal of feed, lethargy; Temp instability (Hypothermia /Hyperthermia); Seizure, Excessive cry, Vomiting; Abdominal distension; Respiratory Distress; Bulging anterior fontanels; Delayed capillary filling time; Chest retraction, grunting, apnea; Sclerema, umbilical sepsis; Bleeding; Jaundice; Shock.

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Exclusion Criteria: Neonates with congenital anomalies. In all cases, complete sepsis screen was done including TLC, absolute neutrophil count, I/T ratio, micro ESR, and CRP. Blood cultures were send only in cases which were not on any antibiotics. Platelet counts were obtained using automated analyser.

RESULTS:

Amongst 70 cases, 49(70%) were males whereas the females were 21 (30%).Majority of these cases was preterm 34(48.5%) whereas the term babies were 36(51.4%). The Low birth weight babies were 52(74.29%).Amongst the cases, 37(52.8%) had early onset sepsis while 33(47.1%)had late onset sepsis. It was seen that the commonest symptoms of neonatal sepsis were refusal to feed andlethargies in 55.7% cases followed by respiratory distress in 31.4% cases. The other manifestations of sepsis were haematological such as bleeding and jaundice in 10% cases, shock in 7.1% cases.

Blood culture was done in 33 cases out of which 30 were positive and 3 were sterile. Of these, 30 cases had organism growth in blood culture, the most common organism isolated was Klebsiella in11 (36.6%) cases followed by coagulase negative Staphylococcus aureus in 9(30%) cases. Out of 30 positive blood cultures,14(46.6%) culture showed gram negative bacterial growth,12 (40%) blood cultures were positive for gram positive bacteria,3 (10%)had fungal growth and remaining 1(3.3%) blood culture showed mixed bacterial and fungal growth. The majority of the cases in this study had gram negative bacteria.

In this study, thrombocytopenia is found in 41(58.5%) cases. Mild thrombocytopenia seen in 8 (11.4%) cases, moderate in 18(25.7%) and severe thrombocytopenia in 15 (21.4%) cases in the study group. In our study, thrombocytosis was seen in only 3 (4.3%) patients of the total number of cases in the study group. Among 41 (58.57%) cases of thrombocytopenia, 33 (47.1%) have birth weight less than 2500gms and 23(32.86%) are preterm. Only three (4.3%) cases are of Thrombocytosis.

2(32.8%) of them had gestational age less than 37 weeks and rest 18 (25.71%) of cases had gestational age more than or equal to 37 weeks. In all these categories of Platelet Counts (i.e., Normal, Thrombocytopenia and Thrombocytosis) there is no significant difference between their respective two samples of Gestational age.

Thrombocytopenia is more commonly seen in culture proven cases of neonatal sepsis .24(80%) of culture positive cases had thrombocytopenia.16.6% of the total had normal platelet count and 3.3% showed thrombocytosis. Among the 3 blood culture negative cases, 2(66.6%) cases had thrombocytopenia and 1(33.3%) case had normal platelet count. In the rest 37 cases with no blood culture, 20(54%) cases had normal platelet count while 15 (40.5%) cases had thrombocytopenia while 2(5.4%) cases showed thrombocytosis. There are total 30 cases in which Micro-organism was found. Amongst them, 3 (10%) cases had fungal infection, 14(46.6.%) cases are of Gram negative and 12(40%) are of gram positive. Among gram negative13(43.33%) are of Thrombocytopenia and 1(3.33%) case is of Thrombocytosis while in Gram positive, 4(13.33%) cases are normal and 8(26.67%) cases had thrombocytopenia.Only one (3.33%) case is of mixed infection (Bacterial and Fungal both) is found of Thrombocytopenia. Thrombocytopenia was more commonly observed than thrombocytosis in cases of neonatal sepsis with complications. About 75 % cases with complications had thrombocytopenia, 6.2 % had thrombocytosis while 18.7% had normal platelet count.The mortality rate was 7(10%) in case group. Amongst them, 2(28.5%) had mild thrombocytopenia while 5(71.4%) had severe thrombocytopenia.

Table 1: Commonly associated organisms with study cases.

Microorganism	No. of cases (n=30)	%Age
Klebsiella	11	36.6%
Coagulase negative staphylococcus aureus	9	30%
Staphylocoocusaureus	3	10%
E.coli	3	10%
Candida	3	10%
Mixed	1	3.3%

DISCUSSION:

The study was conducted on 70 cases admitted in Neonatal Intensive Care Unit with signs and symptoms of neonatal sepsis consists of 70 cases ,of which 49 were males (70%) and 21 were females(30%). It was found that 34(48.5.%) neonates were preterm (51.4%)and 36 were term(≥37 wks). Ann L Anderson et al(2008)[3]also showed increased risk of developing sepsis as the birth weight decreases. In our study, 37(52.8%) cases had early onset sepsis while 33(47.1%) percent had late onset sepsis(table 3).This is consistent to a retrospective study that was

Table 2: Correlation of microorganism with platelet count.

Micro-organism	Platelet count			Total
	Normal	Throbocytopenia	Thrombocytosis	
Gram Negative	0 (0%)	13 (43.33%)	1 (3.33%)	14 (46.67%)
Gram Positive	4 (13.33%)	8 (26.67%)	0 (0%)	12 (40%)
Fungal	1 (3.33%)	2 (6.67%)	0 (0%)	3 (10%)
Mixed (bacterial and fungal)	0 (0%)	1 (3.33%)	0 (0%)	1 (3.33%)
Total	5 (16.67%)	24 (80%)	1 (3.33%)	30 (100%)

Table 3: Correlation of platelet count with gestational age, birth weight and blood culture.

Platelet counts	Gestation age(weeks)			Birth Weight			Blood culture	
	<37	=37	Total	<2500	=2500	Total	positive	negative
Normal	10 (14.3%)	16 (22.9%)	26 (37.14%)	17 (24.3%)	9 (12.8%)	26 (37.1%)	5 (7.1%)	1 (1.4%)
Thrombocytopenia	23 (32.8%)	18 (25.7%)	41 (58.57%)	33 (47.1%)	8 (11.4%)	41 (58.5%)	24 (34.3%)	2 (2.8%)
Thrombocytosis	1 (1.4%)	2 (2.8%)	3 (4.29%)	2 (2.8%)	1 (1.4%)	3 (4.3%)	1 (1.4%)	0
Total	34 (48.6%)	36 (51.4%)	70 (100%)	52 (74.3%)	18 (25.7%)	70	30	3

done by Rabindran et al (2014)[4] to assess the prevalence and course of thrombocytopenia in neonatal sepsis in which the prevalence of early onset sepsis was 17.44% and late onset sepsis was 13.5%. It was observed that refusal to feed, lethargies were the most common presentation seen in 39(55.7%) cases of neonatal sepsis in our study group followed by respiratory distress which is seen in 22(31.4%) cases and least common being CNS manifestation such as seizures 3(4.2%).

Blood culture was done in 33 neonates out of 70 cases. Blood culture was positive in 30 (42.8%) cases in our study as shown in table 3, which is comparable to study done by NawshadUddin Ahmed ASM et al(2002)[5] where blood culture was positive in 35% cases. In our study, the most common organism isolated was Klebsiella in 11(36.6%) followed by coagulase negative staphylococcus in 9(30%) blood cultures. The other isolates were E.coli(10%), Candida (10%) and rest showed mixed bacterial and fungal growth. Hence gram positive organism were seen in 40% cases, gram negative in 46.6%, fungal in 10% and mixed in 3.3% cases. Kumhar G et al[6] performed a study to determine the profile of bacteriological isolates from blood cultures of neonates in a tertiary care hospital in New Delhi, India, Staphylococci and Klebseilla were the most common Gram-positive and Gram-negative organisms, together accounting for 32.3% (266/823) and 33.8% (278/823) isolates respectively. Study done by Parwez Ahmed et al (2015)[7] on 100 newborns on very low birth weight babies with culture documented sepsis showed that 54% had gram negative sepsis, 40% had gram positive sepsis and 6 % had fungal sepsis. Klebsiellapneumoniae was the most commonly isolated organism.

The ability of Klebsiella species to cause outbreak of serious infection in NICU may be related to its virulence, its ability to colonize neonates , to survive in the inanimate environment and the neonates increased susceptibility to Klebsiella that are born without a normal flora and was acquired over first few weeks of life. In our study, thrombocytopenia was found in 41(58.5%) cases out total 70 cases of sepsis.

In our study thrombocytopenia was more commonly seen in neonates with low birth weight and in preterm. It has been suggested that in neonatal sepsis endothelial damage activates reticule-endothelial removal of platelets. Thrombocytopenia occurs as ultimately the rate of platelet production

falls behind platelet consumption, with a causative role for serum thrombopoietin levels). Thrombocytosis was seen in only 3(4.28%)patients of the total. According to the study by Wiedmeier SE and Henry E et al (2010)[8]on thrombocytosis in neonates and young infants in which among 471 infants who had one or more platelet counts performed in this period, 25 had extreme thrombocytosis. No cases were identified in the first week after birth, 40% were recognized between the second and fourth weeks and 40% between the fifth and eighth week. Among total cases of neonatal sepsis, thrombocytopenia was more commonly observed in neonates weighing<2500gms. Thrombocytosis was also observed more commonly in cases with birth wt <2500gms. On statistical analysis, there is no significant difference between their respective two samples of Birth weight (i.e., < 2500 gms and ≥2500 gms). In our study, 58.57% cases are of Thrombocytopenia, 32.86% of them have gestational age less than 37 weeks and rest 25.71% of cases have gestational age more than or equal to 37 weeks. There is no significant difference between their respective two samples of Gestational age. Lea Bonifacioet al(2007)[9] also found that neonates with thrombocytopenia were more frequently born at lower gestational age and birth weight. Thrombocytopenia was more commonly seen in culture proven cases of neonatal sepsis. In our study thrombocytopenia was more commonly seen in gram negative infections (92.8%) followed by fungal and gram positive infections with 66.6% in each. This is similar to the study by Wan-soo Lee et al (2007)[10]who analyzed cases with culture proven sepsis in low birth weight babies and had similar results.

Thrombocytopenia may just be a marker of severity of sepsis, as Gram negative sepsis are more severe than Gram positive ones and sepsis can cause disseminated intravascular coagulation. A direct pathophysiological mechanism of endotoxins produced by Gram negative bacteria in neonatal sepsis could also produce thrombocytopenia. Total 16 patients out of 70 cases of neonatal sepsis showed complications such as seizures, bleeding manifestations, shock and MODS. The overall mortality was 7(10%).Of them the total mortality with mild thrombocytopenia was 2(2.85%) and the mortality with severe thrombocytopenia were 5(7.14%).Hence severe thrombocytopenia was associated with higher mortality. Similar result was observed by M A Bhat et al (2009)[11]who concluded that the incidence of multiorgan failure and death was more in thrombocytopenic neonates. Blood culture was sent in

4 patients out of total death cases (7), all of them showed bacterial growth. The most common organism being Klebsiella in 3 cases and the remaining 1 was positive for E.coli. It is also stated in the literature by Isabelle M.C. Ree, Suzanne F et al (2017)[12], that both thrombocytopenia and Gram negative sepsis are independently associated with mortality.

CONCLUSION:

Based on this study, it can be concluded that neonatal sepsis is more common in preterm babies (<37wks) than term babies(≥37wks) and occur more commonly in babies having birth weight <2500g as compared to babies with a birth weight ≥2500g. Gram negative septicemia is more common than the Gram positive. Most common organism isolated in Blood culture is Klebsiella followed by coagulase negative staphylococcus. Thrombocytopenia is more commonly seen in culture proven cases of neonatal sepsis which being more common in gram negative infections. Thrombocytopenia was more commonly observed in low birth babies and with gestational age <37wks.Thrombocytopenia was more commonly observed than thrombocytosis in cases of neonatal sepsis with complications. Severe thrombocytopenia with gram negative infections are more commonly associated with mortality.

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