Prevalence of thrombocytopenia in neonates admitted in NICU with culture proven sepsis

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ABSTRACT

Background: Thrombocytopenia is a common haematological problem encountered during neonatal period, particularly in the sick, premature neonates admitted in the NICU, and usually indicate an underlying disease process. Thrombocytopenia may be considered as an important and early tool in diagnosis of septicaemia in neonates.

Methods: It is a hospital based cross sectional study. A total 105 neonates with blood and/CSF culture positive sepsis and associated thrombocytopenia admitted in NICU. This study was conducted to find the prevalence of thrombocytopenia in neonates admitted in NICU with culture proven sepsis and to observe the outcome of thrombocytopenia and sepsis.

Results: Out of 105 culture positive neonates K. pneumoniae 47/105 (44.8%) was the commonest micro-organism isolated, followed by Pseudomonas 26/105 (24.8%), E. coli 14/105 (13.3%), Staphylococcus 11/105 (10.5%), Candida 2/105 (1.9%) in decreasing order. Thrombocytopenia was present in 100/105 (95.2%). Among thrombocytopenic neonates 38/100 (38%), 36/100 (36%) and 26/100 (26%) having severe, moderate and mild thrombocytopenia respectively. 38 (38%) newborns of severe thrombocytopenia among them K. pneumoniae (50.0%) was commonest organism, followed by Pseudomonas. (23.7%) and Staphylococcus (15.8%) in the decreasing order. 36 (36%) newborns of moderate thrombocytopenia among them K. pneumoniae (47.2%) again commonest organism associated, followed by Pseudomonas. (25.0%), and E- coli (11.1%). In severe thrombocytopenic newborns both GI and pulmonary (60.50%) haemorrhage was the most common bleeding manifestation. Mortality rate (37.1%) was high in newborns having sepsis.

Conclusions: Bacterial sepsis is significantly complicated by thrombocytopenia. Severe thrombocytopenia in a suspected case of bacterial sepsis might predict Klebsiella sepsis and hence it may be rational to start empirical antibiotics covering the same.

Keywords: Blood culture and micro-organism, Newborns, Sepsis, Thrombocytopenia

INTRODUCTION

Thrombocytopenia is a common haematological problem encountered in the neonates particularly in the sick, premature neonates admitted in the NICU, and usually indicate an underlying disease process. Most of the sick, low birth weight and premature infants have low platelet count. It is also reported that not only bacteria but fungal, protozoal, rickettsial and viral etiology may also cause neonatal septicaemia. Thrombocytopenia is seen frequently in early and late onset of sepsis. It is commonly seen with Gram positive septicaemia as compared to Gram negative septicemia and low platelet is usually seen even before the pathogens are cultured from the blood. Therefore, thrombocytopenia may be considered as an important and early tool in diagnosis of
septicaemia in neonates. A normal platelet count ranges from 150,000 to 450,000 platelets per microliter of blood. Thrombocytopenia is defined as platelet count <150,000 per microliter of blood irrespective of the gestational age. It is the commonest haematological abnormality encountered in the neonatal intensive care unit (NICU).

Neonatal septicemia refers to a clinical syndrome characterized by systemic signs and symptoms due to generalized bacterial infection with a positive blood culture in the first 4 weeks of life. General signs of neonatal sepsis are lethargy/hypotonia, tachycardia/bradycardia, fever/ hypothermia, abdominal distension, and hypotension/delayed capillary refill time, apnea, retractions, and grunting, and increased ventilator requirements. Focal infections associated with sepsis are pneumonia, meningitis, necrotizing enterocolitis (NEC), and urinary tract infections. Superficial infections such as conjunctivitis and oral thrush are not usually included under neonatal sepsis. In developing countries, sepsis is the most common cause of mortality responsible for 30%–50% of the 5 million total neonatal deaths each year. The National Neonatal Perinatal Database (NNPD, 2002-2003) from India has reported an incidence of 23/1000 live births for septicemia. Gram-negative organisms are more commonly reported from India. Conventionally, neonatal sepsis has been classified as early onset sepsis (EOS) and late onset sepsis (LOS) with 72 h of life as a common demarcation. In developed countries, Group B Streptococcus and coagulase-negative staphylococci (CONS) are the most common etiological agents for EOS and LOS, respectively. Define diagnosis of sepsis is made by isolation of the organism in blood specimen culture.

Bacteria or bacterial products may cause endothelial damage leading to platelet adhesion and aggregation or may bind directly to platelets leading to aggregation and accelerated clearance of platelets from circulation. There may be a possibility of immunologically mediated development of thrombocytopenia in septicaemia as there is presence of circulating immune complex in septicemic patients and decrease number of complement in patients with septicemic shock.

Hence, in view of the high incidence of mortality due to thrombocytopenia and neonatal sepsis in NICUs. This study was done to find out association between the two factors. We hope that this study will help us to reduce the morbidity and mortality associated with thrombocytopenia due to neonatal sepsis.

METHODS

This study was conducted at a teaching tertiary care hospital, Department of Pediatrics, NSCB Medical College, Jabalpur, in Madhya Pradesh, India. Investigator had informed the nature, conduct and all possible risks and rights to the parents of participants before the initiation of study. Informed consent was taken from the parents/guardians of all patients. This was a Hospital based cross sectional study conducted over 1.5 years from March 2016 to August 2017. Permission from Institutional Research and Ethical Committee was taken before commencement of the study. Only culture-positive septic neonates, from both inborn and outborn units aged <28 days were included in the study. Babies who were Extremely low birth weight (birth weight <1000 grams), having age >28 days, neonates having maternal history suggestive of placental insufficiency, neonates with family history of bleeding manifestations and newborn’s mother with low platelets counts were excluded from the study. Clinical and laboratory data were collected from day to day admissions of neonates. As per our hospital protocol, septic screening including complete blood counts (CBC) and blood culture was done for all the symptomatic neonates for sepsis.

Following definitions were used in the study, Neonatal period was referring to age less than 28 days after birth. Culture proven sepsis were defined as when an infant having clinical picture suggestive of septicaemia, pneumonia or meningitis along with isolation of pathogen from blood. EOS (Early onset sepsis) was defined as clinical manifestations of sepsis appearing within 72 h of birth, while in LOS (Late onset sepsis), clinical manifestations of sepsis are seen after 72 hours of birth. All the samples for blood cultures were collected from a peripheral vein with proper aseptic precautions before starting any antibiotic therapy. Normal platelets count was defined as when platelets count is >150,000/mm³. Thrombocytopenia was defined as newborn infants having platelets counts below 150,000/mm³. Mild, moderate and severe thrombocytopenia were defined as when platelets counts between 100,000-150,000/mm³, 50,000-100,000/mm³ and <50,000/mm³. Extramural newborn were defined as a baby not born in the study centre and intramural newborn those who were born in side the study centre. Prevalence is the proportion of disease found to have been affecting a particular population.

Blood samples were collected under full aseptic precautions, for that hands were washed and dried, worn sterile gloves prior to the procedure and prepared a patch of skin approx. 5-cm in diameter over the proposed venepuncture site. This area was cleansed thoroughly with 70% alcohol followed by povidone-iodine (1%), followed again by 70% alcohol. Application of povidone-iodine and alcohol was done in concentric circles moving outward from the centre. The skin was allowed to dry for at least 1 minute before the sample is collected. A 1 ml sample of blood were taken for a blood culture bottle containing 5-10 ml of culture media. Blood cultures were collected from a fresh venepuncture site. All blood cultures were incubated at 37°C and observed for 72 hours for growth of micro-organism. Information was collected regarding organism isolated, demographic profile, type of sepsis (early onset sepsis/late onset
sepsis), presentation (non-specific/systemic), and hematology.

**Statistical analysis**

The data were recorded in the predesigned proforma and then were entered in the MS excel and eventually it was analysed by using software -SPSS version 20. Association and correlation of qualitative data were tested by chi-square test and Fischer’s exact test were applied in quantitative data. A P value <0.05 was considered significant.

**RESULTS**

During the study period, on the basis of inclusion criteria total 105 newborns included in the study with culture positive sepsis, in NICU of our hospital. Out of these 105 newborns 34 (32.4%) were females and 71 (67.6%) were male. The male-to-female ratio was 2.9:1. 34 (32.40%) newborns were having normal birth weight, 56 (53.3%) were having low birth weight and 15 (14.3%) were having very low birth weight.

**Figure 1: Proportion of micro-organism isolated.**

47 (44.8%) and 58 (55.2%) newborns were intramural and extramural respectively. 78 (74.3%) cases had early-onset sepsis, while 27 (25.7%) had late-onset sepsis. 82 (78.1%) and 23 (21.9%) newborns were delivered via normal vaginal delivery and lower section caesarean section respectively. 45 (42.9%), 59 (56.2%) and 1 (1.0%) newborns were pre term, term and post term respectively. 88 (83.8%), 14 (13.3%) and 3 (2.9%) newborns were appropriate for date, small for date and large for date respectively.

The most common isolates were *Klebsiella pneumoniae* 44.8% (47/105) newborns followed by *Pseudomonas spp* 24.8% (26/105), *E. coli* 13.3% (14/105), *Staph. aureus* 10.5% (11/105) and *Candida spp* 1.9% (2/105) (Figure 1).

Severe thrombocytopenia was most common 36.2% (38/105) followed by moderate 34.3% (36/105) and mild 24.8% (26/105) thrombocytopenia (Figure 2).

**Figure 2: Proportion of newborns according to severity of the thrombocytopenia.**

**Figure 3: Association of platelets counts with micro-organism.**
Among severe thrombocytopenic 38/105 (36.2%) newborns, *Klebsiella pneumoniae* 50.0% (19/105) were commonest organism, followed by *Pseudomonas spp.* 23.7% (9/105) and *Staph. aureus* 15.8% (6/105) (P value=0.830) (Figure 3).

**Figure 3: Association of platelets count and outcome of newborns.**

The total mortality was high 37.1% (39/105) in newborns having sepsis. Mortality was higher in the newborns having severe 73.70% (28/38) thrombocytopenia compared to newborns having moderate (30.60%) thrombocytopenia (P value<0.0001) (Figure 4).

*Klebsiella pneumoniae* (56.4%) was the leading cause of death in the newborns followed by *Pseudomonas spp.* 20.5%), *E- coli* (10.3%), *Staph. aureus* (10.3%) and *Citrobacter spp.* (2.5%) respectively (P value=0.555) (Figure 5).

**Figure 4: Association of outcome of sepsis with different micro-organism.**

**DISCUSSION**

In the present study of newborns with culture positive sepsis, it was found that Male (67.6%) newborns were higher in proportion compared to female (32.4%). It is comparable to the study by Heena et al (63.4%) and Pramila et al (58.6%).

Present study shows that percentage of thrombocytopenia (platelets counts <150x10³/mm³) was 95.2%. This indicates that the low platelets count in newborns is having an important correlation with sepsis and admission in the neonatal intensive care unit. Prevalence of thrombocytopenia were 36.2%, 34.3% and 24.8% newborns severe, moderate and mild respectively. It represent severity of thrombocytopenia was associated with culture positive sepsis.

It was found that low birth weight (53.3%) newborns were higher in proportion followed by normal birth weight (32.40%) and very low birth weight (14.3%). Heena et al observed that low birth weight (76.20%) newborns were more. Vikram et al also were having similar finding in their research conducted at Karnatak.

In this study, we observed appropriate for date (83.8%) newborns were having more sepsis compared to small for date (13.3%) and large for date (2.9%) newborns. It was similar to Pramila et al study.

It was found that *Klebsiella pneumoniae* (44.8%) was the commonest, *Pseudomonas spp.* (24.8%) was second most common and *E. coli* (13.3%) was the third most common isolated micro-organism. Bacterial pathogens are comparable to a “NNPD study” found that among intramural admissions *Klebsiella pneumoniae* (32.5%) was most frequently isolated organism followed by *Staphylococcus aureus* (13.6%) and *Escherichia coli* (10.6%) however among extramural admissions *Klebsiella Pneumoniae* (30.1%), followed by *Staphylococcus aureus* (16.2%), *E- coli* (13%) and *Pseudomonas* species (9.3%). It is comparable to Heena et al study they were also found that *Klebsiella* (54%) was commonest, followed by *Pseudomonas* (15.9%) and *Escherichia coli* (11.1%). It is also similar to Charoo et al study, *Klebsiella pneumoniae* (62.5%), Parvez et al study, *Klebsiella pneumoniae* (48.1%) was commonest organism followed by *Pseudomonas spp* (18.5%) and *Acetobacter* (14.8%) and Swarnkar et al *Klebsiella pneumoniae* (48.6%). This is in accordance with the literature that most of the Indian studies shows *Klebsiella* as the predominant pathogen in neonatal sepsis. Findings were contradictory to the Torkman et al study-*Enterobacter spp* (39.6%) were the commonest organism, and Tripti et al study *Pseudomonas spp* (40%) was commonest pathogen. This difference is due to, in our study a higher proportion of infected newborns were having sepsis with *Klebsiella pneumoniae*. A study by Kathleen et al found *Group-B Streptococci* (59.8%) was the commonest organism followed by E coli (40.2%). Pramila et al were also found *Staph. aureus* (58.62%) was the most common followed by *Klebsiella* (16.09%) coagulate negative *Staphylococcus* (6.89%). Other than bacterial pathogens, fungal organism were 1.9%. All
were *Candida spp.* in present study. It was similar to Pramila et al (2.29%).

Our study showed, severe thrombocytopenia was found in 36.2% newborns followed by moderate (34.3%) and mild (24.8%) thrombocytopenia. Vikram R et al in their study observed severe and moderate thrombocytopenia was 15% and 15% respectively among septicaemic newborns which was low in comparison to present study.26

In this study it was found that severe thrombocytopenia was commonest among the *Klebsiella pneumoniae* (50.0%) followed by *Pseudomonas spp.* (23.7%) and *Staph. aureus* (15.8%). It is comparable to the study by Charoo et al in which they found that severe thrombocytopenia was 60% among *Klebsiella pneumoniae*.20 Similar observations were also reported by Vikram et al and Arif SH et al.26,27

Fungal organism was isolated in 2.6% of severe thrombocytopenic newborns contradictory to Sartaj et al study, having 60% association with fungal pathogens and Parvez et al study found 33.3% association with severe thrombocytopenia.21,28 Inadequate and less competent sampling as well as culturing techniques in our centre may be the reason for the different findings.

High mortality rate of 37.1% in newborns having sepsis. Our centre being tertiary referral centre with higher rates of complicate deliveries and admissions substantiates the higher mortality rate. Increased patients burden leading to breach in the prevention of cross infection and full aseptic precautions also contributes to the same. *Klebsiella pneumoniae* (56.4%) was the leading cause of death compared to *Pseudomonas spp.* 20.5%, *E. coli* (10.3%), *Staph. Aureus* (10.3%) and *Citrobacter spp* (2.5%) in this study. Vergnano et al also attributes *Klebsiella* and *Pseudomonas* to high case fatality rates.29

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REFERENCES

1. Kaplan C, Morel kopp MC, Clemenceau S. Fetal and neonatal alloimmune thrombocytopenia. Transf Med. 1992;2:265-71.
2. Corrigan JJ Jr, Ray WL, May N. Changes in blood coagulation system associated with sepsicemia. N Engl J Med. 1968;279:851.
3. Neame PB, Kelton JG, Walker IR. Thrombocytopenia in sepsicemia: the role of DIC. Blood. 1980;56:58.
4. Corrigan JJ Jr, Tucson A. Thrombocytopenia: a laboratory sign of septicemia in infants and children. J Pediatr. 1974;85:219-20.

5. Reider GF, Straub PW, Frick PG. Thrombocytopenia in septicemia. A clinical study for the evaluation of its incidence and diagnostic value. Helv Med Acta. 1971;36:23.
6. Platelet count: MedlinePlus Medical Encyclopedia. Available at www.nlm.nih.gov. Accessed on 2015-05-01.
7. Gotoff SP, Behrman RE. Neonatal septicemia. J Pediatr. 1970;76:142- 53.
8. Deorari AK. Neonatal sepsis: Manageable daunting issue for India. J Neonatol. 2009;23:7- 11.
9. Report 2002-2003. National Neonatal Perinatal Database Network. New Delhi: National Neonatology Forum of India; 2004.
10. Mathur NB. Neonatal sepsis. Indian Pediatr. 1996;33:663- 74.
11. Neonatal Morbidity and Mortality. Report of National Neonatal Perinatal Database. Indian Pediatr. 1997;34:1039-42.
12. McGrath JM, Stewart GJ. The effect of endotoxin on vascular endothelium. Jr Exp Med. 1968;129:833-9.
13. Thorne KJI, Oliver RC, MacIntyre DE. Endotoxin-induced platelet aggregation and secretion changes in plasma membrane proteins. J Cell Sci. 1977;28:225-36.
14. Kelton JG, Neame PB, Bishop J. The direct assay for platelet associated IgG (PAIgG) lack of association between antibody level and platelet size. Blood. 1979;53:73-80.
15. Walker LC, Ahlin TD, Tung KSK (1978) Circulating immune complexes in disseminated gonorrheal infection. Ann Intern Med. 1978;89:28-33.
16. Hassan HR, Gohil JR, Desai R, Mehta RR, Chaudhary VP. Correlation of blood culture results with the sepsis score and sepsis screen in the diagnosis of early-onset neonatal septicemia. J Clin Neonatol. 2016 Jul;5(3):193.
17. Verma P, Sadawarte K. Neonatal septicemia: Its etiological agents and clinical associates. Indian J Child Health. 2015;2(3):113-7.
18. Goudar VR, Kabin GM, Joshi SN, Chavan VP, Badiger SL. A study of bacterial sepsis and its relation to thrombocytopenia in neonates. Int J Contemp Pediatr. 2017 Apr;4(3):1032-6.
19. National neonatal perinatal database report, 2002-03. Available at http://www.newbornwhocc.org/pdf/nnpd_report_2002-03.PDF
20. Charoo BA, Iqbal J, Iqbal Q, Mushtaq S, Bhat AW, Nawaz I. Nosocomial sepsis in newborn infants: a prospective study. Hematol/Oncol Stem Cell Therapy. 2009 Apr 1;2(2):349-53.
21. Ahmad P, Kaith R, Gattoo I, Najar BH, Hussain SQ. Thrombocytopenia as a predictor of neonatal sepsis in very low birth weight babies and its correlation with specific organism involved: a hospital based
observational study. Indian J Neonat Med Res. 2015 Jul, Vol-3(3): 7-13
22. Swarnkar K, Swarnkar M. A study of early onset neonatal sepsis with special reference to sepsis screening parameters in a tertiary care centre of rural India. Internet J Infect Dis. 2012;10(1).
23. Torkaman M, Afsharpaiman SH, Hoseini MJ, Moradi M, Mazraati A, Amirsalar S. Platelet count and neonatal sepsis: A high prevalence of Enterobacter spp. Singapore Med J. 2009;50(5):482.
24. Karne TK, Joshi DD, Zile U, Patil S. Study of Platelet Count and Platelet Indices in Neonatal Sepsis in Tertiary Care Institute. MVP J Med Sci. 2017 May 22;4(1):55-60.
25. Mayor-Lynn K, González-Quintero VH, O'sullivan MJ, Hartstein AI, Roger S, Tamayo M. Comparison of early-onset neonatal sepsis caused by Escherichia coli and group B Streptococcus. Am J Obstet Gynecol. 2005 May;192(5):1437-9.
26. Goudar VR, Kabbin GM, Joshi SN, Chavan VP, Badiger SL. A study of bacterial sepsis and its relation to thrombocytopenia in neonates. Int J Contemp Pediatr. 2017 Apr;4(3):1032-6.
27. Arif SH, Ahmad I, Ali SM, Khan HM. Thrombocytopenia and bacterial sepsis in neonates, Indian J Hematol Blood Transfus. 2012 Sep;28(3):147-51.
28. Bhat S, Naik S, Rafiq W, Tariq A. Incidence of thrombocytopenia and changes in various platelet parameters, in blood culture positive neonatal sepsis. Int J Pediatr. 2015;3(4.1):757-66.
29. Vergnano S, Sharland M, Kazembe P, Mwansambo C, Heath PT. Neonatal sepsis: an international perspective. Arch Dis Childhood-Fetal Neonat Ed. 2005 May 1;90(3):F220-F224.

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