Original Research Article

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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.1 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.^{2,3} 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.⁴ Therefore, thrombocytopenia may be considered as an important and early tool in diagnosis of septicaemia in neonates.⁵ A normal platelet count ranges from 150,000 to 450,000 platelets per microliter of blood.⁶ 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 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. 8 The National Neonatal Perinatal Database (NNPD, 2002-2003) from India has reported an incidence of 23/1000 live births for septicemia.9 Gram- negative organisms are more commonly reported from India.10 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. 11 Definite 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. ^{12,13} 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. ^{14,15}

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, $50,000-100,000/\text{mm}^3$ and $<50,000/\text{mm}^3$. 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 povidoneiodine 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 It were entered in the MS excel and eventually it then 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.

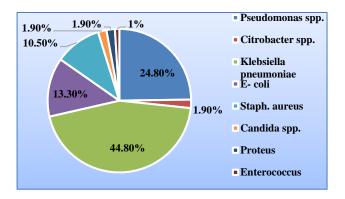


Figure 1: Proportion of micro-organism isolated.

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).

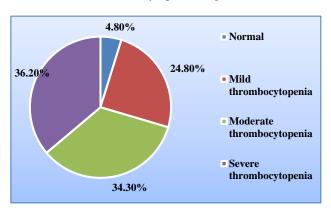


Figure 2: Proportion of newborns according to severity of the thrombocytopenia.

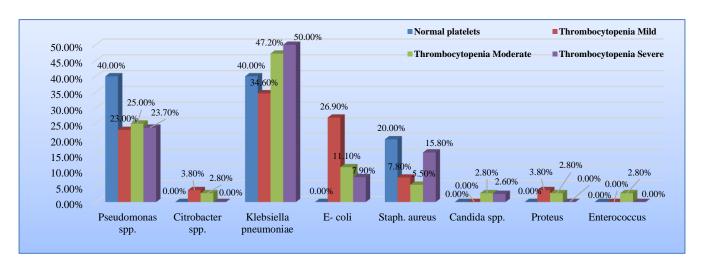


Figure 3: Association of platelets counts with micro-organism.

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).

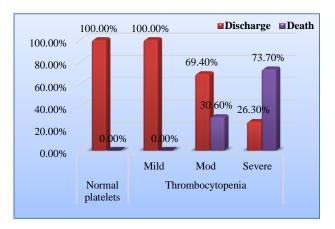


Figure 4: Association of platelets count and outcome of newborns.

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).

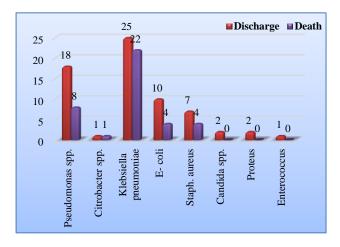


Figure 5: Association of outcome of sepsis with different micro-organism.

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%). 16,17

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. ¹⁶ Vikram et al also were having similar finding in their research conducted at Karnataka. ¹⁸

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.¹⁷

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 Staphylococcus aureus (16.2%), E- coli (13%) and Pseudomonas species (9.3%).¹⁹ 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%).16 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%). 20-22 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.^{23,24} 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%).²⁵ Pramila et al were also found Staph. aureus (58.62%) was the most common followed by Klebsiella (16.09%) coagulase negative Staphylococcus (6.89%). 17 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%).¹⁷

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*. 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. 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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Ethical approval: The study was approved by the

Institutional Ethics Committee

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