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Correlation of Platelet Count with Specific Causative Organism in Culture Positive Sepsis Neonates - An Observational Cohort Study

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Abstract

Introduction: Thrombocytopenia is one of the frequent hematological issues seen in neonatal sepsis. Thrombocytopenia can be noted in both gram-positive and gram-negative septicemia. Hence it can be considered a predictor for sepsis in neonates.

Methods: This study was conducted in Kangaroo Care Women and Children Hospital. Study Design: Retrospective and Prospective Observational Cohort study was conducted. Study Duration: 18 months (January 2022– June 2023). Inclusion Criteria: Neonates admitted to NICU with Culture Positive Sepsis were included in the study. Exclusion Criteria: Neonates with maternal history suggestive of placental insufficiency, low platelet counts, and family history of bleeding disorders.

Results: Out of 429 admissions in NICU, 33 neonates had culture-positive sepsis. Among 60.6% of Gram-negative organisms, Acinetobacter baumannii was the commonest seen in 21.2% of neonates. Among 33.3% Gram-positive organisms, coagulase-negative Staphylococcus was the commonest, present in 15.15% neonates. Among 12.1% Fungal Sepsis, all isolated were Candida spp. Few cases had multiple organism infections. Severe thrombocytopenia was seen in 51.51% of neonates, moderate thrombocytopenia in 6.06%, and mild thrombocytopenia in 9.1%. The total mortality was high (33.33%) in septic neonates all cases were with severe thrombocytopenia. The most common organism causing mortality was *Candida spp.* (27.27%), followed by *Klebsiella pneumoniae* and *Escherichia coli.*

Conclusions: Mortality was higher in Gram-Negative sepsis. A large percentage of newborns admitted with sepsis had thrombocytopenia. Therefore, thrombocytopenia can be regarded as one of the earliest nonspecific predictors of sepsis in newborns admitted to the NICU. It also greatly affects the outcome.

Keywords: Neonatal sepsis; Thrombocytopenia; Blood culture; Gram-negative organism

Introduction

Neonatal sepsis, a critical condition characterized by a systemic infection within the first 28 days of life, continues to be a leading cause of morbidity and mortality in newborns worldwide (50-60%) [1]. Early diagnosis and effective management of neonatal sepsis are essential to improve the outcomes.

Among the various hematological markers that have gained attention in the context of neonatal sepsis, platelet counts have emerged as a potentially

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valuable tool for early detection, risk assessment, and treatment monitoring. Platelets, small anuclear blood cells with key roles in hemostasis and immune response modulation, are increasingly recognized for their involvement in the pathophysiology of sepsis.

Thrombocytopenia is one of the frequent hematological issues seen in neonatal sepsis. This can be noted in both gram-positive and gram-negative septicemia. The emergence of thrombocytopenia in newborns can be either early (less than 72 hours) or late (more than 72 hours). Early-onset thrombocytopenia is typically associated with platelet insufficiency and is mild and self-limiting, but late-onset thrombocytopenia is seen in bacterial sepsis and necrotizing enterocolitis and is frequently severe and protracted. In septic neonates, thrombocytopenia can have a variety of etiologies, including enhanced platelet destruction, decreased platelet production, or mixed etiologies [2].

This study aims to investigate the correlation between platelet counts and the severity, prognosis, and clinical outcomes of neonates with sepsis and also explore their diagnostic significance and prognostic implications. By synthesizing the existing knowledge, we strive to contribute to a deeper understanding of the intricate relationship between platelet counts and neonatal sepsis, ultimately paving the way for enhanced clinical management strategies and improved neonatal outcomes.

Materials and Methods

This study was conducted in Kangaroo Care Women and Children Hospital over 18 months Informed written consent was taken from the parents/guardians of all neonates enrolled in the study. Study Design: Retrospective and Prospective Observational Study. Study Duration: 18 months (January 2022– June 2023). Inclusion Criteria: Neonates with sepsis whose blood culture was positive were included in the study. Exclusion Criteria: Neonates born to mothers with history suggestive of placental insufficiency and thrombocytopenia and a family history of bleeding disorders were excluded.

Throughout the study period a complete blood count, rapid screening assays, and blood culture were performed as per unit protocol for newborns admitted to the NICU who had symptoms of sepsis. Data about demographic information, sepsis type (early onset/late onset), presentation (non-specific/ systemic), hematological parameters, and isolated organisms were collected. A pre-structured proforma was used to record all the data, and standard statistical techniques were used to analyze it. The outcome of death or discharge was noted.

Definitions and Criteria used in this Study:

Culture-positive Sepsis: Neonate presenting with any clinical features suggestive of sepsis along with isolation of the pathogen from blood culture.

Early Onset Sepsis (EOS): Clinical features of Sepsis appearing within 72 hours of life Late Onset Sepsis (LOS): Clinical features of sepsis seen after 72 hours of life.

Normal platelet count: platelet count of >1,50,000/mm^3.

Thrombocytopenia: platelet count of <1,50,00/mm^3

Platelet counts between 1,00,000 and 1,50,000/mm^3 are termed as mild thrombocytopenia 50,000 to 1,00,000/mm^3 as moderate thrombocytopenia and 50,000/mm^3 as severe thrombocytopenia.

Blood Culture: Blood samples were collected from a peripheral vein with proper aseptic precautions before administering antibiotics. A patch of skin approx. 5-cm in diameter was prepared by thoroughly cleansed with 70% alcohol followed by povidone-iodine (1%), followed again by 70% alcohol over the proposed venepuncture site. Application of povidone-iodine and alcohol was done in concentric circles moving outward from the center. The skin was allowed to dry for at least 1 minute before the sample was collected. A sample of 1 ml of blood was taken for culture in a 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 the growth of microorganisms.

Results

Out of 429 admissions in NICU, 33 (7.69%) neonates had culture-positive sepsis. Out of these 33 neonates enrolled, 8 (24.2%) were females and 25(75.8%) were males (Figure.1). 4(12.1%) newborns were having normal birth weight, 2 (6.1%) were having low birth weight, 15 (45.5%) were having very low birth weight and 12(36.4%) were extremely low birth weight (Figure.2). 4 (12.12%) newborns were delivered via normal vaginal delivery, 2 (6.06%) via assisted vaginal delivery and 27(81.8%) via lower section cesarean section. 7(21.2%) newborns were <28 weeks gestation, 20(60.6%) were between 28-32weeks gestation, 2(6.1%) were between 32- 34 weeks gestation, 1(3%) were between 34-37 weeks gestation and 3(9.1%) were above 37 weeks gestation (Figure.3). 29(87.9%) newborns were Appropriate for gestational age, 3(9.1%) newborns were Small for gestational age, 1(3%) were Large for gestational age.

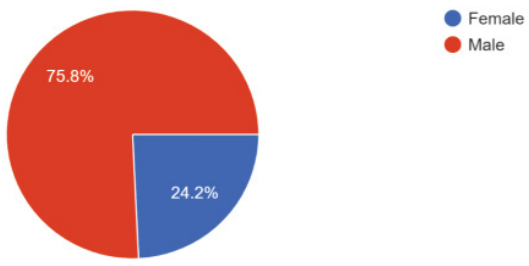

Figure 1: Gender

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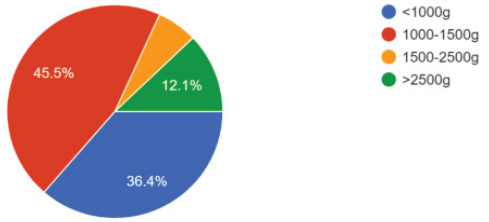

Figure 2: Birth Weight

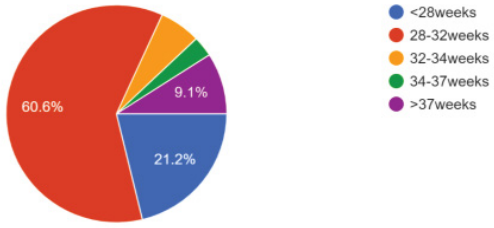

Figure 3: Gestational Age

Out of the 33 neonates enrolled, 12(36.36%) cases presented with early onset sepsis, while 21 (63.63%) with late-onset sepsis. Amongst the 20(60.6%) cases positive for Gram-negative organisms, Acinetobacter baumannii 7(21.21%), Klebsiella species were seen in 6(18.18%), Citrobacter koseri in 2(6.06%), Escherichia coli in 3 (9.09%), Pseudomonas in 1 and Stenotrophomonas maltophilia in 1 neonate. Among 11 (33.33%) neonates in whom gram-positive organisms were isolated, Coagulase-negative staphylococci were seen in 5(15.15%), Staphylococcus aureus in 2(6.06%), Group B streptococcus in 2(6.06%) and 2(6.06%) Enterococcus. 4 (12.12%) had Fungal Sepsis, Candida spp.4(100%) was isolated in all cases. (Figure.4). Few cases had multi-organism infection.

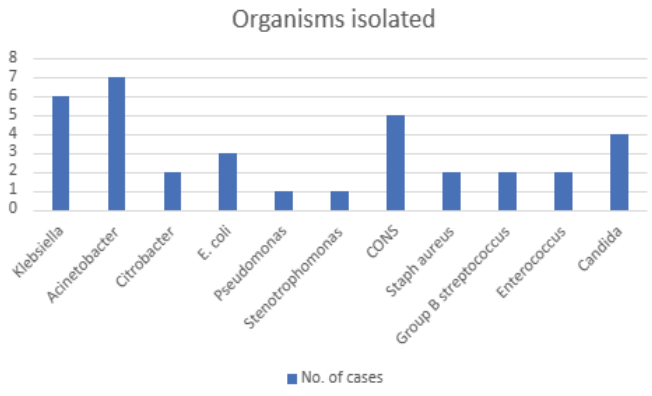

Figure 4: Number of organisms isolated

Among these 33 septic neonates, 4 neonates had multiple organisms infection. One newborn had an infection by Gram-positive, Gram-negative, and Fungus. In the other 3 neonates, two different Gram-negative organisms were isolated.

22(66.66%) neonates out of 33 septic neonates had thrombocytopenia. Among them, severe thrombocytopenia was seen in 17(51.51%), moderate thrombocytopenia in 2(6.06%) and mild thrombocytopenia in 3(9.1%). The total mortality was high 33.33% (11/33) in newborns having sepsis. 100% of mortality was seen in the newborns having severe thrombocytopenia.

Table 1: Neonatal Outcomes in association with platelet counts

Platelet Counts	Total	Discharge (n=22)	Death (n=11)
Severe thrombocytopenia	17	6 (35.3%)	11 (64.7%)
Moderate thrombocytopenia	2	2 (100%)	0
Mild thrombocytopenia	3	3 (100%)	0
Normal platelet count	11	11 (100%)	0

Among 11 deaths, 8(72.72%) were having Gram-negative sepsis, including 1 with multiple organism sepsis. 2(18.18%) were having fungal sepsis and 1(9.09%) Gram positive sepsis. Candida albicans 3(27.27%), including one case with multi-organism sepsis was the leading cause of death in the newborns followed by Klebsiella pneumoniae 2(18.18%), Escherichia coli 2(18.18%), Coagulase negative staphylococcus 2(18.18%) including one case with multi-organism sepsis, Acinetobacter 2(18.18%), Citrobacter 1(9.09%) and Stenotrophomonas 1(9.09%).

Table 2: Outcome of different organisms

Organisms	Death (n=11)
Candida spp.	3*
Klebsiella	2*
CONS	2*
E. coli	2
Acinetobacter	2*
Citrobacter	1
Stenotrophomonas	1
Pseudomonas	1*

* Includes cases with multi-organism sepsis

Discussion

The diagnosis of Neonatal Septicemia necessitates prompt treatment to ensure the survival of the neonate and the normal neurodevelopmental outcome. One of the most frequent hematological signs observed during Neonatal Sepsis is Thrombocytopenia. Low platelet counts may be an early indicator of the diagnosis of Neonatal Septicemia[3].

Out of 429 NICU admissions during the study period, 33 neonates had culture-positive sepsis. Out of these 33 neonates enrolled, 24.2% were females and 75.8% were males.

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Our study shows that, in neonates with sepsis, the percentage of thrombocytopenia was high (66.66%). Severe thrombocytopenia was seen in 45.48%, followed by moderate thrombocytopenia (15.15%), mild thrombocytopenia (9.1%), and normal platelet count (24.24%). Suggesting that the occurrence of thrombocytopenia in neonates has a significant correlation with sepsis in neonates admitted to NICU [4].

In this study involving 33 neonates with sepsis, Normal birth weight was seen in 12.1% of newborns, 6.1% were in the low-birth-weight range, 45.5% were in very low birth weight and 36.4% were in extremely low birth weight range. In a study conducted by Heena et al., higher culture-positive cases were observed in low-birth-weight newborns (76.20%) [5], similar to our study. A similar finding was made in the research conducted by Vikram et al. [6].

In this study, the majority of cases (60.6%) were attributed to Gram-Negative Organisms, 33.3% were attributed to Gram-Positive Organisms and 12.1% were attributed to Fungal Sepsis. Out of the 60.6% of Gram-negative Organisms isolated, 21.21% were Acinetobacter baumannii, 18.18% were Klebsiella spp., and 9.09% were E. coli. Out of the 33.33% of Gram-positive Organisms, Coagulase-negative staphylococci were seen in 5(15.15%), Staphylococcus aureus in 2(6.06%), Group B streptococcus in 2(6.06%) and 2(6.06%) Enterococcus.

Various Indian studies show more common isolation of Gram-negative bacteria. Gram-negative organisms are the most common cause of neonatal sepsis in developing countries [4].

According to the NNPD report, the most common organism isolated was Klebsiella pneumoniae (32.5%), followed by Staphylococcus aureus (13.6%) and Escherichia coli (10.6%) [8]. Heena et al. observed that Klebsiella (54%) was the commonest, then Pseudomonas (15.9%) and Escherichia coli (11.1%) [5]. These findings were similar to the studies by Charoo et al., Parvez et al., and Swarnkar et al., where the most common organism isolated was Klebsiella pneumoniae (48.1%) followed by Pseudomonas spp (18.5%) and Acinetobacter (14.8%) [9,10,11]. In the other studies, by Torkman et al., Enterobacter spp (39.6%) was the most common and by Tripti et al., Pseudomonas spp(40%) was the commonest [12,13]. Pramila et al. found Staph. aureus (58.62%) was the most common followed by Klebsiella (16.09%) coagulase-negative Staphylococcus (6.89%) [7].

In this study, Klebsiella was the second most common organism responsible for 18.18% of all cases. Rehman et al. reported 29% cases of Staphylococcus aureus and Kurein et al. reported 13% cases of Staphylococcus aureus neonatal sepsis respectively [14,15]. In developed countries, the most common causative organism for late-onset sepsis is CONS. Venkateshan S et al. study reported a 5-6% incidence of CONS in neonatal sepsis [16] Sanghvi K Pet al. study reported CONS in 61% of cases of neonatal sepsis [17]. 15.15% of CONS were in our study.

In our study, fungal organisms isolated were in 12.1% (Candida spp). 11% of cases had fungal sepsis in the Venkateshan S et al. study and 8% in the study by Guida et al. [16,18]. In the study conducted by Bhat et al., 8.5% of septic VLBW neonates were reported to have fungal sepsis [19].

In this study, we found severe thrombocytopenia in 51.51% of neonates, moderate thrombocytopenia in 6.06% neonates, mild thrombocytopenia in 9.09% neonates, and normal platelet count in 33.33% neonates.

Guida et al., in 2003 reported significantly low platelet count at the onset of sepsis in gram-negative and fungal sepsis [18]. Akarsu et al. had shown the lowest platelet count in gram-negative than in gram-positive sepsis [19].

In our study, it was observed that among 51.51% severe thrombocytopenic neonates, Acinetobacter baumannii were the most common (n=4), and Candida spp. (n=4) followed by Klebsiella (n=3). Mortality in neonates admitted with sepsis in our study was 33.33%. Our centre is a tertiary referral centre with a high number of complicated deliveries and admissions, which substantiates the higher mortality rate. Among 60.6% gram-negative sepsis, mortality was 40% (8/20) while 33.33% gram-positive sepsis had 18.18% (2/11) mortality, and 12.1% fungal sepsis had 75% mortality (3/4).

Studies by Akarsu et al., and Khassawneh et al. found similar high mortality in gram-negative sepsis [21,19].

Candida albicans 3(27.27%), including one case with multi-organism sepsis, was the leading cause of death in the newborns followed by Klebsiella pneumoniae, Escherichia coli, Coagulase-negative staphylococcus including one case with multi-organism sepsis and Acinetobacter with each 2(18.18%) respectively.

We had one case of 28 weeks gestation, which was positive for the gram-negative organism Pseudomonas, gram-positive organism CONS, and fungus Candida spp. The baby was delivered via LSCS, to a mother with DCDA twin gestation in preterm labor and prolonged rupture of membrane. The baby presented with respiratory distress and feed intolerance, he had severe thrombocytopenia and succumbed to complications of sepsis after 35 days of hospital stay.

There were two other cases where we isolated two different gram-negative organisms, Klebsiella and Acinetobacter, and Escherichia coli and Citrobacter respectively, both babies had severe thrombocytopenia. The former case had a maternal history of pyelonephritis, clinically suspected chorioamnionitis, and prolonged rupture of membranes. The outcome was death after 21 days of hospital stay. The latter

was discharged home after 20 days of hospitalization. There was a history of prolonged rupture of membranes and fever.

There was another case, a term baby with no maternal risk factors, had temperature instability and respiratory distress, baby had severe thrombocytopenia. The outcome was discharge after 25 days of hospital stay.

Conclusion

Neonatal sepsis is one of the leading causes of mortality in neonates admitted to intensive care units. The major cause of mortality was Fungal sepsis followed by Gram Negative sepsis and Gram Positive sepsis. A large percentage of newborns admitted with sepsis also had thrombocytopenia. Severe thrombocytopenia was more prevalent in Gram Negative sepsis followed by Fungal and Gram Positive sepsis. Therefore, thrombocytopenia can be regarded as one of the earliest nonspecific predictors of sepsis in newborns admitted to the NICU. It also greatly affects the outcome of septic neonates.

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