

Organism Specific Response of Platelet Count in Neonatal Sepsis

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Abstract:

Background: Neonatal sepsis is one of the major causes of neonatal morbidity and mortality, particularly in developing countries and it is caused by Gram positive bacteria, Gram negative bacteria and fungi. Thrombocytopenia has been used as an early but nonspecific marker for sepsis. About 75% of culture positive neonates have thrombocytopenia. The severity and duration of thrombocytopenia varies in different types of organism. So, the objectives of this study were to examine platelet counts and platelet indices in neonates with culture proven sepsis and to determine if there was an organism specific platelet response.

Methods: This cross-sectional prospective study was carried out in the special care baby unit (SCABU) under department of Paediatrics and Neonatology, BIRDEM General Hospital, Dhaka from November 2008 to September 2009.

Results: Total 120 newborn babies with culture positive sepsis were included in this study. Gram positive bacteria was

found in 06 (5%), Gram negative bacteria was found in 58(48.3%) and fungi was found in 56 (46.7%) neonates. Thrombocytopenia was found in 95% of culture positive neonates. When compared with neonates with Gram positive sepsis, those with Gram-negative or fungal sepsis had a significantly lower platelet count, platelet nadir and prolonged duration of thrombocytopenia ($p<0.05$). Fungal sepsis was also associated with prolonged duration of thrombocytopenia when compared with that of Gram negative sepsis ($p=0.03$).

Conclusion: Neonatal sepsis is frequently associated with thrombocytopenia. However, Gram negative and fungal sepsis is associated with a lower platelet count, platelet nadir and prolonged duration of thrombocytopenia compared with that of Gram positive sepsis.

Key Words: Neonatal sepsis, thrombocytopenia, Gram positive bacteria, Gram negative bacteria, fungi.

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Introduction:

Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries.¹ Neonatal mortality in Bangladesh is 27 per 1000 live births.² Neonatal sepsis is defined as a clinical syndrome characterized by signs of systemic infection and documented by a positive blood culture in the first four weeks of life.³ Incidence of neonatal sepsis in Asia is 7.1 to 38 per 1000 live births,⁴ in Bangladesh it is 19.6 per 1000 live births.⁵

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The pattern of infection by various organisms varies from one institution to another and even from year to year in the same institution.⁶ The common organisms responsible for neonatal sepsis are Klebsiella pneumoniae, Acinetobacter, Escherichia coli (E.Coli), Pseudomonas aeruginosa, Salmonella, Haemophilus influenzae, Proteus, Coagulase negative staphylococci, Staphylococcus aureus, Streptococcus, Pneumococcus, Flavobacterium freundii, Candida etc.⁷

Blood culture is the gold standard test to diagnosis neonatal sepsis. But it could be positive only in 30-40% cases.⁸ Obtaining blood cultures from neonates can be difficult, sample volumes are small, and a substantial number are negative or contaminated.⁹ Estimation of cytokines and C Reactive Protein (CRP) levels are potentially useful in this respect.¹⁰ Complete blood count including platelet count is a good predictor of sepsis in newborns.¹¹

Thrombocytopenia is a major indicator of sepsis in neonates.¹¹ It has been shown that 75% of culture positive neonates had thrombocytopenia.¹² Majority of newborn developed thrombocytopenia by 36-48 hours

after developing neonatal sepsis and average duration of thrombocytopenia persisted around 6 days.¹³ There is a positive association of Gram negative infection and thrombocytopenia.¹⁴ Fungal infection is also associated with a greater degree of thrombocytopenia.¹⁵ Congenital viral infections like cytomegalovirus (CMV), toxoplasma, rubella and herpes simplex are important causes of thrombocytopenia in neonatal period and early infancy.¹⁶

Analysis of platelet count is a simple and readily available laboratory test. The present study was undertaken to examine platelet counts and platelet indices in neonates with culture proven sepsis and to determine if there was an organism- specific platelet response among 3 groups of infectious agents: Gram positive bacteria, Gram-negative bacteria and fungi.

Materials and Methods:

This cross-sectional prospective study was carried out at special care baby unit (SCABU), BIRDEM General Hospital during November 2008 to September 2009. Total 120 newborn babies with culture positive sepsis were included in this study. Neonates with congenital infections, maternal disorders causing thrombocytopenia, and lethal congenital anomalies were excluded. Maternal history, baby's birth events, clinical features consistent with neonatal sepsis and initial complete blood count including total platelet count and blood culture reports were recorded in a preset structured data collection sheet. After seeing blood culture report, studied neonates were divided into three groups as neonates with Gram positive sepsis, neonates with Gram negative sepsis and neonates with fungal sepsis. After inclusion of culture positive neonates blood was sent to evaluate the total platelet count, changes in platelet count including platelet nadir. Duration of thrombocytopenia was also noted.

Early onset sepsis is acquired from the mother before or during birth and the manifestations is present within 1st week of life. Late onset sepsis is acquired after delivery (in the nursery or in the community) which usually presents after 7 days of life.

Babies with a birth weight of less than 2500 grams irrespective of gestational age are defined as low birth weight babies. Babies with a birth weight of less than

1500 grams irrespective of gestational age are defined as very low birth weight babies. Babies with a birth weight of less than 1000 grams irrespective of gestational age are defined as extreme low birth weight babies.

Thrombocytopenia is defined as a platelet count less than 150,000/cmm of a viable gestational age. The changes in platelet count is defined as the percent change in platelet count at the time of sepsis as compared with a baseline platelet count which was initially done in all newborn at the time of admission. The platelet nadir is the lowest platelet count obtained during the period of hospital stay starting from the time the initial positive blood culture was drawn. The duration of thrombocytopenia was the number of continuous days that the platelet count remained below 100,000/cmm. Data analysis was done by employing Statistical Package for Social Science (SPSS), version-12.0. P value was considered significant when it was less than 0.05.

Results:

Out of 120 neonates, the mean age was 8.5 (\pm 4.6) days and the mean gestational age was 33.4 (\pm 4.0) weeks. Sixty seven (55.8%) babies were male and 53(44.2%) babies were female. One hundred and thirteen (94.2%) babies were born by cesarean section and rests of the babies were born by normal vaginal delivery. Sixty four (53.3%) babies were inborn and 56 (46.7%) babies were out born. Ninety four (78.3%) babies were preterm and rest of the babies was term. Among the study babies 56 (46.7%) had low birth weight, 34 (28.3%) had very low birth weight, 24 (20%) had normal birth weight and 6 (5%) had extreme low birth weight. Sixty five (54.2%) babies developed late onset sepsis and 55 (45.8%) babies developed early onset sepsis.

In this study Gram negative bacteria was found in 58 (48.2%) cases, fungi was found in 56 (46.7%) cases and Gram positive bacteria was found in 6 (5%) cases (Figure-1). most common organism found in this study was nonalbicans Candida (46.7%). Common bacterial pathogens found in this study were Klebsiella pneumoniae (20%) and Serratia (13.3%). Other organism found were: Pseudomonas aeruginosa (5.8%), Citrobacter (5.8%), Acinetobacter (3.3%), Staphylococcus (3.3%) and Enterococcus (1.7%) (Table-I).

Table-I*Distribution of organisms in blood culture (n=120)*

Organism	Number (%)
Nonalbicans Candida	56 (46.7)
Klebsiella pneumoniae	24 (20)
Serratia	16 (13.3)
Pseudomonas aeruginosa	7 (5.8)
Citrobacter	7 (5.8)
Acinetobacter	4 (3.3)
Staphylococcus	4 (3.3)
Enterococcus	2 (1.7)

No significant difference was found in between the baseline platelet count of neonates with Gram positive and Gram negative sepsis but significant differences

were found in between the platelet count at the time of sepsis, the platelet nadir, and the duration of thrombocytopenia of neonates with Gram positive and Gram negative sepsis (P value was <0.05). (Table-II)

No significant difference was found in between the baseline platelet count of neonates with Gram positive and Fungal sepsis but significant differences were found in between the platelet count at the time of sepsis, the platelet nadir, and the duration of thrombocytopenia of neonates with Gram positive and Fungal sepsis (P value was <0.05). (Table-III)

No significant difference were found in between the baseline platelet count, the platelet count at the time of sepsis, the platelet nadir of neonates with Gram negative and Fungal sepsis but significant difference was found in between the duration of thrombocytopenia of neonates with Gram negative and Fungal sepsis (P value was <0.05). (Table-III)

Table-II*Comparison of platelet status between neonates with Gram positive and Gram negative sepsis*

Platelet status	Gram positive sepsis (n=6)	Gram negative sepsis (n=58)	P value
Baseline platelet count (Mean \pm SD/cmm)	276,333 (\pm 59,868)	246,557 (\pm 59,371)	0.123
Platelet count at the time of sepsis (Mean \pm SD/cmm)	161,333 (\pm 60,447)	53,410 (\pm 31,618)	0.000
Platelet nadir (Mean \pm SD/cmm)	102,500 (\pm 79,814)	28,279 (\pm 26,894)	0.000
Duration of thrombocytopenia (Mean \pm SD/days)	2.5 (\pm 1.9)	7.2 (\pm 3.0)	0.000

Table-III*Comparison of platelet status between neonates with Gram positive and fungal sepsis*

Platelet status	Gram positive sepsis (n=58)	Fungal sepsis (n=56)	P value
Baseline platelet count (Mean \pm SD/cmm)	276,333 (\pm 59,868)	253,434 (\pm 90,767)	0.274
Platelet count at the time of sepsis (Mean \pm SD/cmm)	161,333 (\pm 60,447)	50,375 (\pm 29,935)	0.000
Platelet nadir (Mean \pm SD/cmm)	102,500 (\pm 79,814)	24,878 (\pm 22,184)	0.000
Duration of thrombocytopenia (Mean \pm SD/days)	2.5 (\pm 1.9)	8.3 (\pm 3.5)	0.000

Table-IV

<i>Comparison of platelet status between neonates with Gram negative and fungal sepsis</i>			
Platelet status	Gram negative sepsis (n=58)	Fungal sepsis (n=56)	P value
Baseline platelet count (Mean ±SD/cmm)	246,557 (±59,371)	253,434 (±90,767)	0.316
Platelet count at the time of sepsis (Mean ±SD/cmm)	53,410 (±31,618)	50,375 (±29,935)	0.299
Platelet nadir (Mean ±SD/cmm)	28,279 (±26,894)	24,878 (±22,184)	0.23
Duration of thrombocytopenia (Mean ±SD/days)	7.2 (±3.0)	8.3 (±3.5)	0.03

Discussion

In this study, Gram negative bacteria was found in 58 (48.3%) cases, fungi was found in 56 (46.7%) cases and Gram positive bacteria was found in 6 (5%) cases. This finding is similar to that of other studies which showed that gram negative bacteria were responsible in most cases of neonatal sepsis.¹⁷⁻²¹ A few studies reported fungi as the cause of neonatal sepsis.^{17,18} This was in contrast to other studies where gram positive bacteria were the commonest cause of neonatal sepsis^{11,22} while another study showed, the frequency of isolation of both gram positive and gram negative bacteria were equal.²³ These gram negative organisms make up the part of the modern ICU ecology and are usually transmitted from environmental flora via hands of caregivers, intravenous line and canula hubs especially in developing countries.²⁴

The most prevalent pathogens were nonalbicans Candida 56 (46.7%) in the present study. In one study, it has been shown that nonalbicans Candida was reported as the most prevalent pathogens which range from 14-100%.²⁵ In other study Candida species was reported as the leading cause of neonatal sepsis.²⁶ Fungal sepsis emerges due to prematurity, long term use of broad spectrum antibiotics, indwelling central venous catheters, total parental nutrition and hand washing procedures.²⁷

Klebsiella pneumoniae is emerging as a common bacteria in hospital settings^{5,7} and it was the predominant Gram negative organism in the present study. In this study, klebsiella pneumoniae was found in 24 (20%) cases, serratia was found in 16 (13.3%) cases, pseudomonas

aeruginosa was found in 7 (5.8%) cases, citrobacter was found in 7 (5.8%) cases and acinetobacter was found in 4 (3.3%) cases which is similar to those found in other studies.^{5,7}

Staphylococcus aureus was found in 4 (3.3%) cases and enterococcus was found in 2 (1.7%) cases, these two Gram positive organisms were isolated in present study which is similar to that of other studies.^{7,28}

Thrombocytopenia is a major indicators of sepsis in neonates¹¹. In this study 95% of culture positive neonates had thrombocytopenia this was in contrast to other studies where 75% of culture positive neonates had thrombocytopenia.^{12,29,30}

In this study, Gram negative and fungal sepsis was associated with a lower platelet count, platelet nadir and prolonged duration of thrombocytopenia compared with that of Gram positive sepsis which was consistent with that of another studies.^{11,31,32} Fungal sepsis was also associated with prolonged duration of thrombocytopenia compared with that of Gram negative sepsis which was similar to that of other studies.^{11,15,33}

Conclusion:

Sepsis is frequently associated with thrombocytopenia. It also has organism specific responses. Gram negative and fungal sepsis is associated with a lower platelet count, platelet nadir and prolonged duration of thrombocytopenia compared with that of Gram positive sepsis. Platelet count can be easily done to predict neonatal sepsis in any hospital setting. It is a cost effective, simple, easy test for early detection of neonatal sepsis.

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