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Original Research Article

Organism specific platelet response in neonatal sepsis in neonates weighing ≤1800 gm

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ABSTRACT

Background: Thrombocytopenia is an important but non-specific marker of severity of neonatal sepsis. Few studies have observed organism-specific response in platelet count, however this finding in not consistently seen in various studies. We carried out this study to look for organism-specific response of platelet count and indices in neonatal sepsis in our setup.
Methods: A prospective analytical study was conducted during December, 2019 to November, 2020 at tertiary care centre of central Gujarat. Neonates weighing ≤1800 gm (n=100) were enrolled according to eligibility criteria. Sepsis screen including TLC, ANC, platelet count, platelet indices, micro ESR, CRP, and blood culture was done. Patients with culture-proven sepsis were divided according to organisms isolated from blood or CSF. Patients were followed up to the final outcome of their hospital stay. Appropriate analytical tests were used for the results.
Results: Out of 100 patients, 69 had culture-proven sepsis, of which 40 (58%) were gram-negative, 21 (30%) were gram-positive and 8 (12%) had fungal sepsis. Of these 48/69 (70%) patients had thrombocytopenia. Of these patients with thrombocytopenia 60%, 30% and 10% in the first sample while 48%, 38% and 16% in the second sample had gram positive, gram negative and fungal sepsis respectively. Commonest organisms isolated were *Enterococcus* and MRCONS, and thrombocytopenia was not having specific correlation with any particular organism. There was no significant difference between mean and median platelet count of gram-positive, gram-negative, and fungal sepsis.
Conclusions: Thrombocytopenia is significantly associated with neonatal sepsis. The effects of sepsis on platelet count are not organism-specific.

Keywords: Thrombocytopenia, Neonates, Sepsis

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteraemia in the first 28 days of life.[1] Neonatal sepsis is one of the commonest and important causes of neonatal mortality, globally as well as in developing countries like India. Neonatal sepsis is the 3rd common cause of cause-specific mortality in India since 2000 according to Lancet systemic analysis declared in June, 2019.[2] Timely diagnosis of sepsis in neonates is critical as the illness can progress rapidly but signs and symptoms of sepsis in neonates are subtle and non-specific which makes it difficult to diagnose clinically.

Thrombocytopenia is defined as platelet count <150000/cmm. Thrombocytopenia is considered an important indicator of sepsis.[3,4] Blood culture is the gold standard test for diagnosis of sepsis but it takes 48-72 hours for the growth of the organisms. And studies show that it is positive only in 40-60% of cases. Thrombocytopenia is considered a non-specific marker of

sepsis in neonates. There is paucity of literature regarding organism-specific platelet response in neonatal sepsis.

The objective of the present study was to find out any organism-specific response on platelet count and platelet indices in neonatal sepsis.

METHODS

This prospective analytical study was carried out over 12 months from December 2019 to November 2020 at intramural and extramural neonatal nursery, department of paediatrics, S.S.G. hospital and medical college, Vadodara and was approved by the institutional ethics committee on human research of medical college and SSG hospital, Baroda.

The sample size was calculated using MedCalC software and with the statistical data available from monthly statistics of neonatal nursery and reference of published study Bhakri et al with a confidence interval of 95%.[5] The sample size of 88 was calculated.

All the neonates weighing ≤1800 gm, after applying inclusion and exclusion criteria were enrolled for the study. Neonates with birth weight ≤1800 gm and are either suspected to have sepsis based on clinical signs and symptoms of sepsis or having any 2 high-risk factors for sepsis like foul-smelling liquor, maternal intrapartum fever, prolonged rupture of membrane, chorioamnionitis, severe birth asphyxia were included. Neonates having any major congenital malformation, or who have received blood products or IvIg before enrolment or with neonatal alloimmune thrombocytopenia and autoimmune thrombocytopenia, patients already on antimicrobial therapy before enrolment, patients who are not surviving for >72 hours of admission and relatives not willing to give consent were excluded from the study.

Cases with clinical signs and symptoms of sepsis with the isolation of pathogens from the blood (BACTEC), CSF and urine were defined as confirmed neonatal sepsis. To avoid any confounding effects of earlier sepsis or treatment on platelets or other parameters of neonatal sepsis, only the first episode of sepsis in a patient was included in the study. Blood samples for sepsis screen including complete blood count with platelet counts, micro-ESR, CRP and blood culture was collected by venepuncture in patients with suspected sepsis. Second sepsis screen was performed after 24 hours of the first sample and the third sepsis screen 3-5 days after the second sample and as and when required after that depending on clinical basis. A 5-part Automated haematology analyser was used for TLC, ANC, Platelet count with platelet indices.

Positive sepsis screen was considered if 2 or more of the following parameters were present: TLC: leucocytosis (>20000/mm^3) or leukopenia (<5000/mm^3), ANC: Neutropenia or neutrophilia as per Manroe chart, S. CRP: ≥6 microgram/ml, platelet count-thrombocytopenia <150000/mm^3. Blood or CSF or urine showing growth of one or more organisms were noted and considered as gold standard for definite diagnosis of sepsis.

All the enrolled patients were followed up to the outcome of the admission in the form of discharge/ expired/left against medical advice. Data collected were analysed by applying appropriate statistical tests like chi square test. The data was entered by using MS office excel and analysis was done by using Med CalC version 19.6.1. P<0.05 was considered significant.

RESULTS

In our study, a total of 100 patients with ≤1800 gm with suspected sepsis were enrolled after applying inclusion and exclusion criteria and after taking informed written consent from the relatives. Among 100, the proportion of males and females was equal. We had selected babies weighing ≤1800 gm, out of which half were VLBW. Out of a total of 100, 79% cases comprised of preterm babies and 70% of small for gestation age. Out of 100, 70% cases were born of a vaginal delivery and 27% cases were born as a part of multiple gestations. Out of 100, a total of 69 patients had culture-proven sepsis (Table 1).

Table 1: Demographic profile.

Variables		Number (n=100)	Percentage (%)
Sex	Male	50	50
	Female	50	50
Weight	LBW	51	51
	VLBW	49	49
Gestation	Term	21	21
	Preterm	79	79
AGA/SGA	AGA	30	30
	SGA	70	70
Mode of delivery	Vaginal	70	70
	LSCS	30	30
Maternal risk factors for sepsis	Present	20	20
	Absent	80	80
	Single	73	73
	Multiple	27	27

Out of a total of 69, 45% of patients developed sepsis before 72 hours of life (early-onset sepsis) and 56% of patients developed sepsis after 72 hours of life (late-onset sepsis). There is no significant difference between the weight of the patients and development of early or late-onset sepsis as p=0.50.

Out of a total of 69 culture-positive cases, cases caused by gram-negative organisms were 40 (58%), gram-positive organisms were 21 (30%) and fungal sepsis was 8 (12%) (Figure 1). Out of 69 culture-positive cases, the most common organism isolated was *Acinetobacter* in 23

cases (33.39%). 2nd most common organism isolated was Methicillin-resistant CONS in 16 cases (23.18%). Other organisms isolated in descending order were *Klebsiella* (9/69, 13.04%), Candida (8/69, 11.59%), pseudomonas (7/69, 10.14%). *Streptococcus* and *Enterococcus* were isolated in 2-2 cases each and CONS and *E. coli* in 1-1 cases each (Table 2).

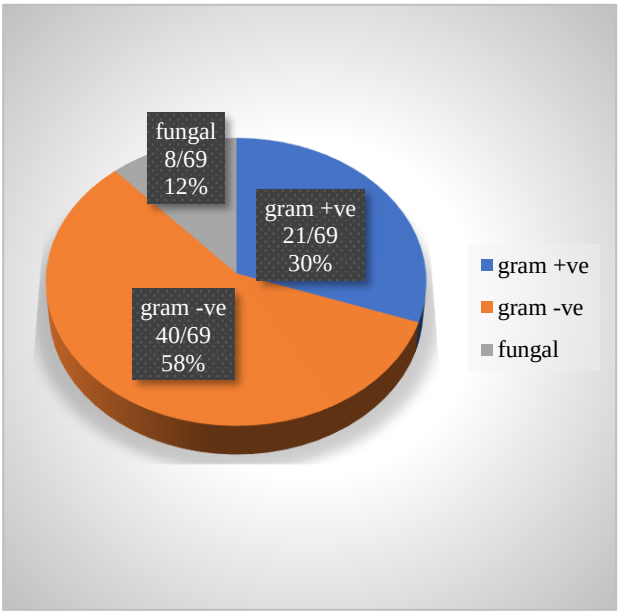

Figure 1: Distribution of cases according to type of organism.

Table 2: Distribution of cases according to organism.

Organisms		No. of cases (n=69)	Percentage (%)
Gram negative organisms	***Klebsiella***	**9**	**13**
	Acinetobacter	**23**	**33**
	E. coli	**1**	**2**
	Pseudomonas	**7**	**10**
Gram positive organisms	***Streptococcus***	**2**	**3**
	Enterococcus	**2**	**3**
	MRCONS	**16**	**23**
	CONS	**1**	**2**
Fungal	***Candida***	**8**	**12**
	total	**69**	**100**

In our study, there was no significant statistical difference between the occurrence of early or late-onset sepsis and specific organisms as p=0.07. Thrombocytopenia was studied in specific organism sepsis. Out of total patients having thrombocytopenia, 60% were gram-negative sepsis, 30% were gram-positive sepsis and 10% were fungal sepsis at the time of the first sample. While at the time of the second sample, 46% were gram-negative sepsis, 38% were gram-positive sepsis and 16% were fungal sepsis among the total of 48 cases (Table 3). 34/40 (85%) cases of gram-negative sepsis had thrombocytopenia at the time of enrolment and increased to 36/40 (90%) at the time of the second sample. Similarly, 17/21 (81%) cases of gram-positive sepsis had thrombocytopenia at the time of enrolment and 18/21 (86%) at the time of second sepsis. In fungal sepsis, 6/8 (75%) cases had thrombocytopenia at the time of enrolment and all 8 cases had thrombocytopenia at the time of the second sample.

Table 3: Type of organism and thrombocytopenia.

Organism	Sample 1 <150000, (n=57) (%)	Sample 2 <150000, (n=48) (%)
Gram negative organisms	34/57 (60)	22/48 (46)
Gram positive organisms	17/57 (30)	18/48 (38)
Fungal	6/57 (10)	8/48 (16)

Mean platelet counts in patients with gram-negative, gram-positive and fungal sepsis were 102350±69370, 113000±69977 and 114000±64171/cmm respectively and there was no significant difference between them as the p=0.81. As there was a large margin of variation among the platelet count values, medians of platelet count of gram-negative, gram-positive and fungal sepsis were taken into consideration. Median platelet counts were 87000, 93000 and 106000/cmm in gram-negative, gram-positive and fungal sepsis respectively and there was no significant difference among them as the p=0.73.

Platelet nadir was seen early in gram-negative sepsis as compared to game-positive and fungal sepsis. And it was improved with the treatment. However, in fungal sepsis highest fall in platelet count was seen later in the course (Figure 2). Platelet transfusion was given according to the clinical condition of the patient and not depending of platelet count. Platelet transfusions were given in 12 cases of culture-proven sepsis. Out of 12, 8 cases of gram-negative sepsis, 2 cases of fungal sepsis, 1 case of gram-positive sepsis and 1 case of culture-negative sepsis.

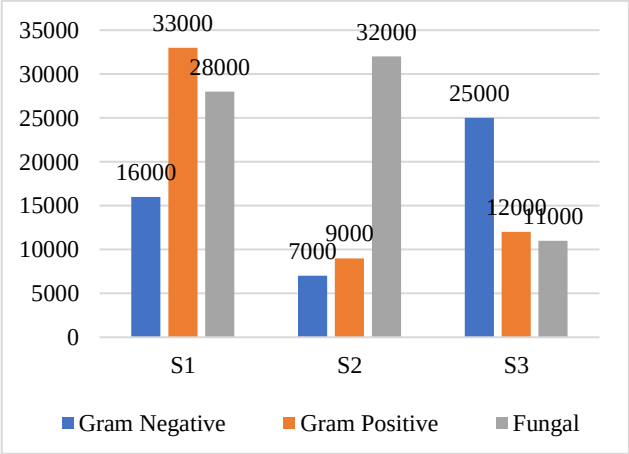

Figure 2: Type of organism and platelet nadir.

DISCUSSION

In our study, thrombocytopenia was present in 82.6% of cases of culture-positive sepsis which was not organism-specific (p=0.81). So, thrombocytopenia is one of the important but non-specific indicators of sepsis. However, Guida et al had concluded that thrombocytopenia is associated with sepsis in VLBW.[6] While Manzoni et al had a similar result to our study that thrombocytopenia is a non-specific marker of neonatal sepsis in preterm VLBW infants.[7]

In our study, gram-negative organisms were the most common organisms for neonatal sepsis. Bhat et al and Couto et al have concluded the similar results.[8,9]

Our study shows changes in platelet kinetics due to sepsis is not an organism-specific response as there is no statistically significant difference in the median and mean platelet count in gram-positive, gram-negative or fungal sepsis. Akarsu et al had shown higher platelet count in gram-positive sepsis as compared to gram-negative sepsis but these findings were only quantitative and not statistical.[10] Manzoni et al also concluded same findings as our study.[7] In contrast, Guida et al concluded that sepsis has organism-specific response over platelet kinetics.[6]

In our study, platelet nadir reached was 7000/cmm in gram-negative sepsis and 9000/cmm in gram-positive within 24 hours of initiation of sepsis. And in fungal sepsis platelet nadir was 11000/cmm which occurred later in the course. Guida et al and Akarsu et al had reported similar findings.[6,10] Bhat et al had concluded that thrombocytopenia was more severe gram-negative and fungal sepsis as compared to gram-positive sepsis. [(8)]Benjamin et al concluded that fungal sepsis is associated with greater degree of thrombocytopenia and poorer outcome as compared to gram-positive or gram-negative organisms.[11]

In our study, the mean platelet count in culture-proven sepsis was 106942±69185/cmm and in no sepsis was 207100±34506/cmm at the onset of sepsis and there was a statistically significant difference between these 2 groups (p<0.0001). Bhakri et al concluded similar findings that there is a statistically significant difference in mean platelet count between confirmed and no sepsis cases.[5] Abdalla et al stated that there is no statistical difference between these platelet responses and the type of microorganism.[12]

Limitations

There were few limitations of our study. Our study has relatively small sample size and data is from single centre. So, it would be desirable to have further multi-centric study with larger sample size to confirm the findings.

CONCLUSION

Thrombocytopenia is significantly associated with neonatal sepsis. However, this response is not related to any specific type of organism causing neonatal sepsis. This association of thrombocytopenia with neonatal sepsis can be utilized as one of the markers of neonatal sepsis and early presumptive diagnosis before we get the definitive diagnosis by blood culture. Further studies should explore its potential role in neonatal sepsis screen.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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