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Original Research Article

Proficiency of platelet parameters as an inexpensive efficient early marker for diagnosis of neonatal sepsis

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ABSTRACT

Background: Neonatal sepsis is an invasive serious infection which is life threatening if not treated early. Though blood culture is the gold standard for diagnosis but it yields positive results in fewer number of cases and it also time consuming. So it is requisite to ordain a cost effective and easy marker for its early diagnosis to initiate treatment to reduce the case fatality.
Methods: A prospective study was done for 12 months upon 48 blood culture proven cases of neonatal sepsis. 48 normal babies were taken as control group. Platelet parameters were studied in all 96 babies of the study population.
Results: It was found that thrombocytopenia, mean platelet volume (MPV), platelet large cell ratio (P-LCR) and mean platelet volume to total platelet count ratio (MPV/TPC) are early helpful markers for diagnosis of sepsis in neonates with p value of 0.0003, <0.0001, <0.0001 and <0.0001 respectively. MPV/TPC has the highest specificity (95.6%) with positive predictive value (90.2%).
Conclusions: Platelet count and its indices are cheap, early and workable marker for diagnosis of neonatal sepsis.

Keywords: Thrombocytopenia, MPV, P-LCR, MPV/TPC, Sepsis, Neonate

INTRODUCTION

The first month of life is the most vulnerable period of child survival, with 2.4 million newborn dying in 2020. Sub-Saharan Africa has the highest neonatal mortality rate in the world (27 deaths per 1000 live birth) with 43% of global newborn deaths, followed by Central and Southern Asia (23 deaths per 1000 live birth), with 36% of global newborn deaths.[1] With the birth of 25 million children each year India accounts for nearly one fifth of the worlds annual child birth. Every minute one of those babies dies. Prematurity (35 per cent), neonatal infections (33 per cent), birth asphyxia (20 per cent)and congenital malformations (9 per cent) are among the major cause of newborn deaths.[2] Neonatal septicemia is considered one of the leading cause of neonatal mortality globally, more in developing countries like India.[3] Septicemia in neonates is a blood infection that can lead to sepsis which is a clinical syndrome of bacteremia characterized by systemic signs and symptoms of infection in less than 28 days of life.[4] Neonatal sepsis has been a leading cause of high morbidity and mortality in newborns and is recognized as a global health challenge.[5,6] The incidence of neonatal sepsis in India was 30/1000, as per the neonatal perinatal database (NNPD).[7] The total neonatal mortality rate was 28/1000 live birth of which one third proportion of deaths occur due to sepsis.[8] It is very hard to find out any particular rapid and cost effective hematological test or specific clinical signs to confirm sepsis in neonates. Although it is very requisite to diagnose early a case of neonatal sepsis to initiate early specific treatment as delay in treatment will significantly increase the case fatality and serious morbidity and early initiation of empirical therapy without diagnosis will lead to serious antibiotic resistance in some cases. Blood culture is the gold standard for diagnosis of neonatal sepsis but it is costly and requires 48-72 hours to get a positive result. Moreover, it is positive only in 35-75% of septic cases and culture become negative in some

spurious organisms.[9,10] There is no ideal tests or combination of tests that will definitely point towards diagnosis of sepsis.[11,12] So it is required to find out a diagnostic tests or markers which is feasible with acceptable sensitivity and specificity as well as cost effective so that every health care facility can afford it. The coagulatory system is frequently involved in case of neonatal sepsis. Bacteria and its toxins can cause damage to endothelial cells leading to platelet adhesion and aggregation or sometimes directly binds to platelets leading to aggregation and dispatch from the circulation.[13]In neonatal sepsis platelets are rapidly expedited from the circulation and destructive thrombocytopenia occurs. As a result of that production of platelets get activated and newer platelets with variable size comes out in the circulation. Mean platelet volume (MPV) (normal 8.5 fl-12.5 fl) is the average size of platelets in the circulation which is increased in septicemia due to platelet production rate and platelet activation.[14,15] Platelet distribution width (PDW) (normal 10-17%) is an indicator of variation in size of platelets in the circulation which is increased in septicemia due to destructive thrombocytopenia and platelet activation.[16] Platelet–large cell ratio (P-LCR) (normal less than 30%) indicates the proportion of platelets greater than 12fl in the circulation in regard to total platelet count which also increased in septicemia due to same cause.[17] MPV/TPC is another important platelet parameter (normal ratio up to 7.2%) which is increased in platelet activation. These platelet parameters can be easily measured by routine blood count analyzer which is rapid and cost effective. There are different studies about platelet patameters in neonatal sepsis which showed beneficial results in most of the studies.[18,19] This study was done to find out the efficiency of these parameters for diagnosis of neonatal sepsis in our setting.

METHODS

This prospective study was done at the sick newborn care unit (SNCU) and neonatal intensive care unit (NICU) of North Bengal Medical College and Hospital, Darjeeling, India for a period of 12 months from July 2021 to June 2022. Ethical permission was taken from institutional ethical committee. Informed and written consent were taken from all the parents of the neonates included in the study.

Inclusion criteria

All newborns admitted during the study periods with symptoms of sepsis like poor feeding, hypothermia, lethargy, bradycardia, tachycardia, cyanosis, apnoea, and hypotension.

Exclusion criteria

Major congenital anomaly, suspected inborn error of metabolism, respiratory distress syndrome (surfactant deficiency), pathological jaundice, who received antibiotics before taking blood culture sample and who not given consent for the study. During the study period 190 neonates were admitted with symptomatology of sepsis of which 39 babies had clinical sepsis (sepsis screen negative and blood culture negative), 97 babies had probable sepsis (sepsis screen positive but blood culture negative) and only 54 babies suffered from blood culture proven sepsis. Six neonates were excluded for birth asphyxia, hypoglycemia, pathological jaundice and congenital malformations. Finally, the study case was 48. Similar number of healthy neonates were taken as control group. So the study population was 96. About 2.5 ml blood was taken from all the babies of study population and incorporated in EDTA vaccume container. Smears are made and stained by Leishman's stain for platelet count determination. Platelet indices were determined by incorporation of blood in the automated analyzer (Sysmex XN 1000).

Statistical analysis

Results found in both the groups were compared by standard statistical method. For stastical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS version 24.0 and GraphPad Prism version 5. P value of less than 0.05 was considered statistically significant.

RESULTS

This study was performed in the SNCU and NICU of North Bengal Medical College and hospital. During the study period 48 neonates had culture proven sepsis. Demographic profile of study population was illustrated in Table 1.

Table 1: Demographic profile of study population.

Study group	Cases	controls	P value
Gender			
Male	30	26	P=0.82
Female	18	22	
Age in days	6.9	3.2	P=0.51
Birth weight (kg)			
<2.5	28	18	P=0.62
>2.5	20	30	

Table 2: Frequency of bacterial isolates in neonates with culture proven sepsis.

Types of microorganism	Frequency	Percentage	P value
Klebsiella	17	35.4	0.3
E. coli	10	20.8	1.000
Enterococcus	4	8.3	0.132
Staph aureus	13	27	0.3
Streptococcus	2	4	1.000
Pseudomonas	0	0	
Candida	2	4	0.143
Total	48		0.132

There was male preponderance in cases and female babies are more in control group. Average age was about 7 days in cases and most of them weing <2.5 kg. Gram negative bacteria was the most common microorganism found (Table 2) in blood culture denoting that most babies acquire them during birth process and suffering from early onset septicaemia.

Table 3: Different platelet parameters and their coalition with study subjects.

Study group	Cases	Controls	P value
Total platelet count (lac/cc)			
>1.5	9	44	0.0003
<1.5	39	4	
MPV (fl)			
>10.5	45	42	<0.0001
<10.5	3	6	
PDW (%)			
>19.1	34	15	0.0002
<19.1	14	33	
P-LCR	29.12±1.35	20.41±1.13	<0.0001
MPV/TPC	10.27±2.5	3.66±1.6	<0.0001

MPV: Mean platelet volume, PWD: platelet distribution width, P-LCR: platelet large cell ratio, TPC: total platelet count

Table 4: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of different platelet parameters.

Parameters	Reference cut-off level	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
TPC	<150000/µl	88.5	22.8	34.6	79.3
MPV	>10.5fl	85.8	32.9	42.7	82.6
PDW	>19.1%	80.2	35.5	41.2	79.5
P-LCR	>45%	79.5	36.3	43.1	77.5
MPV/TPC	≥7.2	48.5	95.6	90.2	71.4

DISCUSSION

Neonatal sepsis is a critical illness which is alarming to all pediatricians due to its high mortality and long-term morbidity. Early diagnosis and specific treatment is necessary for favourable outcome but it is very difficult to diagnose early. Different platelet parameters have been studied around the globe for few decades showing different results. This study is the first in this geographical region which is unique of its kind.

Platelet count is an important parameter for early diagnosis of neonatal sepsis. There was evidenence that significant thrombocytopenia occurs even before the bacteria cultured from the blood of septic neonates.[20] Choudhary et al showed in their study that there was significant thrombocytopenia of 81.12% in septicemic neonates.[19] There are also various studies which showed that thrombocytopenia is a important marker for early diagnosis of neonatal sepsis.[21-23] Our finding in this study reinforces that thrombocytopenia is an early indicator of neonatal sepsis with a high sensitivity and negative predictive value (Table 4). Mean platelet volume (MPV) is the volume of platelets in the circulation which is increased during platelet activation. Platelet shape changes from biconcave discs to spherical with pronounced pseudopod formation which leads to raise of MPV during platelet activation. In this study it was seen that there was marked raise of MPV with p<0.0001 (Table 3) which is supportive of different other studies.[19,21,23] Platelet distribution width (PDW) is an indicator of volume variability in platelet size which is increased in platelet anisocytosis. PDW increased in cases of destructive thrombocytopenia like neonatal sepsis.[24] In this study PDW increased in 70% of cases in comparison to control where only 31% cases showed raise (p=0.0002) with high sensitivity and negative predictive value (Table 4). Majumder et al in their study showed similar results that PWD increased significantly in sepsis group with p<0.0004.[23] Platelet larger cell ratio(P-LCR) is an indicator of circulating larger platelets (>12.5 fl) which is presented as percentage. The normal percentage range is 15-35% which is increased in case of platelet activation like septicemia.[25] Mittal et al in their study showed that there was significant raise of platelet larger cell ratio in cases than in controls.[21] In this study we found similar results with P<0.0001 which reinforces other studies.[19,23] MPV/TPC is a ratio which is another important platelet parameter with limited number of studies till date. In this study it has been found that it has a high specificity (95.6%) and high positive predictive (90.2%) value with p<0.0001 prevailing a low false positivity rate. Panda SK

et al found similar type of results which reinforces the findings in this study.[26]

Limitations

Sample size in this study is not larger and sometimes there is delay in performing the tests after sample collection. So multicentre study with larger sample size with prompt testing after sample collection will require for better results.

CONCLUSION

Sepsis in neonates have significant thrombocytopenia with marked increase in MPV, P-LCR, PWD and MPV/TPC in comparison to healthy neonates. These platelet indices are easily measurable by automated blood analyzer which is available in most of the health care facility. These tests are very cost effective and can be used for early diagnosis of neonatal sepsis.

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