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Original Research Article

Platelet count and its indices as diagnostic markers of neonatal sepsis: a cross-sectional study

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ABSTRACT

Background: Neonatal sepsis is a critical condition posing a significant threat to newborns globally, particularly in developing countries. The non-specific symptoms and time-consuming traditional diagnostic methods highlight the need for rapid and reliable biomarkers. Recent studies suggest platelet count and indices such as mean platelet volume (MPV) and platelet distribution width (PDW) as potential indicators for early diagnosis of neonatal sepsis. This study aimed to assess the correlation between platelet count and its indices and neonatal sepsis.
Methods: A hospital-based cross- sectional study was conducted at NICU of tertiary care hospital involving 80 neonates with suspected sepsis. Platelet count, PDW, and MPV were measured and correlated with neonatal sepsis. Statistical analyses were performed using SPSS software, with a significance set at $p<0.05$.
Results: Of the 80 neonates studied, 22.5% exhibited thrombocytopenia. There was a noteworthy inverse relationship discovered between platelet count and sepsis, while MPV and PDW were higher. Gram-negative organisms were the most common cause of sepsis, out of which *E. Coli* (63.64%) was the most common.
Conclusions: The study confirmed a significant association between platelet count and indices with neonatal sepsis. Platelet count, MPV, and PDW can serve as effective, rapid diagnostic markers, potentially improving early detection and outcomes in neonatal sepsis.

Keywords: Neonatal sepsis, Platelet count, MPV, Thrombocytopenia, PDW

INTRODUCTION

Sepsis in neonates is a main reason of morbidity and mortality among newborn infant in developed and developing countries. Neonatal sepsis is referred to as a systemic illness of bacterial, viral, or fungal origin that is associated with hemodynamic changes and other clinical symptoms resulting in morbidity and mortality in newborn.[1] Recently, the global burden of disease (GBD) Study 2016-17 assessed 1.3 (95% CI 0.8 to 2.3) million annual incident cases of Neonatal Sepsis globally, resulting in 203,000 sepsis related deaths.[2] The case fatality rate of sepsis among neonates in India ranges from 25% to 65%.[3]

Sepsis is a non-specific inflammatory defence mechanism and is considered a generalized process where every organ and system can be involved. The haemostatic system is frequently disturbed during sepsis.

Early and accurate diagnosis is crucial for timely intervention and improved outcomes. However, the non-specific clinical presentation and the time-consuming nature of current diagnostic methods, such as blood cultures, pose significant challenges to early detection and treatment.[4] In this context, there's a growing interest in identifying reliable, rapid biomarkers for early diagnosis of neonatal sepsis. Among these, platelet count and indices such as MPV and PDW have emerged as

potential diagnostic tools. Platelets, traditionally recognized for their role in hemostasis, have recently been appreciated for their function in the immune response, particularly in sepsis. A typical observation in sepsis is thrombocytopenia, or a drop in platelet count, which has been linked to a higher risk of morbidity and mortality in newborns.[5,6]

Recent research has indicated that changes in platelet indices can be an early sign of sepsis and may correlate with its severity.[7,8] A higher MPV, for instance, has been associated with bacterial infections and could reflect an increased turnover of platelets in response to septic conditions.[5] Similarly, PDW, a measure of the variability in platelet size, has been shown to increase in the presence of infection and inflammation.[9] Despite these promising findings, there is a need for more comprehensive studies to validate the utility of platelet count and indices as diagnostic biomarkers in neonatal sepsis, especially in diverse clinical settings.

Platelet indices like MPV and PDW reflect platelet activation and have been studied in various adult populations as indicators of inflammatory and infective conditions.[9,10] However, their role in neonatal sepsis is less clear and has been the subject of fewer studies. Hence the present study was undertaken to evaluate thrombocytopenia and variations in platelet indices in neonatal sepsis.

METHODS

The index cross-sectional research study was carried out from 1st November 2022 to 31st October 2023 at neonatal intensive care unit of tertiary care hospital after taking written and informed consent from the parents of the neonate. Ethical clearance was obtained from the institutional ethics committee.

Sample size

Sample size has been calculated using the formula 4PQ/L2,

Where, p=anticipated proportion of outcome (95%).[11]

q =100-p

l=absolute error (5%)

N = 4×95×5/25

Approximately 80 neonates admitted in neonatal unit of hospital showing signs and symptoms of sepsis, and/or born to mothers with risk factors forsepsis were included in the study.

Inclusion criteria

Neonates admitted to neonatal intensive care unit with signs and symptoms of sepsis and / or born to mothers having risk factors for sepsis, parents who have given consent were included.

Exclusion criteria

Neonates having congenital and acquired cause of thrombocytopenia and platelet indices other than sepsis i.e., Autoimmune alloimmune platelet disorders. Neonates with any congenital abnormality, Hyaline membrane disease, congenital heart disease. Neonates with metabolic disorders, known chromosomal abnormalities, intrauterine growth restriction or birth asphyxia. Mothers who have taken antibiotics within 48 hours of delivery were excluded from study.

Methodology

All neonates admitted to neonatal intensive care unit with clinical suspicion of sepsis or born to mothers having risk factor for sepsis (i.e., maternal fever, significant PV leaking, maternal UTI) were part of the study after taking written and informed consent from parents of neonate. History, examination findings and lab data of neonates were recorded on a structured proforma (Figure 1).

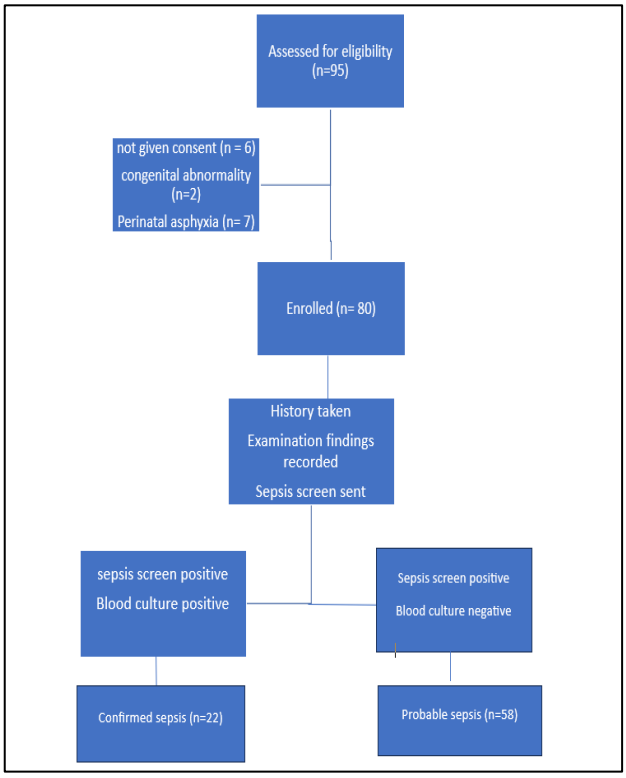

Figure 1: Study flow diagram.

The blood samples were collected by peripheral venepuncture in EDTA (tripotassium ethylenediaminetetraacetic acid) vial using aseptic precautions for evaluation of platelet indices. Platelet count, MPV, PDW were evaluated three times: at admission, 3rd day and 7th day of sepsis.

One millilitre of blood was collected into a K3 EDTA tube (tripotassium ethylenediaminetetraacetic acid) and counts performed within 1 hour ofsample collection using 6-part Sysmex XN-350 fully automated haematology analyser.

Two millilitres of blood drawn into blood culture bottle under all aseptic- precautions and analysed using fully automated BACTEC method.

The study group were categorized into two groups: Confirmed neonatal sepsis: Presence of clinical signs and symptomsof sepsis with isolation of pathogen from blood culture.

Probable sepsis: clinical features and laboratory parameters consistent with infection without a positive culture.

Possibility of clinical sepsis was considered if the following clinical features were present: hypothermia/ hyperthermia instability, convulsions, bulging anterior fontanelle, lethargy or unconscious or drowsy, poor activity, apnea/tachypnea, respiratory distress, tachycardia/bradycardia, hypotension, refusal to feed, abdominal distension and necrotising enterocolitis.

Statistical analysis

Data was entered in excel sheet which was imported in SPSS; licensed version 23.0. Descriptive Analysis was done and expressed in proportion, mean and standard deviation. Quantitative data was analysed using t-test and expressed in mean and standard deviation. Qualitative data was analysed using chi square test and expressed in proportion. P<0.05 was considered statistically significant.

RESULTS

A total of 80 neonates admitted with clinical signs of sepsis were included in the study, out of which 56 (70%) had early onset sepsis (EOS), while, 24 (30%) had late onset sepsis (LOS). Confirmed sepsis was reported in 27.5% neonates, while 72.5% had probable sepsis. The mean age of neonates in the EOS Group was 1.23±0.57 days, and in the LOS group was 18.92±7.09 days. There was nearly equal distribution among males (47, 58.75%) and females (33, 41.25%). Preterm and term babies were 38.7% (31) and 61.3% (49) respectively (Table 1).

The mean platelet counts on day 1, day 3 and day 7 of sepsis was significantly lower in culture-positive neonates compared to culture-negative cases (p<0.05). A progressive increase in the platelet count was observed by day 7 post-antimicrobial therapy (Table 2).

MPV was greater in neonates with culture positive sepsis as compared to culture negative cases and there was significant difference in mean MPV between the two groups (p=0.02). This shows that high MPV has an association with neonatal sepsis (Table 3).

PDW was found to be high in neonates with culture positive sepsis compared to culture negative sepsis (Table 4), though difference statistically insignificant (p>0.05).

Thrombocytopenia was noted in 22.5% (18) neonates with sepsis, while 71.25% (57) neonates had a normal platelet count. Thrombocytosis was present in 6.25% (5) neonates (Table 5). Thrombocytopenia was common on day 1 of neonatal sepsis and platelet count gradually improved as sepsis get controlled after instituting the antimicrobial therapy.

Blood culture was positive in 27.5 % of the neonates (Table 6), *E. coli* was the most common organism (63.64%) isolated in the culture followed by *Klebsiella* (22.73%) and *Staphylococcus aureus* (13.64%).

In our study, age, sex, gestational age, hemoglobin and TLC were not comparable between the two groups.

The results indicate a significant association between various platelet indices and neonatal sepsis. These findings support the potential of platelet count and indices as diagnostic biomarkers in neonatal sepsis.

Table 1: Demographic profile of neonates.

Variables	Culture positive, (n=22)	Culture negative, (n=58)
Mean age (in days)	9.96±7.41	8.64±6.45
Male	13	34
Female	9	24
Preterm	9	22
Term	13	36
EOS	16	40
LOS	6	18

Table 2: Comparison of mean platelet count in culture positive and culture negative at different time interval.

Plateletcount	GROUP	N	Mean	SD	Sig. (2-tailed)
Plateletcount 1st day	Culture positive	22	2.17	1.18	0.0436*
	Culture negative	58	2.75	1.11	
Plateletcount 3rd day	Culture positive	22	2.10	1.16	0.0431*
	Culture negative	58	2.66	1.06	
Plateletcount 7th day	Culture positive	22	2.24	1.16	0.0417*
	Culture negative	58	2.83	1.13	

*Statistically significant (p<0.05).

Table 3: Comparison of mean MPV in culture positive and culture negative at different time interval.

MPV	Groups	N	Mean	SD	Sig. (2-tailed)
MPV 1st day	Culture positive	22	10.22	1.18	0.0214*
	Culture negative	58	9.63	0.93	
MPV 3rd day	Culture positive	22	10.13	1.07	0.0402*
	Culture negative	58	9.53	1.15	
MPV 7thday	Culture positive	22	9.91	1.12	0.0450*
	Culture negative	58	9.32	1.17	

*Statistically significant (p<0.05).

Table 4: Comparison of mean PDW in culture positive and culture negative at different time interval.

PDW	Groups	N	Mean	SD	Sig. (2-tailed)
PDW 1stday	Culture positive	22	11.61	2.34	0.844#
	Culture negative	58	11.49	2.54	
PDW 3rd day	Culture positive	22	11.47	2.45	0.707#
	Culture negative	58	11.24	2.51	
PDW 7th day	Culture positive	22	11.31	2.68	0.801#
	Culture negative	58	11.15	2.10	

#Statistically not significant (p>0.05).

Table 5: Platelet count (in lakhs).

Platelet count (in lakhs)	N	Percentage (%)
<1.5	18	22.5
1.5-4.5	57	71.25
>4.5	5	6.25
Total	80	100

Table 6: Organism isolated in the culture.

Organism	N	Percentage (%)
E. Coli	14	63.64
Klebsiella pneumoniae	5	22.73
Staphylococcus aureus	3	13.64
Total	22	100.00

DISCUSSION

In the present study conducted in NICU, Rohilkhand medical college and hospital, 80 neonates with clinical features of sepsis were considered to explore the diagnostic potential of platelet count and indices as markers of neonatal sepsis. The purpose of this study was to determine the frequency of thrombocytopenia and the variations in different platelet indices in newborn sepsis, particularly concerning duration of illness and specific organisms.

The prevalence of thrombocytopenia in sepsis is variable and different values have been reported in earlier studies conducted in various countries. Studies demonstrate that thrombocytopenia is an important marker of sepsis. In our study, platelet count was significantly lower in culture positive group than the culture negative ones (p<0.05). In this study, thrombocytopenia was noted in 22.5% of the neonates with sepsis. This result is in contrary to that of other studies by Arif et al (83.5%) and Choudhary et al the 81.2%.[12,13] This difference might be because of the small sample size taken in the study. Thrombocytopeniais a common complication in patients who are critically ill, suffering from various diseases and is also correlated with rise in mortality.

Platelet count (low) and MPV (high) were found to be significant predictors of neonatal sepsis, in our study, affixing the findings of the existing literature. In our study mean MPV was greater in neonates with culture positive sepsis (27.5%) as compared to neonates with culture negative sepsis (72.5%) and there was significant difference in mean MPV (p=0.02) between the two groups. This shows that high MPV has an association with neonatal sepsis. Aydemir et al reported significantly higher MPV in neonates with sepsis.[14] Wang et al echoed the findings of our study that higher MPV measures were reported in neonates with sepsis, thus signifying its potential role as predictor of sepsis.[15] Kim et al reported that such an increase in MPV especially during first 72 hours may be a good marker of deleterious outcomes in neonatal sepsis of severe nature.[16] Not just the incidence, the platelet indicators have shown to predict the sepsis severity too (Catal et al).[11] The results of this study are comparable to that reported by Meena et al, Mittal et al and Guida et al, Aydemir et al.[4,14,17,18] reported MPV to be a significant predicator of sepsis.

The PDW was found to be high in neonates with culture positive sepsis, in this study. This difference was statistically insignificant (p>0.05). There was no correlation between a high PDW and culture positive sepsis. These results are in accordance with studies done by Meena et al and Mittal et al.[17,18] In Mittal et al study, more number of neonates with culture positive sepsis had thrombocytopenia and a high MPV and PDW.[18] However, these differences were not statistically significant. Patrick et al report that the PDW was high in

neonates with culture positive sepsis and indicates a significant association between culture positive sepsis and high PDW.[7]

Blood culture was positive in 27.5 % of the neonates, *E. coli* was the most common organism (63.64%) isolated in the culture followed by *Klebsiella* (22.73%) and *Staphylococcus aureus* (13.64%) which is similar to the findings of Aydemir et al.[14] Our findings contradict the other existing literature wherein the most common organism reported with neonatal sepsis were *Klebsiella* by Salama et al (31.8%). Turhan et al and Kumar et al reported *Staphylococcus aureus* to be the most common organism (39% and 35.7% respectively).[19-21]

The study found that decreased platelet count was associated with increased MPV in cases of septicemia. Similar to observations by Nelson and Kehlet al and Becchi et al it was found that MPV has an important prognostic value in the early stage of sepsis.[8,10] Increased PDW was also noted in septic neonates, aligning with findings from Guclu et al and Patrick et al who reported significant increases in PDW in the presence of bacteremia.[5,7] Several studies have highlighted the role of platelet indices in diagnosing neonatal sepsis. Guida et al and Bhat et al have documented the utility of platelet count, MPV, and PDW as markers of neonatal sepsis, with variations observed in culture-positive and culture-negative sepsis cases.[4,6] The findings are consistent with these studies, reinforcing the potential of these indices as useful, rapid diagnostic tools in neonatal sepsis.

The significant association of thrombocytopenia with neonatal sepsis indicates that platelet count and indices can be valuable additions to the diagnostic and prognostic tool kit for neonatal sepsis. Their routine assessment in suspected cases could lead to earlier diagnosis and more targeted treatment, potentially improving outcomes.

Strengths

All observations and data for the study was collected by single investigator thus eliminating interrater bias.

Limitations

The study included participants from a single center, hence, the external validity is limited. As the sample size of our study was small, the findings are not representative of all neonates with sepsis. EDTA was used as an anticoagulant, and platelet indices may be affected by these anticoagulants.

CONCLUSION

Thus, to conclude, our study reports that the commonly used platelet indices (platelet count, MPV and PDW) are significant predictors of the incidence of the neonatal sepsis in NICU settings. Neonates with confirmed sepsis had severe thrombocytopenia and high MPV and PDW, which is an indication of poor prognosis. Platelet count and platelet indices are hematologic parameters that can be easily evaluated, and thus, can be adopted as valuable tools for diagnosing neonatal sepsis, especially in remote and resource-limited regions in countries such as India. Blood culture positivity was low in our study which may be due to mostly referred patient who are already on antibiotic and due to small sample size, thus emphasizing on the need to conduct more such studies. These parameters should be taken into consideration for the diagnosis in cases suspected to have sepsis, so that treatment can be initiated promptly and morbidity and mortality can be reduced. However, more studies with a larger sample size are needed to confirm these results and to know the actual relation of changes in different platelet indices with that of organisms and duration of sepsis.

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

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