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Platelet indices as an earlier and economical marker of neonatal sepsis

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Abstract:

BACKGROUND: Neonatal sepsis is a life-threatening condition which needs urgent diagnosis and proper management. Blood culture and sepsis screening are currently used methods, but their utility is limited due to delayed reporting and increased cost. However, in newborn infants, a close relationship between sepsis and thrombocytopenia and other changes in platelet indices such as increased mean platelet volume (MPV) and platelet distribution width (PDW) has been suggested by few studies.

OBJECTIVE: This study aimed to assess the diagnostic value of platelet indices in the early detection of neonatal sepsis.

MATERIALS AND METHODS: A retrospective study with diagnostic testing was carried out by collecting data from medical records of neonates with neonatal sepsis who were admitted to the Neonatology Department in DR. B. C Roy PGIPS, Kolkata, over the period from January 2019 to December 2019. One hundred neonates were included in the study, 50 were proven to have sepsis by culture, and others are used as controls (apparently healthy babies). Sensitivity, specificity, positive predictive value, and negative predictive value of platelet count, MPV, and PDW in neonatal sepsis were determined using a 2 × 2 table.

RESULTS: The platelet count was significantly decreased, whereas PDW and MPV were increased in septic babies ($P < 0.0001$).

CONCLUSION: Platelet indices can be used to diagnose neonatal sepsis as easily available and cheaper markers.

Keywords:

Neonatal sepsis, platelet indices, thrombocytopenia

Introduction

Neonatal sepsis is one of the commonest causes of neonatal mortality contributing to 15% of all neonatal deaths.[1] The situation is even worse in underdeveloped countries. The most important approach is the availability of early diagnosis and thereby early treatment of infants with sepsis, because, early diagnosis and treatment is the life-saving for most of the case.[2] However, it is a diagnostic challenge as there are overlapping signs and symptoms which preclude a specific diagnosis of sepsis. A high index of suspicion and its confirmation are necessary for the early diagnosis of sepsis. Various tests are traditionally applied.[3] Although blood culture is a gold standard for diagnosis, it is not without limitations. Supreetha *et al*. reported that a definite diagnosis of septicemia by a positive blood culture required a minimum period of 48–72 h and yielded a positive result in 30%–70% of cases.[4] The negative predictive value (NPV) of various sepsis screen parameters is too low to confidently rule out sepsis. Hisamuddin *et al*. reported 70% diagnostic accuracy of C-reactive protein levels for diagnosis of neonatal sepsis and suggested that C-reactive protein levels alone are not specific enough to be relied upon as the only indicator of neonatal sepsis.[5] There is no ideal test or combination of tests that are benchmarkers of an excellent test.[6-8] And

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thus, the need for better diagnostic parameters arises which should be with good sensitivity and specificity as well as of low cost so that any health care facility can use it.

The hemostatic system is frequently disturbed during sepsis. In particular, in newborn infants, a close relationship between sepsis and thrombocytopenia and other changes in platelet indices such as increased mean platelet volume (MPV) has been suggested by a few studies.[9-11] Vander Van der Lelie *et al*. suggested that an increased MPV could be associated with invasive infections. Under physiological conditions, MPV and platelet distribution width (PDW) are directly related. When there is an increase in PDW, MPV increases.[12] Advantages of platelet indices are that all these indices are readily available with no additional cost while performing routine blood counts using autoanalyzers. There have been studies showing significant changes in platelet indices in patients with neonatal sepsis.[13] Still, there is no clear consensus, so more studies are needed on this subject. Hence, the present study was undertaken to evaluate thrombocytopenia and variations in platelet indices in neonatal sepsis.

Materials and Methods

This retrospective study was conducted in the Department of Pathology in collaboration with the Department of Paediatrics and Microbiology of Dr. B. C. Roy PGIPS, Kolkata, over a period of 1 year extending from January 2019 to December 2019. Informed and written consents were obtained from the parents of all enrolled neonates.

A total of 60 children with sepsis (cases) and 50 without sepsis (as controls)were included in the study. The children with sepsis were diagnosed on the basis of the signs and symptoms of bradycardia (<100/min), tachycardia (>200/min), hypotension, respiratory distress, irritability, lethargy, cyanosis, apnea, tachypnea, bluish skin color and poor perfusion, feeding difficulty. The patients (10 in number) with incomplete medical record data, immunodeficiency diseases, autoimmune diseases, malignancies, hematological disorders, and major congenital anomalies were excluded from the study.Finally, the study included 50 septic newborns (sepsis group) and 50 healthy newborns (control group).

This study aims to study the relation between neonatal sepsis and platelets and its indices (platelet count, MPV, PDW). For these tests, we drew approximately 2 ml of venous blood from each neonate through peripheral veins in ethylenediaminetetraacetic acid tube. Smears are made from peripheral blood and stained by Leishman's stain and examined to confirm thrombocytopenia. Platelet indices were collected from an automated machine (Sysmex XE 2100). Bacterial and fungal organism type is detected by blood culture and Gram staining. Neonates were evaluated through detailed history from the mother and clinical examinations. Peripheral venous blood was collected from all the newborns and sent for investigations for blood culture, sepsis screen, and platelets indices. On the results obtained, they were classified into three groups: proven sepsis – culture positive; suspected-screen positive but culture negative; and clinical sepsis – both screen and culture negative.

Data collected in this study were gender, gestational age, birth weight, blood culture result, platelet count, MPV, and PDW. Data analysis was carried out using SPSS software (Statistical analysis was carried out using the IBM SPSS Statistics for Windows, Version 20.0. IBM Corp. Armonk, NY). Sensitivity, specificity, positive predictive value (PPV), and NPV of MPV in neonatal sepsis were determined by a 2 × 2 table.

Results

Table 1 summarizes the demographic profile of the control and sepsis groups [Table 2]. It demonstrates platelet count and platelet indices (MPV and PDW) in cases and control groups. There were significant differences between control and sepsis groups in terms of platelet count ($P = 0.0002$) in addition to significant differences between control and sepsis groups related to MPV ($P = 0.0001$) and PDW ($P = 0.0004$). The sensitivity and specificity of platelet indices for diagnosis of neonatal sepsis were assessed by comparing them against blood culture which is the gold standard for diagnosis of neonatal sepsis [Table 3]. It was observed that thrombocytopenia was the most sensitive marker (86.8%) followed by MPV and PDW in detecting babies with culture-positive sepsis. However, it has a low specificity (23.4%). Table 3 shows that the sensitivity of platelet counts was highest (86.8%) followed by MPV (84.9%) and PDW (79.5%). Platelet count as a parameter has low specificity (23.4%). PPV and NPV of MPV were highest.

Discussions

The current study included 50 sepsis cases out of 100 neonates, with a mean age of 10.16 days, male-to-female ratio of 1.5:1, 56% were preterm, and mean birth weight of 2.28 kg with 52% of <2.5 kg.

Platelet count is an important hematological parameter in neonatal sepsis. Various workers have determined a specific platelet response with different degrees of thrombocytopenia to sepsis in neonates.[14-16] In

Table 1: Demographic characteristics of the study population

	Study group	
	Cases (*n*=50), *n* (%)	Controls (*n*=50), *n* (%)
Gender		
Male	30 (60)	26 (52)
Female	20 (40)	24 (48)
Gestational age		
Preterm	28 (56)	29 (58)
Term	22 (44)	21 (42)
Birth weight (kg)		
>2.5	24 (48)	25 (50)
<2.5	26 (52)	25 (50)

Table 2: Association between platelet indices in both case and control groups

	Case (*n*=50), *n* (%)	Control (*n*=50), *n* (%)	*P*
Platelet count			
>150,000/µl	10 (20)	45 (90)	0.0002
<150,000/µl	40 (80)	5 (10)	
MPV			
>10.5 fl	43 (86)	10 (20)	0.0001
<10.5 fl	7 (14)	40 (80)	
PDW			
>19.1%	36 (72)	18 (36)	0.0004
<19.1%	14 (28)	32 (64)	

MPV: Mean platelet volume, PDW: Platelet distribution width

Table 3: Correlation of platelet indices with culture-positive sepsis

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Platelet count <150,000/µl	86.8	23.4	37.9	78.2
MPV >10.5 fl	84.9	33.7	41.4	80.5
PDW >19.1%	79.5	36.6	40.9	77.7

PPV: Positive predictive value, NPV: Negative predictive value, MPV: Mean platelet volume, PDW: Platelet distribution width

the present study, 80% of cases with neonatal sepsis developed thrombocytopenia. The prevalence of thrombocytopenia is variable and different values have been reported by workers across the globe. Studies by Bhat *et al*. were revealed that 66.25% developed thrombocytopenia in cases of neonatal sepsis.[17] Again, Choudhary *et al*. showed in their study 81.12% cases of thrombocytopenia[18] and Mittal *et al*. found 83.08% cases of thrombocytopenia in their studies which are similar to what we documented in this study.[19] Our study reinforces the result that thrombocytopenia is an important marker of neonatal sepsis for early diagnosis which has been already demonstrated by other investigators previously.[20]

MPV in our data was increased in 86% of neonatal sepsis. Mittal *et al*. found, in their study, that MPV was increased in 70.7% of neonatal sepsis.[19] Choudhary *et al*. also found a 70.9% increase in MPV value in sepsis cases.[18] It was also seen that sensitivity and specificity of increase in MPV in the diagnosis of neonatal sepsis were found to be 84.9% and 33.7%, respectively. In a study by Arad *et al*., it was seen that sensitivity and specificity of an increase in MPV in the diagnosis of neonatal sepsis were 54% and 46%, respectively.[21] The studies conducted on neonatal sepsis patients reported that MPV values were high and the increase in the MPV values was significant in terms of prognosis and mortality.[22] The MPV cutoff point of 10.5 fL had 84.9% sensitivity, suggesting that MPV may be a marker of neonatal sepsis. The PPV in our study was 41.4%, indicating that a positive diagnostic outcome (MPV ≥10.5 fL) was actually neonatal sepsis 41.4% of the time. Further examination (such as blood culture test) would be needed to confirm the diagnosis. The NPV in this study was 80.5%, indicating that 80.5% of subjects did not suffer from neonatal sepsis if their MPV value was <10.5 fL; however, we must consider the prevalence of neonatal sepsis in the region because PPV and NPV were influenced by the prevalence of the disease.

PDW was found to be increased in 72% cases when compared with controls (36%) ($P < 0.0004$). Guclu *et al*. showed that MPV and PDW were significantly different between sepsis patients and control group.[23] Patrick and Lazarchick reported that there is a significant association of bacteremia in those neonates with MPV>10.8 fL and/or PDW >19.1%.[24]

Thrombocytopenia (platelet count <1.50.000/µl) had the highest sensitivity to detect sepsis (87.91%) followed by MPV and PDW with a sensitivity of 84.9% and 79.12%, respectively, in culture proved group which is comparable to the study done by Ishwar *et al*.[25]

Conclusion

Thrombocytopenia is a common complication in neonatal sepsis. The platelet count decreases with the development of sepsis and platelet indices such as PDW and MPV increase in septic babies. Neonates with culture-proven sepsis have a high prevalence of thrombocytopenia, high MPV, and high PDW, so these can be used as early diagnostic biomarkers of neonatal sepsis and it may be combined with existing sepsis screen to specifically exclude nonseptic case. Our study is an attempt in the direction of defining the value of these cheap and widely available hematological parameters in detecting neonatal sepsis. A limitation of this study was its retrospective design. We did not evaluate the effect of involved organisms on platelet indices and value of MPV after treatment. Therefore, we suggest more larger studies in India, and serial measurements of MPV before and after treatment in larger population during different periods of sepsis would be helpful indices following up of those patients.

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Conflicts of interest
There are no conflicts of interest.

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