Original Article

Diagnostic Accuracy of Mean Platelet Volume in Neonatal Sepsis taking Blood Culture as Gold Standard

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ABSTRACT

Objective: To find out the diagnostic accuracy of mean platelet volume (MPV) in neonatal sepsis by taking blood culture as a gold standard.

Methodology: This cross-sectional study was carried out at Hematology Department, Combined Military Hospital, Lahore from May 2019 to August 2020. Two hundred and five neonates of either gender aged 0 to 28 days with suspected neonatal sepsis were included. Peripheral venous blood samples were collected in ethylenediaminetetraacetic acid (EDTA) and blood culture bottles. Two separate Sysmex KX-21 hematology analyzers were used to evaluate MPV. The mean of each was used as the final reading. On culture, neonatal sepsis was considered as positive for samples that yielded bacterial pathogens. The diagnostic accuracy of MPV was calculated utilizing blood culture as a gold standard.

Results: The mean age of patients was 14.52±8.31 days. There were 99(48.3%) male and 106(51.7%) female cases with a higher female to male ratio. The cutoff value of MPV was 10.2 fL. Fifty three (26%) cases were diagnosed positive for MPV and 47(23%) cases had positive blood cultures. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of MPV were 82.98%, 91.14%, 73.58%, 94.74%, and 89.27%, respectively.

Conclusion: Mean platelet volume has a high diagnostic accuracy and hence in future, this biomarker can be utilized as a diagnostic tool for rapid diagnosis of neonatal sepsis.

Keywords: *Neonatal sepsis. Blood culture. Mean platelet volume. Sensitivity. Specificity.*

INTRODUCTION

Neonatal sepsis (NS), which can occur with or without bacteremia, is a disease characterized by infection-related symptoms and signs in the first month after birth.[1] It is a serious condition in neonatal intensive care units, and it is one of the leading causes of neonatal deaths with a prevalence rate of 20%.[2] It is further estimated that 17.6% of all neonates die globally with sepsis.[3] It is caused by bacterial, viral, fungal, or protozoal pathogens.[4] The clinical picture of neonatal sepsis is subtle and non-specific which renders detection challenging for clinicians. Blood culture has been the standard criteria for diagnosis of septicemia, but it requires a lot of time and is mostly not easily accessible. This delay in diagnosis can add a risk of mortality due to delayed treatment.

Platelet indices have also gained popularity as inflammation and infection indicators.[5] Platelets are essential in primary hemostasis and are often involved in secondary hemostasis. Platelets play a function in inflammation, and their antimicrobial efficacy has been shown without a shadow of a doubt in a number of acute and chronic infections.[6] Infectious diseases have been related to shifts in platelet volume indices. Patients with sepsis had higher MPV and platelet distribution width values than patients who did not have sepsis. Platelet indices are cheap and easily available routinely performed tests so these can be used for the diagnosis of neonatal sepsis.[7]

Prompt diagnosis and treatment of neonatal sepsis is an important factor in reducing morbidity and mortality. No local study is available and international data published yet has inconsistent sensitivity and specificity. Hence, this study can help to know the diagnostic accuracy of MPV in our population. In future, this biomarker can be utilized as a diagnostic tool as there is an urgent need for rapid diagnosis of neonatal sepsis.

METHODOLOGY

A cross-sectional study was carried out at the Hematology Department, Combined Military Hospital, Lahore from May 2019 to August 2020. A consecutive sampling technique was utilized to draw the blood sample of neonates with clinical suspicion of sepsis. A sample size of 205 was calculated at a 5% significance level and taking the expected prevalence of neonatal sepsis as 19.3%.

All neonates of either & gender aged 0 to 28 days with suspected neonatal sepsis were included. Neonates who had suffered birth asphyxia (assessed on clinical presentation or medical record), low birth weight of less than 1500 grams (as defined by their birth card/record), gestational age at birth of less than 32 weeks (as determined by ultrasound at the time of birth) and serious congenital malformations such as meningomyelocele (as determined by clinical presentation) were excluded.

After taking approval from the hospital ethical review

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committee 205 patients reporting to the Pediatric Emergency Department fulfilling the study criteria were included in the study. Informed written consent from the parents was taken. Peripheral venous blood samples, 3 mL in EDTA were taken along with blood culture samples (5 mL) in blood culture bottle as advised by the Clinical Microbiologist of Combined Military Hospital, Lahore. The samples were deposited at the Pathology Department of Combined Military Hospital, Lahore within half an hour time-lapse. Two separate Sysmex KX-21 hematology analyzers were used to evaluate MPV and platelet count. The mean of each was used as the final reading. For the risk assessment and management, thrombocytopenia was classified according to different severity levels (severe thrombocytopenia <50,000/µL, moderate thrombocytopenia 50,000-1,00,000/µL, mild thrombocytopenia 1,00,000-1,50,000/µL).[8] On culture, neonatal sepsis was considered as positive for samples that yielded bacterial pathogens. Mean platelet volume was measured in fL and a cutoff was determined by the receiver operating characteristic curve. On the proforma, the results of blood cultures and MPV were reported. Specificity, sensitivity, negative predictive value, positive predictive value, and diagnostic accuracy were calculated.

STATISTICAL ANALYSIS

All the collected data was entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 22. Mean±SD was calculated for quantitative data (age in days). Frequency and percentages were used for qualitative data like the gender of the neonate, diagnosis of neonatal sepsis on blood culture, and MPV. A 2x2 table was made to calculate sensitivity, specificity, positive, and negative predictive values of MPV taking blood culture as a gold standard.

RESULTS

The mean age of patients was 14.52±8.31 days with minimum and maximum age of 1 and 28 days, respectively. There were 95(46.34%) neonates who were 1-13 days old and 110(53.66%) cases were 14-28 days old. There were 99(48.3%) male and 106(51.7%) female cases with a higher female to male ratio. There were 30(14.6%) patients with normal platelet count, 100(48.8%) with mild thrombocytopenia, 55(26.8%) with moderate thrombocytopenia, and 20(9.8%) with severe thrombocytopenia (Table 1).

The cutoff value of MPV was 10.2 fL. There were 53(26%) patients diagnosed positive for MPV and 47(23%) cases had positive findings on culture. There were 39(74%) cases that had positive findings on both culture and MPV and 144(95%) cases had negative findings on both culture and MPV. There were 14(26%) cases that had negative findings on culture but had positive findings on MPV while 8(5%) cases had positive findings on culture but had negative findings on MPV (Table 2). The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of MPV were 82.98%, 91.14%, 73.58%, 94.74%, and 89.27%, respectively.

Table 1: Degree of Thrombocytopenia in Study Subjects

Thrombocytopenia	Frequency & Percentage
No Thrombocytopenia	30(14.6%)
Mild (1,00,000-1,50,000/µL)	100(48.8%)
Moderate (50,000-1,00,000/µL)	55(26.8%)
Severe (<50,000/µL)	20(9.8%)

Table 2: Comparison of Diagnosis of Neonatal Sepsis on Blood Culture & MPV

Diagnosis on MPV	Diagnosis on Blood Culture		Total
	Positive	Negative	
Positive	39(74%)	14(26%)	53(26%)
Negative	8(5%)	144(95%)	152(74%)
Total	**47(23%)**	**158(77%)**	**205(100%)**

DISCUSSION

Neonatal sepsis is a widespread and significant cause of morbidity and mortality, responsible for one-quarter of all neonatal deaths.[8] Since the clinical signs and symptoms of sepsis in newborns may be subtle, diagnosing it involves a strong level of skepticism. There is no single laboratory test that is both sensitive and accurate.[9] It is impossible to render an early diagnosis of NS, as it is often identified late owing to the wide variety of clinical symptoms. The gold standard diagnostic technique for NS is positive blood culture but it results in a delay in the initiation of

antibiotic therapy, resulting in high mortality.[10] Mean platelet volume is a simple platelet parameter that can be used for the diagnosis of sepsis.[11]

In the current study, the mean age of patients was 14.52±8.31 days with minimum and maximum age of 1 and 28 days, respectively. There were 99(48.3%) males and 106(51.7%) females with a higher female to male ratio. Thrombocytopenia was found in 85.4% of patients and 14.6% of cases had normal platelet levels. Similar results were found in another study conducted by Sri Laxmi et al. They reported thrombocytopenia in 80% of cases.[8]

Fifty three (26%) were diagnosed positive for MPV and 47(23%) cases had positive findings on culture. In this study, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of MPV were 82.98%, 91.14%, 73.58%, 94.74%, and 89.27%, respectively. A case-control study conducted by Meabed et al., included 50 patients with neonatal sepsis and 50 healthy neonates as a control. They found a significantly higher level of MPV in patients as compared to controls. They concluded that MPV can be utilized as an early diagnostic marker in NS.[12] A study was conducted in Bali to assess the diagnostic accuracy of MPV in neonatal sepsis. They concluded that a cutoff point of 7.44 fL of MPV is used for the diagnosis of neonatal sepsis with a specificity of 84.2% and sensitivity of 80%.[13] Another prospective case-control analysis found 80% specificity and sensitivity of MPV at a cutoff point of 10.2 fL.[5]

On contrary, a study was conducted in Iran to evaluate the diagnostic role of MPV in neonatal sepsis. They included 72 diagnosed cases of newborns with sepsis and 50 healthy infants as a control. Mean platelet volume, white blood cell count, and C-reactive protein (CRP) were compared in both groups. Mean platelet volume was high in the neonatal sepsis group but its sensitivity and specificity were inadequate. The study concluded that MPV cannot be used as a diagnostic test. C-reactive protein is a better diagnostic marker and MPV can be used in combination with CRP.[14]

A study was conducted by Hanaganahalli et al., to assess the predictive role of MPV in the diagnosis of neonatal sepsis. In NS, the sensitivity and accuracy of MPV were both 100%. Its sensitivity and accuracy were 96% and 100%, respectively when paired with CRP. As a consequence, the use of CRP and MPV in conjunction should be regarded in the early diagnosis of NS and uric acid levels should only be used as a secondary method to validate the diagnosis. In the management of neonatal sepsis, MPV is more responsive and precise than CRP and uric acid. They concluded that in patients with culture-proven sepsis, MPV was significantly high as compared to controls. So, MPV can be utilized as a specific economical marker of neonatal sepsis.[15] A study was conducted to evaluate the efficacy of MPV in the initial diagnosis and follow-up of patients with sepsis. They also compared its efficacy with CRP and interleukin-6 levels in sepsis. The study showed that at the MPV cutoff value of 10.35 fL, the sensitivity was 97.8% and the specificity was 78.7%. The mean platelet volume can be used for diagnosis and follow-up of sepsis.[16] Another study reported that MPV and platelet distribution width have a diagnostic role in neonatal sepsis.[17] All these studies effectively correlate with the results of the present study.

CONCLUSION

Mean platelet volume has high diagnostic accuracy and hence in future, this biomarker can be utilized as a diagnostic tool for rapid diagnosis of NS. By early detection of the condition, the treatment can be planned timely which can surely reduce the risk of mortality.

LIMITATIONS & RECOMMENDATIONS

The limitation of this study, required to be conceded, is that it was a single-centered study including a small sample size as compared to the affected population. Secondly, the media utilized for blood culture was only helpful for the isolation of bacteria and fungi. Other etiologies of neonatal sepsis such as viruses could not be detected. Quantitative CRP can also be performed along with MPV and blood culture for more accurate results. Large-scale studies using diagnostic strategies for the determination of other pathogens are required to establish the diagnostic role of MPV in neonatal sepsis.

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