DOI: 103126/JNPS.V4113

Original Article

Mean Platelet Volume as a Marker of Sepsis in Newborn

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Article History
Received On : 03 Apr, 2022
Accepted On : 09 Dec, 2022

Funding sources: None

Conflict of interest: None

Keywords: Mean platelet volume; newborn; sepsis

Abstract

Introduction: Neonatal sepsis is the leading cause of death in developing country like India and we need early diagnosis and treatment to prevent mortality so we require better diagnostic marker for sepsis. Mean platelet volume (MPV) is a measure of average platelet volume which represents inflammatory burden of disease. In our study MPV rises in septic neonates significantly and can be helpful to diagnose sepsis early with other blood counts.

Methods: This case-control study was done on 500 newborns, out of which 452 included in study are classified into two groups that is group A (n = 226): apparently healthy neonates, group B (n = 226): diagnosed with neonatal sepsis by septic screening positive. All patients in the study were go through adequate valuation of their history, clinical examination, complete blood count including MPV, C-reactive protein (CRP) and blood culture.

Results: Septic neonates showed statistically higher values of MPV than the control group. The diagnostic cut-off value of MPV NS was 10.2 fl.

Conclusions: MPV which is a platelet index obtained from complete blood count can be used an additional marker along with established septic screen to ensure early diagnosis in neonatal sepsis.

Online Access

DOI:
https://doi.org/10.3126/jnps.v42i2.44272

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Introduction

Neonatal sepsis is characterized by signs and symptoms of infection along with or without microorganism in first 28 days of life. Neonatal sepsis is a continual and important reason of morbidity and mortality which collectible for one fourth of neonatal deaths.[1] Fatality due to sepsis is between 30% and 50%. The clinical signs and symptoms of sepsis in newborns may be subtle and hence requires a high degree of suspicion to diagnose it.

There is no single laboratory test with 100% sensitivity and specificity. Blood culture remains to be the gold standard test to diagnose neonatal sepsis but it takes almost about two to eight days for the results to come, it is relatively expensive and it has a low positivity rate. All newborns suspected to have sepsis should go through a septic screen which include total leucocyte count (TLC), absolute neutrophil count (ANC), immature to mature neutrophil ratio (I:T ratio), micro erythrocyte sedimentation rate (uESR) and C-reactive protein (CRP).

The need of the hour is to identify a test that is cheap, accurate, and easy to perform

with quick availability of reports to complement the early detection of sepsis in neonates as early diagnosis and treatment decreases the neonatal morbidity and mortality.[2] The aim of the study is to determine any change in MPV with neonatal sepsis.

Methods

Institutional Ethical Committee of Rewa permitted for the study, and after taking consent from the parents of the patients this case-control study was carried out on full-term neonates admitted in Gandhi Memorial Hospital, Rewa, India. During this interval from January 2019 to December 2019, all neonates were classified into two groups. Group A (n = 226): apparently healthy neonates and Group B (n = 226): diagnosed with neonatal sepsis by septic screening positive. Term neonates more than 37 weeks, with one or more maternal risk factors for early onset sepsis and neonates with history of maternal premature rupture of membrane were included in the study. Similarly, neonates with dimorphic features suggestive of chromosomal abnormalities, perinatal asphyxia and neonates who had already received antibiotics before arrival in our institute were excluded from the study. After taking consent from the parents, babies who were suspected to have sepsis were enrolled in the study. Detailed obstetric history (any previous abortion, still birth, sibling death, previous NICU admission), including antenatal history was documented. Detection of clinical signs of sepsis such as temperature instability, cardiorespiratory dysfunctions, GIT dysfunction, neurological dysfunction and renal dysfunction were noted. Septic screen was sent and neonates with ≥ 2/4 positive parameters were considered to have sepsis or blood culture proven sepsis. Laboratory parameter for sepsis were total leukocyte count < 5000 / mm^3 or > 20,000 / mm^3, u ESR > 15 mm in first hour, C reactive protein (CRP) positive, Absolute Neutrophil Count: As per Manroe and Mouzinhos chart and blood culture measurement. Four ml blood sample of venous blood was collected aseptically by venipuncture. Two ml whole blood was put in EDTA vacuum container and mixed up and down gently which was used to measure CBC, MPV and u ESR. One ml of blood was put in plain tube without anticoagulant for the assay of CRP. Laboratory investigations CBC was done for all samples using automated cell counter Mindray BC 3600. CRP was measured by using the CRP latex slide agglutination test for qualitative detection of CRP. Latex particle coated with goat IgG anti human CRP are agglutinated when mixed with sample containing CRP. The sensitivity of 0.6 ml /dl of CRP according to the world health organization (WHO) international reference preparation positive and negative controls are recommended to monitor the performance of the procedure, as well as comparative pattern for better result interpretation. Data were analyzed using SSPS software. Quantitative data were conveyed as mean ± SD and qualitative data were conveyed as frequency and percentage. Independent sample t-test of significance was used when comparing two means. The w2-test of significance was used to analyse proportions in between two qualitative parameters. P value < 0.05 was considered as significant. Receiver operator curve (ROC) was generated and the area under curve (AUC) was evaluated. Sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) were also calculated.

Results

Five hundred neonates were eligible for the study, of which 48 neonates were excluded for various reasons. Among the two large groups: Total 452 neonates divided into Group A healthy neonates comprised 67.6% (n = 153) males and 32.3% (n = 73) females while Group B septic neonates comprised 62.3% (n = 142) males and 37.1% (n = 84). In our study, maximum neonates were admitted with dull / lethargic (or refusal to feed) 35% (n = 79), convulsion 16% (n = 36), respiratory distress (includes tachypnea / subcoastal retraction / intercostal retraction / grunt) and 11.5% (n = 26) as shown in Table no. 1

Table No 1. Showing frequency and percentage of clinical characteristics

S.No	Clinical characteristics	N	%
1.	Lethargic / dull	79	35
2.	Convulsion	36	16
3.	Respiratory distress	26	11.5
4.	Fever	25	11
5.	Cold peripheries	18	8
6.	Low urine output	16	7
7.	Skin rash	5	2

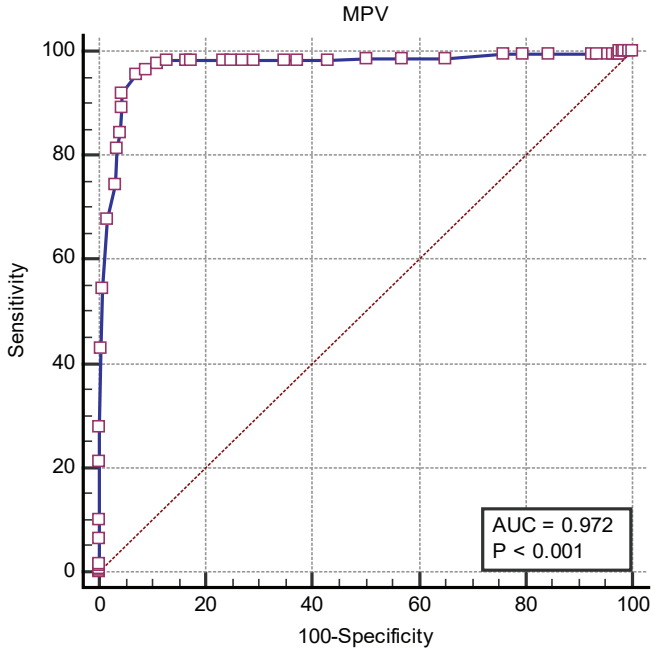
When we compared the study groups, there was significant difference between the two groups (septic and non septic) regarding the septic screening profiles. TLC, ANC, u ESR, MPV showed statistically significant increase in the septic group B than healthy group A and platelets were significantly decreased in the septic group B. There was no significant statistical difference found between septic and healthy groups among the parameters of hemoglobin and RBC.

Table No 2. Showing Mean ± SD and p value of case and controls

PARAMETER	GROUP A	GROUP B	t-VALUE	P VALUE
Haemoglobin	9.54 ± 16.2	7.11 ± 15.45	-0.948	0.3438
RBC	0.87 ± 4.58	0.88 ± 4.44	-1.701	0.0897
WBC	3174 ± 9979	8367 ± 16761	11.393	< 0.0001
ANC	2535 ± 5585	6143 ± 9852	9.653	< 0.0001
u ESR	3.23 ± 9.07	4.95 ± 20	27.8	< 0.0001
Platelets	1.1 ± 1.9	1.2 ± 1.6	-2.770	0.0058
MPV	0.5 ± 8.6	1.1 ± 10	17.418	< 0.0001

The sensitivity of the test is 95% and specificity is 93% positive predictive value of 95% wharesas negative predictive value is 93% with a MPV cutoff value of 9.2fl. Area under curve is 0.972

Figure 1 Receiver Operating Curve of MPV



Discussion

Sepsis remains to be one of the most important causes for neonatal mortality. To prevent further complications of sepsis, we need to diagnose early and treat it.[1] Present study aimed to determine the role of MPV as a diagnostic marker of neonatal sepsis. The easily accessible, cheap, and common laboratory tests for are very important in determining the screening of the disease in neonatal sepsis. MPV is universally available with routine blood counts by automated hemograms and a simple and easy method of assessing platelet function in correlation with sepsis. To achieve a larger surface, platelets go through changes in structure during activation. Their shape varies from discoid to spherical and pseudopodia are also formed. Platelet vertical diameter is important in determining platelet volume, which is achieved by a hematology analyzer, using deformation of electrical field, based on impedance technology. Volume is determined by measuring the cross diameter of the platelet cell using analyzers with laser optical technology. Consequently, activated platelets seem larger in surface area independently of the principle of measurement.[2] In recent studies it has been reported that MPV is increased in RDS, NEC, BPD IVH, acute appendicitis etc.[3-6] There have been previous studies that have looked at the co-relation between the MPV and neonatal sepsis. In present study, MPV was significantly higher (10 ± 1.1) in the study group as compared to the control group (8.6 ± 0.5). Similar results were found in the study done by Prathyusha et al where 106 neonates included in the study showed statistically significant MPV difference between the study groups (mean 12.8 ± 1.52, 10.82 ± 1.20 respectively) at a cut of value of 10.2 fl and a sensitivity of 93%, specificity of 84 % with a positive predictive value of 83% and negative predictive value of 94%.[7] Difference of cutoff is there which may be because of age difference / preterm neonates as well as from different MPV measurement methods. In a study done by Mehmet Yekta Oncel et al, a total of 100 patients with sepsis (35 with proven sepsis and 65 with clinical sepsis) and 50 healthy controls were enrolled. Comparison of markers of sepsis obtained at baseline revealed MPV levels to be significantly higher in newborns with sepsis compared to healthy controls p value 0.001.[4] Similar finding of 82 % sensitivity was seen in a study conducted by Aydin B et al at a cut off value of 10.4 fl.

Also recently a study done by Yao et al found that out of 315 neonates who were confirmed to have sepsis divided into two groups: proven sepsis (with a positive blood culture; n = 207) and clinical sepsis (with a clinical diagnosis; n = 108) with 132 hospitalized neonates with noninfectious diseases were enrolled as the control group. Here MPV was significantly higher in the two sepsis groups than in the control group (P < 0.05) with optimal cut-off point of 11.4 fL, with sensitivity of 40.5% and specificity of 88.4%.[8] In the study done by Catal F, preterm neonates were grouped as control (n = 100) and sepsis (n = 91). MPV value of 10.35 fl was identified as the cut off to identify patients with probable sepsis with a sensitivity of 97.8% and specificity of 78.7% and a MPV value of 10.75 fl was determined as the cut off value for patients with high risk of mortality (death) at diagnosis of sepsis with a sensitivity of 95.2% and a specificity of 84.9%.[9] In contrast to present study, Aksoy et al concluded that there was no significant difference in MPV between septic and control babies. This may have resulted as they had mainly done their study on the respiratory infection (respiratory syncytial virus) in preterms and extremely low birth weight newborns which we had excluded in our study.[10]

Platelets have an important role in thrombogenesis.[11] The correlation between platelet activation and adverse clinical outcome of vascular diseases including coronary artery disease (CAD), stroke, and venous thromboembolism has been established. The mechanism of alteration of platelet function in sepsis is still unclear. Young platelets are larger as compared to older ones. Inflammation induce platelets production by over consumption resulting in increase in the young platelets in peripheral smear. In comparison to small platelets, larger platelets are functionally, metabolically, and enzymatically more active as they contain more intracellular thromboxane A2 and increased expression of procoagulant surface proteins such as p-selectin and glycoprotein IIIa, causing greater prothrombotic potential. Moreover, platelet-neutrophil interactions and platelet-endothelial interactions facilitate a variety of immune activation instances.[12-15] By this MPV also increases as well as the number of young platelets.

Conclusions

Neonatal sepsis is almost always accompanied by thrombocytopenia. Although important platelet indices are readily available, they are less studied among neonates. MPV can be used as an additional marker along with established septic screen to ensure early diagnosis and treatment of neonatal sepsis with no additional expense as it simply generated with CBC. Our case-control study concluded that MPV increases significantly in neonates with sepsis. However further studies also need to be carried out for serial monitoring of MPV with sepsis so that can show changes with treatment also.

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