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Original Article

Diagnostic Sensitivity and Specificity of Platelet Indices in Sepsis

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ABSTRACT

Objective: to determine the diagnostic sensitivity and specificity of platelet indices [platelet count (PLT), mean platelet volume (MPV), MPV/PLT ratio] in sepsis.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Fauji Foundation Hospital, Rawalpindi Pakistan, from Jun to Dec 2019.

Methodology: Adult patients (18-70 years old) with clinically diagnosed Sepsis (n=150) and their age-matched controls (n=150) were recruited. Platelet indices were measured, and blood culture samples were sent to the microbiology lab. Septic patients were compared to the control group. Receiver operating characteristic (ROC) curves were generated for diagnostic sensitivity and specificity of platelet indices.

Results: Mean platelet volume and MPV/PLT ratios were significantly raised in sepsis, culture-positive sepsis and culture-negative sepsis compared to the control group. In ROC analysis, MPV had 67.3% sensitivity and 65% specificity, whereas the MPV/PLT ratio had 64.7 % sensitivity and 61% specificity to diagnose sepsis. Higher sensitivity (78%) and specificity (70%) were obtained in Culture positive cases for MPV as compared to sensitivity (64%) and specificity (59%) seen in Culture negative cases. MPV/PLT ratio showed the same sensitivity (64%) and specificity (61%) in both Culture positive and Culture negative cases.

Conclusion: The study concludes that MPV and MPV/PLT ratios are significantly higher in sepsis, culture-positive sepsis and culture-negative sepsis than in the control.

Keywords: Mean platelet volume (MPV), Mean platelet volume/platelet ratio (MPV/PLT ratio), Platelet count (PLT), Receiver operating characteristic (ROC) analysis, Sepsis.

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INTRODUCTION

Sepsis is one of the most common causes of death in hospitalized patients. The incidence of sepsis is increasing worldwide, and the survivors of sepsis may have lasting ailments leading to a remarkable impact on health care.[1] In the United States, almost 750,000 cases of sepsis were seen in a year, which led to 215,000 deaths and more than $20 billion (5.2%) of total US hospital costs.[2]

Platelets play an important role in inflammatory conditions like sepsis. Activated platelets increase in size and secrete cytokines and chemokines, which are involved in controlling infection.[3,4] This can be identified by considering mean platelet volume (MPV) in routine blood cell analysis.[5] MPV/Platelet count ratio (MPV/PLT ratio) is a new parameter significantly raised in sepsis patients.[6]

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Clinical diagnosis of sepsis is based on non-specific physiological criteria, whereas the Definite diagnosis depends on blood culture and CRP. We must wait for cultural results; they are positive only in one-third of the cases.[7] CRP is an expensive test and is not available in every laboratory. The delay/cost involved in blood culture and CRP levels for the definite diagnosis of sepsis results in diagnostic ambivalence, therapeutic impediment and inappropriate use of antibiotics.[8] The time needed to identify new investigations that can help make prompt diagnoses, risk stratification, therapeutic decisions and monitoring the therapeutic response. Literature evidence of variations in the values of MPV, PLT and MPV/PLT ratio in sepsis raises the possibility that these platelet indices might be a quicker and cheaper alternative to blood culture and CRP for the definite diagnosis of sepsis if their diagnostic sensitivity and specificity are proven.[9,10] However, there is a lack of evidence regarding the diagnostic efficiency of PLT, MPV and MPV/PLT ratio. Our study aimed to explore the

diagnostic sensitivity and specificity of these platelet indices in sepsis (as a whole) and culture-positive and culture-negative sepsis so that their utility may be validated as additional indicators to diagnose sepsis.

METHODOLOGY

The cross-sectional study was conducted at the Pathology Department of Fauji Foundation Hospital, Rawalpindi, from June to December 2019 after obtaining permission from the Hospital Ethical Board (FF/FUMC/215-67/Phy/20). The sample size was calculated by an online calculator, after putting the platelet count values (x10^9/L) in Sepsis cases (112±117) and healthy controls (174±123) from a previous ssstudy.[11] Consecutive non-probability sampling technique was used.

Inclusion Criteria: Adult patients (18-70 years old) with clinically diagnosed sepsis who presented in an emergency department or were admitted to the ward were included. The age-matched control group was selected from the patients admitted to the ward with a diagnosis other than the infectious disease/systemic inflammatory response syndrome (SIRS), with CRP levels & white blood cell count within the normal range.

Exclusion Criteria: Patients were excluded if they had immune thrombocytopenia, Bernard Soulier disease, Ischemic heart disease, myeloproliferative disorders, and chronic liver disease, or taking antiplatelet drugs, immunosuppressants or antibiotics.

In order to explore the diagnostic sensitivity and specificity of Platelet indices in sepsis, two groups were made: Group-A, consisting of clinically diagnosed septic patients (n=150), and Group-B, consisting of age-matched control (n=150). Platelet indices were compared between these two groups, and ROC was generated for diagnostic sensitivity and specificity of platelet indices in sepsis. To explore the diagnostic sensitivity and specificity of Platelet indices in Culture-positive and Culture negative septic patients respectively, three groups were made: Group-A consisting of Culture Positive Sepsis (n=50), Group-B consisting of Culture Negative Sepsis (n=100) and Group-C consisting of Control (n=150). Platelet indices were compared among these three groups, and ROC was generated for diagnostic sensitivity and specificity of platelet indices.

Patients were diagnosed as having sepsis if two or more of the following features were present: Temperature<36°C (96.8°F) or >38°C (100.4°F), Heart rate>90 /min, Respiratory rate>20/min or $PaCO_2$ <32 mmHg (43 kPa), WBC<4 x10^9/L (<4000/mm^3), >12x 10^9/L (>12,000/mm^3), or 10% band.[1,12] All study participants signed written informed consent. Venous blood (2.5ml) was collected in bottles containing EDTA (ethylene diamine tetra acetic acid) as an anti coagulant. It was sent to the haematology lab and analyzed on an automated haematology analyzer Sysmex XT 1800i system, which measures platelet count and MPV by impedance technology (electrical resistance detecting method).[13,14] All samples were processed within 1 hour of sampling as MPV is sensitive to the differences in blood sample anticoagulation, storage temperature, and delay in processing.[5,15] Results were verified by the haematologist in the lab of Fauji Foundation Hospital. PLT and MPV values were recorded, and the MPV/PLT ratio was calculated.

Under sterile conditions, venipuncture was performed for blood culture results, and 10ml of blood each was put in an aerobic and anaerobic culture bottle. Bottles were transported to the Microbiology laboratory of the hospital, where the blood cultures were processed according to the laboratory protocol.[16] and analyzed by microbiologists to identify the pathogens.

Data were analyzed through Statistical Package for the Social Sciences (SPSS) version 20. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. The receiver operating characteristic (ROC) analysis was performed to analyse diagnostic sensitivity & specificity. The *p*-value ≤0.05 was considered significant.

RESULTS

This study included 150 patients with Sepsis and 150 as a Control Group. The age ranged from 18-70 years. The mean age of the septic patients in this study was 41±17 years, and the Control Group was 42±19 years. ROC curve was drawn to evaluate the diagnostic sensitivity and specificity of PLT, MPV, and MPV/ PLT ratio in sepsis (Figure-1).

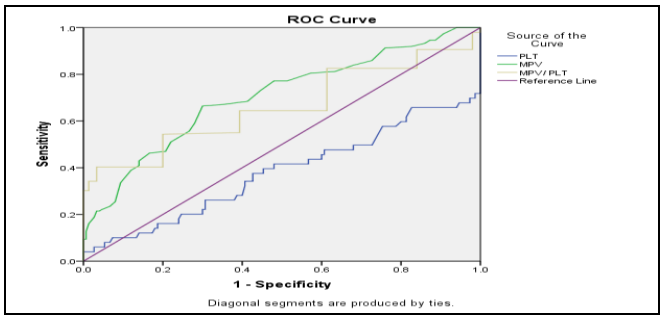

Figure-1: Receiver Operating Characteristic (ROC) curve for Platelet Count (PLT), Mean Platelet Volume (MPV) and MPV/PLT ratio in Sepsis (n=300)

The highest cut-off values for sensitivity and specificity have been shown in Table-I. The area under the curve for PLT, MPV and MPV/PLT ratio was 0.38 (fail), 0.705 (fair) and 0.65 (poor), respectively. The test should not be interpreted because the PLT curve falls below the diagonal line. The sensitivity and specificity of MPV were 67.3% and 65%, respectively, whereas the sensitivity and specificity of MPV/PLT were 64.7% and 61%, respectively.

Higher sensitivity (78%) and specificity (70%) were obtained in culture-positive cases for MPV (Table-II) as compared to the sensitivity (64%) and specificity (59%) seen in culture-negative cases (Table-III).

DISCUSSION

We found significantly higher MPV and MPV/PLT ratio values in septic patients compared to the control group. Our results favour Guclu *et al*., who studied the sequel of severe sepsis on platelet count, MPV and platelet distribution width (PDW) in patients with sepsis versus the control group. He found significantly raised MPV and PDW (p<0.05) in septic patients compared to the Control Group.[2] PLT did not differ significantly in sepsis vs. control in our study, a finding contrary to Yilmaz *et al*., who studied platelet count and its parameters in a canine model of endotoxemia. He showed that MPV was increased, whereas platelet count was reduced in endotoxemia. This discrepancy in results could be due to the variations in the experimental model.[17]

One study conducted a prospective study to see sepsis's mean platelet volume trend as a prognostic parameter. They performed serial monitoring of MPV

Table-I: The result of Receiver Operating Characteristic Analysis for Platelet Count (PLT), Mean Platelet Volume (MPV) and MPV/PLT ratio in Sepsis and Control Group (n=300)

Parameters	AUC	95%CI Lower–Upper	Cutoff Value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	*p*-value
Platelet count (PLT)109/L	0.38	0.316 – 0.444	264	34	60	90.4	58.5	<0.001
Mean platelet volume (MPV)fL	0.705	0.646 – 0.764	9.75	67.3	65	69.6	60.1	<0.001
Mean platelet volume/ platelet count ratio (MPV/PLT) fL/(109/L)	0.659	0.596 – 0.722	0.04	64.7	61	60	60.7	<0.001

ROC curve was drawn to evaluate if PLT, MPV, and MPV/ PLT ratio levels are suitable for diagnosing culture-positive and culture-negative sepsis (Figure-2).

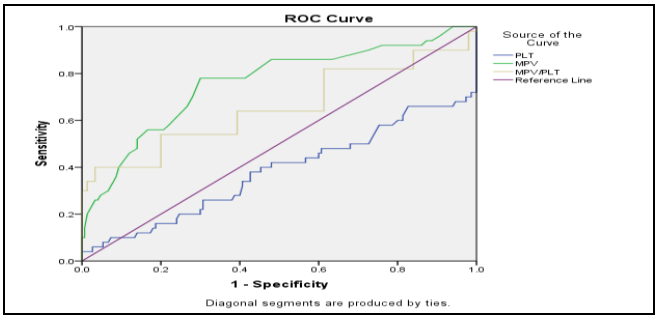

Figure-2: Receiver Operating Characteristic Curve for Platelet Count (PLT), Mean Platelet Volume (MPV) and MPV/PLT ratio in Culture Positive Sepsis (n=300)

Table-II: The result of Receiver Operating Characteristic Analysis for Platelet Count (PLT), Mean Platelet Volume (MPV) and MPV/PLT ratio in Culture Positive and Control Group (n=300)

Parameters	AUC	95%CI Lower-Upper	Cutoff Value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	*p*-value
Platelet count (PLT)109/L	0.38	0.279–0.481	266	32	60	39	78.6	0.011
Mean platelet volume (MPV)fL	0.759	0.677–0.841	9.85	78	70	47.5	84.4	<0.001
Mean platelet volume/ platelet count ratio (MPV/PLT) fL/(109/L)	0.654	0.553–0.756	0.04	64	61	33.7	82	0.001

Table-III: The result of Receiver Operating Characteristic Analysis for Platelet Count (PLT), Mean Platelet Volume (MPV) and MPV/ PLT ratio in Culture Negative and Control Group (n=300)

Parameters	AUC	95%CI Lower-Upper	Cutoff Value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictiv Value	*p*-value
Platelet count (PLT)109/L	0.380	0.305–0.455	264.5	34	60	86.1	67.8	0.001
Mean platelet volume (MPV)fL	0.678	0.610–0.746	9.65	64	59	58.1	67.6	<0.001
Mean platelet volume/ platelet count ratio (MPV/PLT) fL/(109/L)	0.654	0.579–0.729	0.04	64	61	50.4	69.5	<0.001

on all patients with the first sample after a delay of 48 hours. They demonstrated that although MPV was within the normal range at enrolment, MPV values were much higher in non-survivors than in survivors.[9] However, their study involved fewer patients (70 only). Our MPV findings were based on a single reading at presentation only, and our number of patients was more than their study.

Aydemir *et al*. studied the dynamics of platelet count and MPV in 214 adult patients with culture-positive sepsis. They reported significant thrombocytopenia and high MPV in the first three and five days of Gram-positive and Gram-negative sepsis. However, he included patients who survived the first ten days of sepsis and had microbiologically proven sepsis.[18] Blood cultures are positive only in one-third of cases of sepsis due to sampling error, previous antimicrobial treatment or slowgrowing pathogens.[19,20]. Therefore, they already excluded two-thirds of sepsis cases and studied the changes only in one-third of the septic patients. We included all the cases of clinically proven sepsis, which was not necessarily Culture and still, we found a significant increase in MPV.

Guclu *et al*. studied the sequel of severe sepsis on platelet indices in patients diagnosed with sepsis by infectious disease specialists. They reported the sensitivity and specificity of MPV as 53.47% and 87.41%, respectively. They considered an MPV value of more than eight fl as raised, which is quite low.[2] In our study, we used Sysmex XT 1800i, whose reference range for MPV is between 7.0 and 11fL.

Therefore, we chose a higher cut-off of MPV as raised, i.e., 10.35fL. One study used Siemens Advia 2120 in their study, whose normal range for MPV is 6.7-9.6fL, which is lower than the range given by the Sysmex XT 1800i.[21]

CONCLUSION

The study concludes that MPV and MPV/PLT ratios are significantly higher in sepsis, culture-positive sepsis and culture-negative sepsis than in the control.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AL & LZ: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

SF & HZ: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

MK & RL: Concept, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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