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Original Article

Association of Mean Platelet Volume / Platelet Count Ratio with Clinical Severity and Infarct Volume in Patients with Acute Ischemic Stroke

Muhammad Wasi Nayyar, Asad Mahmood, Jahanzeb Liaqat*, Helen Mary Robert, Rafia Mahmood, Ayesha Khurshid

Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Pak Emirate Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To examine the clinical severity and infarct volume of acute ischemic stroke (AIS) compared to control subjects by comparing the mean platelet volume/platelet count (MPV/PC) ratio.

Study Design: Cross-sectional (validation) study.

Place and Duration of Study: Acute Stroke Unit, Pak Emirates Military Hospital (PEMH), Rawalpindi, from Jul and Dec 2020.

Methodology: This study included 50 consecutive AIS patients (Group-1) and 50 healthy subjects (Group-2). An automated haemanalyser determined MPV and MPV/PC ratios. In addition, a modified Rankin Scale for the severity of AIS and ABC/2 method for infarct volume was used.

Results: This study comprised 69 males and 31 females. Statistical analysis showed that MPV and MPV/PC have significantly different mean values between Group-1 and Group-2 at a *p*-value of 0.001. In addition, according to the Rankin scale, a significant difference of means (*p*-value <0.001) of MPV and MPV/PC ratio was present between stroke patients with different infarct sizes. A higher CVA score per Rankin scale was associated with greater infarct size and higher MPV and MPV/PC values.

Conclusion: Higher MPV and MPV/PC ratios are related to AIS compared to healthy individuals. Even greater MPV and MPV/PC ratio values are associated with increased infarct size. MPV and MPV/PC ratio measurements are simple, rapid, and highly cost-effective laboratory markers for risk stratification and early detection of cerebrovascular stroke.

Keywords: Infarct volume, Mean plate volume, Platelet count, Rankin scale, Stroke.

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INTRODUCTION

In acute ischemic stroke, clinicians and researchers must assess the extent of a clinical and anatomical injury.[1] The platelets are already established as instrumental in innate and adaptive immunity. In addition, antimicrobial peptides in platelets exert an immediate, strong, and direct antimicrobial effect that helps in the restriction of the risk.[2] As a result of erosion or rupture of atherosclerotic plaques, platelets become crucial in the pathophysiology of ischemic stroke.[3] As hemostasis maintains vessel integrity, platelets play a critical role. The hemostatic factor, thromboxane A2, and the prothrombotic agent serotonin released by platelets, are directly responsible for the hemostasis of circulating cells.[4,5] Markers of platelet activity, such as thromboxane A2, platelet factor 4, and β-thromboglobulin, correlate positively with MPV, which is a determinant of platelet size.[6, 7] In combination with the elevated platelet counts (PC), platelet size increases the thrombotic potential.[3] Platelets that are larger in size are more responsive than smaller-sized platelets and generate additional prothrombotic factors like thromboxane A2 and show greater accumulations of substances like adenosine diphosphate (ADP), collagen, and adrenaline because of their higher granular content.[8] Studies report that platelets with larger size have been associated with cardiovascular risk factors, such as myocardial infarction, diabetes mellitus, hypercholesterolemia, metabolic syndrome, smoking, and ischemic stroke.[9,10] The objective of this research work was to examine the association of increased MPV/PC ratio with the severity of acute ischemic stroke, as well as the volume of infarcts.

Correspondence: Dr Muhammad Wasi Nayyar, Department of Haematology AFIP Rawalpindi-Pakistan
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METHODOLOGY

The cross-sectional (validation) study was conducted from July 2020 to December 2020 at Acute Stroke Unit at Pak Emirates Military Hospital (PEMH), Rawalpindi, after Institutional Review Board approval (letter number FC-HEM19-9/READ/21/244). The sample size was calculated using the WHO sample size calculator.

Inclusion Criteria: This study included all patients admitted to the Acute Stroke Unit during study period. Fifty patients suffering from their first ischemic stroke were included in this study (Group-1). At the same time, Group-2 had 50 individuals without any evidence of previous vascular events and no prior use of any medication that affects platelet function.

Exclusion Criteria: Patients who had a prior stroke, transient symptoms of cerebrovascular diseases, cranial trauma, acute infection, malignancies, acute myocardial infarction, intracranial haemorrhage, pregnancy, peripheral vascular disease, hematomas, positive C-reactive protein or inflammatory conditions, were excluded from the study as these conditions may affect platelet function and morphology.

Clinical Assessment of patients was done at PEMH, and Blood Samples were analysed in the Department of Haematology at the Armed Forces Institute of Pathology (AFIP). In addition, a non-probability convenience sampling technique was used after informed consent. During each patient's treat-ment, they were subjected to a complete medical his-tory, including medications, cerebrovascular accidents, or ischemic heart disease, an in-depth examination of the nervous system and general health, and an investigation of all recommended biochemical parameters.[11]

Patients with evidence of acute ischemic stroke were considered for the study. The stroke was clinically identified (related to a sudden onset of neurological deficits lasting 24 hours or more) and confirmed via brain imaging (magnetic resonance imaging MRI and CT computed tomography).[12,13]

According to the Modified Rankin scale,[14] the severity of an ischemic stroke is measured from 0–6, with 0 being asymptomatic and six being dead. In most stroke patients, scores between 0 and 2 indicate a "good" stroke outcome. They have a fair-to-good quality of life and can usually perform their daily activities after recovery. Patients with a score of 3 or more will likely require considerable assistance with daily living activities.

In the Trial of Org, 10172 in the Acute Stroke Treatment rating system,[15] ischemic strokes are categorised based on the type of stroke. An MRI scan or CT was done three days after enrollment to measure the infarct size. Infarcts with diameters ≥3 cm were considered large, whereas those under 3 cm were deemed minor infarcts. The ABC/2 formula was used to determine the infarct volume.

A forearm vein was punctured to collect fresh venous blood samples into tubes containing ethylene-diamine-tetra-acetic acid (EDTA) as an anticoagulant. A maximum of 2 hours was allowed for samples to be processed after venipuncture. Samples were stored at room temperature (25°C) between venipuncture and processing. An automated haematology analysis system (Sysmex XN-3000) was used to determine the platelet count and mean MPV (in fL). FUJIFILM Medical System USA's Synapse PACS System, Version 3.2.0, measured the infarct volume.

The data analysis was performed using Statistics Package for Social Sciences (SPSS) version 21.0 software. Results were determined as mean and standard deviation. Independent samples t-test was used to determine the significant difference of means for MPV, PC, and MPV/PC among Group-1 and Group-2. Group-1 was further categorised based on Cerebrovascular Accident (CVA) score using Rankin Scale and infarct volume. An Independent sample t-test was used to determine the difference in mean values of the parameters mentioned above between cases of different infarct sizes and CVA scores. The *p*-value of ≤0.05 was taken as statistically significant.

RESULTS

We selected 50 patients with a history of confirmed cerebrovascular acute ischemic stroke as Group-1 and 50 healthy individuals with no known comorbid conditions as Group-2. There were 37 males and 13 females in the Group of stroke patients (Group-1), while Group-2 with healthy individuals consisted of 32 males and 18 females. The mean age of Group-1 (CVA patients) was 58.6±8.2 years, and that of Group-2 was 61.0±8.3 years.

The mean platelet count of the group of CVA patients was 278.2±36.84 x 109/L, lower than the Group-2 mean platelet count, i.e., 309.7±58.85 x 109/L, which was statistically significant at *p*-value 0.002. At the same time, the Mean platelet volume (MPV) for Group-1 was 8.46±0.78 fL, which was much higher than the MPV of Group-2, i.e., 7.59±0.50fL was also statistically significant at *p*-value <0.001. Also, a difference of <0.001 was found between the MPV/PC ratio, which is statistically significant, where the MPV/PC ratio for Group-2 was 0.0253, much lower than the MPV/PC ratio of Group-1 at 0.0310 (Table-I).

Of 50 stroke patients, 22 had CVA scores ≥3 (based on the Rankin scale) associated with the worst stroke outcome, whereas 28 had CVA scores of 0-2. There were no significant differences in platelet counts

between groups (p>0.05). However, those with a larger Rankin scale CVA score had a substantially higher MPV than those with a CVA score of 0-2 (p-value <0.001). MPV/PC ratio also showed a marked difference in mean values among both these groups; MPV/PC ratio was much higher in cases with a higher CVA score (≥3) as compared to the MPV/PC ratio in lower CVA score of (0-2) respectively (p-value 0.001) (Table-II).

Table-I: Mean differences of Characteristics among Study Groups (n=100)

Variables	Study Groups	n(%)	Mean	*p*-value
Platelet Count (x109)	Group-2	50(100%)	309.705±58.85	0.002
	Group-1	50(100%)	278.24±36.84	
MPV(fl)	Group-2	50(100%)	7.59±0.506	0.001
	Group-1	50(100%)	8.46±0.782	
MPV/PC-ratio	Group-2	50(100%)	.025±0.004	0.001
	Group-1	50(100%)	.031±0.005	

Table-II: Distribution of Cases Based on CVA-score of Rankin Scale (n=50)

Variables	CVA-Score	n(%)	Mean	*p*-value
Platelet Count (x109)	CVA score 0-2	28(56%)	280.82±41.91	0.05
	CVA score ≥3	22(44%)	274.95±29.81	
MPV(fl)	CVA score 0-2	28(56%)	7.95±0.516	0.001
	CVA score ≥3	22(44%)	9.11±0.534	
MPV/PC-ratio	CVA score 0-2	28(56%)	0.28±0.004	0.001
	CVA score ≥3	22(44%)	0.033±0.004	

Results showed that 23 out of 50 cases had an infarct size of <3cm and 27 had an infarct size of >3cm. Patients with infarcts of smaller and larger volumes showed statistically significant differences in their MPV (p-value <0.001). Mean values of MPV/PC ratio were also higher for patients with larger infarct size (0.028) as compared to the mean PMV/PC ratio value (0.033) of stroke patients with smaller infarct size with significant p-value <0.001 (Table-III).

Table-III: Comparison of Infarct Size among Cases (n=50)

Variables	Infarct Size	n(%)	Mean	*p*-value
Platelet Count (10^9)	<3cm	23(46%)	286.78±40.33	0.05
	>3cm	27(54%)	270.96±32.59	
MPV(fl)	<3cm	23(46%)	7.94±0.60	0.001
	>3cm	27(54%)	8.90±0.63	
MPV/PC-ratio	<3cm	23(46%)	0.028±0.04	0.001
	>3cm	27(54%)	0.033±0.04	

DISCUSSION

In thromboembolic conditions, MPV has been shown to have great clinical value. Increased MPV values worldwide have been noticed in stroke and ischemic heart disease patients. MPV has been considered a predictive factor of stroke in patients of early cerebrovascular accidents.[15] A high MPV/PC (MPV to platelet count) ratio is observed as a risk factor for several diseases, including anaemia, myocardial infarction, and hepatocellular carcinoma. A higher MPV/PC ratio has been recognised concerning AIS both in the acute phase and later as the disease progresses in patients.[2,16,17] Additionally, stroke patients with a low platelet count have been shown to have higher mortality. According to these results, MPV/PC might be a factor that influences stroke outcomes (genesis or deterioration). Recent studies have proposed a new form of measuring infarct volume that uses the ABC/2 method as a convenient means to determine infarct volume effectively. This calculation can be performed in an acute setting because it is quick, readily available, and feasible.[13] Our study presented that MPV and MPV/PC ratios were substantially higher in Group-1 (Cerebrovascular accident/ stroke) than in normal healthy individuals. O'Malley *et al*. similarly found increased values of MPV in patients with acute ischemic stroke than in controls. Contrary to our finding, Cho et al.18 observed no differences between cases and controls in MPV values. Our study showed that MPV and MPV/PC ratios are greater in those stroke patients with a higher CVA score (≥3) according to the Rankin scale as compared to stroke patients with a lower CVA score (0-2), thus highlighting the significance of using MPV and MPV/PC ratio in CVA patients for early detection of clinical severity of stroke. This indicates the possible release of more reactive platelets in the blood in response to mediators released from ischemic sites in the periphery. The importance of higher MPV in predicting stroke severity was established by the PROGRESS study,[19] which showed a rise of 11% in the relative risk of stroke for an increase of one femtoliter of MPV upon studying 3134 individuals with a history of CVA. Hence, people with large platelets are more likely to have an ischemic stroke. Results in Butterworth et al.20 studies showed lesser platelet count in the stroke group, according to our result. In our study, a statistically substantial difference was found in the mean value of MPV in stroke patients with large infarct sizes (>3cm) and those with small infarct sizes (<3cm). Similarly, it was shown in our study that the MPV/PC ratio was also higher in patients with larger infarct sizes as compared to stroke patients having smaller infarct size, which was also demonstrated in a study carried out by Guenancia *et al*.[21] Thus, MPV/PC ratio can be utilised as a convenient, clinically

significant parameter for early detection, as well as a direct correlation of clinical severity and infarct volume, of Acute Ischemic Stroke.

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CONCLUSION

Compared to healthy individuals, higher values of MPV and the MPV/PC ratio are associated with cerebral stroke. Even greater increments in MPV and MPV/PC ratio values are associated with increased infarct size. MPV and MPV/PC ratio measurements are simple, rapid, and highly cost-effective laboratory markers for risk stratification and early detection of cerebrovascular stroke.

Conflict of Interest: None.

Author's Contribution

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

MWN & AM: Data acquisition, critical review, approval of the final version to be published.

JL & HMR: Conception, study design, drafting the manuscript, approval of the final version to be published.

RM & AK: Data analysis, data interpretation, critical review, 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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