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Original Research Article

PLATELET INDICES AS A MARKER OF SEVERITY IN NON-DIABETIC NON-HYPERTENSIVE ACUTE ISCHEMIC STROKE PATIENTS

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Abstract

Background: Platelet activation and aggregation play a crucial role in the pathogenesis of acute ischemic stroke. Mean platelet volume (MPV) and platelet distribution width (PDW) are markers and determinants of platelet function. Larger platelets are more metabolically active, produce more prothrombotic factors, aggregate more easily, and serve as indicators of homeostasis and thrombosis dysfunction. **Materials and Methods:** We studied 45 non-diabetic, non-hypertensive ischemic stroke patients without previous thrombotic events and not on antiplatelet medications within 24 hours of symptom onset. These patients were compared with an equal number of age- and sex-matched controls. Stroke severity was assessed using the Canadian Neurological Scale (CNS), and platelet indices were obtained from the SYSMEX KX-21 analyzer. **Result:** The mean age of patients was 53 ± 6.15 years, and the mean age of controls was 52 ± 5.37 years. According to the CNS, patients were divided into two groups: those with a comprehension deficit and those without a comprehension deficit. The mean PDW and MPV values for the 1st group were 18.675 ± 3.494 and 12.894 ± 1.270, respectively, and for the 2nd group were 18.62 ± 3.387 and 12.42 ± 0.984, respectively. These values were significantly higher than the mean PDW and MPV values in controls, which were 15.694 ± 3.127 and 10.46 ± 1.273, respectively. In both patient groups, PDW and MPV were significantly associated with the severity of motor deficits. **Conclusion:** In ischemic stroke patients, platelet indices such as PDW and MPV may be useful for predicting the severity of motor deficits. However, larger sample sizes and multivariate analyses are needed before these indices can be routinely used in clinical practice.

INTRODUCTION

Stroke is defined by the World Health Organization as a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin. Acute ischemic stroke results from sudden loss of blood circulation to an area of cerebral hemisphere leading to irreversible brain injury and neurological deficits persisting for more than 24 hours or until death. It accounts for 80-87% of all strokes. Several risk factors like hypertension, diabetes mellitus, dyslipidaemia, tobacco smoking are instrumental in the pathogenesis of acute ischemic stroke largely by their link to atherosclerosis.[1]

Platelets are small, discoid and non-nucleated structures derived from fragmentation of megakaryocytes. Platelets play a pivotal role in the pathogenesis of atherosclerosis. Platelets secrete a large number of substances that are important mediators of coagulation, inflammation, thrombosis and atherosclerosis. Within an individual there is a wide variation in platelet size and density. Larger platelets contain more dense granules and produce more thromboxane A2. Thus, larger platelets are metabolically more active and have thrombotic prothrombotic potential.[2]

Mean platelet volume (MPV) is a commonly used biomarker of platelet function and activation. Increased MPV has been associated with greater in vitro aggregation in response to ADP and collagen. Mean platelet volume is a cost-effective and routinely available test. Elevated MPV levels are associated

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with increased risk of myocardial infarction in patients with coronary artery disease, as well as death or recurrent vascular events after myocardial infarction. Also, higher MPV is observed in patients with diabetes mellitus, hypertension, hypercholesterolemia, smoking and obesity.[3,4]

Platelet distribution width (PDW) represent variation in platelet size. Larger PDW also indicates prothrombotic status. So far there is a paucity of data on the association between MPV, PDW and stroke severity or stroke outcome. The aim of our study was to investigate the relationship between platelet indices, MPV and PDW, and severity and outcome of acute ischemic stroke.[5]

Both type II diabetes mellitus and hypertension are important risk factors of acute ischemic stroke. Several studies have demonstrated that type II diabetes mellitus and hypertension are associated with endothelial dysfunction leading to platelet activation and altered platelet-endothelial interaction. The uniqueness of our study lies in the fact that it deals with non-diabetic and non-hypertensive stroke patients. Thus, it clearly upholds the view that increased platelet activity is itself an independent risk factor of acute ischemic stroke.[6]

Rathindra Nath Sarkar, Chandan Kumar Das Urmimala Bhattacharjee conducted a study prospective cohort study at department of general medicine, Medical College Hospital Kolkata January 2015-june 20151.70 non diabetic non hypertensive ischemic stroke patients without previous thrombotic events & not on anti-platelet medications within 24 hours of onset of symptoms & compared with equal number of age and sex matched controls. Severity of stroke was calculated by Canadian neurological scale (CNS). According to CNS patients were divided in two groups; with comprehension deficit (1st group, 32 patients) & without comprehension deficit (2nd group, 38 patients). Mean value for PDW & MPV in 1st group was 18.675 ± 3.494 & 12.894 ± 1.270 respectively and in 2nd group was 18.62 ± 3.387 & 12.42 ± 0.984 respectively and was significantly higher than mean value of 15.694 ± 3.127 & 10.46 ± 1.273 of PDW & MPV respectively in controls. In both study groups PDW & MPV was found to be significantly associated with severity of motor deficit. Thus, concluded that patients of ischemic stroke platelet indices may be used for predicting severity and outcome of motor deficit. Although larger sample size and multivariate analysis is required before this can be used regularly in clinical practice.

Milind Vyawashree department of general medicine Maharashtra conducted study to find association of platelet indices in acute ischemic stroke.[7] 100 consecutive cases of acute ischemic stroke and equal number of age and gender matched healthy controls were enrolled in study. Blood sample was collected at time of admission from cases and control for laboratory investigations. Modified Rankin score, ECG, BMI and NIHSS scale score of every patient carried out at time of admission, also modified

Rankin score was calculated on day 7 or discharge. Incidence of hypertension, diabetes, alcohol, obesity, dyslipidaemia well as mean MPV, PDW and platelet count were more in cases than controls. Platelet indices increased in severe stroke, amongst MPV and platelet count increase was statistically significant. Thus, concluded that platelet indices can be used as positive predictor for acute ischemic stroke. Mean platelet volume can be used as a prognostic indicator and high mean platelet volume is well correlated with severity and outcome of acute ischemic stroke at the time of admission itself.

Al Amir Bassiouny Mohamed examined 157 patients with ischemic stroke, admitted to the Sohag University Hospital, August 2013-October 2014. The diagnosis of stroke was performed clinically and confirmed by brain CT and MRI when needed. Platelet indices including MPV and PCT were assessed immediately (within 2 h) after admission. After 3 months, the functional outcome was assessed using the modified Rankin Scale with assessment of the relationship between platelet indices and stroke outcome. MPV was significantly higher in the unfavourable group (10.4 ± 2.3 fL) than in the favourable one (8.7 ± 1.3 fL) (P < 0. 001). MPV was an independent predictor of poor short-term outcome of acute stroke after controlling for confounders like diabetes mellitus. The mean PCT was significantly higher in the unfavourable group (0.28 ± 0.1%) than in the favourable one (0.25 ± 0.1%) (P = 0. 04) but not considered as an independent predictor of poor short-term outcome of acute stroke. Thus, concluded that MPV and PCT were significantly correlated with poor functional outcome, only MPV was an independent predictor of poor short-term outcome of acute stroke after controlling for confounders like DM, and these platelet indices can be used as a prognostic tool.[8]

Priyanka Meena conducted a study from December 1st 2013 to July 31st 2014 at SMS Medical College and Hospital Jaipur. The study was carried out among fifty patients diagnosed with an acute ischemic stroke and presenting to the hospital within forty-eight hours of onset of symptoms. Fifty age and sex matched controls were also recruited. The samples were then taken to the Advanced Haematology Lab department of pathology (SMS medical college) between 2 hours of collection and to measure the platelet count and mean platelet volume (MPV). Comparison of different haematological parameters was also performed between the cases and the controls, which showed significance in Mean RBC, Mean Hb , mean MPV and mean platelet count among the two groups. In conclusion, this study has shown an elevation of MPV and reduction of platelet count in acute stroke. Within this relationship and adjusting for other significant variables in multivariate regression analysis, an increase in MPV is independently associated with stroke.[9]

Narasimhamurthy, Department of General Medicine, ESIC Medical College & PGIMSR, Bangalore, Karnataka conducted a prospective study was

undertaken among patients admitted in ESIC Medical College & PGIMSR from January 2017 to June 2018.[10] Study comprised of around 150 cases of acute ischemic stroke without previous thrombotic events. Severity of ischemic stroke was assessed by the Modified Rankin Scale. Patients were divided into 2 groups based on Rankin score (Group 1: Score 0-2, and Group 2: Score 3 or more). Blood samples were taken to measure MPV and PDW. MPV and PDW were significantly elevated in patients who suffered a severe stroke defined as modified Rankin score of 3 to 6. Patients with higher MPV had worse outcome at the end of one week. After controlling for the risk profile associated with ischemic stroke in the multivariate logistic regression model, the effect of MPV in ischemic stroke remained statistically significant. MPV and PDW can be considered as laboratory markers for the risk of acute ischemic stroke. The MPV is associated with ischemic stroke severity and has a high value for discriminating severe from mild ischemic stroke.[11]

Platelet distribution width (PDW) measures the variability in platelet size. An increased PDW is associated with a prothrombotic status. Currently, there is limited data on the correlation between mean platelet volume (MPV), PDW, and the severity or outcome of strokes. The aim of our study was to explore the relationship between platelet indices, specifically MPV and PDW, and the severity and outcome of acute ischemic stroke.

MATERIALS AND METHODS

A Prospective study was undertaken among patients admitted in Raichur Institute of Medical Sciences, Raichur with ischemic stroke diagnosed by history, detailed clinical examination, routine investigations and brain imaging studies. Controls are students, nursing staff with no ischemic stroke and no comorbidities affecting the platelet indices. 90 with 45 patients with non-diabetic and non-hypertensive acute ischemic stroke are taken for the study and 45 healthy controls are taken for the study. Sample size calculated using the formula n= Zpq/d2.

All Acute Ischemic Stroke patients more than 18 years old based on history, physical examination and computed tomography (CT) scan that was performed at Emergency department during presentation were included in the study. CT features of cerebral hemorrhage, history of hypertension, diabetes mellitus and other co-morbidities like liver and kidney failure, cardiac dysfunction, recent episode of infection, history of transient ischemic attacks (TIA), stroke, autoimmune disorders and peripheral vascular disease, patient on anti-platelet medications, medications for dyslipidaemia, immunosuppressants were excluded from the study.

After obtaining institutional ethics committee clearance and written informed consent, the patients getting admitted to hospitals affiliated to Raichur Institute of Medical Sciences, Raichur, during the period of 15 august 2021 to 14 august 2022 were taken up for the study. 45 non diabetic non hypertensive patients with acute ischemic stroke and 45 healthy controls were included in the study. Information was collected, detailed history and clinical examination done CNS Score is calculated on day 1 and day 7. CNS score ≥8 is mild, score 5-7 is moderate and 1-4 is severe stroke. During the first day and 7th day of admission blood samples for the measurement of platelet indices were collected in ethylene diamine tetra acetic acid (EDTA) tubes and sent to the hospital laboratory. The blood samples were analyzed by the SYSMEXKX-21 automated hematological analyzer which is based upon the Coulter principle and recorded using pre-formed proforma (Annexure 2) at the time of admission. The study group of 45 patients was divided into two broad groups, with comprehension deficit (1st group) and without comprehension deficit (2nd group), based on Canadian Neurological Scale.

The control group of 45 healthy age and sex matched subject from the same hospital which included patients, doctors, nurses and other staffs who did not have any past history of stroke/ TIA or other vascular risk factors.

Investigations like complete blood picture, peripheral smear, platelet indices, RBS, LFT, RFT, ECG, 2D - ECHO, NCCT BRAIN and other investigations as and when required were done. All the data collected were tabulated in the Microsoft Office Excel Worksheet. Statistical evaluation was done using SPSS and suitable statistical method.

RESULTS

The [Table 1] presents a comparison between two groups: patients with acute ischemic stroke (n=45) and control subjects (n=45). The mean age of the stroke patients is 53 years (±6.15), slightly higher than the control group's mean age of 52 years (±6.37). Gender distribution is similar in both groups, with 75.56% of the stroke patients and 71.11% of the controls being male, and 24.44% of the stroke patients and 28.89% of the controls being female. Among the stroke patients, 44.44% have a comprehension deficit, while 53.33% do not, indicating that nearly half of the stroke patients experience difficulties with comprehension.

The mean PDW values for the 1st group, 2nd group, and control group were 18.675±3.494, 18.62±3.387, and 15.694±3.127, respectively. Similarly, the mean MPV values for the 1st group, 2nd group, and control group were 12.894±1.270, 12.42±0.984, and 10.46±1.273, respectively. This indicates that the mean values of both PDW and MPV were significantly higher in patients with acute ischemic stroke compared to the control subjects.

The correlation coefficients between motor deficit scores (based on CNS) and platelet indices in stroke patients were calculated. The severity of motor deficits showed a significant correlation with PDW (r=-0.556, p<0.01) and MPV (r=-0.46, p<0.05). This

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indicates that patients with lower CNS scores for motor deficits (indicating more severe deficits) had higher mean platelet volumes and platelet distribution widths. [Figures 2 and 3] display scatter dot diagrams illustrating the relationship between motor deficit scores and MPV and PDW, respectively.

Table 1: Demographic characteristics of cases and controls.

	Patients with acute ischemic stroke (n=45)	Controls (n=45)
Mean Age	53±6.15	52±6.37
Male	34 (75.56%)	32 (71.11%)
Female	11 (24.44%)	13 (28.89%)
With comprehension deficit (1st group)	20 (44.44%)	
Without comprehension deficit (2nd group)		24 (53.33%)

DISCUSSION

The Canadian Neurological Scale (CNS) is a straightforward and validated tool for assessing stroke severity. It combines components such as comprehension, level of consciousness, speech, and motor function of the arms, legs, and face. Lower CNS scores indicate greater stroke severity, with scores of 8 or higher considered mild, scores of 5-7 moderate, and scores of 1-4 indicating severe stroke.[13,14]

Our study demonstrated that platelet indices like MPV (mean platelet volume) and PDW (platelet distribution width) are significantly elevated in acute ischemic stroke patients compared to controls. Additionally, higher MPV and PDW values are significantly associated with greater functional impairment, as indicated by motor deficits. This suggests that platelet activation plays a critical role in the pathogenesis of stroke.

MPV and PDW are simple, easily measurable indices. When platelets are activated, they change shape from discoid to spherical, with pseudopodia formation. Automated hematological analyzers using impedance technology measure platelet volume based on changes in the electric field, which depends on the platelet's vertical diameter.[15]

Research worldwide has investigated the association between platelet indices and acute thrombotic events. The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) found that MPV is positively associated with stroke risk, with an 11% increased relative risk of stroke per femtoliter increase in MPV. Another study by Slavka et al,[16] showed that individuals with higher MPV (>11.01 fl) had 1.5 times higher vascular mortality risk than those with low MPV (<8.7 fl). Arevalo-Lorido et al. concluded that higher platelet indices are linked to overall mortality and morbidity, including cardiovascular mortality. However, a study by Cho et al. did not find a statistically significant difference in MPV values between patients and controls.[17]

Type II diabetes mellitus and hypertension are significant risk factors for acute ischemic stroke, and several studies have shown that they are associated with endothelial dysfunction leading to platelet activation and altered platelet-endothelial interactions. Our study is unique because it focuses on non-diabetic and non-hypertensive stroke patients, clearly indicating that increased platelet activity is an independent risk factor for acute ischemic stroke.

CONCLUSION

Our study supports the view that elevated platelet indices, such as MPV and PDW, are associated with increased platelet activity and can be considered independent risk factors in stroke patients who are non-diabetic and non-hypertensive.

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