ORIGINAL ARTICLE

Association of Mean Platelet Volume with Acute Ischemic Cerebrovascular Accident Among Patients with Type 2 Diabetes Mellitus: A Hospital-Based Study

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Abstract

Objective: To study the association of MPV (mean platelet volume) and acute ischemic stroke in patients of type 2 diabetes mellitus (DM).

Methods: This was a 1-year cross-sectional hospital-based study involving 79 patients presented with acute ischemic stroke. Among them, 25 were diabetic and 54 were nondiabetic. Demographic data and history of the patients were recorded. Investigations such as haemoglobin estimation, platelet count, MPV, HbA1c, imaging studies were conducted and evaluated for acute ischemic brain stroke. All the patients underwent neurological examination according to National Institute of Health Stroke Scale (NIHSS) at the time of admission and MPV was noted. Outcome of stroke was assessed during discharge by modified Rankin morbidity (MRM) score. SPSS 20 was used to analyse the data.

Results: Among 79 them, 25 patients (31.6%) had history of diabetes which formed the diabetic subset and the remaining 54 (68.35%) were considered in non-diabetic subset. MPV in patients with DM was significantly high (10.16 ± 0.89 fL) compared to nondiabetic patients (8.25 ± 0.91 fL; $p<0.001$). The mean NIHSS scores were significantly high in patients with diabetes compared to nondiabetic patients (20.38±3.19 vs. 17.76±3.74; $p=0.006$). Also, the mean MRM scores were significantly high in diabetics than that of nondiabetics (4.12 ± 0.66 vs. 3.00 ± 0.61; $p<0.001$). History of stroke was present in 12% of patients with DM compared to 1.85% of the non-diabetic patients (p=0.091).

Conclusions: Acute ischemic stroke in diabetic patients is significantly associated with raised MPV level, which is likely to be severe with high morbidity and mortality. Hence, MPV is an easily available blood parameter, which defines platelet reactivity and proves to be a good predictor of severity and outcome of stroke in diabetics. Also, higher percentile of patients showed history of recurrent stroke in diabetics as compared to non-diabetics in whom the MPV was considerably raised compared to other diabetic stroke cases.

Introduction

Stroke is a major cause for death and acquired disability in world population after myocardial infarction. Majority of the strokes are ischemic (80%) while others result from primary haemorrhage either intracerebral or into subarachnoid space.[1] Acute ischemic stroke is more common than haemorrhagic stroke and is a result of thrombosis or embolism. Various risk factors involved for stroke include hypertension, cigarette smoking, hyperlipidaemia, and diabetes mellitus.[2] Among these, risk factors, DM, and ischemic stroke often ascends together.[3]

Platelets play a vital role in normal haemostatic process. The mean platelet volume (MPV) is the mostly used laboratory marker of platelet function and activation. Increased platelet reactivity has emphasized to play an important role in developing various vascular complications.[4] Particularly, the patients with DM show increased platelet activity. The factors that contribute to this increased platelet activity are not clearly elucidated; however, metabolic abnormalities such as insulin resistance, hyperglycaemia, hyperlipidaemia, and conditions such as oxidative stress, endothelial dysfunction and inflammation have been presumed.[5] Studies also have stated that high MPV acts as a risk factor for several vascular complications of DM, which include thromboembolism, myocardial infarction and stroke.[6-9]

Furthermore, an increase in MPV is associated independently with stroke and increased levels of MPV have been found in acute ischemic stroke patients than in normal subjects. The patients with highest quintile of MPV had a >2 fold risk of severe stroke than those with lower quintiles.[10] These findings postulate that, the increase of MPV, specifically in diabetic patients might have a critical role for genesis or worsening of acute ischemic stroke. This prompted us to describe association between MPV and acute ischemic cerebrovascular events, which may serve as a valuable indicator for outcome of the event. MPV, being a cheap and easily available blood parameter, helps to prognosticate stroke both in diabetics and non-diabetics. The objective of this study was to study the association between MPV and acute ischemic stroke in patients with type 2 DM (outcome).

Material and Methods

Study design

This 1-year cross-sectional hospital-

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Received: 04.10.2017; Revised: 22.11.2017; Accepted: 11.04.2018

Table 1: Baseline characteristics of the study population

Findings	Group A (Diabetic), n (%)	Group B, (Non-diabetic) n (%)	*p*-value
Sex			
Male	18 (72 %)	37 (68.52 %)	0.754
Female	7 (28 %)	17 (31.48 %)	
Age-wise distribution			
30 or less	0	2 (3.70 %)	0.551
30-40	1 (4 %)	6 (11.11 %)	
41-50	4 (16 %)	11 (20.37 %)	
51-60	5 (20 %)	11 (20.37 %)	
61-70	8 (32 %)	11 (20.37 %)	
71-80	7 (28 %)	9 (16.67 %)	
81-90	0	4 (7.41 %)	
Previous history of stroke	3 (12 %)	1 (1.85 %)	0.091
Hypertension	5 (20 %)	10 (18.52 %)	0.551
Arterial supply			
ACA	2 (8 %)	5 (9.26 %)	0.890
ACA/MCA	2 (8 %)	4 (7.41 %)	
MCA	17 (68 %)	31 (57.41 %)	
MCA/PCA	1 (4 %)	6 (11.11 %)	
PCA	3 (12 %)	8 (14.81 %)	
Circulation			
Anterior	21 (84 %)	40 (74.07 %)	0.328
Posterior	4 (16 %)	14 (25.93 %)	
Severity of based on NIHHS			
Minor stroke	0	1 (1.85 %)	0.095
Moderate stroke	3 (12 %)	9 (16.67 %)	
Moderate to severe	13 (52 %)	37 (68.52 %)	
Severe	9 (36 %)	7 (12.96 %)	
Outcome based on MRM scores			
Slightly disability	0	8 (14.81 %)	<0.001
Moderate disability	3 (12 %)	40 (74.07 %)	
Moderate to severe disability	17 (68 %)	4 (7.41 %)	
Severe disability	4 (16 %)	2 (3.70 %)	
Death	1 (4 %)	0	
MPV (fL)			
9.5 or less	7 (28 %)	49 (90.74 %)	<0.001
> 9.5	18 (72 %)	5 (9.26 %)	

ACA, Anterior cerebral artery; MCA, Middle cerebral artery; PCA, Posterior cerebral artery; NIHSS, National institute of health stroke scale; MPV, Mean Platelet volume; MRM, Modified Rankin Morbidity score

Table 2: The comparison of baseline clinical characteristics between the diabetic and non-diabetic subsets

Findings	Diabetic, n (%)	Non-diabetic, n (%)	p value
Age (years)	62.04±10.88	58.11±16.75	0.217
Mean blood pressure			
Systolic (mmHg)	160.37±15.78	161.60±12.81	0.714
Diastolic (mmHg)	94.07±7.90	95.60±5.07	0.305
Hemoglobin (gm%)	13.86±1.06	13.87±1.64	0.968
Platelet count (lakhs/m^3)	2.61±0.51	2.76±0.64	0.290
NIHSS	20.08±3.19	17.76±3.74	0.006
MPV	10.16±0.89	8.25±0.91	<0.001
MRM scores	4.12±0.66	3±0.61	<0.001

NIHSS, National Institute of Health Stroke Scale; MPV, Mean platelet volume; MRM, Modified Rankin Morbidity Score

Table 3: Association of MPV with different parameters studied

Parameters	MPV (fL)		*p*-value
	> 9.5, n (%)	9.5 or less, n (%)	
Duration (years)			
5 or less	11 (73.33 %)	4 (26.67 %)	0.601
> 5	7 (70 %)	3 (30 %)	
Treatment			
Oral	12 (75 %)	4 (25 %)	0.746
Insulin	5 (62.50 %)	3 (37.50 %)	
Unknown	1 (100 %)	-	
HbA1c			
≤ 7	1 (50 %)	1 (50 %)	0.807
7.1 to 8.5	4 (80 %)	1 (20 %)	
> 8.5	13 (72.22 %)	5 (27.78 %)	
Previous stroke			
Present	2 (66.67 %)	1 (33.33 %)	0.645
Absent	16 (72.73 %)	6 (27.27 %)	
Hypertension			
Present	4 (80 %)	1 (20 %)	0.564
Absent	14 (70 %)	6 (30 %)	
NIHSS			
Moderate	3 (100 %)	0	0.564
Moderate to severe	8 (61.54 %)	5 (38.46 %)	
Severe	7 (77.78 %)	2 (22.22 %)	
MRM score			
Moderate disability	2 (66.67 %)	1 (33.33 %)	1
Moderate to severe disability	12 (70.59 %)	5 (29.41 %)	
Severe disability	3 (75 %)	1 (25 %)	
Death	1 (100 %)	0	

NIHSS, National Institute of Health Stroke Scale; MPV, Mean platelet volume; MRM, Modified Rankin Morbidity Score; HbA1c, glycated hemoglobin

based study (January 2014 to December 2014) was conducted at the Department of General Medicine and Department of Neurology. The ethical clearance was obtained from Ethics and Research Committee. Patients screened based on selection criteria were informed about the nature of the study. In case of comatose patients, the relatives/caretakers were informed about the study. The patients/caregivers expressing their willingness to contribute in the study were enrolled after obtaining a written informed consent.

Selection criteria

This study included acute ischemic brain stroke patients with or without prior history of DM. Exclusion criteria included patients who had anaemia with haemoglobin levels <12 gm% in men and 10 gm% in women, coronary artery disease, diagnosed with any other malignancy, immune thrombocytopenia purpura, acute poststreptococcal glomerulonephritis, renal failure, valvular heart disease, cyanotic congenital heart disease, and deep vein thrombosis.

Based on inverse sampling method, all the patients who presented with acute ischemic stroke fulfilling the selection criteria were involved in the study till sample size of patients with acute ischaemic stroke having history of type 2 DM was 25.

Data collection

Demographic data such as age and sex were recorded. History of other comorbid conditions including hypertension, DM, previous stroke, personal history such as habits of alcohol consumption, and smoking, were noted. A thorough physical examination was conducted for vitals (respiratory rate, pulse rate, and blood pressure) followed by systemic examination. The diagnosis of stroke was entertained after fulfilling WHO definition of stroke by the patient. The ischemic nature of stroke was

established by computed tomographic/magnetic resonance imaging scan. Evaluation of stroke severity was carried out based on National Institute of Health Stroke Scale (NIHSS). All the outcomes were noted on a predesigned as well as pretested proforma. Clinical investigations such as haemoglobin estimation, platelet count, MPV, HbA1c, imaging studies (Magnetic resonance imaging or computed tomography scan of brain) were conducted and evaluated for acute ischemic brain stroke.

Estimation of mean platelet volume

Under all aseptic conditions, 2 mL of blood sample drawn from antecubital vein of the patient at the time of admission was collected in ethylenediaminetetraacetic acid (EDTA) vials and transported for analysis to laboratory. The MPV was estimated on Beckman and Coulter LH 780 haematology analyser. The MPV value of ≥ 9.5 fL was considered as raised.

Data analysis

The data obtained was coded in a Microsoft Excel Worksheet. SPSS statistics software version 20.0 was used to analyse the pooled data. The categorical data was expressed in terms of rates, ratios, and proportions and compared using chi-square test or Fisher's exact test. The continuous data was expressed as mean ± standard deviation (SD) and compared using independent sample t-test. In case of more than two means, one-way ANOVA was used to compare the data. A $p \leq 0.05$ was considered as statistically significant.

Results

A total of 79 patients presented with acute ischemic stroke during the study period. Among them, 25 patients (31.6%) had history of diabetes, which formed the diabetic subset and the remaining 54 (68.35%) were considered in nondiabetic subset. The baseline study characteristics of the diabetic set and nondiabetic set are presented in Table 1. No significant difference was found between the diabetic subset and nondiabetic subset regarding sex, age, hypertension, arterial supply and type of circulation ($p>0.005$). However, severity of stroke (MRM) and MPV was found statistically significant between the diabetic and nondiabetic set. Also, history of previous stroke was present in 12 % of the patients with DM compared to 1.85% of the non-diabetic patients (p=0.091). Out of 25 diabetic patients, 3 cases were reported to have alarmingly high values of MPV who had history of recurrent stroke. Though the sample size was not sufficient to predict anything strongly.

The mean age of diabetic set was 62.04±10.88 years, whereas that of nondiabetic set was 58.11±16.75 years. The comparison of baseline clinical characteristics between diabetic and nondiabetic subset is provided in Table 2. No significant difference was observed between the diabetic and nondiabetic subset regarding mean age, mean systolic and diastolic blood pressure, NIHHSS score, haemoglobin, and platelet count. However, MPV (10.16±0.89 fL vs. 8.25±0.91 fL; $p \leq 0.001$) and MRM scores (4.12±0.66 vs. 3±0.61; $p \leq 0.001$) were found statistically significant between two subsets.

Among the diabetic patients, no statistical association was observed between MPV and duration of DM, treatment modality, HbA1c, prior history of stroke, hypertension, NIHSS score and MRM score (Table 3).

The mean MPV level in diabetic subset with duration >5 years was 10.29±1.4 fL as compared to 10.07±0.80 fL with duration >5 years or less. However, the difference observed was not significant ($p=0.585$). The mean MPV levels among the diabetic subset who were on treatment with insulin was 10.36±1.09 fL as compared to 9.98±0.75 fL who received OHA's (p=0.404). The mean MPV in diabetic population with HbA1c levels ≤7 was 9.75±0.35 fL, 7.01 to 8.50 was 9.98± 0.74 fL, and >8.50 was 10.39±1.00 fL. However, the difference was not significant ($p=0.678$).

Discussion

Acute ischemic stroke is a condition that is frequently associated with DM. It is known that DM may contribute to systemic as well as intracranial atherosclerotic disease. This augmented risk has been related to pathophysiological changes observed in the cerebral vessels of diabetic patients.[11] Correlating and prognosticating the effect of hyperglycaemia on stroke and its outcome is need of the hour.

As mentioned earlier, platelets with increased size/volume are more reactive. Platelet volume is estimated at the level of progenitor cell. Recent studies stated that cytokines—interleukin-3 (IL-3) or interleukin-6 (IL-6), influence the megakaryocyte ploidy and leads to the production of more reactive and larger platelets.[12] Thus, it is rational to speculate that a proinflammatory state followed by cerebrovascular event may consequence in higher MPV and pro-thrombotic event. This provided a platform to associate MPV to a cohort of diabetic stroke and also to compare it to non-diabetic stroke to assess the severity of stroke (NIHSS) and predict the outcome of stroke (MRM score).

The male sex has been listed as the major risk factor for stroke.[13] In this study, a male predilection was observed. Although the difference was not significant, age is the most nonmodifiable risk factor for stroke. In the study, the mean age among diabetic patients was 62.04 ± 10.88 years compared to 58.11 ±16.75 years in nondiabetic patients. Likewise, a study by Shah et al.[14] to assess the role of MPV in ischemic stroke also reported mean age as 58 years. These observations showed that acute ischemic stroke in this study was common in elderly age group.

It is postulated that higher MPV may predispose to the occurrence of ischemic strokes, which is proved by other research workers.[14] In present study, the majority of diabetic patients had raised MPV levels as compared to nondiabetic patients. Correspondingly, the mean MPV was significantly high in patients with history of DM as compared to nondiabetics. These findings confirm the positive association between MPV and acute ischemic stroke in patients with DM. The positive association observed between ischemic stroke with MPV in diabetic patients was independent of treatment of diabetes ($p=0.404$), duration of diabetes ($p=0.585$), glycaemic control ($p=0.678$), and hypertension ($p=0.564$). There is lack of data to comment on these findings, as this study is first of its kind to study acute ischemic stroke in diabetic patients and study its association with MPV.

Similar results were reported by PROGRESS collaborative group. In this study, stroke rates were greater among individuals with higher measurements of MPV. The study reported that for each 1-fL increase in MPV was associated with 12% increase in relative risk of stroke. Hence, MPV

is known as an independent risk factor of stroke among high-risk individuals. The measurement of MPV may also add useful prognostic information for clinicians in the management of patients with cerebrovascular disease.[15]

The association between MPV with both inflammation and thrombosis has also become a pinpoint of interest in last few decades. Studies reported that MPV levels are significantly high in acute ischemic stroke patients.[16] In this study, 12% of the patients with DM presented with history of stroke compared to 1.85% of the nondiabetic patients. Among these diabetic patients, all 12% of patients had history of recurrent stroke in those MPV was highly raised and thus, associating the raised MPV to recurrence of stroke. However, in this study, owing to a lesser sample size, there was no significant association between history of stroke and raised levels of MPV (p=0.645). This observation is in conformity with bulk of other published reports.[16-19]

The patients with high MPV (>11.01 fL) had 1.5 times greater vascular mortality risk than those with low MPV (<8.7 fL) value. Also, a significant relation was found between patients with high MPV and ischaemic heart disease.[20] Similarly, the current study indicated several other implications regarding severity of stroke and outcome. The severity of stroke is likely to be severe in diabetics based on NIHSS scores (20.38 ± 3.19 vs. 17.76 ± 3.74; p=0.006) and are likely to have higher mortality and morbidity based on MRM scores (4.12 ± 0.66 vs. 3.00 ± 0.61; p<0.001). Likewise, a prospective study conducted by Shah et al.[14] also testified that patients with higher MPV had worse outcome at the end of 1 week, as measured by MRM score. The similar finding has been stated in former studies.[10,16,19]

Moreover, it has been proposed that patients with large platelets are more susceptible to risk factors such as diabetes and obesity, and therefore have an increased risk of acute ischemic stroke.[21] Diabetic patients are known to have higher incidence of myocardial infarction and stroke. Also, presence of high MPV in diabetics might augment the risk of thrombotic complications. It has also observed that diabetics with retinopathy and other complications have higher MPV than those without this complications.[14] Presence of significantly higher MPV in impaired fasting glucose patients as compared to nondiabetic subjects is also reported in the literature.[11]

Altogether, this is a first study to associate MPV in diabetic stroke and nondiabetic strokes with a positive outcome. Thus, stating MPV was highly raised in diabetic strokes than in nondiabetic strokes and has bad prognosis and worst outcome.

Conclusion

Diabetes being a procoagulant state, patients are at risk of any thrombotic event. MPV a valuable predictor of platelet reactivity is a simple test available in panel of hemograms. Based on findings, the current study lights there is a positive association between MPV and acute ischemic stroke in patients with DM. Also, acute ischemic stroke in diabetic patients with raised MPV is likely to be severe (as assessed by NIHSS score) and may results in high morbidity and mortality (as assessed by MRM). In order to correlate MPV to predict recurrence of stroke, a larger sample size of diabetic strokes has to be considered.

Acknowledgments

Both authors have contributed equally in the development of manuscript

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