Original Article

Association of Mean Platelet Volume with Acute Ischemic Stroke and its In-Hospital Outcome amongst Type II Diabetic, Non-Diabetic and Impaired Fasting Glucose Patients : A Prospective Observational Study

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ABSTRACT

Objective : To study the association of mean platelet volume (MPV) with severity and outcome of acute ischemic stroke in type II diabetic, non-diabetic and impaired fasting glucose patients.

Material : This was a 2-year hospital based prospective observational study involving 180 patients presented with acute ischemic stroke. Amongst them, 60 were diabetic, 60 were non-diabetic and 60 had impaired fasting glucose levels. Demographic data and history of the patients were recorded. Investigations such as radiological imaging, platelet count, MPV, FBS, PPBS, RBS, HbA1c, Lipid profile were done to evaluate for stroke. All the patients were examined according to National Institute of Health Stroke Scale (NIHSS) at the time of admission and MPV was noted. Modified Rankin Morbidity (MRM) score was applied to assess the outcome of stroke during discharge. STATA 14.0 was used to analyse the data.

Results : Among 180 patients, each subset had equal distribution i.e 60 patients were in diabetic subset, 60 in non-diabetic subset and remaining 60 in impaired fasting glucose subset. The mean NIHSS scores were significantly high in patients with diabetes mellitus (23.98 ± 9.26) compared to impaired fasting glucose patients (21.83 ± 10.04) and non-diabetic patients (13.7 ± 6.38; p = < 0.0001). MPV in patients with diabetes (9.94 ± 1.17) and in patients with impaired fasting glucose (9.81 ± 1.49) was significantly high compared to non-diabetic patients (9.27 ± 1.27; p = 0.0136). The mean MRM scores were significantly high in diabetic (4.08 ± 1.58) and impaired fasting glucose group (3.65 ± 1.90) compared to non-diabetic group (2.98 ± 1.99; p = 0.0050).

Conclusion : Diabetic patients with acute ischemic stroke have raised MPV levels, which is further associated with high morbidity and mortality. Hence, MPV can be used as a predictor for severity and outcome of acute ischemic stroke.

Introduction :

Stroke is the second leading cause of death worldwide[1]. The incidence for both ischemic and hemorrhagic stroke is higher among males than females (132 versus 99 per 10000 [95% UI] and 65 versus 56 per 10000 [95% UI] for ischemic and hemorrhagic respectively)[2]. Majority of the strokes are ischemic (87%) while others result from hemorrhage. The major risk factors that contribute to stroke are Systemic hypertension, Diabetes mellitus, dyslipidemia and cigarette smoking[3]. These risk factors when modified and kept under control have substantial influence in preventing its occurrence and reducing its severity.

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Platelets are heterogenous blood elements with diverse sizes and densities. In addition to aggregation, platelets modulate important pathophysiological processes including inflammation and coagulation. Platelet size when measured as mean platelet volume (MPV), is a marker of platelet function and is positively associated with indicators of platelet activity. An increased MPV, an indicator of larger and more reactive platelets, has been associated with various vascular complications.

Diabetes mellitus is a prothrombotic state which has been shown to exhibit increased platelet activity. This has been attributed to both insulin resistance and insulin deficiency. Insulin has been shown to antagonize the effects of platelet agonists like collagen, adenosine diphosphate, epinephrine and platelet activating factor[4]. Hyperglycemia contributes to heightened platelet reactivity directly as well as through glycation of platelet proteins.

MPV was found to be significantly higher in diabetic patients and it was hypothesized that platelets with altered morphology are likely to be associated with increased risk of vascular complications in diabetes[5]. Larger platelets contain more dense granules and hence are more potent and thrombogenic[6]. Hence, MPV, which is a cheap and easily available blood parameter, can be used to assess the severity and outcome of acute ischemic stroke among patients with type 2 diabetes.

Materials and Methods "

Study Design :

This was a 2-year hospital based prospective observational study (November 2018 to October 2020) conducted at the department of General Medicine at tertiary care hospital in central India. Ethics clearance was obtained from Institutional Ethics committee. Patients were screened based on selection criteria and enrolled in the study after obtaining a written informed consent. In case of comatose patients, consent was obtained from the caregivers.

Selection Criteria :

This study included acute ischemic brain stroke patients with or without risk factors without prior history of stroke. Exclusion criteria included patients having type 1 diabetes, hemorrhagic stroke, patients on anti-platelet drugs or patients who were known case of hereditary disorders of platelets.

Data Collection :

Demographic data of the patients were recorded. History of risk factors such as DM, hypertension, smoking, alcoholism were noted. Examination of vital parameters (Blood pressure, Pulse rate) was conducted followed by systemic examination. Ischemic nature of stroke was confirmed by imaging techniques (CT scan/MRI). Severity of stroke was assessed on admission by applying National Institute of Health Stroke Scale (NIHSS). Further evaluation was done by estimating Platelet count, Mean platelet volume, Blood sugar levels (FBS, PPBS, RBS, HbA1c) and Lipid profile. Outcome of stroke was assessed after 7 days of hospital stay using Modifies Rankin Morbidity (MRM) score.

Estimation of mean platelet volume :

Under all aseptic precautions, 2 ml blood from the patient at the time of admission was collected in ethylene diamine tetra acetic acid (EDTA) vials. The MPV was estimated with the help of PROKAN PE-6000 analyser in the laboratory. The MPV value of $\geq$ 9.5 fl was considered as raised.

Statistical analysis :

Collected data were entered into Microsoft excel spreadsheet. Tables and Graphs were prepared using Microsoft word and excel software. Continuous variables were presented as Mean ± SD. Categorical variables were expressed in frequency and percentages. Continuous variables were compared between 3 groups by performing One-way Repeated ANOVA test.Categorical variables were compared by performing chi-square test. Mean platelet and MPV were compared between mortality and survivors by performing independent t-test. $P < 0.05$ was considered as statistical significance. Statistical software STATA version 14.0 was used for data analysis.

Results :

A total of 180 patients were enrolled in the study, among whom 60 were diabetic, 60 were non-diabetic and 60 had impaired fasting glucose levels. No significant difference was found between the subsets regarding risk factors such as systemic hypertension, smoking and alcoholism ($p > 0.05$) ***(Table 1).*** However, the mean NIHSS scores were significantly high in patients with diabetes mellitus (23.98 ± 9.26) compared to impaired fasting glucose patients (21.83 ± 10.04) and non-diabetic patients (13.7 ± 6.38; p = < 0.0001) ***(Table 2).*** MPV in patients with diabetes (9.94 ± 1.17) and in patients with impaired fasting glucose (9.81 ± 1.49) was significantly high compared to non-diabetic patients (9.27 ± 1.27; p = 0.0136) ***(Table 3).*** The mean MRM scores were significantly high in diabetic (4.08 ± 1.58) and impaired fasting glucose group (3.65 ± 1.90) compared to non-diabetic group (2.98 ± 1.99; p = 0.0050) ***(Table 4).***

The number of patients with severe stroke in diabetic group was significantly high (45.45%) as

Observation -

Table 1 : **Risk factors in study population.**

Risk factors	Non Diabetic group		Impaired fasting glucose patients		Diabetic group		p-value
	Frequency	%	Frequency	%	Frequency	%	
Smoking	18	30.51	19	32.20	22	37.29	0.721, NS
Alcohol	23	33.82	21	30.88	24	35.29	0.848, NS
Hypertension	40	33.61	42	35.29	37	31.09	0.624, NS
CAD	17	31.48	19	35.19	18	33.33	0.924, NS

Table 2 : **Comparison of NIHSS Score between diabetic, impaired fasting glucose and non diabetic patients**

	Non Diabetic group		Impaired fasting glucose patients		Diabetic group		p-value
	Mean	SD	Mean	SD	Mean	SD	
NIHSS Score	13.7	6.38	21.83	10.04	23.98	9.26	<0.0001, HS

Table 3 : **Comparison of platelet indices between diabetic, impaired fasting glucose and non diabetic patients**

Platelet indices	Non Diabetic group		Impaired fasting glucose patients		Diabetic group		p-value
	Mean	SD	Mean	SD	Mean	SD	
Platelet	2.69	0.59	2.45	0.54	2.62	0.56	0.0648, NS
MPV	9.27	1.27	9.81	1.49	9.94	1.17	0.0136, S

Table 4 : **Comparison of MRM Score on day 7 between diabetic, impaired fasting glucose and non diabetic patients.**

	Non Diabetic group		Impaired fasting glucose patients		Diabetic group		p-value
	Mean	SD	Mean	SD	Mean	SD	
MRM Score	2.98	1.99	3.65	1.90	4.08	1.58	0.0050, HS

Table 5 : **Comparison of outcome between diabetic, impaired fasting glucose and non diabetic patients**

Outcome	Non Diabetic group		Impaired fasting glucose patients		Diabetic group		p-value
	Frequency	%	Frequency	%	Frequency	%	
Deaths	10	29.41	11	32.35	13	38.24	0.776, NS
Survivors	50	34.25	49	33.56	47	32.19	

Table 6 : **Comparison of stroke severity between diabetic, impaired fasting glucose and non diabetic patients**

Stroke severity	Non Diabetic group		Impaired fasting glucose patients		Diabetic group		p-value
	Frequency	%	Frequency	%	Frequency	%	
0 No stroke	0	0	0	0			Chi2=36.9968 P<0.001, HS
1 - 4 Minor	1	100	0	0	0	0	
5 - 15 Moderate stroke	39	46.43	25	29.76	20	23.81	
16 - 20 Moderate to severe	7	100	0	0	0	0	
21 - 42 Severe	13	14.77	35	39.77	40	45.45	

Table 7 : **Association of Mean of platelet indices with severity of stroke in diabetic patients**

	Minor	Moderate	Moderately severe	Severe	p-value
Platelet	-	2.59 ± 0.53	-	2.64 ± 0.57	0.7467, NS
MPV	-	9.09 ± 0.92	-	10.36 ± 1.05	<0.0001, HS

Table 8 : **Association of Mean of platelet indices with disability of stroke in diabetic patients**

	No Significant Disability	Slight disability	Moderate disability	Moderate--ly severe disability	Severe disability	Death	F-value	p-value
Platelet	2.78 ± 0.56	2.62 ± 0.45	2.43 ± 0.60	2.52 ± 0.68	2.86 ± 0.51	2.46 ± 0.49	1.14	0.3505, NS
MPV	9.3 ± 1.00	8.92 ± 0.77	9.11 ± 1.07	10.13 ± 1.05	10.01 ± 1.23	10.99 ± 0.40	6.22	0.0001, HS

Table 9 : **Association of MPV with Modified Ranking Scale Score on day 7**

MPV	Modified Ranking Scale Score for disability of stroke				P-value
	0 - 2		3 - 6		
	Frequency	%	Frequency	%	
7. 6 - 9.0	6	50.0	11	22.92	Chi2 = 11.9925 P=0.007, HS
9.1 - 9.8	4	33.33	4	8.33	
9.9 - 10.6	1	8.33	5	10.42	
10.7 - 11.4	1	8.33	28	58.33	

compared to impaired fasting glucose group (39.77%) and non-diabetic group (14.77%; p < 0.001) ***(Table 6).***

Also, higher MPV in diabetic patients with stroke was associated with severe disability (p = o.ooo1) ***(Table 8).***

Among total deaths, 38.24% were diabetic, 32.35% were from impaired fasting glucose group and 29.41% were non-diabetic which shows the high mortality among acute ischemic stroke patients with diabetes compared to those who were non-diabetic or had impaired fasting glucose levels, but the data was not statistically significant (p = 0.776) ***(Table 5).***

Discussion :

Acute ischemic stroke is being recognised as an important cause of morbidity and mortality worldwide. Thrombus formation at atherosclerotic plug is the main pathophysiology for acute ischemic stroke. As diabetes mellitus is a major risk factor for development of atherosclerosis and thus, for development of stroke, correlating and prognosticating its effects on stroke severity is the need of the hour.

Platelet indices are indicators of platelet activity. Large size platelets are more reactive, and as they have more thrombotic value they tend to cause ischemic events like stroke, myocardial infarction and other vascular complications. A study by Shah et al to assess the role of MPV in ischemic stroke postulated that higher MPV may predispose to occurrence of ischemic strokes[7].

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[8]. Diabetic patients are known for higher vascular complications. Presence of high MPV might increase the risk of thrombotic events. Presence of significantly higher MPV in impaired fasting glucose patients compared to non-diabetic patients is also reported in literature[9].

PROGRESS collaborative group also reported similar results. In this study, stroke rates were greater among individuals with high MPV. The study reported that each 1-fl increase in MPV was associated with 12% increase in relative risk of stroke. Hence, MPV is an independent risk factor for stroke among high risk individuals[10].

In our study, the mean MPV was significantly high in stroke patients with diabetes. Also, high MPV was associated with more severe stroke, and occurrence of death was high among stroke patients with diabetes compared to non diabetic and impaired fasting glucose patients. These findings confirm that MPV can be used as a positive predictor of severity and outcome of acute ischemic stroke in diabetic patients.

Conclusion :

Diabetes being a prothrombotic state, poses a high risk for development of vascular complications. MPV is a cheap and easily available blood parameter which can be used to assess severity and prognosis of acute ischemic stroke patients. Based on findings, our study shows that there is a positive association between MPV and acute ischemic stroke in patients with diabetes. Also, diabetic patients with acute ischemic stroke who had raised MPV value, had severe stroke (as assessed by NIHSS score) and high mortality and morbidity (as assessed by MRM score).

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