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A cross sectional study of association between mean platelet volume and acute ischemic cerebrovascular stroke in patients with known case of Type 2 Diabetes Mellitus:A hospital-based study.

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Introduction

Stroke is the second leading cause of mortality and permanent disability globally, causing 200,000 deaths in the US and 334-424/100,000 fatalities in India annually. 20% of stroke survivors remain hospitalized, and 15% to 25% experience permanent disability.[1]

Stroke risk increases with age, with India's stroke mortality doubling by 2030. In 1990, stroke was the sixth most common cause of disability-adjusted life years, but by 2030, it is predicted to be the fourth most common cause. The burden of stroke is expected to grow automatically due to the increasing ageing population. Most stroke patients experience focal neurologic deficits, leading to residual physical, cognitive, and behavioral impairments.[1]

Most strokes (80%) are ischemic, with thrombosis or embolism being more common. Risk factors include high blood pressure, smoking, hypertension, diabetes mellitus, and haemophilia, with diabetes mellitus and ischemic stroke often rising together. Primary hemorrhage causes the remainder.[2]

Platelets are essential for normal haemostatic processes, homeostasis, thrombosis, and coagulation. Large platelets are more active metabolically and enzymatically, producing more prothrombotic factors and prone to aggregate. Mean platelet volume (MPV) is a measure of platelet size and function. Increased platelet reactivity is linked to vascular problems, particularly in patients with diabetes. Metabolic irregularities, oxidative stress, endothelial dysfunction, and inflammation may contribute to this elevated platelet activity. High MPV is a risk factor for DM vascular complications, including thromboembolism, myocardial infarction, and stroke.[3]

MPV levels are higher in acute ischemic stroke patients and independently linked to stroke. Individuals with the highest percentile of MPV have a higher risk of a major stroke, suggesting an increase in MPV, particularly in diabetic patients, may significantly impact the development or exacerbation of acute ischemic stroke.[4]

Few studies have examined the connection between type 2 DM diabetics' MPV (mean platelet volume) and acute ischemic stroke .Therefore the present study is conducted to look for association between MPV and acute ischemic stroke in patients of type2 diabetes mellitus (DM).

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Aims and Objectives:

The study investigates the correlation between mean platelet volume (MPV) and acute ischemic cerebrovascular stroke in type2 diabetes patients compared to the control population.

Materials and Methods

SOURCE OF DATA:

The study was done on those who had presented with ischemic stroke (first event) in the medical wards or at the medical outpatient department of the Medical College.
Sample Size: 200 patients
Study deigns: Cross sectional study
Study place: Government Medical College, Surat, Tertiary care center
Study duration: 1st August 2021 to 30th January 2022.
After giving their assent, the patients and controls had a comprehensive history, clinical examination, and investigations, all in compliance with the proforma.

The patients included in the research group were chosen based on the following criteria.

Inclusion criteria

1. Age greater than 18 years.
2. Diagnosed case of Ischemic stroke (confirmed by MRI or CT Scan Brain) with or without Diabetes
3. Patients who are conscious and cooperative and willing to give a proper history.
4. If in case the patient is not capable of giving a proper history, in that case history given by the accompanying person after getting consent will be used for documentation.

Exclusion criteria

1. Patient not giving informed consent.
2. Recurrent stroke
3. Hemorrhagic stroke
4. Patient already on antiplatelet agents
1. Pregnant women
2. Hereditary disorders of Large platelet.
3. Malignancy
4. Cyanotic congenital heart disease, valvular heart disease
5. Deep vein thrombosis.

Sample source: During the six-month trial period (August 1, 2021–January 30, 2022), all patients with acute ischemic stroke who presented in the IPD and OPD and met the selection criteria were included in the study.

Estimation of mean platelet volume

Two milliliters of blood were extracted from the patient's antecubital vein at admission, collected in an EDTA vial, and transported to a laboratory for analysis while maintaining aseptic conditions. Using an automated haematology analyzer, the MPV was calculated. An MPV value of greater than 9.5 fL was regarded as high.

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We gathered information on patients who were hospitalized for acute ischemic cerebrovascular stroke between August 1, 2021, and January 30, 2022.

We examined the subsequent standards.

Clinical symptom:

1. Numbness or weakness of the face, arm or leg, especially on one side of the body.
2. Sudden confusion
3. Difficulty speaking, diminished vision
4. Dizziness, loss of balance or coordination
5. severe headache with no known cause

INVESTIGATIONS:

All the patients and controls underwent the following investigations.

- Complete hemogram
- Fasting Blood sugar
- Post prandial Blood sugar
- Electrocardiogram
  Fasting Lipid profile
- Glycosylated Hemoglobin (HbA1c)
- Imaging studies for patients alone (CT , MRI)
- Severity of stroke was measured by modified Rankin morbidity score.

CASE DEFINITION OF STROKE

(1) **DIAGNOSIS OF DIABETES MELLITUS**:

(a) Fasting Plasma Glucose > 126mg/dl and 2 Hours post prandial plasma glucose > 200mg/dl or HbA1c ≥ 7.0.

(b) Known cases of type 2 Diabetes Mellitus taking/not taking medications.

(2) **HYPERTENSION**:

(a) Blood Pressure > 140/90 mm of Hg recorded in sitting posture on each of 2 or more visits.

(b) Known hypertensive patients taking/not taking medications

(**3) DYSLIPIDEMIA:**

(a) Total cholesterol ≥200 mg/dl.

(b) Known cases of dyslipidemia with or without medications

(4) Modified Rankin's Scale:

It is one of the commonly used clinical outcome measures in patients with stroke

0 → No symptoms

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1 → No significant disability, able to carry out all usual activities despite some symptoms

2 → Slight disability, able to look after own affairs without assistance, but unable to carry out all

the previous activities.

3 → Moderate disability, requires some help, but able to walk unassisted.

4 → Moderately severe disability. Unable to attend own bodily needs without assistance and

unable to walk unassisted.

5 → Severe disability, requires constant , nursing care and attention, bed ridden and incontinent.

6 → Dead.

(4) STROKE:

Diagnosed on the basis of history, clinical examination and imaging studies (CT/MRI).

(5)Abnormal ECG features

• Left ventricular hypertrophy.

• Ischaemic heart disease – ST – T changes

• Features of old myocardial infarction.

Statistical Analysis

The SPSS application for Windows, version 25, was used to do statistical analysis after data was entered into the Microsoft Excel program (SPSS, Chicago, Illinois). Categorical data were shown as absolute numbers and percentage, whereas continuous variables were shown as mean ± SD. Prior to statistical analysis, the normality of the data was examined. To determine the overall characteristics of the study population, descriptive analysis was used.

Either the Fisher's exact test or the chi square test was used to analyze categorical variables. The mean was compared using one method of ANOVA. To determine the correlation between two continuous variables, person correlation analysis was conducted. Statistics were deemed significant if $P<0.05$.

Observation and Results

Table 1: General characteristics of the patients with and without diabetes

	With Diabetes		Without Diabetes		P value
	Mean	SD	Mean	SD	
Age	58.18	18.095	61.45	19.626	0.051
HbA1c	6.504	1.9783	7.633	2.5421	0.001
PP2BS	172.85	38.607	292.49	104.797	<0.001

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FBS	138.02	29.962	165.66	9.680	<0.001
Creatinine (mg/dl)	0.982	.2245	.992	.2176	0.761
SBP	148.10	11.128	150.32	10.620	0.151
DBP	91.46	5.147	91.92	5.415	0.539

The mean age of diabetes in my study was 58.18±18.09 years, while the mean age of non-diabetics was 61.45±19.62 years (p>0.05). The clinical features of the baseline subgroups of individuals with and without diabetes are contrasted in Table 1.

There was no appreciable change in mean serum creatinine levels or mean systolic and diastolic blood pressure between the non-diabetic and diabetic categories. Nonetheless, it was discovered that there were statistically significant differences in HbA1c (6.5±1.97 vs. 7.6±2.5), PP2BS (172.85±38.60 vs. 292.49±104.79; p0.001), and FBS (138.02±29.96 vs. 165.669.68; p0.001) between the two categories.

Table 2: Age (yrs) wise distribution with diabetes status

			Diabetes		Total	P value
			No	Yes		
Age; years	21-40	Count	23	26	49	0.530
		%	11.5%	13.0%	24.5%	
	41-60	Count	30	32	62	
		%	15.0%	16.0%	31.0%	
	61-80	Count	37	34	71	
		%	18.5.0%	17.0%	35%	
	>80	Count	10	8	18	
		%	5.0%	4.0%	9.0%	
Total		Count	100	100	200	
		%	100.0%	100.0%	100.0%	

The age group that comprises the majority of patients (35%) is 61-80 years old, followed by 41-60 (31%) and 21-40 (24.5%) years old. Regarding age group distribution, there was no statistically significant difference between the two groups (p>0.05).

Table 3: Gender distribution among stroke patients

Gender	Frequency	Percent
Male	106	53.0
Female	94	47.0
Total	200	100.0

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In our analysis, there is a greater proportion of male patients (53%) than female patients (47%). The male prevalence is also seen in the patient group that does not have diabetes.

Table 4: Comparing ECG findings in patients with and without diabetes

		Diabetes		Total	P value
		No	Yes		
Abnormal	Count	57	62	119	0.471
	%	57.0%	62.0%	59.5%	
Normal	Count	43	38	81	
	%	43.0%	38.0%	40.5%	
Total	Count	100	100	200	
	%	100.0%	100.0%	100.0%	

The ECG results showed no discernible difference between the two groups (p>0.05).

Table 5: Comparison of blood parameters with diabetes status

	Diabetes				P value
	No		Yes		
	Mean	SD	Mean	SD	
Hb	13.099	1.2121	13.092	1.2099	0.967
Platelet count (in lakhs)	1.941	.2837	2.024	.2831	0.061

The mean hemoglobin level did not significantly differ between the non-diabetic and diabetic subgroups. The difference in platelet count between non-diabetics (1.94±0.28 lacs) and diabetics (2.02±0.28 lacs; p≤0.001) was determined to be statistically insignificant.

Table 6: Comparing MPV with diabetes

Diabetes	Mean	Std. Deviation	P value
No	8.751	1.1991	<0.001
Yes	10.247	1.3176	
Total	9.499	1.4634	

Patients with diabetes had a mean platelet volume that was considerably greater (10.24±1.31) than non-diabetic subgroups (8.75±1.19) (p<0.05).

Table 7: Pearson correlation between MPV and FBS

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		FBS
MPV (fL)	Pearson Correlation	0.377
	Sig. (2-tailed)	0.001
	N	100

substantial increase in correlation. MPV rises in tandem with an increase in FBS.

MPV and FBS were found to have a statistically significant positive connection in patients with the diabetic subgroup.

Table 8: Pearson correlation between MPV and PP2BS

		PPBS
MPV (fL)	Pearson Correlation	0.576
	Sig. (2-tailed)	0.001
	N	100

notable increase in correlation. MPV rises in tandem with an increase in PP2BS.

PP2BS and MPV showed a statistically significant positive correlation in patients with the diabetic subset.

Table 9: Pearson correlation between MPV and HBA1C

		HBA1C
MPV (fL)	Pearson Correlation	0.433
	Sig. (2-tailed)	0.001
	N	100

substantial positive correlation. MPV rises in tandem with rising HBA1C.

In patients with the diabetic subset, there was a statistically significant positive correlation between MPV and HBA1C.

Table 10: Pearson correlation between MPV and Modified Rankin morbidity scale (Severity)

		Modified Rankin morbidity scale (Severity)
MPV (fL)	Pearson Correlation	0.302
	Sig. (2-tailed)	<0.001
	N	200

notable increase in correlation. MPV also rises as the Modified Rankin score does.

Between MPV and the Modified Rankin Morbidity Scale (Severity) in patients with and without diabetes subsets, a statistically significant positive correlation was observed.

Table 11: Comparing mean MPV with Modified Rankin morbidity scale (Severity)

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Modified Rankin morbidity scale (Severity)	Mean	Std. Deviation	P value
2	8.767	1.1081	<0.001
3	8.954	1.1169	
4	9.651	1.3422	
5	10.120	1.6518	
Total	9.499	1.4634	

Between subjects with diabetes and those without, there was statistically significant differences in the Modified Rankin Morbidity Scale for stroke severity and MPV. The Modified Rankin Morbidity Scale indicates that mean MPV increases with increasing severity.

Table 12: Comparing Modified Rankin morbidity scale (Severity) with diabetes status

			Diabetes		Total	P value
			no	yes		
Modified Rankin morbidity scale (Severity)	2	Count	16	12	28	0.038
		%	16.0%	12.0%	14.0%	
	3	Count	28	15	43	
		%	28.0%	15.0%	21.5%	
	4	Count	30	32	62	
		%	30.0%	32.0%	31.0%	
	5	Count	23	40	63	
		%	23.0%	40.0%	31.5%	
Total		Count	100	100	200	
		%	100.0%	100.0%	100.0%	

When the MRM scale was used to compare the severity of the strokes, it was discovered that the group with diabetes had significantly more severe strokes than the group without diabetes. This difference was statistically significant ($p<0.05$).

Table 13: Comparing territory of Infarcts with Diabetes status

Territory of Infarction			Diabetes		Total	P value
			No	Yes		
	MCA	Count	40	46	86	
		%	20%	23%	43%	
	ACA	Count	3	3	6	

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		%	1.5%	1.5%	3%	0.630
	ICA	Count	2	3	5	
		%	1.0%	1.5%	2.5%	
	MCA +ICA	Count	24	28	52	
		%	12%	14%	26%	
	VBA	Count	24	19	43	
		%	12%	9.5%	21.5%	
	VBA+ICA	Count	5	3	8	
		%	2.5%	1.5%	4%	
Total		Count	100	100	200	
		%	100.0%	100.0%	100.0%	

There was no significant correlation found between the stroke patients' diabetes status and the infarct territory (p>0.05).

Table 14: Comparing MPV with territory of infarct

Infarct Territory	Mean	Std. Deviation	P value
MCA	11.100	1.6972	0.880
ACA	9.301	1.2621	
ICA	9.236	1.7035	
MCA + ICA	10.229	1.4634	
VBA	9.600	1.4942	
VBA+ ICA	9.626	1.7394	

In both groups, there is no significant correlation between the MPV and the infarct territories (p value>0.05).

DISCUSSION

One illness that is commonly linked to diabetes mellitus is acute ischemic stroke. It is well known that both intracranial and systemic atherosclerotic disease may be exacerbated by DM. This elevated risk has been associated with pathophysiological changes in the cerebral arteries of diabetics. [5] Correlation and prediction of the effects of hyperglycemia on stroke and its outcome are urgently needed.

Recent studies suggest that increased platelet volume and size, influenced by interleukin-3 or IL-6, may lead to increased megakaryocyte ploidy and prothrombotic events, potentially causing a higher risk of stroke, compared to non-diabetic strokes.[6]

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Hypertension and Stroke

Hypertension is a common risk factor for both diabetic and non-diabetic stroke, with mean systolic blood pressure 148.10±11.128 in diabetics and 150.32±10.62 in non-diabetics, with no statistical difference. Hypertension is the most prevalent independent risk factor for ischemic cerebrovascular stroke.[7]

Age of Stroke and Diabetes status

The study's mean age for the diabetic group was 58.18±18.09 years, while the non-diabetic group's mean age was 61.45±19.62 years. The statistical difference between the two groups was not significant ($p>0.05$). The age group of 61–80 years old accounts for the majority of patients in both groups (35%), followed by 41–60 years old (28%) and 21–40 years old (24.5%). Similarly, in the Patil et al. study, the mean age of patients with diabetes was 62.04 ± 10.88 years, while that of patients without diabetes was 58.11 ± 16.75 years. The mean age of Shah et al.'s study, which evaluated the role of MPV in ischemic stroke, was 58 years, which is consistent with our findings.[8] In these findings demonstrated that the elderly age group in this study experienced acute ischemic strokes frequently.[8]

Our demographic data matched that of the Shubhash et al. study.[46] observed that the mean age of stroke patients with diabetes was 57.5 ± 12.7 years, while the mean age of stroke patients without diabetes was 61.3 ± 12.9 years. The majority of patients (40%) in the diabetic stroke group and (27.5%) in the non-diabetic group were in the 60-69 age range.[9] The stroke patients with diabetes were 3.2 years younger than the stroke patients without diabetes in the Kamel et al. stroke study.[10] Similar to previous research, the current study found that strokes happen earlier in life in individuals with diabetes than in those without the disease.[9] According to studies, people with diabetes experience the onset of peripheral vascular disease earlier than people in general.[11]

Stroke and Gender

Male sex is a major risk factor for stroke, with 53% of diabetic and non-diabetic patients having a higher risk. Men with diabetes have a 27% higher risk of stroke. However, sex differences in diabetic patients' outcomes are unclear, and women often do not seek healthcare due to belief in natural cures or native medicine.[12,13]

Stroke association with Hemoglobin and Platelet count

The study found no significant difference in mean hemoglobin levels between diabetic and non-diabetic individuals, and platelet count was statistically insignificant. Lower MPV correlates with higher platelet count in physiological conditions, but in inflammation-related pathologies, increased thrombopoietin generation and cytokine activation lead to high platelet count and large platelets. MPV is suggested as a prognostic marker in cardiovascular and cerebrovascular diseases.[14]

MPV and Diabetes status among Stroke patients

Higher mean platelet volume (MPV) may predispose patients to ischemic strokes, as evidenced by studies. Patients with diabetes had significantly higher MPV levels compared to non-diabetic patients. The PROGRESS collaborative group reported similar outcomes. People with higher MPV readings had higher stroke rates. The relative risk of stroke increased by 12% for every 1-fL increase in MPV. MPV is recognized as a stand-alone risk factor for stroke in high-

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risk patients, providing clinicians with important prognostic data when treating patients with cerebrovascular disease.[15]

MPV correlation with HbA1c, PP2BS and FBS in relation to Diabetes status

The study found significant correlations between HbA1c, PP2BS, and FBS in patients with type 2 diabetes mellitus (DM). Increased platelet activity is linked to vascular complications in DM. Platelet activation, measured by the MPV, is used to study stroke. A higher MPV indicates more active and aggregatable platelets, while a lower MPV indicates less active ones. Multiple studies have found strong correlations between MPV, FBS, PP2BS, and HbA1c. A large-scale prospective study in China found that both hyperglycaemia and hypoglycaemia are associated with an increased risk of intracerebral hemorrhage.[16,17,18]

MPV and Stroke severity

Patients with high MPV values (>11.01 fL) were 1.5 times more likely to die from vascular causes than patients with low MPV values (<8.7 fL). Additionally, a strong correlation was discovered between ischemic vascular disease and patients with high MPV.52In patients with diabetic and non-diabetic subsets, our study revealed a significantly positive correlation between MPV and the Modified Rankin Morbidity Scale (Severity). The area of infarcts, however, did not significantly correlate with either group's history of MPV or diabetes ($p>0.05$). There was a statistically significant difference in MPV and stroke severity (MRM) between the non-diabetic and diabetic groups. The Patil et al. study revealed various other implications concerning the severity and outcome of stroke. Diabetics are more likely to experience severe strokes.[19-21]

It is commonly known that inflammation plays a part in the instability of atherosclerotic plaque, which leads to ischemic vascular events. Increased P- and E-selectin expression results from this inflammatory milieu, aiding in platelet adhesion. Platelets then become activated and release a variety of inflammatory mediators.65 Megakaryocyte size may be influenced by IL3 and IL6, which can also result in larger, more activated platelets.[22, 21]

SUMMARY

In our tertiary care center, an observational prospective study was conducted from August 2021 to January 2022 to examine the relationship between acute ischemic stroke and MPV (mean platelet volume) in patients with type 2 diabetes mellitus (DM).

Data were gathered from patients who were admitted for acute ischemic cerebrovascular stroke between August 1, 2021, and January 30, 2022.

imaging studies like CT scans and MRIs, as well as baseline investigations like CBC, RFT, HB1AC, FBS, PP2BS, and ECG. Modified Rankin morbidity score scores were used to gauge the severity of the stroke.

The findings of the study sum up:

• There was a statistically significant ($p>0.05$) difference in the mean age of the diabetic group (58.18±18.09 years) and the non-diabetic group (61.45±19.62 years).

• There was statistical significance between the two subsets for HbA1c (6.5±1.97 vs. 7.6±2.5; $p\leq0.021$), PP2BS (172.85±38.60 vs. 292.49±104.79; $p\leq0.001$), and FBS (138.02±29.96 vs. 165.66±9.68; $p\leq0.001$).

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• The age group of 61–80 years old accounts for the majority of patients in both groups (35%), followed by 41–60 years old (31%), and 21–40 years old (24.5%).

• In our study, there was a greater percentage of male patients (53%) than female patients (47%).

The platelet count between the two subsets was found to be statistically insignificant (1.94±0.28 lacs vs. 2.02±0.28 lacs; p≤0.001).

• Patients with diabetes had a mean platelet volume that was significantly higher (10.24±1.31) than non-diabetic subsets (8.75±1.19) (p<0.05).

• A substantial positive correlation between PP2BS, FBS, and

CONCLUSION

Diabetes patients are at risk of thrombotic events, and platelet vesicle (MPV) is a valuable predictor of platelet reactivity. A study found a significant correlation between MPV and type 2 diabetes mellitus in ischemic stroke, and a statistically significant correlation between stroke severity and MPV. Poor glycemic control, high FBS, PP2BS, or HbA1c, and longer diabetes duration were linked to higher risk of vascular complications like cerebral stroke in type 2 diabetic patients. High MPV was also associated with stroke and severe acute ischemic stroke, potentially indicating its potential as a cost-effective marker for monitoring vascular complications in type 2 diabetic patients.

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