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Research Article,

A Study of Association of Mean Platelet Volume with Vascular Complications in Type-2 Diabetes

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Abstract:

Background: Type-2 diabetes is considered as a life-long disease which increases morbidity, mortality and decreases the quality of life. Diabetes is a pro-thrombotic state associated with accelerated atherosclerosis and inflammation. MPV is an indicator of the average size and activity of platelets. MPV reflect the state of thrombogenesis deducing an easy way of predicting vascular complications of Type 2 DM and would help in preventing it.

Methods: This cross-sectional study was conducted among 110 patients in the hospitals attached to Bangalore Medical College and Research Institute (BMCRI). To assess vascular complications, patients were subjected to fundoscopy, urine examination, 2D echo, ECG, CT scan of brain, doppler of arterial and venous systems. And diabetic neuropathy was evaluated clinically. Statistical analysis was performed using SPSS software. A p value of <0.05 was considered significant.

Results: The mean platelet counts and MPV were higher in diabetics with vascular complications compared to those without complications, 9.16 ± 0.86 fl versus 7.7 ± 0.6 fl (P< 0.001), respectively. MPV showed a positive correlation with fasting blood glucose (regression (r) = 0.30)(P=0.0013), post prandial glucose (regression (r) = 0.31)(P=0.0009) and HbA1C levels (regression (r) = 0.26)(P=0.0058) which were significant. Although glycemic status of the patient did not correlate with the duration of diabetes, MPV showed positive correlation with duration of T2DM (regression(r) = 0.19) (P=0.045) which was significant.

Conclusion: Our results showed significantly higher MPV in diabetic patients with vascular complications and longer duration. Hence, platelets may play a role and MPV can be used as a simple parameter to assess the vascular events in diabetes

Keywords: MPV, T2DM, vascular complications

Introduction:

Prevalence of Diabetes mellitus is very high**,** As per IDF (International Diabetes Federation) 463 million people have diabetes all over the world in 2019, it is estimated that it will increase to 700 million in 2040.(1) Diabetes Scenario in India is worse , with the Fact that India is ranked second in the world in diabetes prevalence, just behind China(2) adding to morbidity and mortality significantly leading to significant loss of DALY(Disability Adjusted life years)(3). Hence it is Vital to prevent vascular complications, hence monitoring of DM becomes important. Platelets have a key role in homeostasis maintenance. Platelets are disc shaped non-nucleated, tiny flattened structures which are derived from megakaryocytes and influenced by persons wellbeing and nutritional status. MPV gives an estimate of the average size of platelet. Mean Platelet Volume ranges from 7.5 and 10.5 fl.(4) . The density of granules present in the platelets largely decides the size of the platelets.(4) Studies have found that the endothelial dysfunction and Vascular Lesions occurring as a part of diabetes complication is due to Sustained High Blood sugars and Platelets in turn respond to stimuli generated by the endothelium of blood vessels, by adhering to sub endothelial surfaces and secrete

their intracellular contents to cause platelet aggregation and thrombus formation and advanced atherosclerosis[5][6] It is already found that glycated Hb(HbA1c),which is a long term gluco-regulation marker, should be below 7% to have reduced risk of micro-vascular and macro vascular complications in Diabetic Patients.[7] With the fact that Plasma glucose is the major energy source for Platelets Higher Blood sugars increases platelet activity.[4] With many costly biomarkers of diabetic thrombocytopathy are considered for clinical practice, Mean platelet volume (MPV) is a quick and simple, easy-to-measure parameter of platelet size and hence the enzymatic activity and prothrombotic potential consequently. Larger platelets contain more dense granules and hence are more thrombogenic.

Hence this MPV can be used as a relationship between the platelet function and diabetic vascular complications [8].Hence this Study was undertaken.

Aims and Objective:

To determine the Mean Platelet Volume in diabetics.

1. To Compare and Correlate Mean Platelet Volume in diabetics with and without vascular complications

Materials and Methods

Inclusion Criteria

- Age >18 years
- Patient willing to give informed consent
- Diagnosis as per American diabetes association 2018 guidelines[9]
- Hb > 13 mg/dl (male)
- Hb >12 mg/dl (female)

Exclusion Criteria

- Diabetics on anti-platelets and anti-coagulants
- Patients with malignancy

Methodology:

This study was conducted among patients admitted under medicine department between November 2018 to May 2020 at Victoria hospital and Bowring & Lady Curzon hospital, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India. A study population of 111 diabetic patients with and without vascular complications was taken with 56 patients with complications and 55 without complications. Approval and clearance were obtained from the institutional ethics committee on 15/11/2018-BMCRI/PG/124/2018-19.Information was collected from the patients on their duration of T2DM, treatment history, age, and sex. Data were collected on the anthropometric parameters and vitals of the patients (height, weight, BMI), Pulse rate and Blood pressure. Both fasting and post prandial blood samples of 5 ml each were collected in plain vacutainer and processed immediately for routine biochemical analysis. Spot urine sample was collected and looked for presence of albuminuria. Such patients underwent ultrasonography abdomen for the evaluation of the kidney echotexture and size. Digital fundoscopy was done to assess diabetic retinopathy. Diabetic retinopathy was diagnosed using The Early Treatment Diabetic Retinopathy Study criteria (ETDRS).[10] Patients who had neuropathic symptoms were clinically examined for diabetic neuropathy. Patients who had symptoms and signs of lower limb ischemia were evaluated with respective limb arterial and venous doppler. Also, patients were screened and evaluated clinically for macrovascular complications and relevant investigations like ECG, 2D ECHO for cardiovascular complications and neuroimaging for cerebrovascular complications. MPV and platelet counts were measured in the above subjects using an automated blood counter. The blood glucose (fasting, post-prandial) levels and HbA1c levels were also measured all relevant investigations were done on out-patient and in-patient basis.

Statistical Analysis:

Statistical methods: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions.

Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. **Independent t test** was used as test of significance to identify the mean difference between two quantitative variables.

ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram and ROC Curve

P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results:

The study of Mean platelet volume as a predictor of vascular complications in type 2 diabetes was done in patients admitted in Bangalore Medical College and Research Institute from 2018-2021. Total of 111 patients who were admitted in our institute were included in the study after considering inclusion and exclusion criteria.

Age Distribution:

Mean age was 55.66 ± 13.675 years. In the study, 15.3% were <40 years, 24.3% were in 41 to 50 years, 24.3% were in 51 to 60 years, 22.5% were in 61 to 70 years, 9.9% were in 71 to 80 years and 3.6% were >80 years. Table 1

Table 1: Age distribution of subjects in the study

		Count	%
Age	<40 years	17	15.3%
	41 to 50 years	27	24.3%
	51 to 60 years	27	24.3%
	61 to 70 years	25	22.5%
	71 to 80 years	11	9.9%
	>80 years	4	3.6%

Sex Distribution:

Out of 111 patients 63 patients (56.8%) were Male and 48 patients (43.2%) were Female. In this study male patients were more than female. Table 2

Table 2: Gender distribution of subjects in the study

		Count	%
Sex	Female	48	43.2%
	Male	63	56.8%
	Total	111	100.0%

Distribution of Cases According To Duration of Diabetes:

In the study, Duration of Diabetes was Newly Detected in 16.2%, <5 years in 37.8%, 6 to 10 years in 30.6% and >10 years in 15.3%. Table 3

Table 3: Duration of Diabetes distribution among subjects

		Count	%
Duration of Diabetes	Newly Detected	18	16.2%
	<5 years	42	37.8%
	6 to 10 years	34	30.6%
	>10 years	17	15.3%

Glycemic Profile of Subject's Comparison With respect To Duration of Diabetes:

Mean FBS (mg/dl) in Newly Detected Diabetes was 202.77 ± 70.93, in < 5 years was 242.5 ± 84.35, in 6 - 10 years was 230.44 ± 74.60 and in >10 years was 249.41 ± 57.67. There was no significant difference in mean FBS (mg/dl) comparison with respect to duration of diabetes. Table 4.

Mean PPBS (mg/dl) in Newly Detected Diabetes

was 265.67 ± 63.67, in < 5 years was 281.38 ± 78.14, in 6 - 10 years was 276.29 ± 92.39 and in >10 years was 285.82 ± 62.58. There was no significant difference in mean PPBS (mg/dl) comparison with respect to duration of diabetes. Table 4.

Mean HBA1C (%) in Newly Detected Diabetes was 9.42 ± 1.56, in < 5 years was 9.86 ± 1.93, in 6 - 10 years was 9.58 ± 2.1 and in >10 years was 9.34 ± 2.09. There was no significant difference in mean HBA1C (%) comparison with respect to duration of diabetes. Table 4.

Table 4: Glycemic Profile of subject's comparison with respect to Duration of diabetes

	Duration of Diabetes										P value
	Newly Detected		<5 years		6 to 10 years		>10 years		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
FBS(mg/dl)	202.77	70.93	242.5	85.35	230.44	74.6	249.41	57.67	233.42	77.12	0.13
PPBS(mg/dl)	265.67	63.67	281.38	78.14	276.29	92.39	285.82	62.58	277.95	78.87	0.55
HbA1c (%)	9.42	1.56	9.86	1.93	9.58	2.1	9.34	2..09	9.63	1.97	0.45

Complications in Diabetic Subjects:

In the study patients had no vascular complications in 49.5%, had micro-vascular complications in 22.5% and macro-vascular complications in 28.8%. Table 5, Figure 1.

Table 5: Complications distribution among subjects

		Count	%
Complications	No Vascular Complications	55	49.5%
	Micro complications	25	22.5%
	Macro complications	32	28.8%

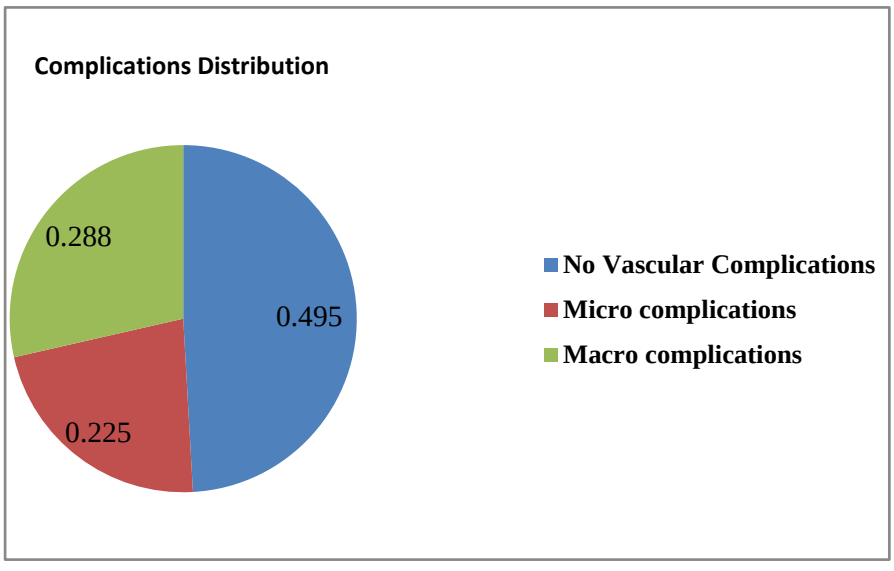

Figure 1: Pie Diagram Showing Complications distribution among subjects

Mpv Comparison With Respect To Duration of Diabetes:

In this study there was significant correlation between MPV and duration of diabetes. Table 6, Table 7.

Table 6: MPV comparison with respect to Duration of diabetes

	Duration of Diabetes										P value
	Newly Detected		<5 years		6 to 10 years		>10 years		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
MPV(fl)	8.69	4.95	8.1895	0.475	8.63	0.5	8.275	0.55	8.432	0.1	0.045

Table 7: Correlation between MPV with Duration of diabetes

		Mean Platelet Volume(fl)
Mean Platelet Volume(fl)	Pearson Correlation	1
	P value	
	N	111
Duration of diabetes(years)	Pearson Correlation	0.19
	P value	0.045787
	N	111

Mpv Comparison With Respect To Glycemic Status:

In this study there was significant correlation between MPV with FBS, PPBS and HbA1c. Table 8.
https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html

Table 8: MPV comparison with respect to Glycemic status

		Mean Platelet Volume(fl)
Mean Platelet Volume(fl)	Pearson Correlation	1
	P value	
	N	111
FBS(mg/dl)	Pearson Correlation	0.30
	P value	0.0013
	N	111
PPBS(mg/dl)	Pearson Correlation	0.31
	P value	0.0009
	N	111
HbA1C (%)	Pearson Correlation	0.26
	P value	0.0058
	N	111

Mean Platelet Volume Comparison With Respect To Complications:

Mean Platelet Volume (fl) in patients with no Vascular Complications was 7.7 ± 0.6, In patients with Micro-vascular Complications was 9 ± 0.8 and in Macro-vascular Complications was 9.2 ± 0.9. There was a significant difference in Mean Platelet Volume (fl) comparison with respect to vascular complications in patients with T2DM. Table 9.

Table 9: Mean Platelet volume Comparison with respect to Complications

	Complications						F	t-value	P value
	No Vascular Complications		Micro complications		Macro complications				
	Mean	SD	Mean	SD	Mean	SD			
Mean Platelet Volume (fl)	7.7	0.6	9.0	0.8	9.2	0.9	52.781	10.231	<0.001 *

Table 10: Validity of Mean platelet Volume in predicting Vascular Complications
Area under the ROC curve (AUC)

Area under the ROC curve (AUC)	0.925
Standard Error	0.0261
95% Confidence interval	0.859 to 0.966
z statistic	16.270
Significance level P (Area=0.5)	<0.0001

Youden index

Youden index J	0.7659
95% Confidence interval	0.6395 to 0.8558
Associated criterion	>8.3
95% Confidence interval	7.9 to 8.5

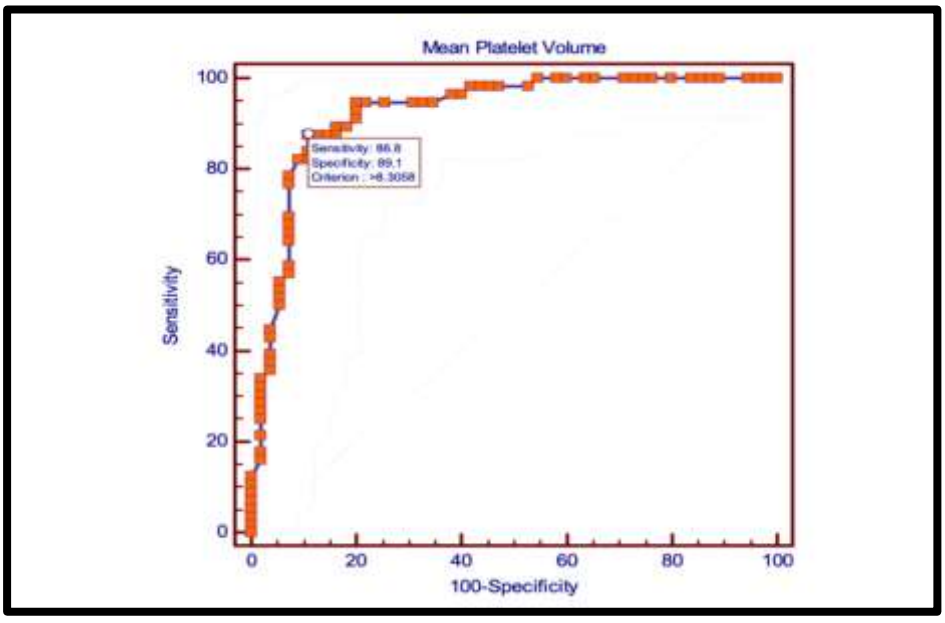

Figure 2: ROC Curve showing Validity of Mean Platelet Volume in predicting Vascular Complications

Criterion values and coordinates of the ROC curve

Criterion	Sensitivity	95% CI	Specificity	95% CI	+PV	95% CI	-PV	95% CI
>8.3	87.50	75.9 - 94.8	89.09	77.8 - 95.9	89.1	77.6 - 95.9	87.5	75.9 - 94.8

MPV of >8.3 had highest sensitivity of 87.5%, Specificity of 89.09%, PPV of 89.1% and NPV of 87.5% in predicting Vascular complications among diabetics.

Discussion:

Diabetes is a growing health problem associated with increased risk of micro and macro-vascular complications. With the easy availability of various blood tests such as platelet volume indices (PVI), efforts are made to identify and prove their utility to act as biomarkers for early detection of diabetic complications.

This is a cross sectional study conducted over a period of 2 years from Nov 2018- May 2020 to study association of MPV with vascular complications in Type 2 DM. 111 patients were included in this study, where 56 patients were diabetics with vascular complications and 55 patients were diabetes without vascular complications.

AGE:

In this study the most common age group was 51-60 (22 patients) with mean age of 55.66±13.67. Most of the patients were of 40-70 years. The IDF Diabetes Atlas which tracks the global impact of diabetes also shows the more common age group of diabetes is between 20-79 years of age.[11] This is important because of increasing risk within population and failure to control factors such as obesity and poor diets. This would further cause a rising prevalence as each person getting diagnosed at a earlier age stays longer.

SEX:

In this study there was male predominance i.e., 56.8% of patients and female patients were 43.2%, which was similar to study done by Mohammed Haghighatpanah et al, Correlation of glycosylated hemoglobin levels with fasting and postprandial glucose in South Indian Type 2 Diabetic patients.[12]

Duration of Diabetes:

In this study, Duration of Diabetes was Newly Detected in 16.2%, <5 years in 37.8%, 6 to 10 years in 30.6% and >10 years in 15.3%. Ours being a tertiary care center most of the patients were incidentally diagnosed patients and duration more than 6 years who were on regular follow up for their medications.

There was no significance in mean FBS, mean PPBS, mean HBA1C compared with the duration of the diabetes.

It was found that MPV was significantly correlating with duration of diabetes. This was also seen in many other studies.[13],[14],[15] Although some showed discordant results.[16] Platelet number and re-activity contributes to the progression of diabetes and its effect on platelet indices.

Glycemic Profile:

In this study, there was a significant positive correlation found in between MPV and FBS, MPV and PPBS and MPV and HBA1C.

There are multiple studies which are showing positive correlation with MPV and glycemic status of the patient.[16] It has been proposed that increase in MPV could be because of raised blood sugar leading to osmotic swelling and shorter life span of platelets in diabetic patients. Alternatively, this may suggest that platelet activation is related to glycemic control. Therefore, it may be concluded that glycemic control decreases the hyper activity of the platelet function and thus may prevent or delay possible diabetic vascular complications.

Mean Platelet Volume Comparison With Respect To Complications:

Study done by Archana buch et al, platelet volume indices as predictive bio markers for diabetic complications in Type 2 DM patients, showed MPV was significantly increased in diabetic patients with complications compared to those without complications.[17]

Insulin resistance and hyperglycemia are said to be the important factors causing increased platelet re-activity in diabetic patients. Platelet hyper re-activity is a well-known factor contributing for prothrombotic state in diabetics which is measured by MPV.[17]

In this study there was a significant difference in

Mean Platelet Volume comparison with respect to vascular complications in patients with Type 2 DM. Also this study suggests MPV is associated with poor glyco-metabolic control and it is reflected in many complications such as retinopathy, nephropathy, coronary artery disease, cerebrovascular accidents and diabetic foot.

Conclusion:

From this study we can conclude that MPV is significantly increased in diabetic patients with complications compared to diabetics without complications showing that increment is more in diabetics with poor glycemic control. The platelets become more reactive and aggregable, and their mean volume (MPV) is increased. The increased platelet size may be one factor in the increased risk of atherosclerosis associated with diabetes mellitus and associated vascular complications. Hence, MPV would be a useful marker of vascular complications in diabetes both micro and macro-vascular. It was observed that MPV increased with duration of the diabetes. Also, it was seen that increase in HbA1c concentration was directly proportional to increased MPV. Hence, it can be shown that MPV can be used as a simple and cost-effective tool to monitor the progression and control of DM and its vascular complications.

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Declarations:

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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