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Increased Mean Platelet Volume as a predictor of peripheral neuropathy in Type 2 Diabetes Mellitus patients

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Abstract: ***Background:*** *Diabetes mellitus is one of the most common cause of peripheral neuropathy. In diabetes the platelets produce prothrombotic factors which is implicated in peripheral neuropathy. Mean platelet volume is one simple test to predict the presence of peripheral neuropathy .*
Aims: *(1)To estimate mean platelet volume in type 2 diabetes mellitus. (2)to record the prevalence of diabetic peripheral neuropathy. (3)To correlate mean platelet volume with peripheral neuropathy.*
Methods: *A cross sectional study was conducted in 132 patients dividing them into a group of each 44 as non diabetic, diabetic without peripheral neuropathy(or microvascular complications) and diabetic with peripheral neuropathy and other microvascular complications respectively. Mean platelet volume(MPV) was done within 1 hour of sample collection.*
Results: *The mean platelet volume was more in group diabetic with peripheral neuropathy(11.376±0.567) when compared to other groups and the difference was statistically significant.*
Conclusion: *Type 2 diabetic patients have a higher MPV, compared to non- diabetic controls. Peripheral neuropathy patients with diabetes have higher MPV when compared to diabetics without peripheral neuropathy.*
Keywords: *Type 2 diabetes mellitus, mean platelet volume, peripheral neuropathy*

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I. Introduction

Diabetes mellitus (DM) is a major global health problem.[1] In 2014 the global prevalence of DM was established to be 9% among adults aged 18 years.[2] The global prevalence of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population. According to estimates of the World Health Organization, there were 346 million people suffering from diabetes worldwide in 2013.[3] WHO projects that diabetes will be the 7th leading cause of death in 2030[4]. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Platelet volume is a marker of platelet function and activation. It can be quantified as mean platelet volume (MPV). Normal mean platelet volume in healthy subjects ranges between 7.2 and 11.7 fL. . It has been reported that platelets from diabetic patients synthesize more thromboxane than normal platelets. Hyperglycemia has been found to be associated with larger platelets[5], which release more prothrombotic factors such as thromboxane A2[6]. MPV is simple and effective and cheap test that may predict micro vascular complications like neuropathy in type 2 DM. Defects in insulin action in diabetes also leads to disordered platelet activity, which in turn leads to macrovascular and microvascular events

II. Material And Methods

SOURCE OF DATA: Data was collected from patients fulfilling the inclusion and exclusion criteria visiting medicine OPD of Sri venkateshwaraa medical college hospital and research centre,Ariyur,Puducherry .
Sample Size: The Sample size was 44 Cases in each group (Study Population = 132 Cases)**.** Detailed history including regarding diabetes, hypertension and drug intake was taken. Family history was enquired. MPV and platelet count in the above diabetic and non-diabetic subjects was done using an automatic blood counter (Alere H 560). Venous blood samples from brachial vein was collected and within 1 hour of collection, samples were analyzed to minimize variations due to sample aging. Renal parameters such as blood urea, serum creatinine,

and urine micro albumin and urea albumin/serum creatinine were done[7]. 10 gm Monofilaments test was done to look for neuropathy. The study was done over a period of 13 months, from December 2016-december 2017

Inclusion criteria of cases:
- Patients diagnosed with type 2 DM with diabetic peripheral neuropathy.
- Adults more than 18 years of age

Exclusion criteria of cases:
- Male patient and female patients with hemoglobin below 12mg/dl and below 11mg/dl respectively.
- Diabetics on antiplatelet drugs such as aspirin and clopidogrel
- Pregnant women
- Malignancy
- Collagen Vascular disease
- Infections

Inclusion criteria of controls:
- Non-diabetics above the age of 18 years

Exclusion criteria of controls:
- Male patient and female patients with hemoglobin below 12mg/dl below 11mg/dl respectively.
- Pregnant women
- Malignancy
- Collagen Vascular disease
- Infection

Study design: It is a cross sectional study. The study was carried out in 132 patients, and they were divided into three groups
1. Group A: Normal healthy non-diabetic
2. Group B: Diabetics without microvascular complications.
3. Group C: Diabetics with microvascular complications.

Complete case history was taken from all the subjects, and a thorough clinical examination was done. The investigations done for all the subjects are Complete blood count, Fasting blood glucose, Post prandial blood glucose, HbA1c (glycosylated hemoglobin), Blood urea , Serum creatinine, Urine routine examination, 10 gm monofilaments test,and other relevant investigations whenever needed. MPV was done as a part of complete blood count using Alere H 560 - Automated Hematology Analyzer. Venous blood samples were collected in di-potassium EDTA and tested within one hour of collection to minimize variations due to sample aging. Samples for plasma glucose estimation and HbA1c were collected in sodium fluoride and di-potassium EDTA, respectively. 10 gm monofilaments test was done to look for features of neuropathy.

Statistical analysis: Data will be entered into Microsoft excel data sheet and will be analyzed using SPSS 22 version software. Results are expressed as Mean ± SD (Min-Max). Microsoft Excel 2016 was used to plot graphs and for the masterchart. The following were the statistical tests used: (1)Categorical data will be represented in the form of Frequencies and proportions.(2)Continuous data will be represented as mean and standard deviation. (3)Independent samples t test for comparative analysis**.** (4)One way analysis of variance with Duncan's multiple range test for pair wise comparisons. (5)Pearson's correlation coefficient**.** (6)Chi square test**.** A "p value" of < 0.05 is considered as statistically significant.

III. Result

Statistical analysis was carried out to meet the objectives of the study. The statistical results are compared at 0.05 level of significance. (p value ≤ 0.05 implies significance)
Group 1= Non diabetics,
Group 2= Diabetic without peripheral neuropathy or other microvascular complications
Group 3= Diabetic with peripheral neuropathy and other microvascular complications

Table 1: Distribution of subjects across age

Age	Frequency	Percent
26-40 years	18	13.6
41-55 years	45	34
56-70 years	60	45.45

>70 years	9	6.8
Total	132	100

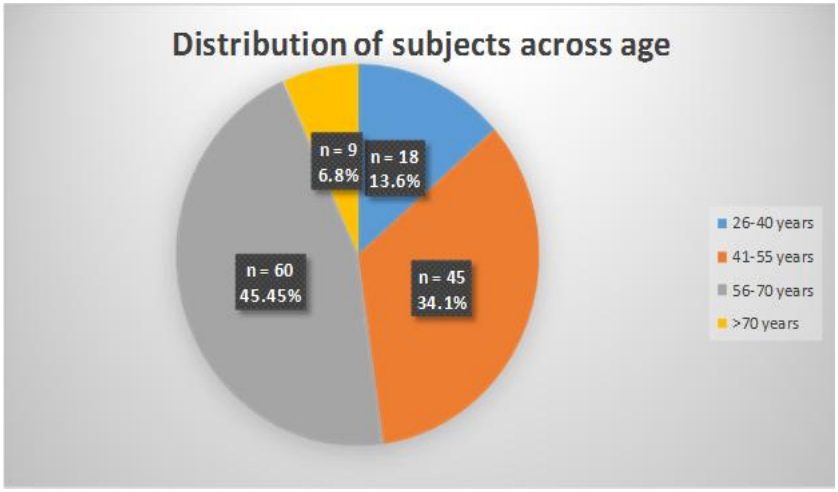


Figure 1:-Distribution of subjects across

Table 2:- Distribution of subjects according to age among the groups

AGE Group	GROUP			Total
	1	2	3	
26-40yrs	18	0	0	18
	40.9%	0%	0%	13.6%
41-55yrs	26	4	15	45
	59.1%	9.1%	34.1%	34.1%
56-70yrs	0	40	20	60
	0%	90.9%	45.5%	45.5%
>70yrs	0	0	9	9
	0%	0%	20.5%	6.8%
Total	44	44	44	132
	100.0%	100.0%	100.0%	100.0%

Mean age of the Group1 was 42.41 $\pm$ 4.5 yrs. Mean age of the Group2 was 59.57 $\pm$ 2.7 yrs. Mean age of the Group 3 was 63.75 $\pm$ 10.3 yrs. P Value = <0.001, There was a statistically significant difference between the Age groups among the groups.

Table 3:- Distribution of subjects according to sex among the groups

SEX	Group			Total
	1	2	3	
Female	17	18	17	52
	38.6%	40.9%	38.6%	39.4%
Male	27	26	27	80
	61.4%	59.1%	61.4%	60.6%
Total	44	44	44	132
	100.0%	100.0%	100.0%	100.0%

P value = 0.351, There was no statistically significant difference between sex among the groups.

Table 4:- Comparison of mean MPV between the age groups

Age Group	Mean MPV	Std. Deviation	P Value
26-40yrs	5.41	.33	<0.001
41-55yrs	7.81	3.06	
56-70yrs	8.90	1.65	
71yrs	11.34	1.19	

There was a statistically significant difference of Mean MPV between the age groups.

Table 5:- Comparison of mean MPV among sex

	Sex	Mean MPV	Std. Deviation	P Value
MPV	Female	8.161538	2.3850148	.821
	Male	8.262500	2.6689198	

There was no statistically significant difference of Mean MPV among sex

Table 6:- Comparison of mean MPV and duration of DM

Duration of DM	Mean MPV	Std. Deviation	P Value
1-5yrs	8.48	1.59	<0.001
5-10yrs	10.43	1.58	
>10yrs	12.02	.764	

There was a statistically significant difference of Mean MPV with duration of DM

Table 7:- Comparision of mean MPV among groups

Group		MPV
1	Mean	5.434
	Std. Deviation	.3409
2	Mean	7.793
	Std. Deviation	.480
3	Mean	11.44
	Std. Deviation	.8657
Total	Mean	8.22
	Std. Deviation	2.55
	P value	<0.001

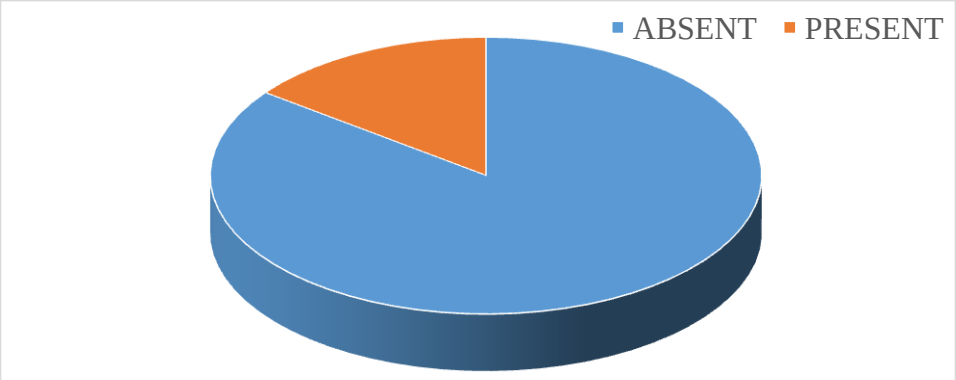
P value <0.001 shows that the is a significant correlation between increased MPV and diabetes mellitus

Table 7: Mean MPV levels and Neuropathy in diabetic patients

Neuropathy	Number	Mean MPV	Std. Deviation	P value
Absent	75	9.312000	1.9583473	.000
Present	13	11.376923	.5673827	

The Mean difference in MPV between those with Neuropathy and those without Neuropathy was statistically significant

Figure 2: Graph showing distribution of diabetic subjects according to Neuropathy



IV. Discussion

India leads the world with the largest number of diabetic patients. Also, the morbidity and complications associated with diabetes are well known. This warrants a detailed knowledge of pathogenesis of the disease. The aim of this study was to evaluate the platelet activity in diabetic patients. MPV is an indicator of the average size and activity of platelets. Larger platelets are younger, more reactive and have greater potential to aggregate. High MPV is emerging as a new risk factor for the vascular complications of DM of which atherothrombosis plays a major role.[8] The main aim of this study was to evaluate MPV in diabetics and to determine if MPV was significantly higher in diabetics, and also establish its association with peripheral neuropathy and glycemic control. This study was done on 132 cases divided into a group of 44 each.

V.1.Association between age and MPV: All subjects were above 18 years of age. In this study the age group range was 26 to >70 years, with maximum patients being in 56-70 years (45.45%). The mean age of group 1 was 42.41±4.5 years, group 2 was 59.57±2.7 years and mean age of group 3 was 63.75± 10.3 years. There was statistically significant difference between the age group among the groups.

According to this study there was no statistically significant difference between sex among the groups. According to this study, there is statistically significant association between age groups and MPV (p<0.001).

The results of previous studies like Ulutas et al [9], who established that there is no significant difference in MPV in relation to age (p value= 0.90). According to Ezgi Coşkun Yenigün et al[10], there was no significant

difference in MPV in the various age groups (p value = 0.62). In a study done by Papanas et al [5] also, there was no association between MPV and age.

V.2.Association between gender and MPV: In this study, there were 80 males and 52 females. Out of 80 males, Group 1 had 27, group 2 had 26 and group 3 had 27. Out of 52 females, group 1, 2 and 3 had 17, 18 and 19 respectively in each group. Males had a mean MPV of 8.1615±2.38fL, whereas females had a mean MPV of 8.26±2.66 fL. There was no significant difference in MPV between males and females (p=0.821). This was similar to the results of studies done by Ezgi Coşkun Yenigün et al [10] (p=0.62) and Papanas et al [5]

V.3.Comparision of MPV in diabetics and non-diabetics: The main goal of this study was to determine the mean platelet volume in non-diabetics and diabetics. In this study, the mean MPV in group 1 i.e. in patients without diabetes was 5.434±0.3409 fL and mean MPV in group 2 i.e. in patient with diabetes and without peripheral neuropathy was 7.793±0.480 fL. The MPV in group 3 ie diabetics with peripheral neuropathy was 11.44±0.8657. This difference was statistically significant (p value<0.0001), thus reinforcing the concept that platelet activity, reflected by mean platelet volume is higher in diabetic patients, compared to non-diabetic individuals. These findings were in agreement with several studies done over the last few years.

Two recent studies done in India also came with similar findings: Kodiatte et al[5] did a study in Kolar, Karnataka, in 2012 and demonstrated that MPV was higher in diabetics (8.29±0.735 fL), when compared to non-diabetics (7.47±0.73 fL) [p value < 0.001]. Vadatti et al[11] did a study in Guntur, Andhra Pradesh, in 2015, and they demonstrated that MPV was significantly higher in diabetics, when compared to non-diabetics (7.91 ± 0.87 fL vs 6.91 ± 0.71 fL respectively [p value < 0.00001])

V.4.MPV and glycemic control: In our study, mean MPV was highest in group 3 (11.44±0.8657) followed by group 2 (7.793±0.480) and MPV was lowest in group 1 (5.434±0.3409) and this inter-group difference was statistically significant (p value<0.0001).

In the study done by Kodiatte et al, the diabetic subjects were divided into 2 groups: Group A with HbA1c <6.5 % and Group B with HbA1c ≥6.5%, they found that the mean MPV in Group-A (7.95±0.72 fL) was significantly lower, compared to Group-B (8.35±0.724), p-value being 0.003. In the study done by Demirtunc et al[12], diabetics with HbA1c >7% had a mean MPV of 9.0±0.7 fL which was significantly higher than the group with diabetic patients having HbA1c ≤7%, who had a mean MPV of 8.4±0.8 fL, p-value being 0.01.

Also, in this study, there was significant correlation between MPV and HbA1c and p value <0.0001

V.5. MPV and peripheral neuropathy: In the current study, the mean platelet volume was more in group 3 i.e. diabetes with peripheral (11.376±0.57) when compared to other groups and the difference was statistically significant.

Similar results were obtained in the study done by Yenigün et al where diabetics with peripheral neuropathy had a higher MPV (9.38 ± 1.47 fL) compared to the diabetics without peripheral neuropathy (8.47 ± 0.49 fL), this difference was statistically significant (p value=0.048) .Similar results were obtained in the study of Papanas et al[5], where mean MPV of diabetics with microvascular complications was significantly higher compared to that of diabetics without microvascular complications.

In our study, Mean difference in MPV between those with neuropathy (11.37±0.56) and those without neuropathy (9.31±1.95) was statistically significant (p<0.001)

Inference: Diabetic patients having a higher mean platelet volume should be carefully examined to look for any peripheral neuropathy. Greater the platelet hyperactivity, greater will be the predisposition for developing peripheral neuropathy.

V.6. MPV and duration of diabetes: In this study, the association of MPV with duration of diabetes was statistically significant, (p<0.001). However, there was a significant association between the duration of diabetes and peripheral neuropathy. Longer the duration, greater is the likelihood to develop complications.

V. Conclusion

Type 2 diabetic patients have a higher MPV, compared to non-diabetic controls. Higher MPV indicates increased platelet activity and greater aggregation of platelets, which in turn predisposes the diabetic patients to microvascular complications. Peripheral neuropathy of diabetes are associated with a higher MPV, as compared to diabetic patients without peripheral neuropathy. Diabetic patients having good glycemic control have a lower MPV when compared to diabetics with poor glycemic control. There is association between MPV and duration of diabetes, according to this study. MPV can be used as a simple and cost-effective tool to monitor glycemic control and neuropathic complication in diabetic patients. It would be feasible even in rural centers which have cell count analyzers. However, its usefulness and sensitivity, when used on a larger scale requires further studies.

VI. Limitations of the study

This study population may not be representative of the general population, as all our subjects were patients visiting the hospital**.** There were confounding variables like hypertension and dyslipidemia which may interfere with some variables in the study**.** This was a small scale study, hence, further studies are required to assess the utility of MPV in diabetes**.**

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