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Relation of Mean Platelet Volume with Diabetic Retinopathy in Diabetes Mellitus Type 2 Patients

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ABSTRACT

Background: Diabetic retinopathy (DR) is one of micro vascular complications of Diabetes mellitus and leading cause of blindness. Mean Platelet volume is a marker of average size and activity of platelets. Larger platelets are younger and exhibit more activity and related to these complications.**Objective:**to study the association between mean platelet volume and Type 2 Diabetes, and its correlation with diabetic retinopathy.**Methods:** In this study, 100 patients with Type 2 diabetes and without retinopathy, 50 patients with type 2 diabetes and with diabetic retinopathy and 50 healthy age and gender matched controls were chosen and evaluated clinically and laboratory data including MPV, platelet count,HbA1C,Fasting and post prandial blood glucose, lipid profile,creatinine levels were obtained and studied. All study was done by SPSS software. **Results:** Mean MPV among subjects with DM with Retinopathy was 11.7 ± 1.3, among subjects with DM without Retinopathy was 10.7 ± 0.9 and among normal controls was 8.8 ± 0.5. There was significant difference in MPV b/w 3 groups. In the study there was significant positive correlation between MPV and duration of DM, FBS, PPBS and HbA1c i.e. with increase in Duration of DM, FBS, PPBS and HbA1c there was increase in MPV and vice versa

Conclusions: In Diabetic patients ,the risk of retinopathy development increases with higher MPV values and hence MPV can be used as cheap and easy tool for monitoring diabetic retinopathy

Keywords: Mean platelet Volume, Type 2 Diabetes,Diabetic retinopathy

INTRODUCTION: Diabetes mellitusis an important public health problem worldwide [1] In India, people affected by diabetes is estimated to rise to 79.4 million by 2030, making it the diabetic capital of the world.[2] Diabetic retinopathy (DR) is a long-term, micro vascular complication of diabetes mellitus which is most common preventable cause of blindness.[3] .WHO has estimated that diabetic retinopathy is responsible for 4.8% of the 37 millioncases of blindness in the world. [1,4]

Diabetes mellitus (DM) has been considered as a 'prothrombotic state' with increased platelet activity.[5]However it might be due to circulating factors that affect platelet function.[14] Insulin is a natural antagonistof platelet hyperactivity and reduces the pro-aggregatoryproperties. In diabetics there is loss of sensitivity to the normal restraints exercised by prostacyclin (PGI2) and nitric oxide (NO) and increased sensitivity to proaggregatory agents thereby causing rapid platelet aggregation and adherence to vascular endothelium.[6]In diabetes von Willebrand factor is released which promotes platelet clumping by binding to the platelet. Hyperglycemiacan increase platelet reactivity by inducing nonenzymatic glycation of surface proteins on the platelet, by the osmotic effect of glucose and activation of protein kinase.[7]

MPV is easy to quantify and inexpensive test, measured as a part of complete blood count which can identify platelet hyperactivity.[3,8] MPV is an indicator of the average size and activity of platelets.[4,3] The function of platelets seems to be related to their sizes. Larger platelets are younger, more reactive, contain more dense granules and produce large amounts of thromboxane A2 and hence exhibit hyperresponsivenessto ADP- or collagen-induced aggregation when compared with smaller and less active platelets.[2,3,8]

Higher MPV means more platelet activity and greater platelet turnover.High MPV is emerging as a new risk factor for micro vascular complications of DM.[9] Higher values of MPV are seen in diabetic patients with micro vascular complications like retinopathy.[10] The purpose of this study is to compare MPV and PDW values in diabetic with and without retinopathy and to find their association with various degrees of diabetic retinopathy.

MATERIALS AND METHODS: In this study, 100 patients with type 2 diabetes and without retinopathy,50 diabetic patients with diabetic retinopathy and 50 healthy age matched controls

were considered after taking proper informed written consent. The study was performed in Karnataka Institute of Medical Sciences, Hubli after obtaining ethical committee approval.

Patients with type 1 diabetes ,pregnancy,anemia,fever,infection,current or previous history of thyroid disease,acquired or congenital platelet disorders,patients on antiplatelet and anticoagulant medications, hematological disorders were excluded as per exclusion criteria

After history and clinical examination, patient's blood sample was taken and sent for evaluation of Hemoglobin, platelet counts,mean platelet volume,lipid profile,Fasting and post prandial glucose, creatinine.

All patients underwent ophthalmic assessment and fundoscopy.Diabetic retinopathy was defined as presence of atleast 2 micro aneurysms and/or other signs of retinal damage and classified as either normal study,non proliferative and proliferative retinopathy.Non proliferative retinopathy (NPDR)is classified as mild, moderate and severe NPDR.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Chi-square testwas used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t testwas used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively. ANOVA (Analysis of Variance)was the test of significance to identify the mean difference between more than two groups for quantitative data.Pearson correlationwas done to find the correlation between two quantitative variables and qualitative variables respectively.p value(Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS: Total study included 100 diabetics with retinopathy(69 males and 31 females),50 diabetics without retinopathy(31 males and 19 females) and 50 healthy controls(30 males ,20 females).Mean age of subjects in DM with Retinopathy group was 57.8 ± 8.8 years, in DM without Retinopathy group was 60.2 ± 10.1 years and in control group was 59.1 ± 10.8 years. There was no significant difference in age distribution. Mean BMI among subjects in DM with Retinopathy was 28.1 ± 2.8, in DM without Retinopathy was 27.7 ± 3.2 and in Normal Controls was 26.8 ± 2.9. There was significant difference in BMI b/w 3 groups. Mean duration of DM among subjects in DM without Retinopathy group was 6.6 ± 3.3 years and in subjects with DM with Retinopathy was 8.3 ± 2.9 years. There was significant difference in duration of DM b/w two groups. Majority of subjects in three groups were males and there was no significant

difference in gender distribution between three groups. Among DM with Retinopathy subjects 60% had HTN, among subjects with DM without Retinopathy 60% had HTN.

Table 1: Profile of subject's distribution and comparison between three groups

		Group						P value
		DM with Retinopathy		DM without Retinopathy		Normal Controls		
		Mean	SD	Mean	SD	Mean	SD	
Age		57.8	8.8	60.2	10.1	59.1	10.8	0.360$
BMI		28.1	2.8	27.7	3.2	26.8	2.9	0.047*
Duration (years)		8.3	2.9	6.6	3.3	-	-	<0.001*@
Gender	Male	69	69.0%	31	62.0%	30	60.0%	0.484
	Female	31	31.0%	19	38.0%	20	40.0%	
HTN	Yes	60	60.0%	30	60.0%	0	0.0%	<0.001*#
	No	40	40.0%	20	40.0%	50	100.0%	
Drugs (OHAs/Insulin)	OHA	69	69.0%	40	80.0%	-	-	0.362
	Insulin	9	9.0%	3	6.0%	-	-	
	Insulin + OHA	22	22.0%	7	14.0%	-	-	

 # Chi-square test, @Independent t test, $ANOVA test

Table 2: Glycemic Profile of subject's comparison between three groups

	Group						P value$
	DM with Retinopathy		DM without Retinopathy		Normal Controls		
	Mean	SD	Mean	SD	Mean	SD	
FBS	157.4	42.2	134.4	17.9	101.4	6.4	<0.001*
PPBS	250.5	52.6	213.7	39.6	134.0	9.1	<0.001*
HbA1c	8.4	1.7	8.5	1.8	5.1	0.3	<0.001*

$ANOVA test

Mean FBS among subjects with DM with Retinopathy was 157.4 ± 42.2 mg/dl, among subjects with DM without Retinopathy was 134.4 ± 17.9 mg/dl and among normal controls was 101.4 ± 6.4 mg/dl. There was significant difference in mean FBS b/w three groups. Mean PPBS among subjects with DM with Retinopathy was 250.5 ± 52.6 mg/dl, among subjects with DM without Retinopathy was 213.7 ± 39.6 mg/dl and among normal controls was 134.0 ± 9.1 mg/dl.

There was significant difference in mean PPBS b/w three groups. Mean HbA1c among subjects with DM with Retinopathy was 8.4 ± 1.7, among subjects with DM without Retinopathy was 8.5 ± 1.8 and among normal controls was 5.1 ± 0.3. There was significant difference in mean HbA1c b/w three groups.

Table 3: Laboratory parameters distribution comparison between three groups

	Group						P value$
	DM with Retinopathy		DM without Retinopathy		Normal Controls		
	Mean	SD	Mean	SD	Mean	SD	
Hb%	11.2	1.1	11.3	1.3	12.3	1.1	<0.001*
MPV	11.7	1.3	10.7	0.9	8.8	0.5	<0.001*
Platelets	241.5	61.6	241.1	44.8	233.9	43.8	0.697
Total Count	8018.2	2618.1	8045.4	3110.6	7219.8	3160.2	0.233
Blood Urea	32.1	7.9	30.9	4.2	33.9	7.1	0.108
Creatinine	1.2	0.5	1.2	0.6	1.1	0.6	0.610

$ANOVA test

Mean MPV among subjects with DM with Retinopathy was 11.7 ± 1.3, among subjects with DM without Retinopathy was 10.7 ± 0.9 and among normal controls was 8.8 ± 0.5. There was significant difference in MPV b/w 3 groups.

Similarly there was significant difference in mean Hb% b/w three groups.

There was no significant difference in mean Platelet count, Total count, Blood urea and creatinine b/w 3 groups.

Table 4: Grade of Retinopathy

Grade of Retinopathy			DM with Retinopathy	
			Count	%
Fundus	1	Mild NPDR	56	56.0%
	2	Moderate NPDR	28	28.0%
	3	Severe NPDR	11	11.0%
	4	PDR	5	5.0%

In the study among DM with Retinopathy subjects 56% had Mild NPDR, 28% had Moderate NPDR, 11% had Severe NPDR and 5% had PDR.

Table 5: Mean platelet volume with respect to grade of retinopathy among subjects DM with retinopathy

			MPV		P value
			Mean	SD	
Fundus	1	Mild NPDR	10.0	0.9	<0.001*
	2	Moderate NPDR	11.2	1.0	
	3	Severe NPDR	12.5	0.8	
	4	PDR	11.8	2.2	

In DM with Retinopathy subjects, Mean MPV among subjects with mild NPDR was 10.0 ± 0.9, among moderate NPDR was 11.2 ± 1.0, among severe NPDR was 12.5 ± 0.8 and among PDR was 11.8 ±2.2. There was significant difference in mean MPV with respect to grade of DR.

Table 6: Correlation between MPV and diabetic profile of subjects

		MPV
Duration (years)	r (Correlation coefficient)	0.707**
	P value	<0.001*
	N	199
FBS	r (Correlation coefficient)	0.505**
	P value	<0.001*
	N	200
PPBS	r (Correlation coefficient)	0.560**
	P value	<0.001*
	N	200
HbA1c	r (Correlation coefficient)	0.716**
	P value	<0.001*
	N	200

In the study there was significant positive correlation between MPV and duration of DM, FBS, PPBS and HbA1c i.e. with increase in Duration of DM, FBS, PPBS and HbA1c there was increase in MPV and vice versa.

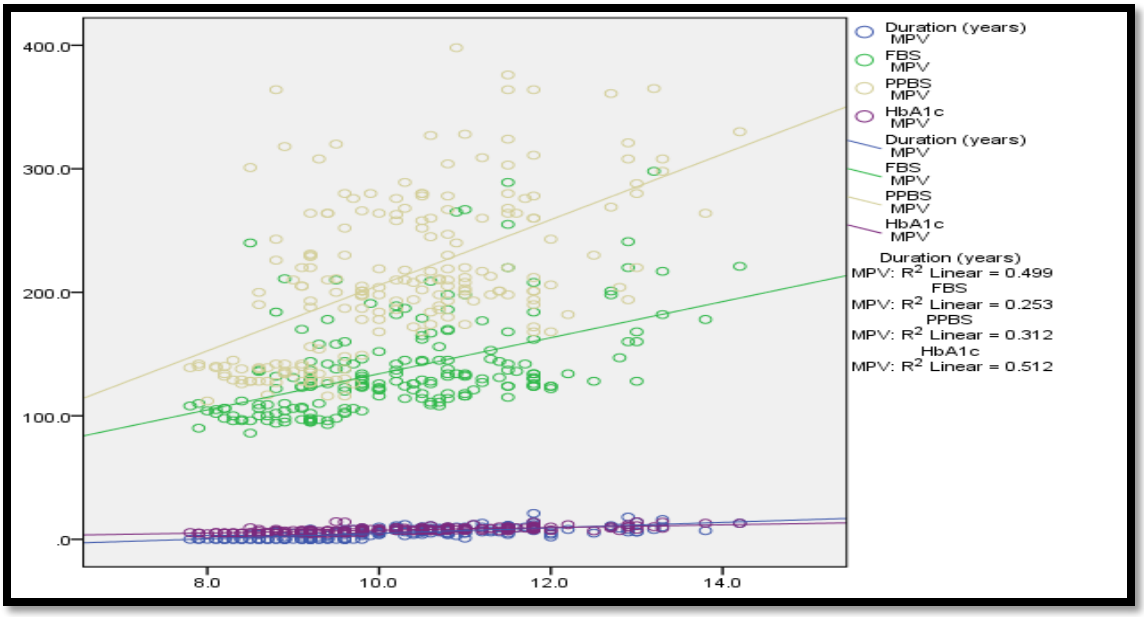

Figure 1: Scatter plot showing correlation between MPV and Glycemic Profile

DISCUSSION: DM is global pandemic and is associated with micro and macrovascular complications. Platelets are anucleated large particles with proaggregatory particles and thrombogenic.

Mean Platelet volume is indicator of the average size and platelet activity.Normal mean platelet volume in healthy subjects is 7.fl-11.7fl .High MPV indicates large and highly active platelets.Larger platelets store and release serotonin,thromboxane A2,β thromboglobulin and are proaggregatory in nature.Mechanisms for increased MPV in DM is not clear but can be attributed to osmotic swelling of platelets and insulin stimulating megakaryocytes to produce larger platelets.DM also tends to shorten the lifespan of platelets and hence larger platelets are seen.

In our study mean age and gender remains same for both cases and controls .Among diabetics, group of diabetics with retinopathy have observed to have higher fasting blood glucose , post prandial blood glucose and HbA1C levels in comparison to diabetics without retinopathy

In our present study, MPV values were studied in diabetics with and without retinopathy and also healthy controls. Significantly higher MPV values were seen in diabetics as compared to healthy controls. MPV values were significantly higher in diabetic patients with retinopathy when compared to diabetics without retinopathy.This is in accordance with other studieslike Jindal et al,[11]Buch et al,[12]Alhadas et al,[13]Yilmaz et al,[14] also found that MPV levelswere

associated with DR. Kodiatte et al,[15] Rajeshkanna,[2]Gungor et al,[16]Ates¸et al,[10]Dindar et al,[17] foundsignificant correlation between MPV and DR.But as per study of Aydinli et al[18] and Demirtunc et al[19] advocatedthat there was no association between MPV and DR.

In our present study , we also studied MPV values and degree of diabetic retinopathy and an increasing trend was seen . Mean MPV values in all stages of retinopathy were significantlyhigher compared to control group. A positivecorrelation was present between the degree ofretinopathy and values of MPV.

Yilmaz et al[14] found an associationbetween mean platelet volume and DR stage. Ateset al[10] found an increase inMPV with the stage of retinopathy. But Kodiette et al[15]found no correlationbetween MPV values and stages of retinopathy. MPV values were higher in advanced stages of retinopathy.

Our study suggests that increased MPV is associated with poor glycemic control. This coincideswith the results of Kodiatte et al[15]Dindar et al,[17]Gungor et al[16.]

CONCLUSION: We found an association between MPVand diabetic retinopathy. Moreover, an increase in MPV values was observed with increasing severity of DR. This finding suggests a role of platelets in the pathogenesis of diabetic retinopathy and that mean platelet volume would be useful in monitoring thedisease progression. MPV can emerge as an important, simple, effortless, and cost-effective tool for monitoring and for early recognition of microvascular complication in Diabetes Mellitus.

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