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Study on Mean Platelet Volume in Type 2 Diabetes Mellitus Patients vs Non Diabetic Patients

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ABSTRACT
Increased prevalence of vascular disease is seen in patients with Diabetes Mellitus (DM). Enhanced reactivity of platelets in patients with diabetes has been postulated to play a role in the microvascular and macrovascular complications of diabetes. MPV is being evaluated as a marker of increased platelet activation. This is a cross-sectional prospective study to evaluate MPV in patients with type 2 diabetes versus non-diabetic patients and to investigate the potential association between MPV and chronic diabetic complications. Our study revealed that MPV is increased in Diabetes mellitus (DM) and that platelets become more reactive and aggregable. The increased platelet size may be a risk factor for atherosclerosis associated with DM and its vascular complications. Hence, MPV would be a useful prognostic marker of cardio-vascular complications in Diabetes mellitus (DM).
Keywords: *cardiovascular complications , diabetes mellitus, HbA1c, mean platelet volume.*

Introduction

According to International Diabetes Federation (IDF), in 2013, 382 million people in the world have diabetes. By 2035, this number will rise to 592 million. In fact, India ranked second in the world in diabetes prevalence, just behind China. Thus preventing vascular complications and monitoring of DM is important. Sustained hyperglycemia leads to a series of interrelated alterations that can cause evident endothelial dysfunction and vascular lesions in diabetic complications. Platelets in response to stimuli generated by the endothelium of blood vessels, changes shape, adhere to subendothelial surfaces, secrete the contents of intracellular organelles, and aggregate to form a thrombus leading to development of advanced atherosclerosis in diabetes. Mean Platelet Volume (MPV) is an indicator of the average size and activity of platelets. Larger platelets contain more dense granules and hence are more potent and thrombogenic. This suggests a relationship between the platelet function especially MPV and diabetic vascular complications thus indicating changes in MPV reflect the state of thrombogenesis. The data of MPV value in diabetics and their association with vascular complications are scarse in India. The aim of this

study in to determine the MPV values in diabetics compared to non diabetics, and in diabetics association between MPV and vascular complications.

Aims and Objectives

1. To determine the MPV in diabetics compared to non-diabetics
2. To find out among the diabetics, if there is an association between MPV and chronic diabetic complications
3. To determine the correlation of MPV with fasting blood glucose, glycosylated hemoglobin (HbA1c), body-mass index and duration of diabetes in the diabetic patients.

Materials and Methods

Inclusion Criteria

- Group A - patients already diagnosed with Type 2 DM and
- Group B- nondiabetic patients without known coronary artery disease, cerebrovascular disease, peripheral vascular disease.
- Age between 20 - 80yrs

Exclusion Criteria

- Male patients with hemoglobin below 13g% and female patients below 12g% (nutritional anemias can be a reason for reactive thrombocytosis and hence increased MPV)
- Patients with abnormal hematocrit and/or abnormal white blood cell count and/or abnormal platelet number
- Nondiabetics with coronary artery disease, cerebrovascular disease, peripheral vascular disease and diabetics on anti-platelet drugs like aspirin and clopidogrel
- Subjects diagnosed with any malignancy

Our study was a cross-sectional and prospective study done in a tertiary care centre after getting ethics committee approval. This study was carried out in 108 previously diagnosed Type 2 diabetic patients and 108 non diabetic patients. The group of diabetic patients were further divided into those without complications and those with one or more of the microvascular and macrovascular complications and also features of metabolic syndrome like hypertension, obesity and dyslipidemia. 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 along with urine for microalbuminuria. After baseline evaluation, diabetics were divided into two groups according to their HbA1c levels. Appropriate statistical evaluation using chi square test were performed to find out the difference in MPV between diabetics and non-diabetics and also to find correlation of MPV with FBS, HbA1c, Body mass index (BMI=weight/height^2) and duration of diabetes.

Results

A Total of 216 subjects were included in the study. These subjects were divided into two groups; group A (n=108) consisted of diabetic subjects and group B (n=108) consisted of non-diabetic subjects. There were 66(61.1%) male diabetics and 42 (38.9%) female diabetics in the study (n=108).There were 75 (69.4%) non-diabetic males and 33 (30.6%) non-diabetic females in the study (n=108). Among the total 216 subjects, the minimum age was 22 years; maximum age was 80 years, mean age was 50.12 years. The mean age of the diabetic population was 54.89 ± 10.201 years whereas that of non-diabetic population was 45.34 ± 11.899 years. This was statistically significant ($P<0.05$). The mean duration of diabetes was 8.45 ± 4.096 years. The mean FBS level in the diabetic group was 150.52 ± 54.861 mg/dl while that of the non-diabetic group was 97.78 ± 24.407 mg/dl. This was also statistically significant ($P<0.05$). The mean HbA1C level in the diabetic group was 8.563 ± 1.981% as compared to 6.3185 ± 0.652% of the non-diabetic group which was also statistically significant ($P<0.05$) (table 1).

In the diabetic group (Group A), MPV was significantly higher (11.25 ± 2.342 fl) as

compared to the non-diabetic group (8.9861 ± 1.599fl). This was found to be statistically significant (P < 0.05). Out of the 108 diabetics (group A), 96 diabetics (88.86%) had complications such as Microalbuminuria (67), Retinopathy (56), Hypertension (83), CAD (44), Dyslipidemia (61), Neuropathy (6), Diabetic Foot (22), and 12 diabetics (11.1%) did not have any complications (table 2). Among patients of Group A, significantly higher MPV was associated with Retinopathy (P=0.30), Microalbuminuria (P=0.39) and Diabetic foot. However, no statistical correlation was seen between MPV and duration of diabetes, BMI, CAD, Dyslipidemia, Hypertension and Neuropathy (table 3,4).

We also divided the diabetic group (group A) based on the HbA1c levels into group with HbA1c <6.5% and group with HbA1c ≥ 6.5%. Out of 108 diabetic patients, there were 15 patients in group with HbA1c < 6.5%. (mean HbA1c = 6.14 ± 0.352%) and 93 patients in group with HbA1c ≥ 6.5% (mean HbA1c = 8.95 ± 1.853%). The mean MPV in group with HbA1c < 6.5% (9.1467 ± 1.0894 fl) was significantly lower than that of group with HbA1c ≥ 6.5% (11.5903 ± 2.316 fl; p< 0.05).

Similarly, the mean duration of diabetes was significantly higher (p<0.05) in group with HbA1c ≥ 6.5% (8.80 ± 4.055 years) than in group with HbA1c < 6.5% (6.33 ± 3.811 years). There was no correlation between age, gender and HbAlc levels. Among the complications, there was positive statistical significance seen in diabetic foot patients and their HbA1c levels (p<0.05) (table 5)

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Table 1 : comparison of FBS,PPBS, HbA1c,BMI and MPV among two groups.

Group	Mean	S.D	Statistical inference
Duration of Diabetes(yrs)			
Group A (n=108)	8.45	4.096	t=21.451 Df=214
Group B (n=108)	.00	.000	.000<0.05 Significant
FBS (mg/dl)			
Group A (n=108)	150.52	54.861	t=9.128 Df=214
Group B (n=108)	97.78	24.407	.000<0.05 Significant
HbA1c %			
Group A (n=108)	8.5630	1.98144	t=11.181 Df=214
Group B (n=108)	6.3185	.65255	.000<0.05 Significant
PPBS (mg/dl)			
Group A (n=108)	226.79	82.027	t=11.305 Df=214
Group B (n=108)	123.92	47.050	.000<0.05 Significant
MPV(Mean Platelet Volume)fl			
Group A (n=108)	11.2509	2.34284	t=8.297 Df=214
Group B (n=108)	8.9861	1.59921	.000<0.05 Significant
BMI (kg/m2)			
Group A (n=108)	23.8917	3.49673	t=3.422 Df=214
Group B (n=108)	22.2972	3.34864	.001<0.05 Significant

Table 2: Diabetic group and its complications and correlation with MPV.

MPV *(Group A) (n=108)*	Mean	S.D	t	df	Statistical inference
Micro albuminuria					
Present (n=67)	11.6134	2.29538	2.088	106	.039<0.05 Significant
Absent (n=41)	10.6585	2.32583			
Retinopathy					
Present (n=56)	11.7196	2.28763	2.196	106	.030<0.05 Significant
Absent (n=52)	10.7462	2.31758			
Diabetic foot					
Present (n=22)	12.4682	1.71725	2.818	106	.006<0.05 Significant
Absent (n=86)	10.9395	2.38733			
CAD					
Present (n=44)	11.6432	2.17164	1.450	106	.150>0.05 Not Significant
Absent (n=64)	10.9813	2.43355			
Dyslipidemia					
Present (n=61)	11.1656	2.29571	-.430	106	.668>0.05 Not Significant
Absent (n=47)	11.3617	2.42304			
Hypertension					
Present (n=83)	11.3229	2.28870	.580	106	.563>0.05 Not Significant
Absent (n=25)	11.0120	2.54891			
Neuropathy					
Present (n=6)	12.1167	2.40035	.931	106	.354>0.05 Not Significant
Absent (n=102)	11.2000	2.34149			

Table 3: Correlations relationship between MPV vs other variables

MPV	Duration of diabetes	BMI	HbA1c	FBS	PPBS	Microalbuminuria	Retinopathy
r	.151	.059	.563(**)	.463(**)	.507(**)	-.199(*)	-.209(*)
p	.119	.543	.000	.000	.000	.039	.030
n	108	108	108	108	108	108	108
Statistical inference	Not Significant	Not Significant	Highly Significant	Highly Significant	Highly Significant	Significant	Significant

***<0.01 Highly Significant / *<0.05 Significant*

Table 4: Correlations relationship between MPV Vs other variables

MPV	Diabeticfoot	CAD	Dyslipidemia	Hypertension	Neuropathy
r	-.264(**)	-.139	.042	-.056	-.090
p	.006	.150	.668	.563	.354
n	108	108	108	108	108
Statistical inference	Not Significant	Not Significant	Not Significant	Not Significant	Not Significant

***<0.01 Highly Significant / *<0.05 Significant*

Table 5: comparison of HbA1c with complications

	(Group-A) HbA1c %						Statistical inference
	Below 6.5%		Above 6.5%		Total		
	(n=15)	*(100%)*	*(n=93)*	*(100%)*	*(n=108)*	*(100%)*	
Micro albuminuria							
Present	7	46.7%	60	64.5%	67	62.0%	X^2=1.747 Df=1 .186>0.05 Not Significant
Absent	8	53.3%	33	35.5%	41	38.0%	
Retinopathy							
Present	5	33.3%	51	54.8%	56	51.9%	X^2=2.393 Df=1 .122>0.05 Not Significant
Absent	10	66.7%	42	45.2%	52	48.1%	
Diabetic foot							
Present	0	.0%	22	23.7%	22	20.4%	X^2=4.456 Df=1 .035<0.05 Significant
Absent	15	100.0%	71	76.3%	86	79.6%	
CAD							
Present	4	26.7%	40	43.0%	44	40.7%	X^2=1.429 Df=1 .232>0.05 Not Significant
Absent	11	73.3%	53	57.0%	64	59.3%	
Dyslipidemia							
Present	8	53.3%	53	57.0%	61	56.5%	X^2=.070 Df=1 .791>0.05 Not Significant
Absent	7	46.7%	40	43.0%	47	43.5%	
Hypertension							
Present	10	66.7%	73	78.5%	83	76.9%	X^2=1.016 Df=1 .314>0.05 Not Significant
Absent	5	33.3%	20	21.5%	25	23.1%	
Neuropathy							
Present	0	.0%	6	6.5%	6	5.6%	X^2=1.025 Df=1 .311>0.05 Not Significant
Absent	15	100.0%	87	93.5%	102	94.4%	

Discussion

In our study, the diabetics group had significantly higher MPV than the non-diabetic group. This is similar to findings seen in studies done by Hekimsoy et al, Demirtunc et al., Zuberi et al., Ates et al., Jindal et al., Papanas et al., and Kodiatte et al. [2,3,4,6,9,10]

Higher values of MPV were observed in our study among the diabetic subjects with microvasular complications such as Retinopathy and Microalb-uminuria which was statistically significant. Higher values were also seen in studies done by Papanas et al and Ates et al. [9,10] This suggested a role for the increased platelet activity in the pathogenesis of vascular complications.

On the contrary, in the studies done by Hekimsoy et al and Demirtunc et al.,[3,6] MPV was not significantly different in subjects with diabetics complications. Their possible explanation was centered on the rapid consumption of activated platelets in diabetic without complications.

In our study, MPV was significantly higher in diabetics with HbA1c levels ≥ 6.5% than in diabetics with HbA1c levels < 6.5%. There was also a significant association between HbA1c and MPV, which was also observed in the studies done by Demirtunc et and Saigo et al.[6,7]

But studies like Papanas et al., Sharpe and Trinick[8,9] did not show any association between HbA1c and MPV.

Therefore, it may be concluded that glycemic control deceases the hyperactivity of the platelet function and thus may prevent or delay diabetic vascular complications. However, larger studies are needed to confirm our data. The reason for a high number of diabetics with HbA1c levels ≥ 6.5% in the current study might have been due to poor dietary practices and lack of knowledge regarding the diet and exercise regimens that should be followed in diabetics.

MPV was strongly associated with complications like Retinopathy which was similar to studies done by Ates et al[10] where they went one step further to correlate MPV with degree of Retinopathy.

Conclusion

Our study revealed that MPV is increased in Diabetes mellitus (DM) and that platelets become more reactive and aggregable. The increased platelet size may be a risk factor for atherosclerosis associated with DM and its vascular complications. Hence, MPV would be a useful prognostic marker of cardio-vascular complications in Diabetes mellitus (DM). Our study also showed that increase in HbA1c concentration was directly proportional to increased MPV. However, these results may be of clinical relevance (ie., MPV as the cause or end result of vascular complications) in the future, if further studies determine the contribution of platelet activation to the pathogenesis of diabetic micro and macrovascular diseases. Hence, MPV can be used as a simple and cost-effective tool to monitor the progression and control of DM and its cardio-vascular complications.

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