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Original Research Article

Platelet indices and their correlation with HbA1c and association with microvascular complications in type-2 diabetes mellitus

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ABSTRACT

Background: Depending on the aetiology of the DM, factors contributing to hyperglycaemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. Mean platelet volume (MPV) and platelet distribution width (PDW) are important, simple, effortless, and cost-effective tools measured by hematology analyser which assess the volume and function of platelets. Analysing the platelet parameters can act as an alarm for progression of complications of DM. Hence, we studied the platelet parameters in diabetic patients with good and poor glycaemic control and their association in microvascular complications.
Methods: This study was conducted on 100 patients having diabetes mellitus. All the patients were subjected to detailed history regarding age, sex, occupation, socioeconomic status, GPE and systemic examination.
Results: Out of 100 cases, 29 patients had a good glycemic control (HbA1c<7%) and 71 had poor glycemic control (HbA1c>7%). Mean FBS was 118.59±19.36 mg/dl in good control group and 158.79±29.21 mg/dl in poor control ($p<0.001$). Mean PPBS was 159.86±37.78 mg/dl in good control group and 235.80±53.28 mg/dl in poor control group ($p<0.001$). Good glycemic control group had mean MPV of 7.89±0.63 fl and poor glycemic control group had mean MPV 10.06 fl ($p<0.001$). Mean PDW was 12.32±1.94 in good control group and 13.81±2.25 in poor control group.
Conclusions: Our study indicates that MPV and PDW are increased in diabetic patients, more so in patients with microvascular complications than in those without complications. Hence, they can be used as markers in predicting the microvascular complications in diabetes mellitus.

Keywords: DM, Microvascular complications, MPV, PDW

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia. Depending on the aetiology of the DM, factors contributing to hyperglycaemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.[1]

India is having highest burden of the diabetic subjects. A majority of patients with type 2 DM, as well as subjects with IGT, have signs of the metabolic syndrome (also called dysmetabolic syndrome, insulin resistance syndrome or syndrome X). Insulin resistance plays a central role in this syndrome.[2] Diabetes and uncontrolled hyperglycaemia are known to play a significant role in the development of cardiovascular disease since Framingham study.[3,4] Additionally, besides the diabetes and classical risk factors, the presences of microvascular complications are also predictor of coronary heart events especially when it is prolonged and/or poorly controlled.[5]

The risk of developing diabetic retinopathy or other microvascular complications of diabetes depends on both the duration and the severity of hyperglycemia. Development of diabetic retinopathy in patients with type 2 diabetes was found to be related to both severity of hyperglycemia and presence of hypertension in the UK Prospective Diabetes Study (UKPDS), and most patients with type 1 diabetes develop evidence of retinopathy within 20 years of diagnosis.[6]

There have been few studies in the available literature on platelet indices in patients with T2DM. Mean platelet volume (MPV) is an indicator of the average size and activity of the platelets. Large circulating platelets are reflected by increase in MPV and increase in MPV has been documented in patients with metabolic syndrome, stroke and DM.[6] Larger platelets are younger, more reactive and aggregable. Hence, they contain denser granules, secrete more serotonin and β-thromboglobulin, and produce more thromboxane A2 than smaller platelets.[7]

Platelet distribution width (PDW) which refers the size variability of circulating platelets.[8] Since PDW is not affected by swelling of the thrombocytes, it was considered as a better predictor of platelet activation than MPV. Platelet anisocytosis term is used when the PDW elevated to normal range of 9-14%.[9] It is increased during platelet activation. The platelets which are activated are different in size than nonactivated ones because of pseudopodia formation and change in shape from discoid to spherical giving rise to increased PDW.[10]

Mean platelet volume (MPV) and platelet distribution width (PDW) are important, simple, effortless, and cost-effective tools measured by hematology analyser which assess the volume and function of platelets and thus have potential to be used as indicators of presence of microvascular complications. Analysing the platelet parameters can act as an alarm for progression of complications of diabetes mellitus. Hence in a view of this, we studied and compared the platelet parameters in diabetic patients with good and poor glycaemic control and their association in microvascular complications.

Aims and objectives

To compare mean platelet volume (MPV) and platelet distribution width (PDW) in type 2 diabetes mellitus patients with good glycaemic control (HbA1c<7.0 gm%) with that of poor glycaemic control (HbA1c>7.0 gm%).

METHODS

This study was conducted after taking approval from institutional ethical committee among the patients who were treated from April 2020 to December 2020, in the department of general medicine, RNT Medical College Udaipur, Rajasthan.

A total of 100 patients having diabetes mellitus were selected. All the patients were subjected to detailed history regarding name, age, sex, occupation, socioeconomic status, general physical examination and systemic examination.

Systolic and diastolic blood pressures (SBP and DBP) were measured after a 5 minutes rest in a supine position with a sphygmomanometer. BP was determined at least 3 times from the right upper arm for analysis, the mean of the 3 was used. Patients with mean blood pressure levels >140/90 mm of Hg or patients already on antihypertensive medications were diagnosed as having hypertension.

Known type 2 diabetes mellitus patients on treatment with OHA/Insulin of either sex age >30 years and newly detected type 2 diabetes mellitus patients were included in the study.

All patients with type 1 diabetes mellitus, gestational diabetes mellitus, male patients with Hb<12 mg% and female with Hb <11 mg%, patients on antiplatelets and antithrombotics, patients with diagnosed malignancy and patients with known chronic kidney disease were excluded from the study.

Methods

Venous samples were collected after 12 hours of overnight fasting at 8:30 am for Mean Platelet Volume, Platelet Distribution Width, HbA1C, FBS, PPBS, Hb, triglyceride (TG) and serum creatinine levels.

HbA1c was measured by high performance liquid chromatography. measurement of MPV and PDW was done using an automatic blood counter (Sysmex XS1000i). Plasma glucose estimation (FBS and PPBS) was carried out by the glucose oxidase method in the autoanalyzer. Hypertriglyceridemia was defined as having triglyceride levels >150 mg/dl.

Microalbuminuria, which is the hallmark of diabetic nephropathy was examined using spot urine albumin creatinine ratio (ACR). Patients with ACR of <20 mg/gm for men and <30 mg/gm for women were categorized as proteinuria negative and those with >20 mg/gm and >30 mg/gm respectively as proteinuria positive.

Diabetic retinopathy was defined by direct ophthalmoscopic examination. Patients with at least 2 microaneurysms and/or retinal haemorrhage, and/or other signs of retinal damage were diagnosed as having retinopathy.

After baseline evaluation, the patients were divided into 2 groups based on HbA1C levels. Diabetics with good glycemic control (patients with HbA1c<7%) and those with poor glycemic control (patients with HbA1c>7%). All the parameters were compared between both the

groups. These groups were further sub grouped based on the presence or absence of complications.

MPV (range 6.4 fl to 10 fl) was divided into 4 class intervals with the width of 1.2 fl and PDW (range 9 fl to 17 fl) was divided into 5 class intervals with width of 2fl. The MPV and PDW in each group (according to glycemic control and microvascular complications) were compared.

Statistical analysis

All continuous variables were expressed as mean standard deviation (SD) or medians (range), and categorical data were calculated as percentages. Differences between variables were evaluated using ANOVA tests. Statistical analysis was performed using SPSS and $p<0.05$ was statistically significant.

RESULTS

In good glycemic control group mean age was 49.38 years and in poor glycemic control group mean age was 52.06 years. The differences in the values of mean age were statistically significant with p value of 0.008.

In good glycemic control group majority were males (55.17%) and majority in poor glycemic control group were females (52.11%).

Majority in good glycemic control group (44.83%) belonged to 6-10 years duration of diabetes class interval with a mean duration of diabetes of 6.69 years and majority in poor glycemic control group (47%) belonged to same duration of diabetes class interval with a mean duration of diabetes of 7.46 years. The p value for the observations was 0.13 which was statistically not significant (Table 1).

Table 1: Demographic data.

	Good glycemic control		Poor glycemic control		Total	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (years)	49.38	9.67	53.15	10.35	52.06	10.26
Mean duration	6.69	3.65	7.46	3.45	7.24	3.51

Table 2: Distribution of hypertension, TGL, FBS levels and PPBS level according to glycemic control.

		Good glycemic control		Poor glycemic control		Total	
		No.	**%**	**No.**	**%**	**No.**	**%**
Hypertension	Yes	18.00	62.07	45.00	63.38	63.00	63.00
	No	11.00	37.93	26.00	36.62	37.00	37.00
TGL (mg/dl)	<150	1	3.45	4	5.63	5	5.00
	150-200	20	68.97	47	66.20	67	67.00
	201-250	6	20.69	14	19.72	20	20.00
	251-300	2	6.90	5	7.04	7	7.00
	>300	0	0.00	1	1.41	1	1.0

Table 3: Mean FBS according glycemic control.

	Good glycaemic control		Poor glycaemic control		Total	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Fasting blood sugar (mg/dl)	118.59	19.36	158.79	29.21	147.13	32.33
PP blood sugar	159.86	37.78	235.80	53.28	213.78	60.08

In good glycemic control group incidence of hypertension was 62.07% and in poor glycemic control group incidence of hypertension was 63.38%. The p value was statistically not significant at 0.90.

On analysing TGL levels both good and poor glycemic control group had majority of patients in class interval of 150-200 (68.97% and 66.20% respectively) (Table 2).

FBS distribution, it was observed that, majority in good glycemic control group (37.93%) belonged to 101-120 mg/dl FBS class interval with a mean FBS of 118.59 mg/dl and majority in poor glycemic control group (80.28%) belonged to >140 mg/dl FBS class interval with a mean FBS of 158.79 mg/dl. The difference in the values for FBS in both the group is highly significant with a p value of <0.001.

PPBS distribution, it was observed that, majority in good glycemic control group (58.62%) belonged to ≤150 mg/dl PPBS class interval with a mean PPBS of 159.86 mg/dl and majority in poor glycemic control group (35.21%)

belonged to 201-250 mg/dl PPBS class interval with a mean PPBS of 235.80 mg/dl. The p value for the means of PP blood sugar was <0.001 which was statistically significant (Table 3).

There was a statistically significant association between MPV distribution and glycemic control based on HbA1c levels (p<0.001) exhibited by the increased mean MPV levels in poor glycemic control group compared to good glycemic control group (2.17 fl higher).

There was a statistically significant association between PDW distribution and glycemic control based on HbA1c levels (p=0.008) exhibited by the increased mean PDW levels in poor glycemic control group compared to good glycemic control (1.49% higher) (Table 4).

Table 4: Mean MPV and PDW according to glycemic control.

	Good glycaemic control		Poor glycaemic control		Total	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Mean MPV	7.89	0.63	10.06	1.02	9.44	1.35
Mean PDW	12.32	1.94	13.81	2.25	13.38	2.26

On statistical analysis the difference in the mean MPV in diabetics with and without retinopathy was statistically significant with p value of <0.001.

On statistical analysis the difference in the mean PDW in Diabetics with and without proteinuria was statistically significant with p value of <0.001 (Table 5).

Table 5: Mean MPV according to proteinuria.

	Proteinuria present		Retinopathy present	
	Mean	**SD**	**Mean**	**SD**
Mean MPV	10.35	0.99	10.48	0.98
Mean PDW	14.37	2.27	14.44	2.35

DISCUSSION

In the present study, 100 cases of type 2 diabetes mellitus were studied in the medical wards of Maharana Bhupal Government Hospital, RNT Medical College, Udaipur.

Out of hundred cases, 29 patients had a good glycemic control defined by HbA1c level <7% and 71 had poor glycemic control HbA1c level >7%. The age distribution was between 30-70 years with mean age of patients with good glycemic control and poor glycemic control being 49.38±9.67 years and 52.06±10.26 respectively. The difference was statistically significant with p=0.008. The results were similar to those obtained in study done by Goyal et al.[11]

In our study 18 patients from good control group and 45 patients from poor control group had history of hypertension and association of hypertension with glycemic control was statistically insignificant. Same was the association between TGL and glycemic control with majority of diabetics having TG levels between 150 to 200 mg/dl. 20 patients from good control group and 47 patients from poor control group had TG level of above-mentioned range.

While analysing FBS distribution and glycemic control, mean FBS was found to be 118.59±19.36 mg/dl in good control group and 158.79±29.21 mg/dl in poor control group. The difference in the values for FBS in both the group was highly significant with a p value of <0.001. This significance was exhibited by the increased mean in FBS levels of poor glycemic control group compared to good glycemic control group. We observed similar results in study conducted by Rajagopal et al.[12]

On comparing PPBS distribution and glycemic control, mean PPBS was found to be 159.86±37.78 mg/dl in good control group and 235.80±53.28 mg/dl in poor control group. The difference in the values for PPBS was highly significant with a p value of <0.001. This significance was exhibited by the increased mean in PPBS levels of poor glycemic control group compared to good glycemic control group.

While analysing proteinuria status, it was observed that, in good glycemic control group incidence of proteinuria was 20.69% and in poor glycemic control group incidence of proteinuria was 53.52%. And analysis of retinopathy status showed that, in good glycemic control group incidence of retinopathy was 10.34% and in poor glycemic control group incidence of retinopathy was 59.15%. The data subjected to statistical chi squared test reveals the existence of statistically significant association between both proteinuria (p=0.003) and retinopathy (p<0.001) status with glycemic control based on HbA1c levels.

In our study, the MPV values were higher in diabetic patients with poor control as compared to diabetic population with good control and there was a statistically significant difference between both the groups. It was observed that good glycemic control group had a mean MPV of 7.89±0.63 fl and poor glycemic control group had a mean MPV of 10.06 fl (p<0.001). This was similar to study conducted by Saluja et al (11.86±0.66 in good control group versus 13.77±1.08 in poor control group, p=0.0001).[13] Similar results were obtained in study

conducted by Walinjkar et al, Demirtas et al, Buch et al, Goyal et al, Rajagopal et al, whereas this was in discordance with studies conducted by Kshirsagar et al and Joshi et al.[11,12,14-18]

On analysing PDW values, mean PDW was 12.32±1.94 in good control group whereas it was 13.81±2.25 in poor control group. This was statistically significant with p value of 0.008. Similar results were obtained in study conducted by Walinjkar et al (14.78±3.21 in patients with HbA1c<7.5,16.26±3.02 in HbA1c group 7.5-10,18.28±2.88 in patients with HbA1c>10 with p=0.005).[14] Studies conducted had no statistical significance between PDW and glycemic control.[11,12,15,17,18]

While comparing the relation between MPV and proteinuria it was found that patients with proteinuria had a mean MPV of 10.35±0.99, whereas it was 8.71±1.15 in patients without proteinuria (p<0.001). On statistical analysis it was significant. Study conducted by Walinjkar et al found similar results with mean MPV of 12.35±1.50 in patients with proteinuria and 10.17±1.12 without proteinuria with p=0.0001.[14] Similar results were obtained in other studies.[16,17,19,20] In studies conducted by other authors had no significant association between MPV and proteinuria.[15,18]

Demirtas et al, In the evaluation of association of retinopathy and hematological indices; there were statistically significant difference of MPV levels between patients with (MPV=9.54±0.88) and without (MPV=9.20±0.92) retinopathy (p=0.006).[15] Similar results were obtained in our study with mean MPV of 10.48±0.98 with retinopathy and 8.95±1.22 without retinopathy (p<0.001). These results were similar to results obtained by studies.[14,16,17,19] Results of our study were discordant to those obtained by Kshirsagar et al.[18]

In our study there was a positive association between PDW and proteinuria depicted by mean PDW of 14.37±2.27 in proteinuria positive group and 12.60±1.94 in proteinuria negative group with p<0.001. This was in concordance with study conducted by Goyal et al (14.16±6.40 in proteinuria group and 12.01±3.55 without proteinuria group).[17] Similar results were obtained in studies.[14,16,19,20] But study done by Demirtas et al and Kshirsagar et al did not show similar association.[15,18]

In study conducted by Kshirsagar et al there was no significant association between PDW and retinopathy.[18] This was in concordance with study conducted by Demirtas et al and Goyal et al.[15,17]

In our study we found the mean PDW was 14.44±2.35 in patients with retinopathy and whereas it was 12.88±2.05 in patients without retinopathy (p<0.001). These results were similar to those obtained in studies conducted by Buch et al (11.40±1.96 in those with retinopathy versus 10.24±2.04 in those without retinopathy, p=0.001).[14,16,19]

We have certain limitations in the study, such as a small sample size, non follow-up study. As few parameters are to be observed with other specialties, hence coordination and evaluation of parameters were little tedious.

CONCLUSION

MPV and PDW were higher in diabetic patients who had poor glycemic control than the diabetics who had good glycemic control. Similarly, elevated MPV and PDW were seen in diabetic patients with complications than diabetic patients without complications.

MPV and PDW are indicators of platelet activity. Increased MPV and PDW are associated with increased risk of thrombogenic events leading to microvascular complications of diabetes mellitus. Our study indicates that MPV and PDW are increased in diabetic patients, more so in patients with microvascular complications than in those without complications. Hence, they can be used as markers in predicting the microvascular complications in diabetes mellitus.

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