

The Role of Platelet Indices to Predict the Vascular Complication in Diabetic Patients in South Tamil Nadu

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Abstract

Background: Diabetic patients have larger young, more reactive and more agregable platelets. Platelet indices such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) are the indicators of increased platelet activity and considered as potential markers for diabetic vascular complications. This study aimed to estimate and compare Platelet count, MPV and PDW between (1) Diabetics patient and Controls (2) Diabetics under glycaemic control and not under glycaemic control.

Methodology: This cross sectional study was conducted at, Tirunelveli Medical College, Tamil Nadu, India, during August 2015 to September 2017. In this study 100 diabetic patients and 100 controls were included.

Inclusion criteria for diabetics were FBS > 126 mg/dl, PPBS > 200 mg/dl, and age between 35-65 years. Exclusion criteria for diabetics were age less than 35 and greater than 65 years. The criteria for controls include normal FBS, PPBS levels, and age from 35-65 years and without any thromboembolic conditions.

Results: Data analysis was done using SPSS 19.0. MPV was significantly increased in (a) diabetics than healthy controls (b) diabetics under glycaemic control than diabetics not under glycaemic control. PDW showed significant difference between (a) diabetics and non-diabetic controls, (b) diabetics under glycaemic control and not under glycaemic control. There was no significance of platelet count among group A and group B. P value < 0.05 was considered significant.

Conclusion: In this study MPV and PDW were significantly increased in diabetic patients than non-diabetic healthy individuals and higher in diabetic patients not under glycaemic control than the diabetic under glycaemic control.

Keywords: Diabetes Mellitus (DM), Platelet Count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW)

Introduction

The prevalence of diabetes has increased by leaps and bounds in India and has reached epidemic proportions. India has more than 62 million diabetic patients. Thus it is vital to obtain epidemiological data on diabetes from all over the world. According to International Diabetes Federation 2013, China has the largest population of diabetics of about 98.4 million, India being second with 65.1 million and USA 24.4 million diabetics. IDF 2013 also gives the data of total diabetics in the world to be around 382 million which is estimated to rise by around 55% to reach 592 million diabetic population by the year 2032. The study also gives the data of SEAR countries to inhabit 72.1 million of diabetic population in 2013 which is postulated to increase to 123 million by 2032 that is a 71% rise from the present diabetic population [1]

Diabetic patients have larger platelets that are young, more reactive and more agregable. They contain denser granules, secrete more serotonin, beta thromboglobulin and thromboxane A₂ than smaller and less active platelets. This suggests an association between the platelet functions and diabetic vascular complications. Hence changes in Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) reflect the state of thrombogenesis. Therefore, MPV and PDW can be considered as predictive markers for vascular complications of diabetes mellitus. Identification of such patients can be easily made by simple routine haematological analysis which helps in easy detection of prothrombotic state of the patients. It is a cost-effective tool that could possibly benefit by preventive actions as a large number of diabetic patients suffer from preventable vascular complications. Analysing the platelet parameters can act as an alarm for diagnosing and progression of complications of diabetes mellitus. Hence in a view of this, we studied and compared the platelet parameters in diabetic patients and healthy controls.

Hence our study aimed to evaluate the platelet indices such as Platelet count, Mean platelet volume and Platelet distribution width in diabetic and non-diabetic patients and to compare platelet indices between diabetic patients who were under glycaemic control and not under glycaemic control.

Methodology

This cross-sectional study was conducted at Diabetic Clinic and Medical Wards, Department Of Medicine, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India, during the period of August 2015 to September 2017. Study was conducted after getting approval from the institutional ethical committee. In this study 100 patients with diabetes mellitus and 100 controls were included

Inclusion criteria for this study populations were Diabetic patients with FBS > 126 mg/dl and PPBS > 200 mg/dl, and age ranging from 35 to 65 years. Exclusion criteria for this study population were Diabetic patients with age less than 35 and more than 65. The control group of this study were selected with following criteria's with individual having FBS < 126 mg/dl and PPBS < 200 mg/dl, age ranging from 35 to 65 years and without any thromboembolic conditions.

Then collection of blood and urine samples were done under aseptic condition. Four to five ml of blood was collected. Venous samples for complete blood count, HbA1C were collected in dipotassium EDTA tube and for plasma glucose (fasting plasma glucose, post prandial plasma glucose) was collected in sodium fluoride tube. Samples were labelled with patients name, age, sex, identification number and

maintained at room temperature. Samples were tested within one hour of collection to minimize variations caused by sample aging.

Complete blood count was done using Sysmex, a three part analyser which gives nineteen parameters per sample including total red cell count, total leucocyte count, differential count, haemoglobin concentration, packed cell volume, mean corpuscular haemoglobin, platelet count, mean platelet volume, platelet distribution width. Standardisation, calibration of the instrument and processing of samples were done as per manufactures instruction. Estimation of plasma glucose level (Fasting plasma glucose and Post prandial plasma glucose) were done by Glucose oxidase - Peroxidase method in fully auto analyser. HbA1C was analysed. Urine microalbuminuria was estimated in random midstream urine sample.

After the baseline investigation, the study population was classified into Group A composed of diabetic patients and Group B composed of non-diabetic healthy controls. Diabetic patients further were classified into different groups according to their HbA1C levels and vascular complication: Group A1 composed of patients with HbA1C \leq 6.5% and Group A2 composed of patients with HbA1C $>$ 6.5%. Platelet parameters such as platelet count, MPV, and PDW were compared between diabetic cases and non-diabetic healthy individuals and also between the different groups. Normal values of platelet count ranges from 1.5 to 4 lakhs/mm³, normal mean platelet volume values ranges from 7 to 9 femtolitres. Regarding platelet distribution width, normal reference value varies from lab to lab. Our lab reference value ranges from 9.4 to 18 femtolitres.

Result

Statistical Analysis was done using SPSS 19. One way analysis of variance (ANOVA) was used to compare more than two independent samples. T-test and independent sample tests were done. $P < 0.05$ was considered to be statistically significant.

In this study 100 of diabetic patients and 100 control groups samples were included. Among the diabetics (group A), 3 patients were less than 40 years, 28 patients were between 41-50 years, 45 patients were between 51-60 years and 24 cases were above 60 years. Among the control population (group B), 12 individuals were below 40 years, 36 individuals were between 41-50 years, 45 individuals were 51-60 years and 7 individuals were above 60 years (Figure 1). In our study, disease prevalence among male in both population (60 males in the diabetic population and 68 males in the control population) were more than the female (40 females in diabetic population and 32 females in the control group (Figure 2). The mean MPV (mean platelet volume) among the diabetic population is 9.79 ± 1.06 fl and the mean MPV among the control population is 8.91 ± 0.81 fl. (Table 1, Figure 3). In our study, 76% of diabetic patients had increased mean platelet volume and 24% of diabetic patient had mean platelet volume within normal range where as 19% of control population had increased mean platelet volume and 81% of control population had mean platelet volume within normal range. So there was a statistically significant difference of mean platelet volume observed between diabetic and non-diabetic population ($P < 0.0001$) (Table 1, Figure 4). The mean platelet distribution width (PDW) was reported to be higher in diabetic population (12.40 ± 2.16 fl) when compared to the mean platelet distribution width in control population (11.23 ± 1.71 fl) as per Figure 5. Even though 99% of both diabetic and control population had platelet distribution width within normal range, the mean platelet distribution width was found to be increased in

diabetic population than nondiabetic and there was a statistically significant difference found between them ($P < 0.0001$) (Table 1). In our study, Mean platelet count of diabetic population was $2.60 \pm 0.85 \times 10^9/L$ and mean platelet count for normal healthy individuals was $2.77 \pm 0.97 \times 10^9/L$. Among the diabetic population, 7% had decreased platelet count, 90% had normal platelet count, 3% had increased platelet count. In case of normal healthy individuals, 1% had decreased platelet count, 97% had normal platelet count, and 2% had increased platelet count. There was no statistically significant difference of platelet count between diabetics and nondiabetic individuals. ($P = 0.207$) (Table 1).

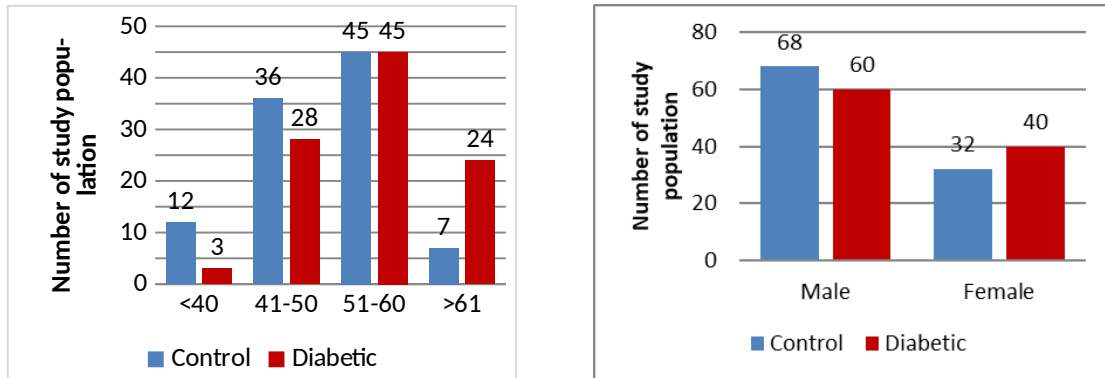


Figure 1 and 2: Age and Gender Distribution of 100 Diabetic Cases and 100 Non-Diabetic Healthy Controls

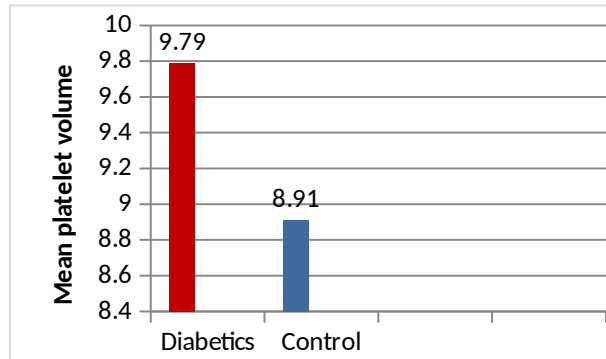


Figure 3: Mean Values of MPV between Diabetic Cases and Non-Diabetic Controls

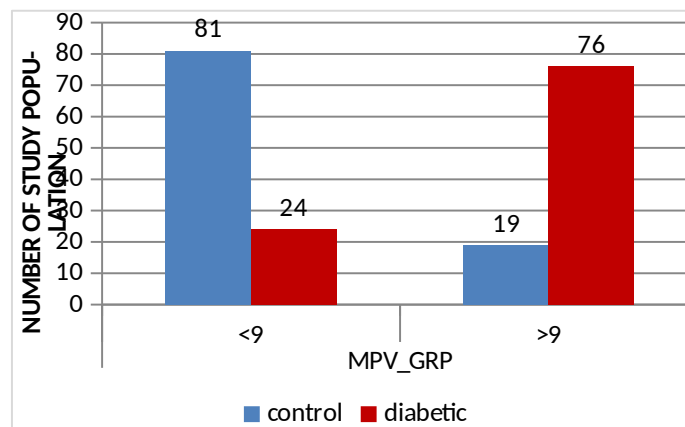


Figure 4: Distribution of Study Population (Controls and Diabetics) based on MPV Values

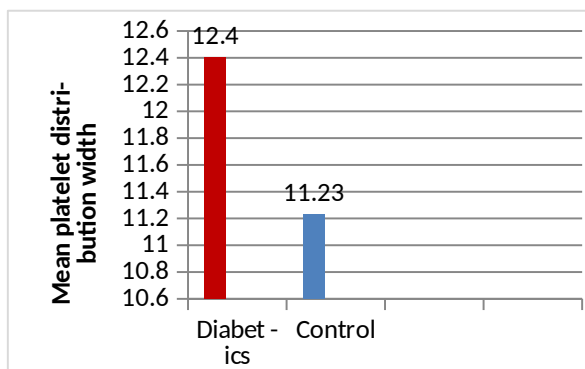


Figure 5: Mean Platelet Distribution Width between Diabetic Patients and Non-Diabetic Control

Table 1: Mean Values of Platelet Parameters between Diabetic Cases and Non-Diabetic Healthy Controls

	Group	Number of Cases	Mean	Standard Deviation	P Value	T Value
MPV	Control	100	8.91	0.81	< 0.0001	6.128
	Diabetic	100	9.79	1.06		
PDW	Control	100	11.23	1.71	< 0.0001	4.220
	Diabetic	100	12.40	2.16		
Platelet Count	Control	100	2.77	0.97	0.207	-266
	Diabetic	100	2.60	0.85		

Platelet Parameters were Compared between Diabetics and Healthy Controls and Statistically Significant Difference of MPV and PDW Values were Obtained (Table 1).

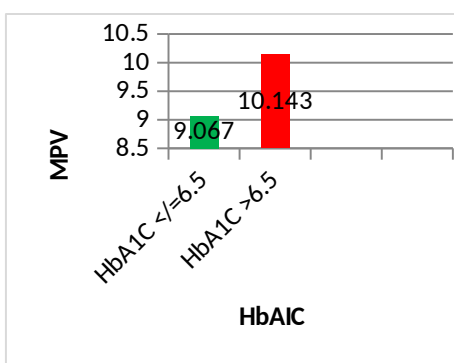


Figure 6: Mean Platelet Volume between Diabetics under Glycaemic Control and not under Glycaemic Control

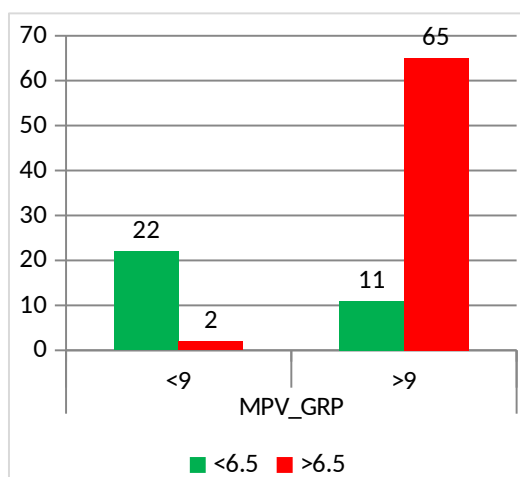


Figure 7: Distribution of Group A1 (Diabetics with Hba1c \leq 6.5) and Group A2 (Diabetics with HbA1C $>$ 6.5) according to their MPV Values

Group A1: Diabetics under glycaemic control (HbA1C \leq 6.5) - 33%
 Group A2: Diabetics not under glycaemic control. (HbA1C $>$ 6.5) - 67%

As per the Figure 6 and Table 2, the mean value of mean platelet volume in diabetics under glycaemic control (9.06 ± 0.98 fl) was decreased than the diabetics who were not under glycaemic control (10.14 ± 0.914 fl) Among the Group A1, 22 patients (67%) had normal mean platelet volume, 11 cases (33%) had increased mean platelet volume. In Group A2, 2 patients (3%) had normal mean platelet volume and 65 patients (97%) had increased mean platelet volume. There was a statistically significant difference between Group A1 and Group A2 ($P < 0.0001$) (Table 2, Figure 7).

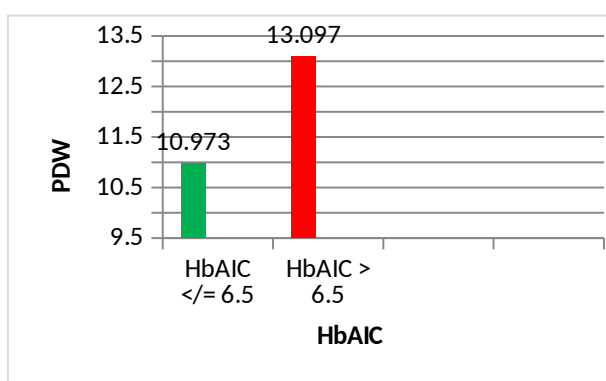


Figure 8: Mean Platelet Distribution Width between Diabetics under Glycaemic Control and not under Glycaemic Control

Table 2: Platelet Parameters between Diabetics under Glycaemic Control and not under Control

		HbA1C Group	Number of Cases	Mean	Standard Deviation	P Value	T Value
MPV	Under Glycaemic Control	\leq 6.5 (group A1)	33	9.067	0.9845	0.0001	

	Not Under Glycaemic Control	>6.5 (group A2)	67	10.143	0.9144		5.398
PDW	Under Glycaemic Control	≤ 6.5 (group A1)	33	10.973	2.0324		
	Not Under Glycaemic Control	> 6.5 (group A2)	67	13.097	1.8733	0.0001	-5.184
Platelet Count	Under Glycaemic Control	≤ 6.5 (group A1)	33	2.6397	1.1320		
	Not Under Glycaemic Control	> 6.5 (group A2)	67	0.5840	0.6401	0.761	0.306

As per Table 2 and Figure 8, the mean platelet distribution width in Group A1 (diabetics under glycaemic, HbA1C ≤ 6.5) was 10.973 ± 2.032 fl and in Group A2 (Diabetics not under glycaemic control, HbA1C > 6.5) was 13.097 ± 1.873 fl. Though 33 patients (100%) of Group A1 and 66 patients (99%) of Group A2 had normal platelet distribution width, there was a statistically significant difference of mean platelet distribution width between Group A1 and Group A2 ($P < 0.0001$).

Discussion

Diabetes Mellitus (DM) refers to a group of common metabolic disorders which share the phenotype of hyperglycaemia. The aetiology of DM includes reduced insulin secretion and decreased glucose utilization. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems which impose a tremendous burden on the individual with DM and on the health care system [2].

The common feature in all the complications of diabetes is vasculopathy both “micro” and “macro”, characterized by progressive narrowing of lumen as well as abnormal permeability to proteins [3]. Macro and microvascular disease are currently the principal causes of morbidity and mortality in patients with type I and type 2 DM. Loss of the modulatory role of the endothelium may be an initiating and a critical factor in the development of diabetic vascular disease [4].

In our study, platelet parameters such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Platelet count were compared between diabetic population and normal healthy individuals. Normal platelet count ranges from 1.5 lakhs to 4 lakhs per cubic millimetre of blood. Increased platelet count is called thrombocytosis and decreased count is called thrombocytopenia

MPV is an indicator of the average size and activity of platelets. MPV is known to increase when there is platelet activation and change from quiescent disks to swollen spheres. Increased MPV in diabetes is due to hyperglycaemia induced osmotic swelling of platelets or due to insulin effect which forces megakaryocytes to produce larger platelets. The large platelets are younger, more reactive and aggregable. Hence, they hold denser granules, secrete more amount of serotonin and β -thromboglobulin, thromboxane A2 and are found to be more 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.

High MPV has also been found to be an emerging independent risk factor for myocardial infarction, cerebral ischaemia and transient ischaemic attack. Thus, DM has been considered as a “prothrombotic state” with increased platelet reactivity. Elevated Platelet distribution width (PDW) is an indication of variation platelet size, and also a marker of platelet activation of active platelet release. In diabetic patients, platelets are hyperactive and these activated platelets differ in size from non-activated ones mainly due to a change from a discoid to a spherical shape and pseudopodia formation, leading to a change in the PDW. In a study by Dalamaga et al. [17] titled platelet markers correlate with glycaemic indices in diabetic patients reported that diabetic patients had increased PDW value when compared with non-diabetic healthy individuals.

Diabetic patients have evidence of increased inflammation and oxidative stress compared to healthy individuals. There is an over production of reactive oxygen species, nitrogen species and potent radicals such as hydrogen peroxide, superoxide anion, which directly cause activation of platelets.

In our study, mean platelet volume values were higher in diabetic patients as compared to non-diabetic population and there was a statistically significant difference between diabetic and non-diabetic population. ($P < 0.0001$). Same observation were found in the study conducted by Buch et al. [5], Bhattacharjee et al [6], Yilmaz et al. [7], Dermatas et al. [8], Gupta AV et al. [9] by Hekimsoy et al. [10], Dermirtunc et al. [11], Zuberi et al. [12], Ates et al. [13], Chang et al. [14], Jindal et al. [15] which revealed that Mean Platelet Volume was significantly raised in diabetics than non-diabetic healthy individuals. But in the study done by Akinbami Akinsegum et al. [16], Mean Platelet Volume was not significantly different between diabetics and non-diabetic population which was against our observation. In this study, Mean Platelet Distribution Width levels were higher in diabetic population when compared with non-diabetic patients. There was a statistically significant difference between diabetic population and nondiabetic healthy controls. This study supported the study conducted by Dalamaga et al. [17], Alhadas et al. [18], Jabeen et al. [19], Buch et al. [5]. Discordant results were found in the study done by Citirik et al. [20], Gupta AV et al. [9].

In our study the Mean Platelet Count in diabetic population was $2.60 \pm 0.85 \times 10^9/L$ and in non-diabetic control population was $2.77 \pm 0.097 \times 10^9/L$. There was no statistically significant difference of Platelet Count between diabetic and non-diabetic healthy individuals ($p = 0.207$). Similar results were found in the study done by Buchet et al. [5], Yilmaz et al. [7], Jabeen et al. [15], Kodiattee et al. [21]. On the other hand study done by Dermataset al. [22] revealed that there was a statistically significant difference of platelet count between diabetic and non-diabetic healthy individuals.

In this study, the Mean Platelet Volume was significantly elevated in diabetic patients with HbA1c level $> 6.5\%$ when compared with the diabetic patients whose HbA1c levels $\leq 6.5\%$. There was a statistically significant difference between them. ($P < 0.0001$). Similar results were also seen in the study done by Bhattacharjee et al. [4], Dermatas et al. [6], Kodiatte et al. [20]. There also a significant difference of mean Platelet Distribution Width between the diabetic population under glycaemic control (HbA1C ≤ 6.5) and

not under glycaemic control (HbA1C > 6.5) in our study. Similar results were seen in the study conducted by Dermitas et al. [22], Bhattacharjee et al. [6]. Furthermore there was no significant difference found in platelet count between the diabetics under glycaemic control (HbA1C \leq 6.5) and not under glycaemic control regulated (HbA1C > 6.5) in our study.

Conclusion

Platelet parameters such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Platelet count were compared between 100 diabetic cases and 100 non diabetic healthy controls. It was found that Mean Platelet Volume and Platelet Distribution Width were significantly increased in diabetic patients than non-diabetic healthy individuals. MPV and PDW were also higher in diabetic patients who were not under glycaemic control (HbA1C \leq 6.5) than the diabetic population who were under glycaemic control (HbA1C > 6.5).

Mean Platelet Volume and platelet distribution width are indicators of platelet activity. Increased MPV and PDW are associated with increased risk of thrombotic events leading to vascular complications of diabetes mellitus. Our study indicates that Mean Platelet Volume (MPV) and Platelet Distribution Width were increased in diabetic patients and they can be used as a marker in predicting the vascular complications in diabetes mellitus.

Conflict of Interest

There is no conflict of interest.

Acknowledgment

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