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A Comparative Study of Mean Platelet Volume in Diabetic Population With and Without Vascular Complication

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Abstract

Diabetes mellitus leads to long-term complications involving multiple organs and systems of the human body. Among the list of complications, a relatively vascular complication increases the morbidity of the condition. Patients with diabetes mellitus are influenced by various factors like hyperglycaemic state, insulin resistance, oxidative stress, and metabolic condition like obesity, and all the mentioned conditions also present with platelet hyperactivity. Mean platelet volume (MPV) can be used as one of the laboratory parameters to know the function and activation of the platelets, which reflects the vascular profile of the patient. So, the present study compares the values of mean platelet volume among the diabetic groups to determine the relation between the vascular complication and the mean platelet volume. This study was conducted with 90 participants, who were divided into three groups. Group A is non-diabetics, group B is type 2 Diabetics, and Group C is type 2 Diabetics with vascular complications and MPV. On analyzing the statistical mean value of mean platelet volume, group B's (type 2 diabetics) value was higher than group A's (non-diabetics) and statistically significant with a p – value of 0.001. Similarly, the mean value of group C (type 2 diabetes with complications) was higher than group B (type 2 diabetics) and statistically significant with a p – value of 0.049 in the diabetics with and without vascular complications. On comparing the MPV of different study groups, the MPV is higher in the diabetic group with complicatiosn compared with the diabetics without complications.

Keywords

Mean Platelet Volume, Type II Diabetes Mellitus, Vascular Complication.

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INTRODUCTION

Diabetes is a comprehensive health burden which is worldwide. Micro- and microvascular complications are common in long term diabetic cases and these complications can involve other systems of the human body (1,2). Diabetes mellitus is one of the most common conditions that is prevalent but undetected in many cases. Most of the cases are incidental findings during the routine investigation of other conditions. Certain cases can present with macrovascular changes like atherosclerotic disease or microvascular changes like retinopathy, neuropathy, and nephropathy even during the time of detection of a new diabetic case (3). Vascular complications from diabetes mellitus are caused by numerous factors, including transformation in the growth factors involving the endothelium of the blood vessels, advanced glycation products, chronic inflammation, altered fibrinolytic ability, and increased platelet aggregation and activation (4). Endothelial dysfunctions and vascular lesions are prominent features of the complications of sustained hyperglycemia. The state of hyperglycemia causes microvascular changes and macro vasculopathy in diabetic patients.

Platelets is a type of blood cell that has a major role in homeostatis, i.e. the spontaneous arrest of bleeding. Platelets take part in temporary homeostatic plug formation in response to stimuli from the site of the endothelial defect by changing their shape, adhering to the sub endothelial surface, and aggregating and releasing their intracellular contents to form a platelet plug. Platelets also augment the process of permanent clot formation by coordinating with activated clotting factors (5).

The normal vasomotion of the blood and its components in the blood vessels determine the normal blood flow and the thromboresistance. There is always an interaction between the blood cells and the endothelial lining of the blood vessels. These interactions initiate the atheromatous plaque formation and also the response from the blood components to the rupture of the plaque. The interaction of the platelet with the plaque rupture site results in the coagulation cascade, which eventually results in vascular events. In a chronic, ongoing inflammatory state, the release of pro-inflammatory cytokines like interleukin 6 is associated with thrombopoietin generation. Interleukin released produces effects on platelet precursor megakaryocyte like increase in megakaryocytic cytoplasmic volume and ploidy of nuclei, which in turn result in the a in large number of platelets (6).

The pathophysiological state of diabetes mellitus with vascular disease can be analyzed by various factors, like the state of hyperglycemia in the patient, oxidative stress, the relation of insulin resistance with atherosclerosis, microRNA, and thrombosis.

In all the above-mentioned states, platelet hyperactivity is of major relevance (3). Hyperglycemia leads to a pro-thrombotic state in diabetic patients. The platelet adhesion is increased by the glycation of the surface proteins of the platelet. Both chronic and acute states of hyperglycemia trigger platelet activation.

Insulin resistance is another prime factor in the development of type 2 diabetes mellitus. Pancreatic beta cells are responsible for the production of compensatory insulin in pre-diabetic cases, eventually leads to a decrease in the pancreatic beta cell mass due to its apoptosis, resulting in insulin deficiency. Insulin controls platelet action by binding to the insulin receptor on the surface of the platelets. The interaction of insulin and platelets also affects plasminogen activator secretion, insulin receptor substrate 1, and insulin-like growth factor -1 (IGF-1) (7).

Increased oxidative stress has been reported in type 2 diabetes mellitus. In these cases, platelet activation and platelet aggregation are due to increased platelet calcium concentration. Oxidative stress causes platelet hyperactivity are due to increased production of F2 isoprostane, signaling platelet reception, and decreased activity of e-NOS (8). Obesity is one of the major metabolic conditions that exacerbates insulin resistance. Obesity presents with an increased platelet count, increased platelet volume and also affects other platelet indices indices, indicating increased platelet adhesion and activation (9).

Activation of the metabolic changes in diabetic patients further leads to vasoconstriction and leads to thrombus formation involving the platelets. All vascular complications are initiated by the inflammatory and thrombotic changes that occur in the endothelium of the vascular structure. When the vascular complication begins, the equilibrium of the vasoconstriction and vasodilation, along with the anti coagulating system is disturbed. The impaired endogenous inhibition of the platelets increases the susceptibility to the platelet activation, and so the altered endothelium becomes a medium for adhesion molecules and platelet agonists. Long-standing cases of diabetes show changes in the morphology and adhering quality of the platelets. Increased platelet activity can be witnessed in acute hyperglycemic states even in a normal individual without diabetes mellitus. All these factors make it necessary to understand the mechanism of endothelium and platelet dysfunction, which are involved in the pathophysiology of diabetes mellitus with vascular complications (10).

Mean platelet volume is a laboratory parameter that quantifies the volume of the platelet and infers its function and activation (11). Morphological variation in the platelet size is associated with differences in the amount of the production of serotonin,

β-thromboglobulin, and procoagulants. Thus, mean platelet volume could be an economical laboratory parameter that reflects the state of thrombogenesis in diabetic patients. Evidence from previous literature has shown that the range of MPV is higher in the diabetic population compared to the non-diabetic population (12).

Including mean platelet volume and other platelet activity in the routine investigations can assess the burden of the complication to diabetics. Since many methods are costly, require specialized equipment, and are time-consuming, these investigations are given less importance in routine assessment methods. Potentially, there are lacunae in the scientific data on the cut-off value, methodology, and procedure, making more interpretation of the results and clinical utility of results even the uncertain. MPV is also found to be higher in various other conditions such as hypertension, cardiovascular diseases, hypercholesterolemia, obesity, and smoking, suggesting a common mechanism and possible comorbid conditions along with diabetes mellitus (13).

The aim of the study is to compare the values of mean platelet volume among the diabetic groups and to determine the relationship between vascular complications and mean platelet volume, with the following objectives: to determine the difference in the mean platelet volume between diabetics and non-diabetics, and to review the difference in the MPV between diabetics with and without complications (established vascular disease).

MATERIALS AND METHODS

This cross-sectional analytical study was conducted after the approval from the institutional ethical committee. With consent, the study was conducted among the patients who attended master health check-ups in a medical college for one month. Patients aged above and 18 were included in the study, except for those with conditions involving blood, liver, bone marrow, chronic systemic inflammatory disorders, any infectious diseases, cancer chemotherapy, patients on antiplatelet therapy, smoking, alcoholism, and pregnancy. A detailed history was elicited from the patients regarding their diabetic profile and the associated complications.

All the participants were examined clinically to screen for the presence of any macro or microvascular complications. Venous blood samples were collected in the hemogram tubes containing sodium fluoride and dipotassium EDTA. Samples were transported to the lab within one hour of collection to minimize variations due to sample aging. The blood samples were used to assess the mean platelet volume (MPV), HbA1C and plasma glucose. MPV was measured by an automatic complete blood count. HbA1C and plasma glucose were

performed to know the diabetic state of the patient. Plasma glucose was measured by the glucose oxidase method in an autoanalyzer. HbA1c was measured by an automated ion-exchange high-performance liquid chromatograph (in a laboratory performed using an NGSP-certified method and DCCT assay standardized) (11).

Following the screening of 150 participants for inclusion and exclusion criteria, a total of 90 participants were included in the study and divided into three groups based on the following criteria:

GROUP A: Non-diabetic controls.

Healthy non-diabetic controls based on their fasting and postprandial blood glucose levels according to the American Diabetic Association Criteria.

GROUP B: Type 2 Diabetes Mellitus without any diabetes-related complications.

Patients diagnosed with Type 2 Diabetes Mellitus according to American Diabetic Association Criteria (14) on oral anti-hyperglycemic drug therapy and without complications related to diabetes.

GROUP C: Type 2 Diabetes Mellitus with complication

Patients diagnosed with Type 2 Diabetes Mellitus based on American Diabetic Association Criteria (14) on oral antihyperglycemic drug therapy and with established complications were analyzed.

Statistical Analysis

Statistical analysis was carried out by using Statistical Package for Social Science (SPSS) 22 with the student's independent sample two-tailed t-test. Values were considered statistically significant when the p value was less than 0.05.

RESULTS

Among the ninety participants of the study group, 58% were male and 42% were female. Statistically, the mean value was calculated between the three groups of study and they were compared. The major parameter compared in the study was the mean platelet volume and the HbA1C among the control and diabetic patients with and without complications.

Mean Platelet Volume

In comparing the mean platelet volume between the diabetic without complication (Group B) and the non-diabetic group (Group A), the MPV value was higher in the diabetic (Group B) and statistically significant (Table 1). On comparing the mean platelet volume of diabetics with complications (Group C) and diabetics without complications (Group B), the MPV value was higher in diabetics with complications (group C) and statistically significant (Table 1 and Figure 1).

Table 1. Comparison of MPV Between Diabetics and Non-Diabetics

	Group	Mean	Std. Deviation	p-value
MPV (fL)	Non-Diabetic	7.5267	0.91196	0.001*
	Diabetic	8.5033	1.20444	
MPV (fL)	Diabetic without complication	8.5033	1.20444	0.049*
	Diabetic with complication	9.1970	1.45780	

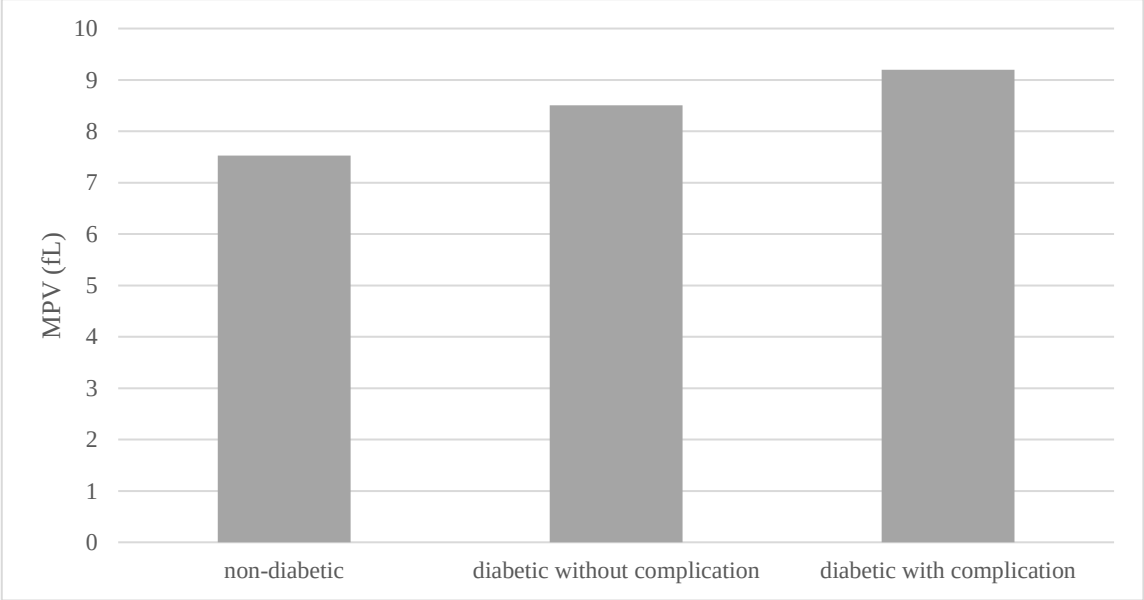

Figure 1. Comparison of MPV Among Diabetics with and Without Complication and Non-Diabetics

DISCUSSION

Diabetes is a major health burden for the world. It is a metabolic disorder that leads to various long-term vascular complications, such as retinopathy, nephropathy, neuropathy, and cardiovascular and cerebrovascular diseases (15). Various factors, such as the state of hyperglycemia, insulin resistance, oxidative stress, and metabolic conditions like obesity are responsible for the pathophysiological state of the condition and have relevance with platelet hyperactivity. Complications are higher among diabetics with poor glycemic control, longer duration of diabetes, and associated comorbidities such as obesity and hypertension, which increase the risk of mortality in diabetics (16). Platelets plays an important physiological role in primary hemostasis (17). They are the main component of the blood, which maintains the integrity of the blood's homeostasis. The size of the platelet determines their thrombogenic nature, in which the large platelets have an increased number of dense granules when compared with the smaller platelets. In the

diabetic population, increased platelets aggregation can cause both micro-and macrovascular complications. Along with diabetes mellitus, other illnesses like hypertension, cardiovascular diseases, hypercholesterolemia, obesity, and smoking are also associated wuth higher MPC levels, pointing to a potential shared cause. The MPV can be used to measure how large highly reactive and pleasant pletelets are. Diabetes results in the deregulation of signaling pathways that can lead to platelet hyperactivity and thrombosis, which can cause vascular lesions to develop and progress (18). In this study, we compared the platelet activity in diabetics and non-diabetics using the mean platelet volume.

Our present study has shown an increased value of mean platelet volume in the diabetic group compared to the non-diabetic group, and similar results have been established in the previous studies, which also show significance in the value of MPV and platelet distribution width in a similar comparison (19,20). A study was conducted in the North Indian Population, in which the case of diabetes and the control group were categorized with the fasting and based on the American diabetes association. The diabetic patients were also examined for vascular complications and categorized based on them. Similar to our present study, the mean platelet volume and other platelet indices were higher in the diabetics with or without complications. However, upon analyzing and comparing the platelet indices between the diabetics with and without complications,the values of platelet distribution width showed significant variability, but the MPV was normal (19). Contrary to the aforementioned-results, another study done to compare the platelet indices in diabetic patients with and without vascular complication showed complications an increased MPV value in diabetics with vascular complications, similar to our study results. In the same study, the other platelet indices values of the diabetic group were higher than those of the control group (20). Few studies have shown a decrease in the platelet count among diabetics when compared to non-diabetics, suggesting that factors such as short survival times, impaired production, and increased turnover of platelest in diabetic patients may be at play. However, the MPV appears to be higher in their studies as well (21).

In another study done to assess the correlation between the mean platelet volume and diabetes, the case and the control groups were divided based on the value of HbA1C. Cases with thrombotic and hematological diseases those and with low hemoglobin counts were excluded. The statistical correlation of the study showed that the mean platelet count in the diabetes was significantly lower than the control group. However, a significant correlation was

established between the mean platelet volume values in both groups.

In another study, the prognosis of diabetes mellitus was assessed by the effectiveness of the platelet parameter analysis. Even though the values of platelet indices were higher in diabetic patients with complications, they were not statistically significant (22).

Most of the studies are done in cases of diabetics with vascular complications, since this leads to increased morbidity and mortality in these cases. Few studies have also concentrated on the involvement in the initiation of the atherosclerotic process, as it is of rising interest. Therefore, the status of platelets was studied in both Type 1 and Type 2 diabetics based on arachidonic acid metabolism. In the aforementioned study, increased platelet aggregation was detected even in a diabetic patient who did not suffer from vascular complications and presented with increased basal arachidonic acid metabolism. This can later stages contribute to increasing the risk of occurrence of vascular complications, both at the micro and the macro level, in diabetic patients (23).

Similar to the previous studies which compared the mean platelet volume between diabetics and the diabetics with retinopathy (a vascular complication). Our present study has also shown an increased mean platelet volume in the diabetic with complication group compared to the diabetic group. This suggests a role for platelets in the vasculopathy of diabetics. The statistical correlation between the HbA1C and the MPV has also been studied previously, and a similar positive correlation has been observed (15,24).

A study was conducted to investigate the relationship between glycaemic control and platelet activity in type 2 diabetes mellitus. In the study, two groups were assessed based on HbA1C. Cases with > 7% HbA1C were put under the glycaemic control measures for 3 months and weekly assessments were done for those cases. At the end of 3 months, 80 % of the cases showed good glycaemic control and also a significant decrease in the level of the mean platelet volume, which supports the result that increased HbA1C concentration increases the mean platelet volume (15).

A cohort study was conducted to estimate the correlation between platelet indices and Type 1 and Type 2 diabetes mellitus. A large sample group with both types of diabetes was taken and the platelet indices were studied under normal and glucose-controlled conditions. In this study, the platelet mass was higher and the MPV value was lower in both type – 1 and type – 2 diabetes when compared with the control group. The assessment of short-term glucose control did not have any effect on the values of the platelet indices (25).

A similar study demonstrated the correlation between the platelet indices and

diabetes with and without complications. They also studied the demographic details of the study group and the statistical influence on the different cases with various complications. 40% of the cases presented with cardiovascular complications, 30% with diabetic foot, and 14% had multiple complications, including retinopathy, neuropathy, and nephropathy. Cases with complications showed increased values of platelet indices in diabetics with complications similar to our study (26).

A similar study was conducted, excluding patients with all possible vascular co-morbid conditions. In the Department of Ophthalmology, fundoscopic examination was done and the degree of retinopathy was assessed. MPV values were studied for both the case and the control groups. The results projected that the patients with diabetic retinopathy at a proliferative state showed significantly higher values of MPV than normal, healthy individuals like our findings (24). Studies conclude that glycemic control decreases the hyperactivity of the platelet function, thus decreasing diabetic vascular complications. The results regarding the duration of diabetes and MPV are similar to a few studies, but are contradictory to others. It is necessary to rule out qualitative platelet disorder to confirm the findings, which is the limitation of the present study.

CONCLUSIONS

Our work leads us to the conclusion that diabetics with vascular problems have greater mean platelet volumes. Comparing the mean platelet volumes of the various study groups, the diabetes group with complications has a higher mean platelet volume than the diabetics without complications. Our findings suggest that an increase in platelet size may be one of the triggers for atherosclerosis linked to diabetes macrovascular and microvascular problems. These findings require confirmation by larger-scale research. As a result, mean platelet volume can be utilized to predict the development of vascular problems in people with diabetes.In this study, we compared the platelet activity in diabetics and non-diabetics using the mean platelet volume.

AUTHOR CONTRIBUTIONS

Ajantha Swamy Vasudhevan: conceptualization, methodology and investigation. Dhivya Mohan Sumathi: original draft writing and reviewing and data curation, Ashwath Kumar & Rajabalaji: investigation and data collection.

CONFLICT OF INTEREST

The author declars there is no conflict of interest.

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