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Original Research Article

Role of mean platelet volume in patients with type 2 diabetes mellitus

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ABSTRACT

Background: In type 2 diabetes mellitus, increased platelet activity is crucial for the emergence of vascular complications. Mean platelet volume (MPV), an indicator of enhanced platelet activity, may be helpful in identifying the thromboembolic events that lead to these vascular complications. This study aims to assess MPV in Type 2 Diabetes patients and investigate the relationship between MPV and glycaemic and diabetic complications.

Materials and Methods: A comparative cross-sectional study was carried out on 266 subjects (133 diabetic patients and 133 nondiabetic controls) at B.P Koirala Institute of Health Sciences for a period of one year. MPV was analyzed in both the groups and the potential association of MPV with diabetic complications and glycaemic parameters was evaluated. Statistical analysis was carried out with Student t-test and Pearson Correlation Coefficient.

Results: The results of the study showed that diabetics' MPV was considerably higher than that of non-diabetic controls (10.07 + 1.41 vs. 7.47 + 0.60 fl, P0.001) and that diabetic patients who had complications had significantly higher MPV than those who did not (10.61 + 1.35 vs. 9.37 + 1.15 fl, P0.001). Retinopathy (p=0.004), nephropathy (p=0.001), and Peripheral artery disease (p=0.03) were diabetes complications with significantly increased MPV. With regard to HbA1C, FBS levels, and the duration of diabetes, MPV demonstrated a statistically significant positive connection (p0.001 and positive r-value).

Conclusion: MPV is a cost-effective tool in the early detection of vascular complications in diabetes and hence proves to be a promising indicator in preventing vascular complications.

1. Introduction

One of the platelet indices used by a hematology analyzer to quantify the size of platelets and, consequently, their activity, is known as mean platelet volume (MPV).[1] Patients with Type 2 Diabetes Mellitus are more likely to experience micro-vascular and macro-vascular problems.[2]

Proangiogenic factors including serotonin and thromboxane A2 are released in greater quantities by large activated platelets than by smaller ones.[3] Hyperglycemia, insulin resistance, oxidative stress, hyperlipidemia, and other metabolic disorders all play a significant part in the onset of endothelial damage and excessive platelet activation. Large activated platelets stick to the damaged endothelial cells and aggregate there because of reduced sensitivity of the platelets to nitric oxide, increased synthesis of von Willebrand factors by the damaged endothelial cells, and elevated levels of advanced glycation end products. This leads to thrombus formation and microcapillary embolization resulting in the development of vascular lesions.[4] It implies a relationship between platelet activity

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and vascular damage in diabetes patients, the primary factor causing morbidity and even fatality in this condition.[4]

In the present study, we compared MPV in Type 2 Diabetes patients with non-diabetic controls, assessed the association between MPV and vascular problems in diabetics, and determined the correlation between MPV and the duration of diabetes, HbA1C, and fasting blood sugar.

2. Materials and Methods

We performed a comparative cross-sectional study after getting ethical clearance (IRC/1671/019) in the Hematopathology Laboratory at B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan for a period of one year (March 2020 to February 2021). Non-purposive sampling technique was used. Sample size calculation was done by using a standard formula based on the normal distribution for comparing two mean sections. The subjects were recruited from the Out-patient Department, Department of Medicine, BPKIHS and then they were separated into two categories: 1) Diagnosed cases of type 2 Diabetes Mellitus and 2) Age and Sex matched controls (individuals who neither have any symptoms and laboratory findings suggestive of diabetes nor have any known vascular complications but had come to the hospital for any other medical reasons). Patients with vascular comorbidities or those receiving anticoagulant medications were not included in our study. Consent was taken from all the participants. All the subjects had undergone complete clinical examinations.

Diabetic patients had undergone investigations such as Fasting blood sugar, HbA1C, and Complete Blood Count (incl. MPV) whereas Control groups had undergone only Complete Blood Count (incl. MPV). However, detailed history was taken from these controls. Only those patients were included as control that had no signs and symptoms or any recent investigation reports suggestive of diabetes or any vascular complications were. These hematological and Biochemical analyses were performed in the respective laboratories of BPKIHS.

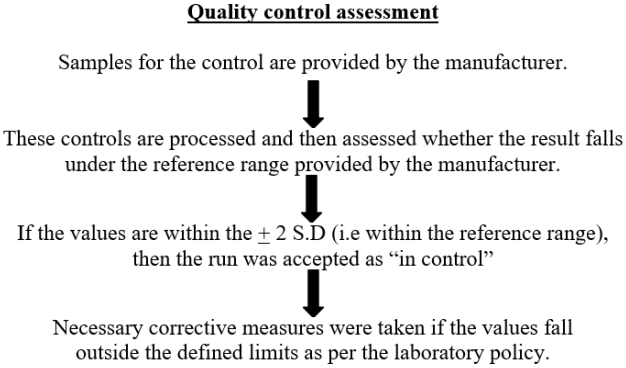
All the diabetic patients were examined for any associated microvascular complications related to the kidney, eyes, and neurons. Similarly, these patients were also examined for macrovascular complications such as Coronary artery disease (CAD), Peripheral arterial disease, and Diabetic foot.

These complications were evaluated and confirmed by the clinicians of respective disciplines for example Diabetic retinopathy was evaluated by an Ophthalmologist. We collected that information by inspecting the medical history (OPD cards, investigation reports) of the patients. Based on the presence or absence of these complications, diabetic patients were divided into two groups: One with complications and another without complications.

To evaluate any association between glycaemic control and MPV, the diabetic subjects were segregated into two categories based on their HbA1C levels: One with HbA1C level <7% and another group with HbA1C level >7%. This cut-off point was selected because the reasonable HbA1C goal in adults according to American Diabetes Association 2019 criteria is <7.[5]

To determine the effects of the duration of diabetes on Mean platelet volume, the diabetic subjects were divided into two groups: 1) One with the duration of diabetes <5 years and another group with the duration of diabetes>5 years.

Under aseptic conditions, two milliliters of whole blood were withdrawn in EDTA vacutainer for Mean Platelet Volume, HbA1C, and five milliliters of whole blood were withdrawn in a plain vacutainer for FBS. Samples were collected from the subjects after giving information about the study and obtaining written consent from the participant. Serum was separated by centrifuging (Remi research centrifuge model R-23, ISO 9001:2000 certified) at 3000 rpm for 12 to 15 minutes at approximately 25°C. All the tests were performed within a few hours of the sample collection. Complete blood count including MPV was analyzed by using BENESPHERA 5-part Hematology Analyzer H51. Biochemical parameters (FBS, HbA1C) were measured by using Cobas c311 Roche-Hitachi Chemistry Auto-Analyzer.



The collected data was entered in Microsoft Office Excel Software 2010. Data analysis was done by using SPSS 20. Mean and Standard Deviation were calculated and along with it graphical and tabular presentations were made. Association between MPV and different variables was assessed using Independent Student T-test and then P value was estimated. Similarly, Pearson's Coefficient of Correlation (r-value) was calculated to establish the correlation between MPV and Duration of diabetes, HbA1C, and FBS. The P-value of less than 0.05 was considered as significant association whereas a positive value of "r" suggested a positive correlation.

3. Results

Two hundred and sixty-six (266) subjects had participated in our study among which one hundred and thirty-three (133) were known cases of type 2 diabetes mellitus and 133 were age and gender-matched controls. Age and gender distribution are depicted in Figures 1 and 2. The diabetic group was subdivided on the basis of the presence or absence of vascular complications, duration, and HbA1C levels. Comparable to the global trend of early diabetes going unnoticed and delay in hospital visits of Type 2 Diabetics, we too have noticed a majority of diabetics in our study presented with complications (56%), with longer duration of diabetes (84%) and with higher HbA1C level (80%), suggesting poor glycaemic control. Among diabetics with complications, patients were also divided based on different types of microvascular and macrovascular complications. Diabetic nephropathy (N=28) was the most common microvascular complication followed by retinopathy (N=20) and neuropathy (N=10) and Coronary artery disease (N=22) was the most common macrovascular complication followed by Peripheral artery disease (N=6) and Diabetic foot (N=2) in our study.

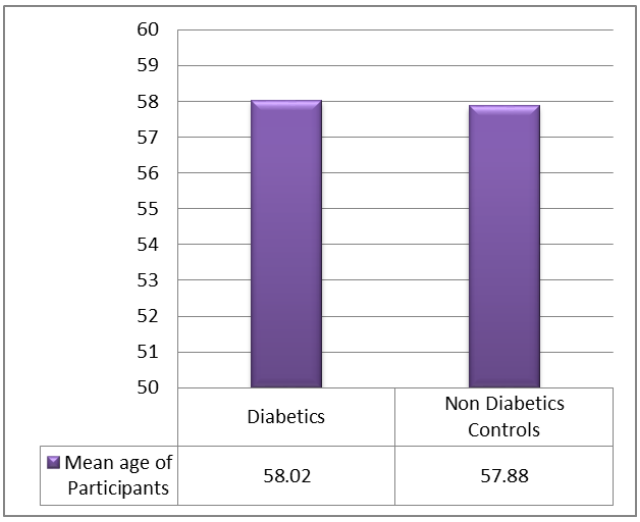


Fig. 1: Age distribution of participants

MPV was significantly raised in the diabetic population in comparison to controls. Similarly, we also observed significantly higher MPV among diabetics with vascular complications in comparison to those without vascular complications (Figure 3). Among diabetics with microvascular complications, MPV showed a significant association with Diabetic Nephropathy and Diabetic retinopathy (Figure 4). Similarly, among those with macrovascular complications, MPV showed a significant association with Peripheral Artery Disease (Figure 5). MPV showed significant positive correlation with HbA1C, fasting blood sugar, and duration of diabetes in our study. All three correlations are reflected by their positive "r" values in (Table 1).

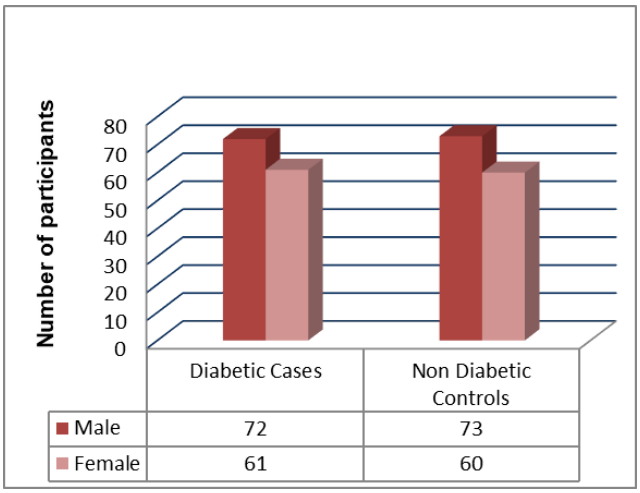


Fig. 2: Gender distribution of participants

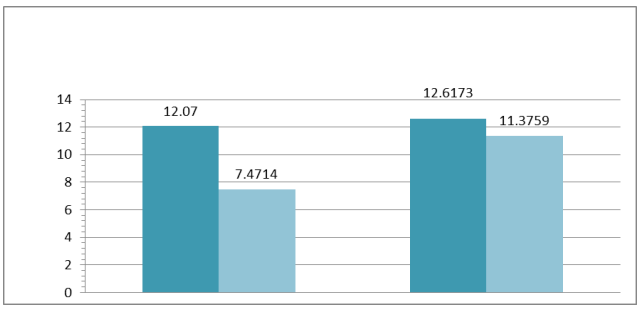


Fig. 3: Comparison of mean platelet volume between diabetic patients & non-diabetic controls and between diabetic patients with & without complication

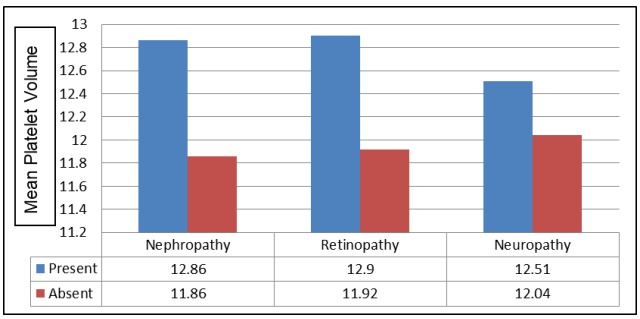


Fig. 4: Comparison of mean platelet volume among diabetic patients with microvascular complication

4. Discussion

Type II Diabetes Mellitus is a chronic metabolic disorder characterized by hyperglycemia and metabolic

Table 1: Correlation of MPV with duration of diabetes, HbA1C & FBS

		Duration of Diabetes (years)	Mean Platelet Volume	Fasting Blood Sugar	HbA1C
Mean Platelet Volume	Pearson Correlation	.389**	1	.486**	.578**
	Sig. (2-tailed)	.000		.000	.000
	N	133	133	133	133

**. Correlation is significant at the 0.01 level (2-tailed).

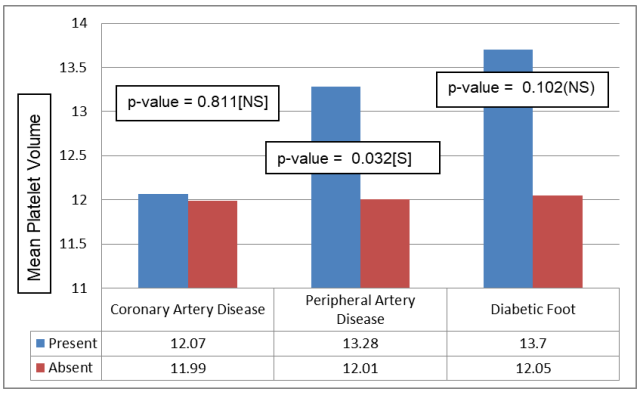


Fig. 5: Comparison of mean platelet volume among diabetic patients with macrovascular complication

dysregulation.[6] Various mechanisms have been proposed to explain how the metabolic abnormalities seen in type 2 diabetes play a vital role in the development of diabetic vascular complications. These include (i) reduced Nitric oxide production by damaged endothelial cells and increased production of endothelin-1 resulting in vasoconstriction, (ii) activating genes involved in raising the production of mediators linked to atherogenesis, (iii) decreased collagen production resulting in formation of unstable plaque and (iv) altered platelet function promoting thrombus formation.[7] Normally insulin prevents thrombus formation by preventing platelet-collagen interaction. Thus, insulin resistance seen in patients with type 2 diabetes results in increased thromboembolic activity leading to development of vascular complications.[8] The mean volume of platelets determines the average platelet size, allowing for the detection of large aggregable platelets that participate in thrombus formation.[3]

When compared to non-diabetic controls, MPV was significantly increased (p-value less than 0.001) in diabetic individuals (12.0759 + 1.4131 vs 7.4714 + 0.6035) in our study. This was in agreement with the majority of studies carried out as ours.[3,6,9–11] This indicates that these large hyperactive platelets are formed due to chronic hyperglycemia. In one study, hyperglycemia has been shown to reduce membrane fluidity and promote platelet activation by increasing the non–enzymatic glycation of proteins on the platelet surface. Persistent hyperglycemia encourages glucose to enter platelets, which are ultimately used for the synthesis of Glycogen in platelets and also results in increased MPV.[12] There have been few studies[9,13] in which mean MPV in diabetic patients was not significantly different compared to non-diabetic controls, contradicting our findings. In our study, compared to Diabetes patients without complications, MPV was significantly raised in those with complications (12.6173 + 1.35909 vs 11.3759 + 1.15839) with a p-value less than 0.001. Similar findings were also seen in a majority of studies carried out similarly to ours.[10,14–18] This suggests that, in the development of vascular complications, a higher activity of platelets plays an important role. Due to the increased production of thromboxane A2 resulting from procoagulant effects that lead to thrombotic vascular complications, larger platelets are hyperactivity and more aggregable than smaller platelets.[4] This was in contrast with a few studies[3,11] in which no significant difference was observed in MPV between patients with diabetic complications and without complications. In our study, we also found significantly increased MPV in patients with diabetic nephropathy which is in concordance with the majority of studies carried out similarly as ours.[19–22] In our study, MPV was significantly higher in patients with diabetic retinopathy. These results were in agreement with various other studies conducted similarly to ours.[6,20–22] The possible reason for the association between MPV and the different microvascular complications such as retinopathy and nephropathy seen in our study is explained by Cakir L et al.[23] According to this study, an altered signalling pathway results in increased platelet activation and aggregation in response to a specific stimulus, leading to thrombus formation and micropapillary embolization with the release of constrictive, oxidative, and mitogenic substances like PDGF and VEGH, that quickens the occurrence of a local vascular lesion such as the neovascularization of the lens in diabetic retinopathies. Despite having a larger MPV in our study, diabetic patients with neuropathy demonstrated statistically negligible increases. This finding was contradicting some studies[14,18] that found significantly high MPV in diabetics with severe neuropathy (NDS more than 6) in comparison to those with NDS less than 6. In our study, we had not divided the neuropathy patients based on NDS. So, there was a possibility that some of our patients have mild neuropathy because of this we did not get significant difference in MPV in patients with diabetic neuropathy.

In our investigation, patients with peripheral artery disease who were diabetic had significantly higher MPV levels. Even while diabetic patients with CAD displayed increased MPV, the increase was statistically insignificant. It was contradicting the other studies.[19,24] Some of the CAD patients included in our study had undergone bypass surgery or PCI. This might have affected the platelet activity resulting in a lowering of MPV as compared to those who had not undergone such intervention. So, though we found an elevated mean MPV in the CAD patients, it was statistically insignificant. In our study, diabetic foot also showed an insignificant rise in MPV which is in contrast to Buch A. et al[25] where they found a significant rise in MPV in patients with diabetic foot as compared to those without diabetic foot. The possible reason for this could be a very less number of participants with diabetic foot in our study, as mostly, they present to Surgery OPD. If we had more patients with diabetic foot, the results could have been different. It was shown that the mean platelet volume and FBS had a significant positive association in our study. Similar results were obtained in other studies conducted as ours.[6,16,20,26] We also found a significant positive correlation between MPV and HbA1C. These results were in concordance with some other studies.[13,16,20–22]

The possible explanation for this could be that diabetic individuals with poor glycaemic control have hyperactive platelets through the glycation of platelet membrane proteins. This leads to early platelet breakdown and enhanced thrombopoiesis, which in turn results in a greater MPV. In one study[27] it was found that the improvement in glycaemic control normalized the MPV values. This indicates the importance of glycaemic control in platelet reactivity. Nevertheless, a small number of studies[28] found no connection between glycaemic variables and MPV.

Our study revealed that between MPV and the duration of diabetes, there was a strong positive association. These results were in agreement with the majority of studies similar to ours.[9,16,21,22] Yeom E et al.,[29] had found that the longer duration of diabetes causes endothelial dysfunction resulting in increased platelet activation and aggregation. This revealed that longer-term diabetic patients may exhibit a higher MPV value. In our study, we had some limitations. We could not do the follow-up of the diabetic cases due to the limited time frame of the thesis. This would have allowed us to compare the reversibility of platelet dysfunction with glycemic management over time and establish a correlation between the two.

5. Conclusion

Statistics in our study showed that variations in mean platelet volume are significantly related to diabetes and its consequences. It is inexpensive, accessible, and straightforward to read, making it a promising marker for spotting thromboembolic events and reducing vascular injury in type 2 diabetes patients. However, to monitor the possibility of reversal of dysfunction in platelets with glycaemic management over time, a study of this type with a bigger sample size and longer duration that includes sample follow-up will be more helpful.

6. Source of Funding

None.

7. Conflict of Interest

None.

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