

Mean platelet volume in impaired fasting glucose subjects and diabetic patients as a risk factor for thrombotic complications.

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Abstract: This study was conducted to compare the MPV in patients with diabetes mellitus (DM), impaired fasting glucose (IFG), and non-diabetic controls and its relation to thrombotic tendency. Large platelets are more thrombogenic and thus put the patient at a higher risk status. Mean platelet volume (MPV) is a determinant of platelet function and increased MPV is associated with increased risk for myocardial infarction, stroke and transient ischemic attacks. This study was conducted at Assiut university hospital, Internal Medicine Department during the year 2012. Confirmed patients with DM, IFG and non-diabetic controls were selected and allocated to respective groups. A total of 60 patients were selected and allocated to three groups of 20 patients each, referred as DM group with thrombotic complications, DM group without thrombotic complications and IFG group. Twenty subjects sex and age matched were included as controls for comparison of MPV, Random blood glucose, platelet counts and MPV and other investigations for thrombotic complications were done. Mean MPV in the DM group with complications was 11.65fl; in DM group without complications was 11.39, in the IFG Group 9.24 fl, and in the non-DM group 8.06 fl. Comparison of MPV values for the three groups showed statistically significant intergroup and intra group differences, with a *P* value of 0.00.

MPV was significantly increased in the IFG group, as compared to the non-DM group, and it increased further when compared to the DM with and without complications.

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1.Introduction

Larger platelets contain more granules and produce greater amounts of vasoactive and prothrombotic factors, such as thromboxane A₂, serotonin and adenosine triphosphate (ATP); they aggregate more rapidly under the stimulus of agonists, such as adenosine diphosphate (ADP), collagen and adrenaline; and finally, they express a greater number of adhesion molecules, such as P-selectin and GpIbIIIa (Lewin *et al.*, 2006).

Mean platelet volume (MPV) is a machine-calculated measurement of the average size of platelets found in blood. The increased platelet activity is emphasized to play a role in the development of vascular complications of this metabolic disorder (Demirtunc *et al.*, 2009).

Platelet volume, a marker of the platelet function and activation, is measured as mean platelet volume (MPV) by hematology analyzers. In fact, increased mean platelet volume values are associated with shortened bleeding time. The belief that platelet size decreases with platelet ageing was wrong. Indeed, platelet age and size are both determinants of platelet activity, but in an independent way. The main platelet parameters seem to be determined in megakaryocytic during platelet production. The increase in MPV is caused by the diabetic state itself, being detectable

from the early phases and persisting for the entire duration of the disease. Positive correlation between HbA_{1c} and MPV, as well as a decrease in MPV values in the patients who achieved improved diabetic control (Hekimsoy *et al.*, 2004). MPV increase might related to the diabetes associated vascular damage, especially considering that, in this disease, platelets are not only larger, but also circulate in an activated state, as demonstrated by the presence of markers of platelet activation, by higher plasma and urinary concentrations of thromboxane A₂ and by an increased spontaneous platelet aggregation (Papanas *et al.*, 2004).

Among diabetic individuals increased platelet aggregation and adhesion are due to increased production of thromboxane A₂ (TXA₂) from arachidonic acid metabolism, and this increases platelet sensitivity. These may play a role not only in the higher risk of developing acute coronary syndrome (ACS) with poorer outcomes observed in DM, but also in the large proportion of diabetes mellitus patients with inadequate response to antiplatelet agents compared to non-diabetic patients. This in itself may contribute to the poorer outcomes observed in diabetic patients despite compliance with the recommended secondary prevention therapy with antiplatelet agents (Eibl *et al.*, 2006).

2. Methods:

This study was conducted at the Assuit university hospitals, Egypt during 2012. Consecutive patients with DM attending the internal medicine department were selected, classified to group with complications and another without.

Diagnosis of DM was established using the criteria of fasting blood glucose (FBG) of ≥ 126 mg/dL on two occasions. Near relatives of diabetic patients were encouraged for blood glucose testing and those with values between 110 mg/dL and 126 mg/dL were allocated to the IFG group and those whose values were < 110 mg/dL were taken as normal subjects and allocated to the non DM group.

Subjects having idiopathic thrombocytopenic purpura and iron deficiency anemia, renal failure, and myocardial infarction or obese patients were excluded. Informed consent was taken from all selected subjects.

3. Results:

A total of 60 patients fulfilling the selection criteria were selected and allocated to three groups of 20 patients each, referred to as DM group with thrombotic complications, DM group without thrombotic complications and IFG group. The three groups were compared to age and sex matched controls. Statistical analysis was performed using the SPSS 21.0 statistical software Package.

- The mean HbA1c of diabetic patients with thrombotic complications was 8.40, in diabetic patients without thrombotic complications was 7.58 and in IFG was 6.18.
- The mean platelet volume of diabetic patients with thrombotic complications, in diabetic patients without thrombotic complications and in IFG were 11.65fl, 11.39fl, 9.24fl respectively which show a significant higher MPV in diabetic patients with or without complications than in normal controls. (Table 1& Fig 1). We demonstrate that mean platelet volume was significantly higher in diabetic patients with complications than in impaired fasting glucose subjects (IFG) (11.39 ± 1.81 vs. 9.24 ± 1.49 $P= 0.001$). (Table 2 & Figure 2).

- Also mean platelet volume was significantly higher in diabetic patients with complications than in impaired fasting glucose subjects (IFG) (11.65 ± 2.13 vs. 9.24 ± 1.49 $P= 0.000$). (Table 2 & Figure 2). There is a significant positive correlation between glycated hemoglobin (HbA1c) in impaired fasting glucose subjects and mean platelet volume in same subjects ($r= 0.368$, $p<0.000$). There is a significant positive correlation between glycated hemoglobin (HbA1c) in diabetic patients with and without complications and mean platelet volume in same patients ($r= 0.4$, $p<0.000$) (Table 3 & Figure 3,4).

Regarding diabetic patients with complications there was significant higher mean platelet volume observed in diabetic patients with ischemic heart disease detected by cardiac enzymes and ischemic changes in ECG than who have not. (12.96 ± 1.23 vs. 9.68 ± 1.59 $P= 0.000$). (Table 4& Figure 5).

4. Discussion:

In our study we stated that mean platelet volume was significantly higher in impaired fasting glucose subjects (IFG), diabetic patients with complications and diabetic patients without complications than in normal controls. Increase in MPV is now emerging as an independent risk factor for thromboembolism, stroke and myocardial infarction (Tavil et al., 2007)

Impaired fasting glucose is probably a frequent glycemic disorder in the general population, and is considered as a pre-diabetic state (Bock et al., 2006). Our data suggest that mean platelet volume is one possible mechanism by which subjects with IFG may be at increased cardio-vascular risk.

We also demonstrate that mean platelet volume was significantly higher in diabetic patients than in impaired fasting glucose subjects.

There was a significant positive correlation between glycated hemoglobin (HbA1c) and mean platelet volume in impaired fasting glucose subjects and diabetic patients with and without complications. In diabetic patients with ischemic heart disease their mean platelet volume was significantly higher than who had not these complications (Khandekar et al., 2006).

Table (1): comparison between mean platelet volume and age in normal controls and impaired fasting glucose, DM patient with and without complications:

	Control group	IFG group		Diabetic patients without complications		Diabetic patients with complications	
	Mean(\pm SD)	Mean(\pm SD)	P value	Mean(\pm SD)	P value	Mean(\pm SD)	P value
MPV	8.06 \pm 0.75	9.24 \pm 1.49	0.011*	11.39 \pm 1.81	0.000**	11.65 \pm 2.13	0.000**

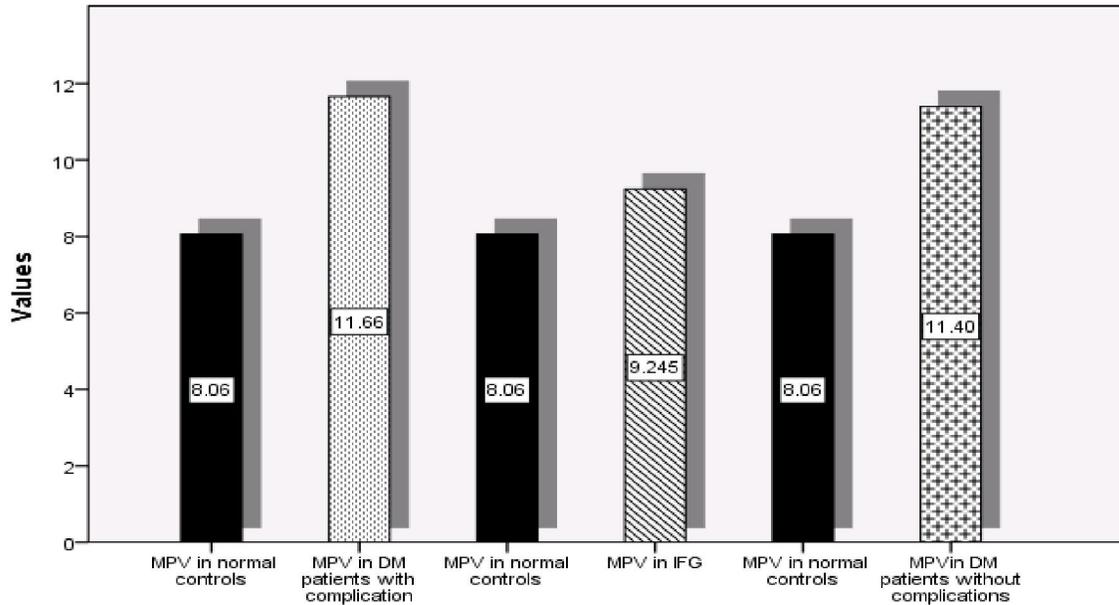


Figure (1): Comparison between MPV in normal controls and IFG, diabetic patient with complications, and diabetic patients without complications.

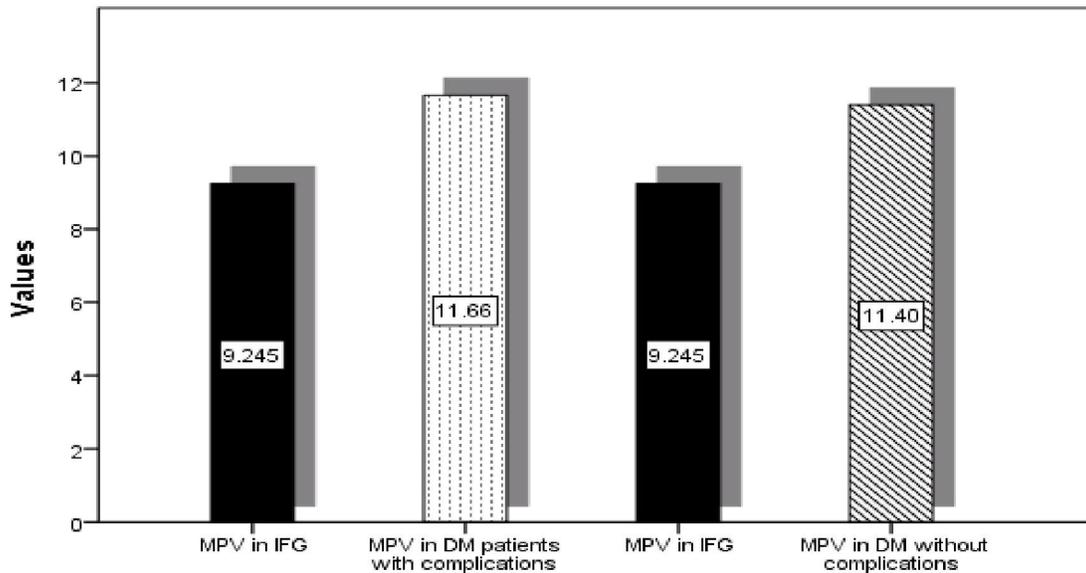


Figure (2): Comparison between MPV in normal controls and IFG, diabetic patient with complications, and diabetic patients without complications.

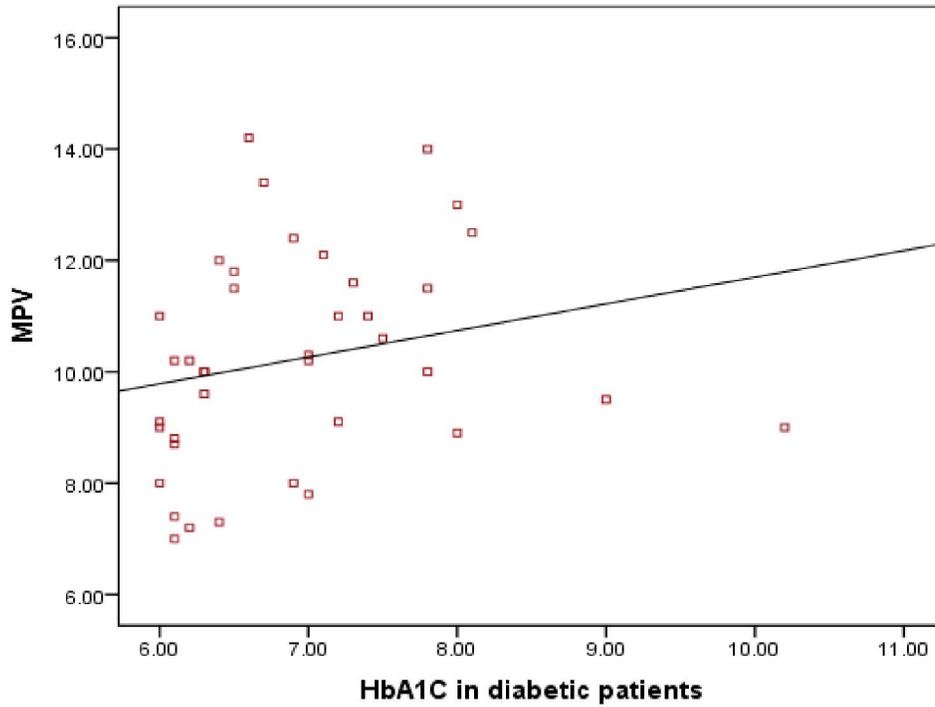


Figure (3): positive correlation between HbA1c and mean platelet volume in diabetic patients ($r= 0.4$, $p <0.000$)

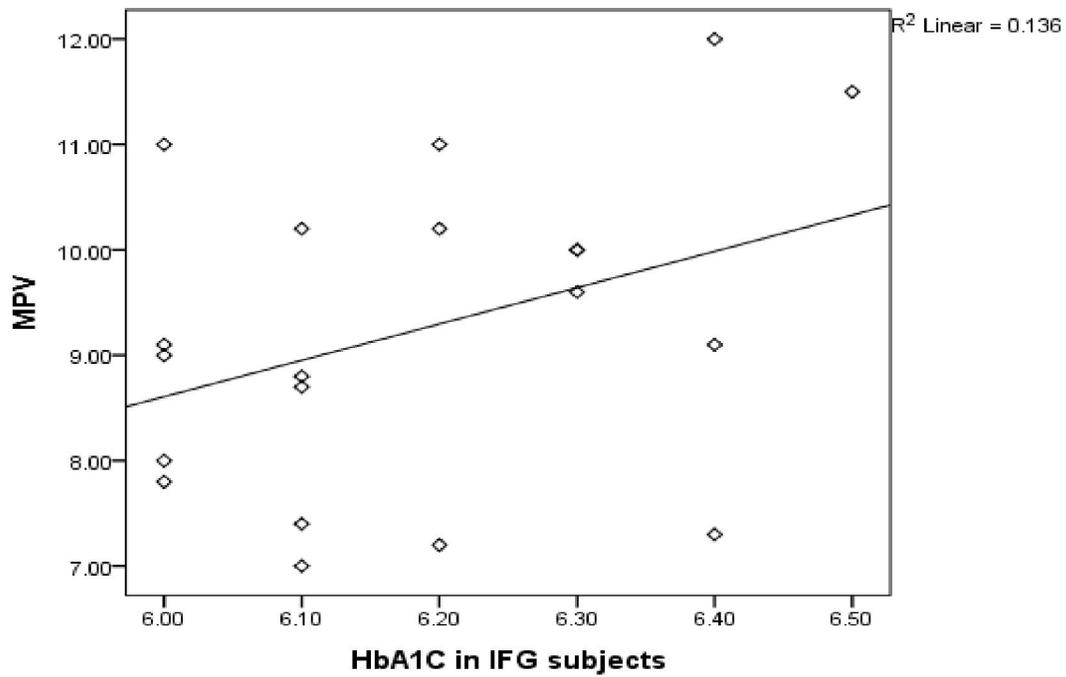


Figure (4): positive correlation between HbA1c and mean platelet volume in impaired fasting glucose subjects ($r=0.36$, $p <0.000$).

Table (2): Comparison between mean platelet volume and age in normal controls and impaired fasting glucose, DM patient with and without complications:

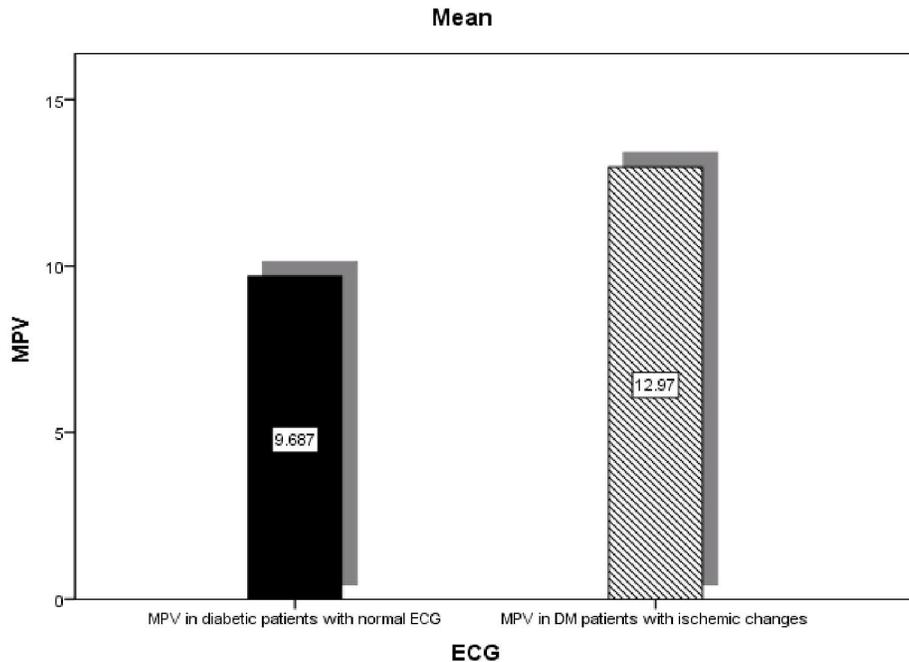
	IFG	Diabetic patients without complications		Diabetic patients with complications	
	Mean(\pm SD)	Mean(\pm SD)	<i>p</i> value	Mean(\pm SD)	<i>p</i> value
MPV	9.24 \pm 1.49	11.39 \pm 1.81	0.001**	11.65 \pm 2.13	0.000**

Table (3): correlation between HbA1c and mean platelet volume in impaired fasting glucose subjects, diabetic patients with and without complications.

HbA1c of	Mean platelet volume	
	R	<i>p</i> -value
Impaired fasting glucose	0.368	<0.000**
Diabetics with and without complications	0.412	<0.000**

Table 4: Comparison between mean platelet volume in diabetic patients with cardiac ischemia by ECG and cardiac biomarkers.

ECG			Cardiac enzymes		
Ischemic changes	Normal		Elevated	Normal	
MPV : Mean(\pm SD)	Mean(\pm SD)	<i>p</i> value	Mean(\pm SD)	Mean(\pm SD)	<i>P</i> value
12.96 \pm 1.23	9.68 \pm 1.59	0.000**	12.81 \pm 1.43	10.23 \pm 2.01	0.004*

**Figure (5): Mean platelet volume is higher in diabetic patients with ischemic changes in ECG than who with normal ECG (*p* <0.000) .****Corresponding author:****Muhamad R. Abdelhameed**

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