



## ARAŞTIRMA/RESEARCH

# Relationship between increased mean platelet volume and glycosylated hemoglobin (HbA1c) in type 2 diabetes mellitus

Tip 2 Diyabet Mellitusda glikozile hemoglobin (HbA1c) ve artış ortalama trombosit hacmi arasındaki ilişki

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### Abstract

**Purpose:** The purpose of the study was to research relationship between mean platelet volume elevation and glycosylated hemoglobin A1c (HbA1c) in Type 2 diabetes mellitus (DM).

**Material and Methods:** The study carried out in 70 patients with type 2 DM and 50 non-diabetic subjects. Diabetic patients were divided into two groups according to their HbA1c levels: DM group1 consisted of patients with HbA1c levels <7% and DM group 2 consisted of patients with HbA1c levels ≥7%.

**Results:** The mean HbA1c levels were as 5.5±0.8, 6.7±0.2 and 9.7±1.9 in the non-diabetic, DM Group 1 and DM Group 2, respectively. MPV was significantly higher in DM Group2 as compared to both non-diabetics and DM Group 1. MPV had a high positive Correlation with HbA1c. MPV was significantly higher in DM Group 2 as compared to both non-diabetics and DM Group 1. MPV had a high positive correlation with HbA1c. It is found that MPV was increased in type 2 DM.

**Conclusion:** This study showed that in diabetes mellitus, MPV is increased and it is indicative of worsening glycemic control. The increased platelet size may be one of the factors in the increased risk of atherosclerosis associated with DM and associated micro and macro vascular complications.

**Key words:** Mean platelet volume, Hemoglobin A1c, diabetes mellitus

### Öz

**Amaç:** Bu çalışmanın amacı tip 2 diabetes mellitus'da (DM) ortalama trombosit hacmi (MPV) yüksekliği ve glikozile hemoglobin A1c (HbA1c) arasındaki ilişkiyi araştırmaktır.

**Gereç ve Yöntem:** Çalışmaya tip 2 DM'li 70 hasta ve 50 non-diyabetik birey alındı. Diyabetik hastalar HbA1c seviyelerine göre iki gruba ayrıldı. DM grup1'e HbA1c < %7 olan hastalar alındı. DM grup 2'ye HbA1c ≥ %7 düzeyleri olan hastalar alınmıştır.

**Bulgular:** Ortalama HbA1c düzeyleri; non-diyabetik grupta 5.5 ± 0.8, DM grup 1'de 6.7 ± 0.2 ve DM grup 2'de 9.7 ± 1.9 olarak saptandı. MPV, hem DM grup ve hem de non-diyabetik bireylerle karşılaştırıldığında DM grup 2'de anlamlı derecede idi. MPV ile HbA1c arasında yüksek pozitif korelasyon vardı MPV, DM grup 2'de non-diyabetik grup ve DM grup 1 ile kıyaslandığında anlamlı olarak yüksek bulundu. MPV'nin tip 2 DM artmış olduğu görülmüştür. Bu çalışma, DM'da artan MPV'nin kötü glikemik kontrole ilişkili olduğunu göstermektedir.

**Tartışma:** Artmış trombosit boyutu DM ile ilişkili aterosklerozun risk faktörlerinden biri olabilir. Bu mikro ve makro vasküler komplikasyonlarla ilişkili bulunabilir. MPV'nin birinci basamak sağlık hizmetlerinde DM'nin progresinin izlemesinde ve vasküler hasarın önlenmesinde basit ve düşük maliyetli bir test olarak kullanılabileceğini düşünüyoruz.

**Anahtar kelimeler:** Ortalama trombosit hacmi, Hemoglobin A1c, Diabetes mellitus.

## INTRODUCTION

Diabetes mellitus (DM) is a great health problem in the world<sup>1,2</sup>. There were 382 million people suffering from diabetes worldwide in 2014. The growing platelet activity is emphasized to play a role in the development of vascular complications of this metabolic disease<sup>3</sup>.

Increase in MPV has been documented in patients with metabolic syndrome, stroke and DM. Diabetic patients have an increased risk of developing micro and macro vascular complications, and platelets may be involved as a causative agent with respect to altered platelet morphology and function. The large platelets contain more dense granules, are more potent than the smaller platelets, and are hence more thrombogenic. Both the size and number of granules in platelets in circulation are under independent hormonal control and don't change during the life span of the platelet. MPV, a determinant of platelet function, is a newly emerging risk factor for atherothrombosis<sup>2</sup>. Many studies have shown that increased MPV is one of the risk factors for myocardial infarction, cerebral ischemia and transient ischemic attacks. Platelet volume, a marker of the platelet function and activation, is measured as MPV by hematology analyzers. Cardiovascular complications are associated with HbA1c and MPV in patients with type 2 DM. The purpose of the study was to research relationship between MPV elevation and HbA1c in Type 2 DM.

## MATERIAL AND METHODS

This is a retrospective study conducted over a period of one year (from January 2014 to January 2015). The study carried out in 70 patients with type 2 DM and 50 non-diabetic subjects. Diagnosis of DM was established using the ADA 2003 criteria of fasting blood glucose (FBG) of  $\geq 126$  mg/dL on two occasions. There was no significant difference among the subgroups for demographic characteristics of study participants, including age, body mass index (BMI) and diabetes duration. Male patients with hemoglobin below 13 gm% and female patients below 12 gm% were excluded from the study because nutritional anemias can be a cause for reactive thrombocytosis and so, increased MPV. Nondiabetic subjects with coronary artery disease and diabetics on antiplatelet drugs such as aspirin and clopidogrel were also excluded. Subjects with any diagnosed malignancy were also excluded.

Diabetic patients were divided into two groups according to their HbA1c levels: DM group 1 consisted of patients with HbA1c levels  $<7\%$  and DM group 2 consisted of patients with HbA1c levels  $\geq 7\%$ .

Statistical evaluation was performed by statistical package for the social sciences (SPSS) version 14 (Chicago, IL) for Windows statistics program using Student's independent sample two-tailed t-test and Pearson correlation test ( $r$  value as the coefficient). Data were expressed as mean  $\pm$  standard deviation. A P value  $<0.05$  was considered statistically significant.

## RESULTS

There were 36 male diabetics and 34 female diabetics in the study (70 in total). There were 26 nondiabetic males and 24 nondiabetic females in the study (50 in total). The mean age of the diabetic population was  $54 \pm 12.14$  years, whereas that of nondiabetic population was  $52.6 \pm 11.2$  years. The mean duration of diabetes was  $6.3 \pm 5.98$  years. The mean BMI in the diabetic group was  $26 \pm 4.08$  kg/m<sup>2</sup>. Nondiabetic group was  $23.95 \pm 4.8$  kg/m<sup>2</sup>. The mean HbA1c levels were as  $5.5 \pm 0.8$ ,  $6.7 \pm 0.2$  and  $9.7 \pm 1.9$  in the non-diabetic, DM Group 1 and DM Group 2, respectively.

MPV was significantly higher ( $8.2 \pm 1.4$  fl) in DM Group 2 as compared to both non-diabetics ( $6.9 \pm 1.6$  fl;  $p < 0.001$ ) and DM Group 1 ( $7.7 \pm 0.9$  fl;  $p = 0.039$ ). MPV had a high positive Pearson Correlation with HbA1c ( $r = 0.393$ ;  $p < 0.001$ ). MPV was significantly higher in DM Group 2 as compared to both non-diabetics and DM Group 1. MPV had a high positive correlation with HbA1c. It is found that MPV was increased in type 2 DM.

## DISCUSSION

DM is a complex syndrome characterized by chronic hyperglycemia responsible for complications affecting the kidneys, peripheral nerves, eyes, macro and micro vascular systems. Diabetes affects more than 300 million patients in the world with significant morbidity and mortality worldwide<sup>4</sup>. It was detected that prevalence of diabetes in Turkish population was reached to 13.7% according to TURDEP II study<sup>5</sup>.

The prevalence of diabetic micro and macro vascular complications is higher in people with poor

glycemic control, longer duration of DM, associated hypertension<sup>6</sup>. A large proportion of patients with Type 2 DM suffer from preventable vascular complications. There is a need to develop risk factor modification interventions to reduce the impact of long-term complications<sup>5</sup>. This leads to increased morbidities in DM. The increased platelet size may be one factor in the increased risk of atherosclerosis associated with diabetes mellitus and associated vascular complications. Hence, MPV could be a helpful prognostic biomarker of cardio-vascular complications in diabetes<sup>5</sup>. MPV could be used as a simple and cost-effective laboratory test in the monitoring of DM and thus helping to curb

morbidities. Study by Kodiatté TA et al., showed that in diabetes mellitus, platelets become more reactive and their mean volume is increased. MPV is an indicator of the average size and activity of platelets. Larger platelets are younger, more aggregable and reactive. So, they contain denser granules, secrete more  $\beta$ -thromboglobulin and serotonin, and produce more thromboxane A<sub>2</sub> than smaller platelets<sup>7,10,11</sup>. All these can produce a pro-coagulant effect and cause thrombotic vascular complications. This suggests a relationship between the platelet function especially MPV and diabetic vascular complications thus indicating changes in MPV reflect the state of thrombogenesis<sup>7,9</sup>.

**Table 1. Clinical and laboratory parameters in study groups**

Parameters	Diabetic group 1	Diabetic group 2	Control group 3
Gender (f/m)	18:17	18:17	26:24
Age (years)	54±12.14	54±12.14	52.6±11.2
BMI (kg/m <sup>2</sup> )	26±4.08	26±4.08	23.95±4.8
Fasting glucose (mg/dl)	130.16±6.6	162.21±5.7	91.12±3.9
HbA1c (%)	6.7±0.2	9.7±1.9	5.5±0.8
Platelet counts	279.6±71.6	282.9±61.9	277.9±59.8
MPV (fl)	7.7±0.9 p=0.039	8.2±1.4 p<0.001	6.9±1.6 p<0.001

There might be small bleeds due to the rupture of atherothrombotic plaques leading to increased platelet recruitment, hyper reactivity, and bone marrow stimulation. High MPV is emerging as a new risk factor for the vascular complications of DM of which atherothrombosis plays a major role<sup>8</sup>. Thus, DM has been considered as a “prothrombotic state” with increased platelet reactivity<sup>12</sup>. Diabetic patients are known to have higher incidence of stroke and myocardial infarction<sup>14</sup>. Another important finding in our study was presence of significantly higher MPV in patients with HbA1c levels >7% as compared to non-diabetic subjects. Therefore, it may be concluded that glycemic control improves platelet activity and function and may prevent or delay possible diabetic vascular complications.

In previous studies, it was shown that MPV increased in diabetic populations<sup>13,14</sup>. In our study, the diabetic group had significantly higher MPV than the nondiabetic subjects. In our study, MPV was significantly higher in diabetics with HbA1c levels  $\geq$  7% than in diabetics with HbA1c levels < 7%. There was also a significant association between HbA1c and MPV. This study showed that in diabetes mellitus, MPV is increased and it is

indicative of worsening glycemic control. The increased platelet size may be one of the factors in the increased risk of atherosclerosis associated with diabetes mellitus and associated micro and macro vascular complications. We found that it increased the MPV increased HbA1c value. We propose that MPV could be used as a simple and cost-effective test to monitor the progression of DM and thereby in preventing vascular injury in primary health care.

Our study showed that in diabetes mellitus, platelets become more reactive and aggregable and their mean volume is increased. Our findings revealed that there is association between MPV and HbA1c. Therefore, MPV may be a potentially prognostic biomarker of cardio-vascular complications in patients with type 2 DM.

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