Iraqi JMS

Published by Al-Nahrain College of Medicine
P-ISSN 1681-6579
E-ISSN 2224-4719
Email: iraqijms@colmed-alnahrain.edu.iq
http://www.colmed-alnahrain.edu.iq
http://www.iraqijms.net
Iraqi JMS 2017; Vol. 15(4)

Remarkable Enhancement of Mean Platelet Volume in Iranian patients with Type 2 Diabetes Mellitus with no Dependence on Hemoglobin A1c Level

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Abstract

Background Diabetes mellitus (DM) is a pandemic disease that leads to several complications. Platelet reactivity plays a major role in diabetes complications. Mean platelet volume (MPV) is a marker of platelet size that is easily determined on routine automated blood counters. Studies have been found that MPV is enhanced in patients with DM.

Objective To assess any relationship between MPV in type 2 Diabetic persons and with glycohemoglobin (HbA1c) level.

Methods The study included a total of 130 subjects who were referred to Samenol Aemme and Mehregan hospitals in Mashhad city, Iran, between April 2013 and November 2014 for a routine check-up. All subjects were divided into two groups as following: Patients with type 2 diabetes group, which comprises 63 subjects and non-diabetic control group, which comprises 57 individuals. Blood sample from each individual was collected after a 12-hour overnight fasting. MPV, HbA1c and fasting blood sugar (FBS) were also monitored.

Results MPV values were found to be 8.7±0.36 fl ($p<0.001$) and 9.8±0.42 fl ($p<0.001$) for control and study groups respectively. FBS values were found to be 95.9±10.3 mg/dl ($p<0.001$) and 202.8±5.1 mg/dl ($p<0.001$) for control and study groups respectively. MPV values were found to be 9.8±0.28 fl and 9.8±0.46 fl ($p=0.813$) for diabetic subgroups with HbA1c <7 and HbA1c ≥7 respectively.

Conclusion The current study showed that: i. MPV was enhanced considerably in patients with DM in contrast to healthy controls. ii. Its increase was not dependent on glycemic control reflected by HbA1c.

Keywords Platelet reactivity, HbA1c measurement, diabetic patients.

Citation Khalili-Hezarjaribi H, Mahdavian S, Mirsadraei M, Farahmand-Bovanlou R, Jahanabad AJ. Remarkable enhancement of mean platelet volume in iranian patients with type 2 diabetes mellitus with no dependence on hemoglobin A1c level. Iraqi JMS. 2017; Vol. 15(4). 377-382. doi: 10.22578/IJMS.15.4.8.

List of abbreviations: DM = Diabetes Mellitus, FBS = Fasting blood glucose, HbA1c = Hemoglobin A1c, MPV = Mean platelet volume

Introduction

Diabetes Mellitus (DM) is an important health problem worldwide and it has been known as the most common endocrine disorder [(1)]. By the year 2025, it is estimated that more than 300 million people worldwide will have DM and by 2030 this would have risen to 552 million [(2-5)]. As the disease progresses, severe diabetic complications will be occurred such as retinopathy, neuropathy, nephropathy, cardiovascular complications and ulceration [(6-8)]. According to previous studies, type 2 DM

and it's related conditions are associated with subclinical inflammation [9-10]. This systemic inflammation may be contributed to platelet reactivity observed in patients with type 2 DM [11]. Platelets play a major role in the normal hemostasis. The large platelets contain more dense granules are more potent than smaller platelets and hence more thrombogenic [12]. Some studies have been shown that acute hyperglycemia results in increased platelet activation [13]. Fasting blood glucose (FBS) and hemoglobin A1c (HbA1c) are parameters widely used to monitor glycometabolic control in patients with DM. HbA1c is a more useful marker to determine mean blood glucose levels over a long-time period [14]. Some studies have been found that levels of FBS and HbA1c are significantly correlated with expression of markers of platelet activation [15-17]. Regarding to the fact that increased morbidity and mortality in type 2 DM are associated with macrovascular (cardiovascular diseases, stroke, and peripheral arterial disease) and microvascular (nephropathy, neuropathy and retinopathy) complications due to platelet dysfunction, the importance of study of platelets is considerable [18-21].

Platelet volume is a marker of platelet activation and function and is measured as mean platelet volume (MPV). MPV is emerging as a new risk factor for vascular complications of DM of which atherothrombosis plays a crucial role [22]. Although several measurements of platelet activity have emerged, many of these measurements are time-consuming, expensive, use a high sample volume, or require specialty training. In contrast, MPV is a marker of platelet size that is easily determined on routine automated blood counters and routinely available at a relatively low cost [23]. MPV was found to be significantly higher in diabetic patients [24,25]. Also, some studies have been shown that in patients with DM, higher MPV correlates with higher HbA1c level [26]. On the other hand, another study has been found that MPV increases independent of HbA1c level [10]. At the present, it is unclear whether MPV is related to FBS, and HbA1c and there is a range of different data about this issue in the literature [30]. Hence, in the current study it was aimed to assess MPV behavior in patients with DM and also evaluate the correlation between HbA1c and MPV in Iranian patients with type 2 DM.

Methods

Study population and sample:

In the current study, a total of 130 subjects were categorized into two groups. One group of diabetic patients and other include non-diabetic controls. All participants under study referred to Samenol Aemme and Mehregan hospitals in Mashhad city, Iran, between April 2013 and November 2014 for a routine check-up. Blood sample from each individual was collected into two types of tubes after a 12-hour overnight fasting as following: non-coagulated blood sample collected in tube containing EDTA, as anticoagulant reagent, was used to assess MPV index and HbA1c Levels and coagulated blood sample in a plain tube without EDTA for evaluation of FBS [27]. The venous blood samples were tested within 30 minutes of collection to minimize variations due to sample aging. MPV was measured using an automatic blood counter system (KX-21 sysmex, Japan).

Also, FBS and HbA1c levels were measured by laboratory standard methods using BT-3000 auto analyzer system, Italy. All obtained data were recorded. Patients with iron deficiency anemia, hypo-hyperthyroidism, congestive heart failure, recent infection were excluded [10]. For the sake of minimizing confounding factors, patients with leukocytosis, anemia or thrombocytopenia were not included as they may affect platelet and erythrocyte size. Patients with known inflammatory conditions such as rheumatoid arthritis, systemic lupus erythematosus, were also excluded [10]. In order to evaluate the correlation between MPV and HbA1c level, then, patients with DM were divided into two groups on the basis of HbA1c

<7 and HbA1c ≥7 and obtained results were recorded [10,26].

Data analysis

Data was assessed by using SPSS program. (SPSS 15.0; SPSS Inc., Chicago, IL, USA). Results expressed as mean±SD. Variables are conducted with either independent samples t test (for normal distributed variables) or Mann-Whitney U test (for abnormal distributed variables). A p value of < 0.05 is considered as statistically significant [10].

Results

The study included a total of 130 subjects who were divided into two groups as following: type 2 diabetic Patients group that comprises 63 subjects (25 males and 38 females) and control group that comprises 57 subjects (٣٢ males and 35 females). Table 1 showed age and gender of both control and study groups. No difference between non-diabetic and diabetic individuals statistically were seen.

Table 1. Demographic characteristics of the diabetic patient and non-diabetic control groups, presented as mean±SD

	Non-diabetic Control Group			Diabetic patients			P value
	Total	Male	Female	Total	Male	Female	
No. of Subjects	67	32	35	63	25	38	0.065
Mean Age	56.91±9.9	56.5±10.2	57.3±9.9	59.41±10.3	58.3±11.8	60.1±9.4	

Figure 1 Compares FBS by autoanalyser and HbA1c blood sugar values between non-diabetic control and type 2 diabetic patient groups and it revealed a statistical significant difference between both groups (p<0.05).

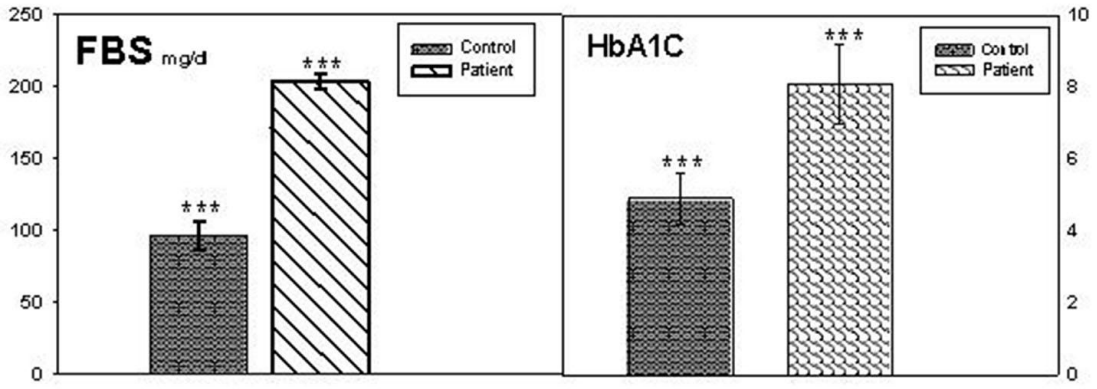

Figure 1. Comparison of FBS and HbA1c blood sugar values between non-diabetic control and type 2 diabetic patients. (p<0.001)

Regarding to the pooled results, FBS and HbA1c values are considerably greater in study groups compared to controls as was expected. This study showed that the MPV was significantly higher in diabetic patients compared to non-diabetic controlled subjects (p<0.001) (Figure 2).

Furthermore, by regrouping of diabetic patients according to HbA1c blood sugar level whether < 7% or ≥ 7% and by comparing the MPV in both groups, no statistical difference was found between those two groups. However, there was statistical significant difference in FBS between the two HbA1c group (figure 3).

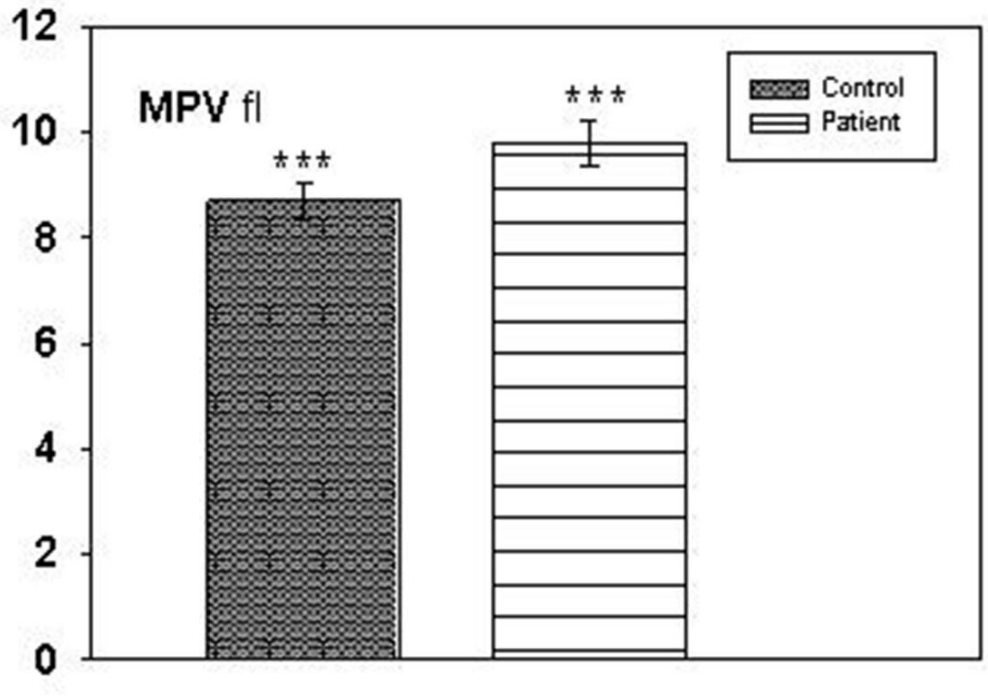

Figure 2. The MPV level in non-diabetic control and type 2 diabetic patient groups, based on estimation FBS by autoanalyzer (p<0.001)

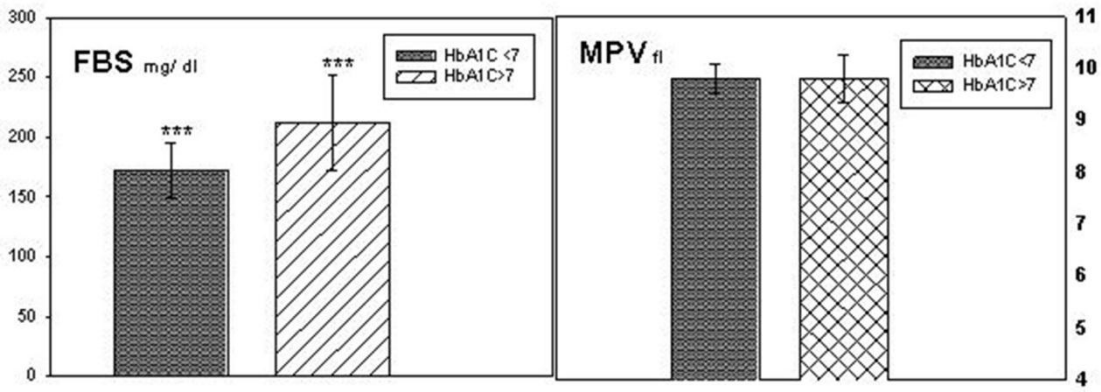

Figure 3. Comparison of MPV values between diabetic subjects based on HbA1c value

Discussion

DM has been known as a pandemic disorder [1]. Many studies have been shown DM as a prothrombic state because platelets function and morphology are usually altered during this disease [28]. Several studies have been shown positive correlation between MPV and DM and also MPV and HbA1c level [26,28]. On the other hand, some studies show that MPV enhancement is consequence of diabetes

complications such as inflammation and no correlation have been found between elevated MPV value and HbA1c level [10]. In the current study, MPV, as one of the important markers of platelet activity, was assessed to understand it's behavior better during DM. According to the obtained results, there was a remarkable enhancement of MPV value in diabetic patients compared to non-diabetic healthy controls. This is inconsistent with majority of previous studies. On the other side, while comparing MPV value based on HbA1c level, no considerable differences have been observed between two groups with HbA1c <7 and HbA1c ≥7. However, when blood sugar was estimated by autoanalyser the MPV was significantly higher in HbA1c ≥7 group compared to HbA1c <7 group. Therefore, it can be concluded that MPV is increased during DM independent of HbA1c level. This is inconsistent with the results obtained by some studies which have shown positive relationship between elevated MPV and HbA1c level [26,28]. According to the previous literatures, higher MPV is related to higher platelet activity. Multiple mechanisms caused by metabolic and cellular abnormalities have been suggested to play a role in the increased platelet activity observed in patients with DM [10,28]. Among them hyperglycemia and insulin resistance can be addressed as the majors and lead to higher platelet activity. Platelets from patients with type 2 DM have increased expression of adhesion molecules and activation markers [28]. Also, a positively significant correlation between platelet activation markers and level of HbA1c has been observed [28]. On the other side, regarding to the obtained results in the present study, it seems that MPV increases independent of HbA1c level. It can be explained in this way that long term glycemic controls may indirectly affects platelet activity, however, there are far more unknown parameters affecting platelet activity in patients with DM. This is an observational study with relatively low size of samples. In order to understand more about molecular mechanisms affecting the platelet activity and consequently MPV value in DM, more studies with greater range of sampling are needed.

According to the obtained results in the current study, it we can be concluded that: i. MPV was significantly increased in patients with DM in contrast to healthy controls. ii. MPV increases independent of HbA1c levels in patients with DM.

Acknowledgments

The authors would like to thank in advance from Samenol Aemme and Mehregan hospital administrators and laboratory staffs.

Authors Contribution:

Dr. Khalili-Hezarjaribi developed the original idea and designed the assessment protocol, wrote the manuscript. Dr. Mahdavian, Dr. Mirsadraei and Dr. Farahmand-Bovanlou collect data and analyzed them and prepared the manuscript. Dr. Jahanabad contributed in the data collection.

Conflict of interest

The authors declare no conflict of interest for the present study.

Funding

No financial support has been provided for this study.

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Received Jan. 22nd 2017
Accepted May. 3rd 2017