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Research Article

Evaluation of the Relationship between Blood Glucose Regulation and Hematological Indices in Patients with diabetes Mellitus

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Abstract

Objectives: Diabetes mellitus is a subclinical and systemic inflammatory endothelial disease. The relationship between erythrocyte and platelet indices and inflammation has been shown in many studies. With good glycemic control, mean platelet volume and red blood cell distribution width levels can be reduced, thus preventing or delaying vascular complications in patients. The aim of our study is to examine the relationship between HbA1c and complete blood count indices in patients with diabetic patients.

Methods: This retrospective study included 8077 diabetic patients aged 18 and over followed in internal medicine outpatient clinics.

Results: In our study, there was a difference between the groups in terms of RDW and MPV levels. The HbA1c levels showed a positive correlation with RDW and MPV levels.

Conclusion: Our study established that high MPV and RDW levels are associated with high HbA1c levels.

Keywords: Diabetes mellitus, glycemic index, HbA1c

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The occurrence of diabetes mellitus is increasing worldwide, and the number of patients diagnosed with diabetes mellitus (DM) is expected to reach 642 million in 2040.[1] The disease itself and its complications cause enormous functional and financial burden annually to the health care systems. The increasing diabetic patients have been largely attributed to the environmental factors that promote the adoption of unhealthy behaviors and development of obesity and overweight around the world.[2] On the other hand, subclinical chronic inflammation is an underlying feature in the pathogenesis of diabetes mellitus and levels of inflammatory biomarkers correlate with prevalent and incident diabetes, as well as major complications and cardiovascular diseases.[2]

Recently, the indices that derived from the routine hemogram test are proposed as novel inflammatory markers and predictors of outcome in chronic conditions. Two of these markers are and red blood cell distribution width (RDW) and mean platelet volume (MPV).[3] RDW measure reflects the extent of anisocytosis, a condition

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that is characterized by pronounced heterogeneity in the volume of circulating erythrocytes. Increased MPV, which indicates larger platelet volume, is considered as an indicator of platelet functions and activation. Associations between these indices and inflammatory diseases have been well established.[3–6] In this retrospective study, we aimed to investigate the relationship between HbA1c and complete blood count (CBC) indices in patients with diabetes.

Methods

This retrospective study was conducted by examining the demographic information and laboratory records of diabetic patients who applied to the Internal Medicine outpatient clinic between January 2018 to December 2018. A total of 8,077 patients over the age of 18 with no missing medical records were included in the study. Patients with acute or chronic renal failure, anemia, thrombocytopenia, leukopenia, polycythemia, thrombocytosis and leukocytosis were excluded from the study. The patients were divided into three groups as Tertile -1 (Hba1c ≤ 7%), Tertile -2 (7%< Hba1c ≤7.9%), and Tertile -3 (Hba1c >7.9% according to the 33rd and 66th percentile values of HbA1c. This study was approved by the Kahramanmaras Sutcu Imam University Clinical Trial Ethics Committee (decision no: 02, dated: 29.12.2021).

Statistical Analysis

The data obtained in the study were statistically analysed using the Statistical Package for Social Sciences (SPSS) version 22.0 software. Conformity of the data to normal distribution was examined visually (histogram and probability graphs) and with the analytical method of the Kolmogorov-Smirnov test. In descriptive analyses, variables with normal distribution were stated as mean±standard deviation (SD), and variables not showing normal distribution were stated as median, minimum and maximum values. Continuous variables were reported as median (min.–max.), and categorical variables as number (n) and percentage (%). The One-Way ANOVA test was applied to evaluate the differences in parametric data between groups. Parameters not showing normal distribution were compared within the groups using the Kruskal-Wallis test. In the comparison of categorical variables between groups, the Chi-square test was applied. The statistical significance was calculated with the Spearman test of numerical variables with normal distribution and the correlation coefficients of numerical variables which did not meet at least one of the normal distribution criteria were calculated with the Pearson test.

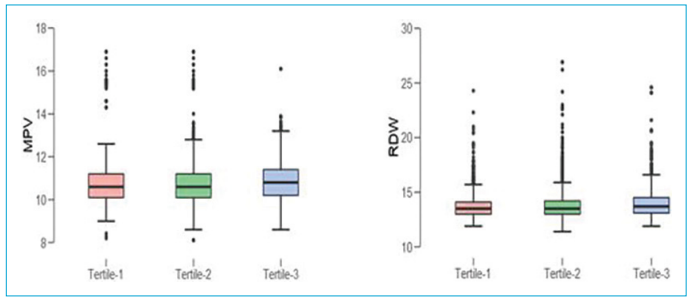

Figure 1. Comparison of mean platelet volume (MPV) and red blood cell distribution width (RDW) between the study groups.

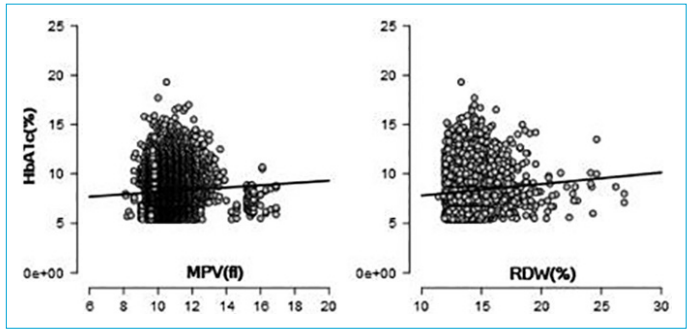

Figure 2. Correlation between mean platelet volume (MPV) and red blood cell distribution width (RDW) with glycated hemoglobin (HbA1c).

Results

A total of 8077 patients, 5127 (63.5%) women and 2950 (36.5%) men, were included in the study, and the mean age of all patients was 58.06±11.32 years. The median age of Tertile-3 was significantly higher than that of Tertile-1 and 2. The median ages of Tertile-1 and 2 were similar. There was no significant difference between the groups in terms of gender. WBC, PT and PDW levels of all three groups were similar. When the groups were examined according to their RDW levels, the Tertile-3 group had higher RDW levels than Terile 1-2 (p values; p= 0.000, p=0.024, respectively) and the Tertile-2 group had higher RDW level than the Tertile-1 group (p=0.008) (Fig. 1). When the groups were examined according to their MPV levels; The MPV level of the Tertile-1 group was higher than Tertile 2-3 (p values; p=0.019, p=0.000, respectively), while the mean of Tertile-2 and 3 were similar (p=0.281). There was a difference between the groups in hemoglobin levels. This difference was due to the fact that the hemoglobin levels of the Tertile-3 group was higher than Tertile-1-2 (p values, respectively; p=0.000, p=0.036) (Fig. 2). The Hb levels of Tertile-1 and 2 were similar (p=0.055). The baseline demographic, clinical and laboratory characteristics of the three groups are shown in Table 1. In the correlation analysis, a positive linear relationship was found between HbA1c levels and RDW and MPV (p<0.001), (Fig. 2, Table 2).

Table 1. Demographic and biochemical characteristics of the HbA1c status

Variables total	A1c Tertile 1 (n=2769)	A1c Tertile 2 (n=2664)	A1c Tertile 3 (n=2644)	p
Sex (male)	971 (12.0)	996 (12.3)	983 (12.2)	0.144
Age (years)	58 (18–98)	59 (19–92)	57 (18–91)	<**0.001**
Glucose (mg/dl)	117 (60–319)	163 (63–465)	250 (64–621)	<**0.001**
WBC (10^3/µl)	7.54 (4.7–12.6)	7.81 (4.5–12.6)	7.61 (4.5–12.6)	0.073
HGB (g/dl)	13.8 (12.1–16.7)	13.9 (12–16.7)	14.1 (12–16.9)	<**0.001**
PT (x10^3 µL)	253 (150–346)	254 (150–350)	253.5 (150–350)	0.155
MPV (fl)	10.6 (8.2–16.9)	10.6 (8.1–16.9)	10.8 (8.6–16.1)	<**0.001**
PDW (%)	12.6 (8.3–22.5)	12.5 (8.1–23)	12.6 (8.1–22.6)	0.532
RDW (%)	13.5 (11.9–24.3)	13.6 (11.4–26.9)	13.7 (11.9–24.6)	<**0.001**

Continuous data are shown as median (maximum–minimun) and categorical data are shown as frequency (%). P-values ≤0.05 are shown in bold. WBC: White blood cell; Hgb: Hemoglobin; PT: Platelet count; MPV: Mean platelet volume; PDW: Platelet distribution width; RDW: Red blood cell distribution width.

Table 2. Correlation between mean platelet volume (MPV) and red blood cell distribution width (RDW) with glycated hemoglobin (HbA1c) and glucose

			Pearson r	p	Lower 95% CI	Upper 95% CI
HbA1c	-	MPV	0.058***	<0.001	0.040	1.000
HbA1c	-	RDW	0.070***	<0.001	0.052	1.000
Glucose	-	MPV	0.079***	<0.001	0.061	1.000
Glucose	-	RDW	0.073***	<0.001	0.055	1.000

All tests one-tailed, for positive correlation. *: p<0.05; **: p<0.01; ***: p<0.001, one-tailed; MPV: Mean platelet volume; RDW: Red blood cell distribution width; CI: Confidence interval

Discussion

In this study, we evaluated the relationship between glycemic control and MPV, RDW parameters in DM patients. MPV and RDW levels increased as glycemic control deteriorated in DM patients. We found a linear relationship between these parameters and HbA1c levels. To the best of our knowledge, we think that our study will contribute to the relevant literature in terms of having a larger sample size compared to similar studies.

Recent studies have shown that DM is associated with low-grade systemic inflammation. Levels of inflammatory markers such as CRP, fibrinogen and pro-inflammatory cytokines are increased in the systemic circulation of patients with DM.[7,8] It has been determined that the cytokine response has increased in parallel with the deterioration of glycemic control.[5,9] Studies have reported that RDW and MPV levels are associated with chronic inflammation.[4,10,11] RDW is the measure of the size variability of red blood cells is associated with the risk of adverse outcomes in patients with heart failure and coronary heart disease.[6,12] MPV is one of the most widely used markers of platelet function and has been shown to reflect the inflammatory burden in different chronic diseases.[13,14] In our study, we think that increased RDW and MPV levels not only reflect poor glycemic control, but also increased cardiovascular risks due to the chronic inflammatory processes.

In studies on hemogram parameters in DM patients in the literature, Hekimsoy et al.[15] found that MPV was significantly higher in the diabetic group in 145 patients but the authors did not detect a correlation between MPV and HbA1c levels in the DM patients. Nada et al.[16] found that MPV and RDW levels were significantly increased in 260 DM patients compared to the control group, but they did not detect a correlation between these two parameters and HbA1c levels. On the contrary, there are studies showing a positive correlation between MPV, RDW levels and metabolic control in patients with diabetes.[17–20] In the study of Cakir et al.[21] which included 46 DM patients, they showed that the MPV level of the patients increased compared to the control group. In the same study, RDW levels increased compared to the control group, but this increase was not statistically significant. The authors attributed this result to the small size of their sample. In our study, we showed that there is a positive correlation between HbA1c level, which is an indicator of glycemic control, and RDW in DM patients.

There are studies are showed that both RDW and MPV levels are not only associated with blood glucose regulation but also with diabetes-related microvascular complications.

While Ma et al. showed that the incidence of diabetic retinopathy increases with increased RDW level in their study,[22] it was stated in the study of Rasoulinejad that MPV value is associated with the presence and severity of diabetic retinopathy, and that MPV can be used in the clinical follow-up of diabetic retinopathy.[23] In the study of Zhang et al.[24] in diabetic patients, it was shown that RDW level is both associated with proteinuria level and is a predictor of patients' progression to end-stage renal disease. Studies have shown that MPV value is also positively correlated with proteinuria and negatively correlated with glomerular filtration rate.[25] Increased MPV is a marker showing increased platelet adhesion and aggregation, as well as increased thrombocyte size. Large platelets are cells with denser granules that produce higher amounts of β-thromboglobulin, serotonin, and thromboxane A2 and are potentially associated with a higher risk of vascular complications.[26,27] There is no clear data explaining why the MPV value is increasing in DM patients physiopathologically. The osmotic expansion of platelets is thought to occur due to high blood glucose and its metabolites.[28] It is a known fact that microvascular complications increase in patients with high HbA1c levels and uncontrolled blood glucose regulation. In this instance, the positive correlation between HbA1c and MPV in our study and the association of MPV level with microvascular complications in previous studies seem to support each other.

However, our study has some limitations. First of all, because of the retrospective design of the study, we could not access the duration of illness and blood pressure data of our participants which could cause the changes on the hemogram parameters; this caused us to ignore the effects of hypertension on hemogram parameters. In addition, we did not have information about the drugs used by the patients and their body mass index. Also that it is a single-center study with data from one hospital, so the results might not be able to be extrapolated to other clinical settings or other ethnic groups.

In summary, our study established that high MPV and RDW levels are associated with high HbA1c levels. Future research is still needed to unveil the biological and physiological mechanisms behind the association and determine whether a causal relationship exists.

Disclosures

Ethics Committee Approval: This study was approved by the Kahramanmaras Sutcu Imam University Clinical Trial Ethics Committee (date: 29.12.2021, number: 02).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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