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Research Article

DIABETIC RETINOPATHY AND MEAN PLATELET VOLUME LEVELS

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ABSTRACT

*Background***:** The aim of the present study was to evaluate the relationship between mean platelet volume (MPV) and diabetic retinopathy. Treadmill exercise test was performed to determine ischemic heart disease in diabetic patients.

*Methods***:** In the present study, data in the files of 73 patients (36 female, 37 male) who were followed and treated in diabetes outpatient clinic and who underwent treadmilll test were used. Diabetes patients who underwent treadmill exercise test were divided into two groups:i.e. treadmill test positive and negative cases. MPV values of the patients and their biochemical parameters, and frequency of retinopathy and hypertension were compared.

*Results***:** There was no significant difference between two groups in terms of sex, hypertension, lipid parameters, HbA1c and retinopathy. Mean age was significantly higher in cases with positive treadmill test results than those with negative results$p<0.05$. In treadmill exercise test positive cases, and overall, MPV values were found to be significantly higher in cases with retinopathy than those without retinopathy, ($p<0.05$).

*Conclusion***:** Diabetic retinopathy associated with elevated MPV levels, in diabetic patients with a postive treadmill test.

Keywords: *Mean Platelet Volume, Diabetic Retinopathy, Treadmill Test*

INTRODUCTION

In a large majority of diabetic patients, micro and macro vascular complications develop in time. The degree and duration of hyperglicemia are strong risk factors for the development of micro and macro vascular complications. Diabetic hyperglicemia may lead to various pathological changes such as alterations in thrombocyte morphology and functions. Thrombocytes are an important target for hypoglicemic injury. However, mechanisms underlying this injury have not been completely understood. Previous studies have shown that in cases with type II Diabetes, increased thrombocyte sensitivity and increase in thrombocyte production may lead to changes in thrombocyte morphology. Hence, increased number of very large and extremely sensitive young thrombocytes appear. The cause of thrombus formation in coronary arteries, which lead to acute ischemic events, is rupture in atherosclerotic plaque or ulceration. In this process, thrombocyte activation plays an important role. Increased mean platelet volume (MPV), indicating larger platelet volume, is considered an indicator of platelet functions and activation, and of increased cardiovascular disease risk. Thrombocytes are cells that play key role in the development of atherosclerosis and acute complications (Vakila *et al.*, 1994). It has been demonstrated that, in the presence of hypertension, which is the major risk factor for the development of atherosclerosis, platelet activation indices such as MPV, P-selectin,beta-thromboglobulin and platelet factor-4 increase, leading to prothrombic state (Nadar et al., 2004). Physical and chemical characteristics of thrombocytes depend on their size. MPV by itself is considered as marker of thormbocyte activation (Bath *et al.*, 1996). Such a parameter can be evaluated along with whole blood count in automated devices, which is an important advantage. Changes in MPV are very important for early diagnosis of

thrombotic and prethrombotic events. Larger thrombocyes contain more granules and platelet derived subtances than smaller ones and are more inclined to adhesion and aggregation. In the cytoplasm of large platelets, substances such as calcium, thromboxane A2, serotonin, PF4 and β-tromboglobulin have been found to be high along with increased expression of adhesion molecule, which is regarded as the indicator of platelet activation (Park *et al.,* 2002). All of these findings indicate that large rthrombocytes are metabolically more active.In the literature, it has been demonstrated that there is a rise in MPV levels in diseases such as diabetes mellitus, acute coronary syndrome, stroke, preeclampsia, renal artery stenosis and hypercholesterolemia. As larger thrombocytes are more active, thrombocyte volume is one of the determinanats of platelet function. Besides, it has been established that high MPV is an independent risk factor for myocardial infarction in patients with coronary heart disease (Endler *et al.,* 2002). It has been stated in the study of Swell et al that thrombocytes, the cause of high MPV in acute coronary syndromes may be that secondary to rapid consumption, thrombocytes with a large volume are released from bone marrow without maturation or that the thrombocytes with smaller size are consumed earlier than the ones with larger size (Sewell, 1984). The aim of the present study was to determine the significance of MPV in the identification and prediction of coronary artery disease and acute myocardial infarction in patients with diabetes and to evaluate its relation with other parameters.

MATERIALS AND METHODS

In the present study, data in the files of overall 73 (36 female, 37 male) patients with type II Diabetes who were followed and treated in Diabates outpatient clinic of Haseki Training and Investigation Hospital and who underwent treadmill exercise test were used. Necessary data were collected retrospetively. In addition, demographic and clinical data were recorded. All cases underwent standard treadmill exercise test in accordance with standrad Bruce protocol. Cases with abnormal findings in resting electrocardiography (ECG), those who have additional diseases and hypertension were excluded from the study. Patients were separated into two groups according to treadmill exercise test results i.e. positive and negative groups. Type II diabetic patients separated into positive and negative test result groups were compared in terms of age, sex, drug use, smoking status, the presence of retinopathy, the frequency of hypertension, fasting blood sugar, total cholesterol, LDL, HDL, trigliceride and MPV values. Hemogram measurment was made with ADVIA 120 blood count device. Study data were recorded to computer and in statistical evaluation SPSS (Statistical Package for Social Sciences) for Windows 10.0 program was used. In addition to descriptive statistical methods (mean±standard deviation), in the comparison of numerical values, in the inter group comparison of normally distributed parameters, Student's t test, and in the comparison of parameters not normally distributed, Mann Whitney U test was used. In intragroup comparisons of parameters, paired sample t test was used. In the comparison of qualitative data, chi-square test was used. Results were calculated at %95 confidence interval, with significance set at $p<0.05$ value.

RESULTS

Mean age of the cases with positive treadmill test results was significantly higher than cases with negative results, $p<0.05$. No significant difference was found between groups with regard to HA1c, lipid parameters,and duration of diabetes. Neither was there any significant difference in sex, frequency of hypertension, smoking status, and retinopathy, (Table-1). No significant correlation was found between MPV values and any parameter in groups, (Table-2). No significant differecne was found in MPV values between cases with positive and negative treadmill test results, those with and without hypertension, smokers and non-smokers. In cases with negative treadmill results, there was no significant difference between cases with retinopathy and without retinopathy in terms of MPV values. However, in cases with positive treadmill exercise test results and overall, MPV values were significantly higher in cases with retinopathy than those without retinopathy, (Table-3).

Table 1: The distribution of sex, hypertension, treatment, smoking status, and retinopathy in groups

		Treadmill (-) patients n(%)	Treadmill (+) patients n(%)	Overall	P value
GENDER	*Male*	15 (45.5%)	22 (55.0%)	37 (50.7%)	0.417
	Female	18 (54.5%)	18 (45.0%)	36 (49.3%)	
HYPERTENSION	*Absent*	13 (39.4%)	19 (47.5%)	32 (43.8%)	0.487
	Present	20 (60.6%)	21 (52.5%)	41(56.2%)	
TREATMENT	*OAD*	17 (51.5%)	18 (45.0%)	35 (47.9%)	0.579
	Insulin	16 (48.5%)	22 (55.0%)	38 (52.1%)	
SMOKING STATUS	*Non smoker*	20 (60.6%)	25 (62.5%)	45 (61.6%)	0.868
	Smoker	13 (39.4%)	15 (37.5%)	28 (38.4%)	
RETINOPATHY	*Absent*	26 (78.5%)	26 (65.0%)	52 (71.2%)	0.195
	Present	7 (21.2%)	14 (35.0%)	21 (21.8%)	

(OAD:Oral antidiabetic drug)

Table 2: The correlation between treadmill test and other parameters in diabetics (r and p values)

	Treadmill negative		**Treadmill positive**		**Overall**	
	r	**p**	**r**	**p**	**r**	**p**
Age	0.029	0.872	0.135	0.406	0.100	0.402
DM duration	0.316	0.073	0.088	0.587	0.072	0.545
HbA1c	0.212	0.236	0.018	0.910	0.107	0.368
Total cholesterol	0.009	0.960	0.206	0.203	0.105	0.375
LDL	0.008	0.967	0.260	0.105	0.125	0.291
HDL	0.021	0.906	0.027	0.870	0.012	0.919
Trigliceride	0.058	0.750	0.075	0.646	0.037	0.754

(MPV:mean platalet volume)

Table 3: The association between MPV and diabetic retinopathy according to treadmill test

	Retinopathy	**MPV Mean (fL)**	**Standard deviation**	**p value**
Treadmill negative	Absent	7.85	0.92	0.284
	Present	8.26	0.72	
Treadmill positive	Absent	7.65	0.85	**0.042**
	Present	8.24	0.88	
Overall	Absent	7.75	0.88	**0.028**
	Present	8.24	0.77	

DISCUSSION

While in some studies on patients with diabetes,it has been revealed that the frequency of coronary artery disease is associated with the duration diabetes not with glicemic control (Bath, 1996). Also, in the present study, no significant difference was found between cases with positive treadmill test results and those with negative results in terms of the duration of diabetes. Although, there was no significant difference between treadmill exercise test positive cases and negative ones in terms of HbA1c values, just as in UKPDS study, in treadmill test positive cases, retinopathy, which is microvascular complication of diabetes, was encountered more commonly, $p<0.05$. In the present study, it was expected that high MPV values would guide us in the early detection of silent ischemia in type II Diabetes patients. However, no significant difference was found in MPV values between treadmill exercise test positive cases and negative ones. Similarly, there was no difference between groups in terms of HbA1c values. In the study of Naka *et al.,* it was found that severity of diabetes was influential in the prevalence of silent myocardial ischemia, but it was also stressed that, HbA1c used to determine this condition, is an insufficient paramer since it indicates short term glicemic control (Naka *et al.,* 1992).In Milan Study on Atherosclerosis and Diabetes (1997), coronary artery disease was found to be more common in diabetic males. In other studies, coronary artery disease was found to be more common in male sex (Janand *et al.*, 1992). Yet, in the present study, there was no significant difference between treadmill exercise test positive cases and negative ones with respect to sex. Although male sex is a risk factor on its own, in the study Koistinen, no difference was found between sexes in diabetic patients and it was suggested that there is fall in the resistance to coronary artery disease among diabetic women. There are many studies reporting that MPV values are high in dyslipidemia (Delanty, 1997). In the present study, in the groups with postive treadmill test results, all lipid values except HDL were found to be higher than the groups with negative test results. However, no statistically significant difference was found between groups in terms of MPV values. In addition, no relation was found between MPV and age, sex, the number of thrombocytes and hypertension. Further studies are required on this issue. Smoking increases MPV in elderly patients with risk of atherosclerosis. Kazuomı et al investigated the impact of smoking on MPV in arterial diseases with cases who are smokers and non smokers and those who have and who do not have atherosclerotic risk factors. It was established that MPV was highest in smokers with atherosclerosis and that smokers without atherosclerosis had significantly higher MPV values, their MPV values decreasing markedly after quitting smoking (Zimmet *et al.*, 1994). In the present study, there was no significant difference was found between cases with positive and negative treadmill exercise test results and between smokers and non smokers with regard to MPV values. In the study of Papanas *et al.*, carried out to determine the relation between MPV and retinopathy,one of the microvascular compications of diabetes, MPV was found to be markedly higher in patients with type II diabetes (Buch *et al.,* 2017). Similarly, in the present study, in cases with positive exercise treadmill test results and retinopathy, MPV values were found to be significantly higher than those in cases without retinopathy, $p<0.05$. It was stated in the study of Swell et al that high MPV in acute coronary syndromes may be due to the release of large thrombocytes from bone marrow prior to maturation secondarily to rapid consumption of thrombocytes or to earlier consumption of small thrombocytes than large ones in coronary events (Libby, 2000). It was also reported that expansion in thrombocytes after blood is drawn is at maximum level at the first minutes, but after samples were kept waiting for 1-2 hours, change in MPV was seen at a lower degree (Mannhalter *et al.*, 2002). Therefore, in the present study, blood transferred to vacuum tubes for MPV measurement were kept waiting for two hours before analysis with an attempt to decrease volume changes, that may occur associated with EDTA to minimum. There was no difference between the diabetes group without retinopathy and the control group in terms of thrombocyte coagulation activity and its size while MPV was found to be increased in the diabetes group with retinopathy (Güngör *et al.,* 2016). In diabetic patients, the risk of retinopathy development increases with higher MPV values. Increased MPV is closely associated with poor glycaemic control, which may be a risk factor for diabetic retinopathy (Yılamz, 2016). MPV values are higher in uncontrolled DM patients when compared with controlled

diabetic patients and a higher percentage of them develop microvascular complications like diabetic retinopathy suggesting that mean platelet volume could indicate and play a more important role in the detection of vascular complications of diabetes (Tuzcu *et al.,* 2014). In the present study, MPV values were found to be significantly higher in cases with positive treadmill exercise test results and overall than in cases without retinopathy, which suggests that MPV may be a marker of microangiopathy.

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