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Diagnostic Value of HbA1c Level in Behcet's Disease and Evaluation of Neutrophil-Lymphocyte Ratio, Mean Platelet Volume and Body Mass Index

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Abstract

Background: Behcet's disease (BD) is a chronic systemic inflammatory disorder. T cells, neutrophils, inflammatory vasculitis and endothelial injury were implicated in the pathogenesis of BD. Hemoglobin A1c (HbA1c) is a minor component of hemoglobin to which glucose is bound, and it was reported to be associated with intima-media thickness, endothelial dysfunction and atherosclerosis in non-diabetic patients. In this study, we aimed to investigate the relationship between markers of glucose metabolism and BD in non-diabetic individuals. To the best of our knowledge, this planned study was the first evaluating the glucose metabolism with HbA1c levels and correlating it with body mass index (BMI), lipid profiles and the other inflammatory markers (mean platelet volume (MPV), neutrophil-lymphocyte ratio (NLR) and sedimentation) in BD.

Methods: Sixty-four patients and 64 controls were enrolled in this study. Clinical manifestations of the disease were recorded. Laboratory analysis including HbA1c, hemogram, hematocrit, platelet count, liver function tests, complete blood count, urine analysis, erythrocyte sedimentation rate, MPV, lipid testes including low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides and total cholesterol levels were measured. Height, weight and BMI of patients were recorded.

Results: Glucose levels were statistically higher in BD ($P < 0.01$). HbA1c level was evaluated, and statistically significant difference was not obtained ($P = 0.9$). Hemoglobin, hematocrit, platelet level and liver-urine analysis tests did not show any significant difference. Cholesterol, triglyceride, and LDL levels were statistically higher in BD group than control group ($P = 0.00$, $P = 0.003$, and $P = 0.001$). BMI was evaluated, and there was a significant difference in BD group ($P = 0.016$). NLR and sedimentation were higher in BD ($P < 0.01$). However, the other inflammatory marker MPV had no significant elevation.

Conclusions: There was no significant association observed between BD patients and HbA1c levels, and this was the first study investigating HbA1c levels and correlating it with other parameters.

Keywords: Behcet's disease; HbA1c; Neutrophil-lymphocyte ratio; Mean platelet volume; Body mass index; Sedimentation

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Introduction

Behcet's disease (BD) is a chronic systemic inflammatory disorder characterized by oral and genital ulcerations, uveitis and vascular, neurological, articular, renal and gastrointestinal manifestations. Its etiology has not been elucidated yet but genetic predisposition, environmental factors and immunological abnormalities were suggested to play a role in its pathogenesis [1, 2]. Stimulation by an unknown trigger was suggested to explain the immunological mechanisms for the initiation of the disease. T cells, neutrophils, inflammatory vasculitis and endothelial injury were implicated in the pathogenesis of BD [3, 4].

Hemoglobin A1c (HbA1c) is a minor component of hemoglobin to which glucose is bound, reflecting the average plasma glucose level for the several months prior to examination, and it has been used in many epidemiology studies as a parameter for glycemic control. It was reported to be associated with intima-media thickness, endothelial dysfunction and atherosclerosis in non-diabetic patients. It has been linked with long-term risk of microvascular complications [5]. Recent studies also proposed that endothelium activation/damage might be a contributing factor in both the procoagulant and clinical conditions of BD [6]. The relationship between markers of glucose metabolism and BD in non-diabetic individuals has not been established clearly yet.

From this point of view, in this study we aimed to investigate the association of HbA1c levels and BD, and whether glucose levels were activated in BD and were related with vascular complications. We selected the non-diabetic individuals with BD to determine the correlation of HbA1c and symptoms of patients and compared with healthy controls. In recently

Table 1. Laboratory Findings in BD and Control Group

Laboratory parameters	BD (mean ± SD)	Control group (mean ± SD)	P value
Hemoglobin	13.40 ± 1.60	13.86 ± 1.16	0.06
Hematocrit	39.75 ± 6.51	42.35 ± 3.39	0.06
Platelet	259.35 ± 61.51	246.65 ± 58.87	0.2
Glucose	95.20 ± 11.25	86.72 ± 8.24	0.00
Cholesterol	176.26 ± 48.90	168.98 ± 29.31	0.3
Triglyceride	130.36 ± 83.94	91.16 ± 52.93	0.003
HDL	50.00 ± 13.02	61.32 ± 14.76	0.00
LDL	111.01 ± 39.63	90.41 ± 26.33	0.001
AST	19.79 ± 5.42	17.01 ± 5.25	0.005
ALT	20.73 ± 11.21	14.88 ± 6.82	0.004
BUN	26.24 ± 11.29	24.16 ± 5.86	0.2
Creatinine	0.84 ± 0.13	0.66 ± 0.13	0.00
MPV	8.95 ± 1.13	9.35 ± 0.77	0.02
Neutrophil	5.07 ± 1.63	4.00 ± 1.31	0.00
Lymphocyte	2.23 ± 0.64	2.45 ± 0.62	0.05
HbA1c	4.87 ± 0.38	4.86 ± 0.18	0.9
Weight	69.28 ± 11.92	61.15 ± 10.72	0.00
Height	1.65 ± 0.06	1.64 ± 0.07	0.7

LDL: low density lipoprotein; HDL: high density lipoprotein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; WBC: lowest white blood cell count; platelet: lowest platelet value; MPV: mean platelet volume; BUN: blood urea nitrogen; SD: standard deviation.

performed studies, BD was also found to be associated with metabolic syndrome, increased risk for the development of metabolic syndrome in BD was detected [1] and, therefore, the important steps of metabolic syndrome, body mass index (BMI) and lipid levels, were also examined in the patients with BD and compared with healthy controls. We also evaluated the association of mean platelet volume (MPV), neutrophil-lymphocyte ratio (NLR) and sedimentation as well-known inflammatory parameters of systemic inflammation to be able to establish a potential connection between these markers and BD. To the best of our knowledge, this planned study was the first evaluating the glucose metabolism with HbA1c levels and correlating it with BMI, lipid profiles and the other inflammatory markers in BD.

Patients and Methods

Sixty-four patients were enrolled in this study with a diagnosis of BD according to the criteria of the International Study Group [7]. Clinical manifestations of the disease were recorded. Laboratory analysis including HbA1c, hemogram, hematocrit, platelet count, liver function tests (aspartate aminotransferase (AST) and alanine aminotransferase (ALT)), complete blood count, urine analysis (blood urea nitrogen (BUN)), erythrocyte sedimentation rate, MPV, lipid testes including low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides and total cholesterol levels were measured. Height, weight and BMI of patients were recorded. Control group was composed of healthy individuals. Exclusion criteria were at age of < 18 years old, diabetes mellitus, chronic systemic disease, systemic collagen disease or chronic inflammatory skin diseases. All participants gave written informed consent before entering the study.

Statistical analysis

Statistical analysis was completed using SPSS 17.0 for Windows (Chicago, IL, USA). Categorical variables are presented as counts and percentages. The Kolmogorov-Smirnov test was used to evaluate whether the distribution of variables was normal. As the data did not conform to normal distribution and could not be normalized by transformation, non-parametric statistical tests were utilized. The two independent sample *t*-test or Mann-Whitney U-test was used to compare continuous variables between the two groups. Continuous variables were presented as mean (standard deviation (SD) or as median inter-quartile range (IQR)). P value of less than 0.05 was considered to be statistically significant. Pearson's Chi-square test was used to compare the categorical variables between groups.

Results

A total of 64 patients (26 male, 38 female) and 64 healthy con-

trols (26 male, 38 female) were included in this study. Mean age (± SD) of the patients was 32.68 ± 10.16 years and for controls was 31.26 ± 10.96 years. There was no statistical difference between patient and control groups according to sex and age (P = 0.4).

Hemoglobin, hematocrit and platelet level did not show any significant difference. However, cholesterol, triglyceride, LDL levels were statistically higher in BD group than control group (P = 0.00, P = 0.003, and P = 0.001). Therefore, BMI was evaluated, and there was a significant difference in BD group (25.39 ± 4.47, control group 22.39 ± 2.99, P = 0.016). NLR was higher in BD (76.46 ± 45.87, 49.41 ± 31.62, P < 0.01). However, the other inflammatory marker MPV had no significant elevation. In addition to this, glucose levels were also statistically higher (95.20 ± 11.25, P < 0.01) and, therefore, the HbA1c level was evaluated and statistically significant difference was not obtained (4.87 ± 0.38, 4.86 ± 0.18, P = 0.9). The other laboratory parameters were normal (AST, ALT, BUN and creatinine). Sedimentation was 14 (8 - 26) in BD group and 5 (5 - 10) in control group. Sedimentation was statistically higher in BD than control group (P = 0.000). The laboratory findings were summarized in Table 1.

Discussion

In this study, we examined the associations of HbA1c, MPV, NLR, sedimentation, lipid levels and BMI in a group of Turkish patients with BD to be able to establish the roles of these parameters in the disease course and pathogenesis. We observed that the glucose, cholesterol, triglyceride, LDL, NLR levels, sedimentation and BMI were statistically higher in BD group than control group; however, we could not detect statistically significant association between the patients and controls in terms of HbA1c and MPV levels. To the best of our knowledge, this is the first study which examined the glucose metabolism with HbA1c levels and connected it with BMI, lipid profiles and the other inflammatory markers. Chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs especially the heart and blood vessels [5, 8, 9]. Increased glucose levels result in increased oxidative stress and protein glycation of vessel walls, accelerating the atherosclerotic process and arterial thrombosis [5, 8, 9]. Endothelial dysfunction is one of the steps of this pathway. Endothelium activation/damage has been postulated both in the pathogenesis and the course of the BD in terms of vascular involvement [6, 10]. Therefore, it is important to know the mean glucose level in about 3 months by means of HbA1c.

Recent studies revealed that there was tendency to increased insulin resistance and metabolic syndrome in BD [11, 12]. Even if the glucose levels were evaluated in these studies, the glucose level in about 3 months (glycemic control) was not examined. Kim et al calculated the plasma glucose level (patients with BD 92.8 + 14.0, control 89.5 + 9.1, P = 0.07), and there was no statistically difference by means of glucose levels; however, fasting insulin level was (patients with BD 5.6 + 4.1, control 3.2 + 2, P < 0.001) statistically higher in BD [9]. Sahin et al investigated the insulin resistance and serum adiponectin levels as cardiovascular risk markers in patients with BD. Fasting plasma glucose, insulin levels and lipid profile were not statistically different from control group, and there was no relationship between insulin resistance, adiponectin levels and inflammatory markers [12]. Yalcin et al evaluated the metabolic syndrome in BD, and they revealed that metabolic syndrome is a risk factor for BD patients [13]. However, HbA1c levels were not assessed. Here in this study, HbA1c levels were evaluated, and statistically significant difference was not obtained in BD. We also could not find a correlation between the BD, its complications and HbA1c levels; however, we would like to point to the importance of HbA1c to avoid metabolic syndrome development which is a new entity for BD.

In our study, cholesterol, triglyceride and LDL levels were statistically higher in BD group than control group. Therefore, BMI was evaluated, and there was a significant difference in BD group. These results were correlated with the findings in the literature [9, 13].

The blood NLR has been recognized as a marker of systemic inflammation. In several diseases, an elevated NLR was implicated as the marker of inflammation and poor prognosis [14]. Therefore, NLR was examined in different studies with various diseases like familial Mediterranean fever (FMF). NLR was suggested to be a useful marker for determining the development of amyloidosis in FMF patients. It was higher in FMF patients when compared with healthy individuals and also higher in amyloidosis-related FMF patients than in amyloidosis-free FMF patients [15]. NLR was studied in cardiac patients as well. It was defined as an emerging marker of inflammation and found to be associated with an increased risk for long-term mortality in acute decompensated heart failure patients and advised to predict subsequent mortality in patients with both ST-segment and non-ST-segment elevation myocardial infarction [16-19]. Since inflammation plays an important role in BD. Ozturk et al suggested that NLR may be a useful index of BD activity [19]. In this study, we also studied the NLR, and it was statistically higher in BD (76.46 ± 45.87, 49.41 ± 31.62, P ≤ 0.01). Our results were also consistent with the previous study, as our results supported the concept that NLR reflected the disease activity in BD. Sedimentation which is the most popular inflammatory marker in BD was also statistically higher and reflected the disease activity (P = 0.00).

The data about the MPV levels and BD are limited, and the results of the studies are conflicting. Ekiz et al and Acikgoz et al detected higher MPV levels in BD and pointed to the prognostic role of this hematological parameter in BD [20, 21]. Nevertheless, in ophthalmologic studies performed in the patients with ocular BD that MPV values were evaluated, any statistically significant correlation was not detected [22, 13]. We also did not observe any significant elevation in MPV levels.

In conclusion, BD is a chronic systemic disease like other inflammatory diseases obesity, hyperlipidemia and diabetes [7, 10], HbA1c, BMI, MPV, NLR, sedimentation and lipid profiles will help us to evaluate the disease course and progress, and therefore, these parameters should not be overlooked in daily practice. Even if there was no significant association observed between BD patients and HbA1c levels, this was the first study investigating HbA1c levels and correlating it with other parameters. In the light of this study, further well-designed stud-

ies with large cohort on different populations and ethnicities will be required to widely investigate the effects of these parameters on the activity and pathogenesis of the disease in order to better elucidate the complex immunopathogenesis and confirm these findings and comprehensively interpret the association between these parameters and BD. A better understanding of the pathogenesis of BD will definitely improve both the diagnosis and treatment of this disease.

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