

# Antistreptolysin O Levels in Patients with Behcet's Disease

## Behçet Hastalarında ASO Düzeyleri

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### Abstract

**Objective:** Behçet's disease is a multisystem inflammatory disorder, and its etiology has not been defined clearly yet. In this study, we aimed to investigate the antistreptolysin O (ASO) levels of patients with Behçet's disease.

**Materials and Methods:** Thirty patients with Behçet's disease and 30 healthy controls were enrolled in this study. We measured erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP), and ASO levels in both groups.

**Results:** There was no statistically significant difference between the two groups with respect to demographic data ( $p>0.05$ ). The ASO levels of the patients and the controls were  $288.4\pm 145.7$  and  $170.6\pm 142.4$  ng/ml, respectively. In the patients with Behçet's disease, ASO ( $p<0.01$ ) and ESR ( $p<0.05$ ) values were significantly higher than in the healthy controls. There was no other significant difference in serum CRP levels between the patients and the controls. We could not find any correlation among ASO, CRP, and ESR values.

**Conclusion:** Our results suggest that serum ASO levels may increase in patients with Behçet's disease. Further studies are needed in order to define the relationship between ASO levels and inflammation status in Behçet's disease.

**Key Words:** Antistreptolysin O, Behçet's disease, Inflammation

### Özet

**Amaç:** Behçet hastalığı multisistemik inflamatuvar bir hastalıktır. Behçet hastalığının etiolojisi henüz tam olarak belirlenememiştir. Bu çalışmada Behçet hastalarında antistreptolizin O (ASO) düzeylerinin incelenmesi amaçlanmıştır.

**Gereç ve Yöntem:** Bu çalışmaya 30 Behçet hastası ve 30 sağlıklı kontrol katıldı. Her iki grupta eritrosit sedimentasyon hızı (ESH), serum C-reaktif protein (CRP) ve ASO düzeyleri ölçüldü.

**Bulgular:** İki grup arasında demografik veriler açısından istatistiksel olarak anlamlı bir fark yoktu ( $p>0.05$ ). Hasta ve kontrollerin ASO düzeyleri sırasıyla  $288.4\pm 145.7$  ve  $170.6\pm 142.4$  ng/ml idi. Behçet hastalarında ASO ( $p<0.01$ ) ve ESH ( $p<0.05$ ) değerleri sağlıklı kontrollerden anlamlı derecede yüksekti. Hasta ve kontrollerin serum CRP değerleri arasında anlamlı bir fark yoktu. ESH, serum CRP ve ASO değerleri arasında herhangi bir korelasyon bulunamadı.

**Sonuç:** Bizim sonuçlarımıza göre Behçet hastalarında serum ASO seviyeleri yüksek olabilir. Behçet hastalarında ASO düzeyleri ve inflamasyon kaskadı arasındaki ilişkiyi belirlemek için yeni çalışmalara ihtiyaç duyulmaktadır.

**Anahtar Kelimeler:** Antistreptolizin O, Behçet hastalığı, İnflamasyon

### Introduction

Behçet's disease was named in 1937 by Turkish dermatologist Hulusi Behçet. It is a multisystem vasculitis with recurrent symptoms that include orogenital ulcerations, skin eruptions, ocular manifestations, and arthritis [1]. In addition, neurological and large vessel involvement can sometimes occur [2]. Behçet's disease is found mostly in the Mediterranean region, the Middle East, and the Far East. The mean age at onset is the third decade [3]. The main histopathological features in the inflamed tissues are infiltration of lymphocytes and monocytes, and sometimes polymorph nuclear leukocytes [4].

The etiology and pathogenesis of Behçet's disease have not been defined clearly, but environmental factors, infectious agents, immune mechanisms, and genetic factors are implicated in the etiopathogenesis of the disease [5]. Recent studies have shown that a wide variety of infectious agents was found to play a role in the etiology of Behçet's disease. However, it is not possible to isolate any organism that emerged consistently. In some studies, streptococcus was found in high concentrations in the oral flora of patients with Behçet's disease which we thought played a role in the occurrence of oral aphthous lesions, the first symptom in Behçet's disease [6-8]. In addition, the intense hypersensitivity reac-

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tion to streptococcal strains was thought to play a role in the symptoms of Behcet's disease patients. After streptococcus-induced tonsillitis, erythema nodosum-like lesions may appear through immunologic manifestation.

Streptococcal antibody tests such as antistreptolysin O (ASO) are commonly used for the diagnosis of poststreptococcal disease. An elevated ASO response is usually seen after a streptococcal upper respiratory tract infection; later, there is a rise in concentration of the antibodies directed against streptococcal streptolysin O. Titers increase as early as 1 week after infection and peak at 3 to 5 weeks. They remain elevated for 2-3 months and return to baseline after 6 months to 1 year [9, 10].

The aim of this study was to investigate the serum ASO levels in patients with Behcet's disease.

## Materials and Methods

Thirty consecutive patients with Behcet's disease who were admitted to our outpatient clinic were included in the study. Of the patients included in the study, 24 had oral aphthae, 14 had genital aphthae, 4 had arthritis, 10 had skin lesions, 2 had eye involvement, and one had thrombophlebitis. This study was performed according to the Helsinki declaration, and informed consent was obtained from all participants. The control group was made up of 30 healthy volunteers whose age and sex were similar to that of the patients. Only three patients were using corticosteroids. All patients except for three were using colchicines. The study was performed as a cross-sectional study.

All patients underwent a complete ophthalmologic and systemic examination to define the ophthalmic and systemic involvement and the disease activity. Diagnostic criteria for Behcet's disease proposed by the International Study Group for Behcet's disease were used for diagnosis [11]. The criteria put forth by the group include recurrent oral ulceration. In addition, a patient must also meet two of the following four criteria for Behcet's disease: recurrent genital ulcerations, eye lesions, skin lesions, and a positive pathergy test. The pathergy test was performed on the patient's avascular forearm skin by introducing a sterile needle in an oblique manner. If there was an indurated erythematous small papule or pustule formation  $\geq 2$  mm in diameter on the applied region, the test was considered positive.

Subjects with a history of acute rheumatic fever or glomerulonephritis were excluded.

The age, height, and weight of all subjects were recorded, and body mass index (BMI) was calculated as weight (kg)/height (m<sup>2</sup>). Demographic data and laboratory values were compared between the groups.

The laboratory personnel were blinded to the clinical diagnosis and grouping of the subjects, matching each blood sample by letter coding. The same procedures were applied

to the patients with Behcet's disease and the control subjects. Erythrocyte sedimentation rates (ESR) and serum C-reactive protein (CRP) were determined in whole blood and serum aliquots, respectively. ESR was determined according to the Westergren method, and serum CRP and ASO concentrations were determined by immunonephelometry with the use of a BN II analyzer.

## Statistical analysis

Student's t-test was used for data that were normally distributed. The Mann-Whitney U test was used for non-normally distributed data. For correlations, we used Pearson's correlation test. A p value  $< 0.05$  was accepted as statistically significant. Statistical analysis was performed with Statistical Package for the Social Sciences for Windows (version 11.0, Chicago, IL, USA).

## Results

The group with Behcet's disease was made up of 30 patients with a mean age of  $31 \pm 8.6$  years. The control group included 30 volunteers with a mean age of  $34.5 \pm 9.7$  years. There was no significant difference between the groups. Demographic values such as weight, height, and BMI were also compared, and we did not find significant differences between the groups (Table 1).

ESR values were significantly higher in the patients than in the controls ( $p < 0.05$ ), but there were no significant differences in serum CRP levels between the patients and the controls.

The ASO levels of the patients and the controls were  $288.4 \pm 145.7$  ng/ml and  $170.6 \pm 142.4$  ng/ml, respectively, shown in a scatter plot (Figure 1). In the patient group, ASO titers were also higher than in the controls ( $p < 0.01$ ) (Table 2). We searched for a correlation of ASO levels with ESR values and serum CRP levels, but we did not find any.

## Discussion

Behcet's disease, a recurrent inflammatory vasculitis with endothelial dysfunction, is a systemic disorder with unknown etiology [12, 13]. Inflammation in Behcet's disease is thought to be mediated by cytokines derived from T helper 1 (Th1) lymphocytes, including tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), interleukin-18 (IL-18), and interferon- $\gamma$  [14]. ASO is commonly used for the diagnosis of poststreptococcal disease [15], and an elevated ASO response is usually seen after a streptococcal upper respiratory tract infection. Recent studies have shown an important role of streptococcus infections in the etiology of Behcet's disease. The proinflammatory cytokines in peripheral blood mononuclear cells are enhanced when stimulated with streptococcal antigen.

**Table 1. The clinical features of the patients with Behcet's disease and healthy controls**

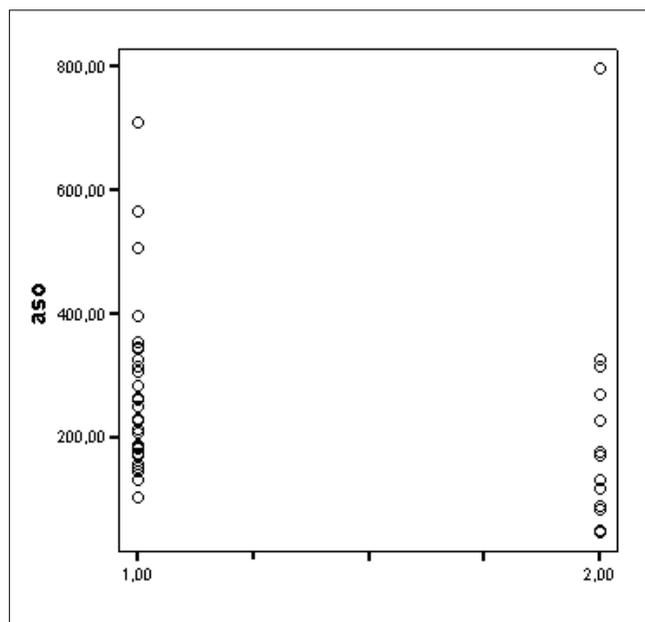
	Patient group	Control group	p value
Age (years)	31±8.6	34.5±9.7	ns
Sex (male/female)	12/18	11/19	
Disease duration (month)	27 (3-180)	-	-
Height (cm)	163.6±8.1	164.3±7.1	ns
Weight (kg)	66.6±12.6	70.4±11.9	ns
BMI (kg/m <sup>2</sup> )	24.7±3.5	26±3.8	ns

BMI: body mass index, ns: not significant

**Table 2. The laboratory features of the patients with Behcet's disease and healthy controls**

	Patient group	Control group	p value
ESR (mm/h)	11.5 (1-86)	10 (2-25)	0.036
CRP (mg/l)	0.5 (0.3-9.7)	0.4 (0.3-1.1)	ns
ASO (ng/ml)	288.4±145.7	170.6±142.4	0.002
Pathergy test positivity (%)	14 (46.6%)	-	-

ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, ASO: antistreptolysin O, ns: not significant



**Figure 1.** ASO levels of patients and controls at scatter plot. Group 1=patient, Group 2=control.

Thus, hypersensitivity to streptococcal antigens was thought to influence the development of symptoms in patients with Behcet's disease [16, 17]. There are few studies investigating the level of ASO in patients with Behcet's disease [15, 18].

In the study conducted by Namba et al., streptococcal antigen levels of patients with Behcet's disease were significantly higher than those of healthy controls and other patients with uveitis [18]. In another study, there was a strong relationship between Behcet's disease and a history of recent streptococcal infections found by Heymann et al. in a study of 26 patients with Behcet's disease and 56 healthy controls [19]. There was another trial on the correlation of ASO and pathergy test, but they could not find any correlation [20]. In our study, we found a significant difference in ASO levels between the controls and the patients, but similarly, we could not find any correlation among ASO, CRP, and ESR values.

In a study of vitamin E supplementation in Behcet's disease, ASO, CRP, and ESR levels were significantly higher in the patient group than in the controls [21]. These data were similar to our results. After 6 weeks of vitamin E supplementation, ASO and CRP levels were significantly decreased, but the decrease in CRP levels was not significant. Vitamin E is an important antioxidative molecule, so it was considered to be helpful for activity of the defense system, which could explain the decrease of CRP. ASO levels were found to be related to streptococcus infections, and they peaked at 2-5 weeks. Even when not treated, ASO levels were reduced after the peak.

Exposure to streptococcal antigens in Behcet's disease has been hypothesized as the main cause of the emergence of the disease, and a trial was conducted on this subject that included two groups of patients with Behcet's disease [22]. One group has only colchicum therapy and the other group has colchicum with benzathine penicillin for 24 months. It was found that penicillin therapy was beneficial as adjunctive therapy in preventing recurrences of arthritis, which may indicate a role of streptococci in the etiology of Behcet's disease.

In conclusion, we found significantly higher ASO titers in the Behcet's disease patients compared to the controls. These results suggested that there is a relationship between ASO and Behcet's disease, but future interventional studies are needed to determine ASO in the prevention and/or treatment of Behcet's disease.

**Conflict of interest statement:** The authors declare that they have no conflict of interest to the publication of this article.

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