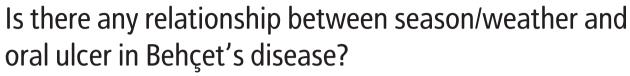


# **Original Investigation**



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# Abstract

**Objective:** Some rheumatic diseases are being influenced by weather conditions. We examined the relationship between oral ulcers and weather/season in Behçet's disease (BD) patients and evaluated the oral ulcers' characteristics by the patients' perspectives.

**Material and Methods:** Patients with BD were evaluated using a self-questionnaire, including patients' clinical and demographical characteristics and detailed characteristics of oral ulcers and the association with season.

**Results:** The most common site of oral ulcers was the tongue (89%). Of 90 patients, there were predisposing factors in oral ulcers. Among patients with BD, 30 believed that seasonal variation aggravated their oral ulcers, especially in winter and autumn.

**Conclusion:** The exacerbation of oral ulcers in patients with BD may be related to the seasons. The weather changes in our study are based on the patients' impression; these should be confirmed by objective findings and clinical assessment in further studies.

Key words: Behçet's disease, season, weather, oral ulcer

#### Introduction

Behçet's disease (BD) is a chronic, relapsing, inflammatory disease characterized by recurrent oral aphthae and any of several systemic manifestations, including genital aphthae, ocular disease, skin lesions, neurologic disease, vascular disease, or arthritis (1). The common clinical feature in patients with BD is the presence of recurrent and usually painful mucocutaneous ulcers (2).

It is an old, popular belief that some rheumatic diseases are being influenced by weather conditions. Seasonal variation has been shown in a number of rheumatic diseases (3).

There has been no previous study that has investigated this issue clearly in Behçet's patients' oral ulcers. The purpose of this study was to investigate the relationship between oral ulcers and weather/season in Behçet's patients and to evaluate the oral ulcers' characteristics by the patients' perspectives. We also examined the possible roles of predisposing factors for Behçet's oral ulcers.

### Material and Methods

One hundred consecutive patients who were followed up at our clinics with a diagnosis of BD according to the International Study Group for BD were included into the study. Data about age, age at diagnosis, age at onset of oral ulcer, disease duration, colchicine using, immunosuppressive agent use, positivity of HLAB51 antigen, and positivity of pathergy test were collected (4). Self-reported questionnaires to assess the oral ulcer characteristics were completed by patients. The questionnaire encompassed questions about patients' clinical characteristics of oral ulcers (site, frequency, healing time, predisposing factors, symptoms before initiation of oral ulcer) and association with season (Questions about seasonal relationship: Do you believe that seasons have a part for the occurrence of oral ulcer? If you believe that there is a relationship between oral aphthous ulcer and seasons, which season aggravates the occurrence of oral ulcer?).

### Statistical analysis

Demographic and clinical variables were summarized as mean±standard deviation (SD) and proportions. Statistical analysis was performed using the SPSS (Statistical Package for Social Sciences) for Windows 9.0 statistical package program (IBM, Chicago, IL, USA).

### Results

# The patients' characteristics

One hundred patients with BD, 48 males and 52 females, were included in this study. Mean age was 35.3±9.8 years, mean age at diagnosis was 30.8±8.8 years, and mean duration of disease was 6.2±6 years.



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Clinical and demographic characteristics of Behçet's patients are shown in Table 1.

#### The features of oral ulcers

Oral ulcers were most commonly reported on the tongue (89%). The number of oral ulcers reported in a year was more than 8 in 73% of patients. The most painful oral ulcers were on the tongue (71%). The mean healing time of oral ulcers changed from 5 to 10 days. Of 90 patients, there was a predisposing factor for oral ulcers. Stress was the most frequent factor in patients (Table 2), and 73% of patients said that some changes had occurred before the oral aphthous ulcer initiated (Table 3).

### Relationship with season

Thirty (30%) BD patients believed that seasonal variation aggravated their oral ulcers, especially in winter (60%) and autumn (20%) (Table 4), although only 5 (20%) of these patients blamed infection as a predisposing factor.

### Discussion

Behçet's disease is a chronic, systemic disease that usually starts with oral ulcers. The prevalence of oral ulcers in BD patients is about 97-100 (2). Although they can occur anywhere in the oral cavity, they are more frequently seen in the tongue, buccal mucosa, mucosal surface of the lips, gingiva, and the soft palate (5-7). We found that oral ulcers are seen more commonly in the tongue. Generally, oral ulcers heal within 7-10 days without scarring, and major oral ulcers are painful (8). In our study, the oral ulcers healed in about 5-10 days, and the site of the tongue was the most painful area.

Various predisposing factors, such as trauma, stress, foods, and microbial factors, can provoke oral ulcers in classic recurrent aphthous stomatitis (RAS) (7, 9). Stress has been implicated in many studies. Sircus et al. (10) reported that emotional and environmental stresses preceded the development of the initial episode of RAS. We found stress, infection, trauma, cold, and some foods as predisposing factors of oral ulcers.

It is believed that weather conditions, such as temperature and moisture, can affect the manifestations of some rheumatic disorders that are especially involving the joints. The incidence of acute gout attacks is highest in spring (11). In systemic lupus erythematosus (SLE) patients, an increased incidence of photosensitive skin rashes occurs predominantly in summer. A survey study found SLE patients to have more joint pain in winter and spring (12). It was reported that the onset of rheumatoid arthritis (RA) was more common in winter

**Table 1.** Clinical and demographical characteristics of Behçet's disease patients

Male, n	48
Female, n	52
Age (years) mean±SD	35.3±9.8
Age at diagnosis (years) mean±SD	30.8±8.8
Age at onset of oral ulcer (years) mean±SD	23.9±9.6
Disease duration (years) mean±SD	6.2±6
Colchicine using n (%)	55 (55%)
Immunosuppressive agent use n (%)	10 (10%)
*HLA B51 antigen positivity n (%)	27 (36%)
**Pathergy test positivity n (%)	41 (46%)

SD: standard deviation; HLA: human leukocyte antigen

**Table 2.** Oral ulcer predisposing factors (total n=90)

	n	%		
Stress	83	92		
Infection	15	16.7		
Trauma	7	7.8		
Smoking cigarette	4	4.4		
Warm	3	3.3		
Cold	11	12.2		
Some foods	11	12.2		

**Table 3.** Symptoms before oral ulcer occurrence

n	%	
20		
26	35.1	
49	66.2	
28	37.8	
21	28.4	
43	59.7	
17	23	
	49 28 21 43	

**Table 4.** Distribution of seasonally aggravated oral ulcers of Behçet's disease patients (total 30 patients)

Season	n	%
Spring	1	3.3
Summer	5	16.7
Autumn	6	20
Winter	18	60

months, and in another RA study, pain was correlated positively with temperature and vapor pressure (13, 14).

The information on the effect of seasonal variation on BD is scarce. We have identified only 3 previous studies that analyzed Behçet's patients' symptoms associated with weather/season, and only 1 of them analyzed the relationship of Behçet's oral aphthous ulcers with season (12, 15, 16) (Table 5). Our study is the first study to evaluate oral ulcer characteristics and their relationship with season by the patients' perspectives in the literature. Krause et al. (12) found no correlation between weather conditions and disease severity of Behçet's patients except for joint symptoms, which were

reported to worsen in autumn and/or spring. They found no correlation between oral ulcer exacerbations and weather/season. In another 2 studies from Korea, they found seasonal variation in the amount of aggravation of BD symptoms. But, in this study, the symptoms were not explained clearly (15, 16). Our results showed that there was increased oral ulcer exacerbation in winter and autumn. The role of environmental factors, especially micro-organisms, is a well known cause in BD pathogenesis and aggravation of BD symptoms (17). Our results can be explained by the increased frequency of viral infections in winter months and other environmental factors. It is well known that upper respiratory infections can be seen more commonly in winter. Viral infections affecting the

<sup>\*75</sup> patients were evaluated \*\*89 patients were evaluated

Table 5. Trials concerning the relationship between Behçet's disease and/or symptoms with seasons

	Our study	Krause et al. (12)	Bang et al. (15)	Kim et al. (16)
Number of patients (Total)	100	16	1155	410
Number of patients thinking or determining that the symptoms are related with seasons	30/100	12/16	246/1155	94/410
Method Self	Self-questionnaires	Activity questionnaires		
		Clinical activity score of Behçet disease	Undefined	Undefined
Searched symptoms related with seasons	Oral ulcer	All Behçet's symptom including oral ulcer	Undefined	Undefined
Outcome	Relation with season was found	No relation was found with oral ulcer Only relation between joint pain and season was found	Disease was aggravated with season	Disease was aggravated with season
Seasons	winter, autumn	autumn, spring	summer, winter	spring, summer

upper respiratory tract, even in healthy people, increase the incidence of oral ulcers during the winter months. In our study, a few patients accused infection as a predisposing factor for the occurrence of oral ulcers in winter and autumn. Seasonal variation as an environmental factor other than infection may facilitate the formation of Behçet's oral ulcer. But, the formation of oral ulcers according to weather changes in our study was based on patients' impressions and could not be confirmed by objective findings and clinical assessments. Also, it is difficult to interpret the results without a control group, such as patients with only recurrent oral aphthous lesions. Another limitation in our study is that the patients reported only subjective complaints. Temperature, barometric pressure, and relative humidity were not taken into consideration during the same period.

In conclusion, this issue can be enlightened more with prospective cohort studies supported by objective meteorological variables.

### Ethics Committee Approval: N/A.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - D.U.C., C.K.; Design - D.U.C.; Supervision - D.U.C.; Resource - D.U.C.; Materials - D.U.C.; Data Collection&/or Processing - D.U.C., T.K.; Analysis&/or Interpretation - D.U.C.; Literature

Search - D.U.C.; Writing - D.U.C.; Critical Reviews - D.U.C., C.K.

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