Sleep quality and its association with disease activity, depression and quality of life in Behçet's disease patients

Behçet hastalarında uyku kalitesinin hastalık aktivitesi, depresyon ve hayat kalitesi ile ilişkisinin değerlendirilmesi

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Abstract

Objective: Quality of sleep is one of the main predictors of quality of life (QoL). Data on sleep quality and associated factors are limited in Behçet's disease (BD), a systemic inflammatory disorder with different organ manifestations. In this study, we assesed depression, anxiety and sleep disorders and their associations with disease activity of Turkish patients with BD to establish the relationship between sleep quality, BD activity and QoL scales.

Methods: A cross-sectional study of 105 BD and 85 healthy controls was conducted. All subjects completed short form (SF-36), health assessment questionnaire, hospital anxiety and depression scale, multidimensional assessment of fatigue scale (MAF), American College of Rheumatology 2010 fibromyalgia criteria and sleep quality assessed with the Pittsburgh sleep quality index (PSQI). Behçet's syndrome activity score was used to determine the disease activity of BD.

Results: PSQI scores of patients with BD were significantly higher compared to the control group (p=0.001). Among patients BD patients, groups with poor or good sleep quality had similar patient characteristics in terms of gender, education level, smoking, depression level, major organ involvement and presence of fibromyalgia. Among the clinical features, only genital ulcers were associated with poor sleep quality (p=0.036). After regression analysis, mean PSQI score of patients with BD was associated with age, mental component score of SF-36 and MAF score. The disease activity was not associated with sleep quality but correlated with fatigue, depression, anxiety, QoL scales (p<0.005).

Conclusion: Sleep quality is poor among patients with BD and is associated with increased fatigue, lower QoL. As sleep is an important predictor of QoL, it should be among the patient-reported outcome measures for assessing BD.

Keywords: Behçet's disease, depression, fatigue, sleep quality

Öz

Amaç: Uyku kalitesi, hayat kalitesinin en önemli belirleyicilerinden biridir. Farklı organ tutulumları ile seyreden sistemik enflamatuvar bir hastalık olan Behçet hastalığında hastaların uyku kalitesi ve bunu etkileyen faktörlerle ilgili yayınlanmış çalışmalar sınırlıdır. Bu çalışmada Behçet hastalarında depresyon, anksiyete ve uyku bozukluklarının belirlenmesi ve uyku kalitesi ile hastalık aktivitesi ve yaşam kalite indeksleri arasındaki ilişkisinin değerlendirilmesi amaçlanmıştır.

Yöntem: Kesitsel çalışmamızda 105 Behçet hastası ve 85 sağlıklı kontrol değerlendirilmiştir. Tüm katılımcılara kısa form (KF-36), sağlık değerlendirme anketi, hastane anksiyete ve depresyon anketi, yorgunluk çok boyutlu değerlendirme anketi, Amerikan Romatoloji Derneği 2010 fibromiyalji kriterleri, uyku kalitesi değerlendirilmesi için Pittsburg uyku kalite indeksi (PUKI), hastalık aktivite değerlendirilmesi için Behçet sendrom aktivite skoru uygulandı.

Bulgular: Behçet hastalarının PUKI skorları sağlıklı kontrole göre anlamlı olarak daha yüksekti (p=0,001). İyi ve kötü uyku kalitesine sahip Behçet hastaları değerlendirildiğinde cinsiyet, eğitim düzeyi, sigara içiciliği, depresyon seviyesi, fibromiyalji ve majör organ tutulumu benzerdir. Klinik özellikler arasında ise sadece aktif genital ülserin varlığı kötü uyku kalitesi ile ilişkili bulunmuştur (p=0,036). Regresyon analizinde Behçet hastalarının ortalama PUKI skoru yaşla, KF-36'nın mental bileşen özeti ve yorgunlukla ilişkili bulunmuştur. Hastalık aktivitesinin uyku kalitesi ile ilişkisi bulunmamakla birlikte yorgunluk, depresyon ve anksiyete ve yaşam kalite ölçütleri ile korelasyonu saptanmıştır (p<0,005).

Sonuç: Uyku kalitesi Behçet hastalarında sağlıklı populasyonla karşılaştırıldığında daha kötüdür ve yorgunluk, düşük hayat kalitesi ile ilişkilidir. Uykunun hayat kalitesinin önemli bir belirleyicisi olduğu düşünüldüğünde Behçet hastalarının değerlendirme ölçütleri arasında olması önemlidir.

Anahtar Kelimeler: Behçet hastalığı, depresyon, yorgunluk, uyku kalitesi

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Introduction

Behçet's disease (BD) is a chronic, systemic inflammatory disease characterized by recurrent oral and urogenital aphthous ulcers, ocular, musculoskeletal, vascular and central nervous system involvement.[1] Although the etiology is unknown, infectious agents, autoimmunity and genetic factors are thought to be associated with the disease. Many studies suggested that physical and psychological stresses also have some influence on the development of immune dysregulation in BD.[1-4]

Chronic inflammation, treatment toxicities and disease-related damage in chronic inflammatory diseases can affect patients' quality of life (QoL) and functional status seriously. Modern health care has focused on the association of mental and social health with physical health, which are all important predictors of QoL and it is essential to evaluate the health-related QoL of patients. One of the important items of QoL is the quality of sleep and a recent study revealed that sleep quality was the most important factor for wellness rated by patients themselves.[5] Psychiatric disorders, depression and anxiety can also affect sleep quality, as well as the disease itself.

There are very limited data of patients with BD with disturbed sleep quality, increased depressive symptoms and anxiety.[6-8] In this study, we assessed depression, anxiety and sleep disorders and their associations with disease activity of Turkish patients with BD to establish the relationship between sleep quality, BD activity and QoL scales.

Materials and Methods

BD patients (n=105) classified using International Study Group (ISG) criteria and 85 healthy controls were recruited to our study between May 2012 and September 2013.[9] Patients who weren't classified as BD according to ISG criteria, with age <18 or more than 65 years, diagnosed psychiatric disease and pregnancy are excluded from our study.

Patient, disease characteristics and demographic information were recorded into study form.

Parameters Used in the Study

Behcet's Syndrome activity score (BSAS) comprised 10 questions, containing visual analog scales for patient's level of discomfort due to oral ulcers, genital ulcers, skin lesions and current disease activity.

Also, the BSAS categorizes the number of oral ulcers, genital ulcers, and skin lesions present and evaluates whether there is an eye, gastrointestinal, or vascular involvement. Physician's global assessment was scored from 0 (inactive) to 10 (active) to assess the disease activity.[10]

Turkish validated short form (SF-36), health assessment questionnaire (HAQ) score, both validated for Turks, were used.[11-14] Hospital anxiety and depression scale (HADS), Multidimensional assessment of fatigue scale (MAF) were also assessed.[15-17] Fibromyalgia is diagnosed on the basis of American College of Rheumatology 2010 criteria.[18]

The Pittsburgh Sleep Quality index (PSQI) evaluates the patient's self-reported sleep quality over the last month. The scale has 19 items and measures 7 components of sleep quality: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. By using these 7 individual scores, a total PSQI score is calculated (range=0-21). The diagnostic specificity of the test for clinical sleep disturbances was high, scores above 5 indicated poor sleep quality.[19,20]

Statistical Analyses

The statistical program SPSS version 21.0 was used for data processing and statistical analysis. Categorical variables are presented as frequencies and percentages. Histogram, normal quantile plot, Kolmogorov-Smirnov, and skewness kurtosis tests were used for normality evaluation of continuous variables. Mann-Whitney U and Kruskal-Wallis tests were used to compare the groups with continuous variables. Correlations for continuous variables were evaluated with the Spearman test, where both rho and p values were presented. As multivariate analysis, binary logistic and ordinal regression models were used, and odds ratios with 95% confidence interval.

Univariate regression analysis showed that age, disease duration, MAF, HAQ, PCS, MCS and HADS-A (p<0.05) were statistically significant variables for poor sleep quality, and all these variables were included for multivariate regression analysis.

The institutional review board of the Medical School approved the study (09.2012.202), and all participants gave informed consent.

Results

Demographic and clinical characteristics of the study population are described in Table 1. There was no difference between BD and control groups regarding gender and age. Thirty (28.6%) of patients with BD were under the immunosuppressive drugs during the study. PSQI scores of patients with BD were significantly higher compared with the control group. The median MAF score also increased in patients with BD compared with the control group (p=0.001, Table 1).

BD (29.5%) patients had increased depression than the control group (13.1%, p=0.008), but there was no difference between the groups in terms of anxiety (18.1% and 11.9% for BD and control group respectively, p>0.05) (Table 1).

Clinical and demographic characteristics of patients with BD with poor or good sleep quality are presented in Table 2. Although there was no difference between the groups in terms of disease activity (BSAS score), among clinical features, only genital ulcers were associated with sleep quality (83% of patients with BD having one or more genital ulcer over last month of evaluation had poor sleep quality compared to 50% in patients without genital ulcers, p=0.036). BSAS was positively correlated with MAF (r:0.39, p=0.000), HAQ (r:0.343, p=0.000) and negatively associated with MCS (r:-0.289, p=0.003) and PCS (r:-0.479, p=0.000).

Mean PSQI score of patients with BD had positively correlated with age (r:0.311, p=0.001), disease duration (r:237, p=0.015), HAQ (r:0.38, p=0.000), MAF (r:0.37, p=0.000), HADS-A (r:0.31, p=0.000) and negatively associated with all subgroups of SF-36, physical, and mental component score: PCS, MCS (r:-0.308 and -0.268 respectively, p<0.005).

Table 1. Demographic and clinical features of patients with BD and healthy controls

		BD (n=105)	HC (n=85)	p
Male		64 (61%)	48 (56.5%)	0.556
Age (years)		39.7±11.2	41.8±10.6	0.190
Smoking		32 (31.1%)	28 (32.9%)	0.875
Disease duration in years		8.8±6.8		
BSAS (median, 25-75 percentile)		20 (7-35)		
The type of disease (n:102)	Mucocutaneous	59 (59.8%)		
	Major organ	43 (42.2%)		
PSQI global score		5.7±3.2	3.4±2.8	**0.000**
Bad sleep quality according to the PSQI		50 (47.6%)	12 (14.1%)	**0.000**
Fibromyalgia		21 (20.4%)	6 (7.1%)	**0.012**
MAF score (median, 25-75)		21 (0-30)	13.3 (0-21.5)	**0.001**
HADS-A (0-21)		6.3±3.7	5.1±3.4	**0.020**
HADS-D (0-16) (median, 25-75 percentile)		5 (2-7)	3 (1-5)	**0.007**
SF-36	PCS	43.3±10.2	52.3±7.5	**0.000**
	MCS	45.1±9.9	51.6±8.0	**0.000**
	HAQ (median, 25-75 percentile)	0.1 (0-0.33)	0.0 (0-0.1)	**0.000**

BD: Behçet's disease, BSAS: Behcet syndrome activity score, HADS-A/HADS-D: Hospital anxiety/depression scale, HAQ: Health assessment questionnaire, HC: Healthy control, MAF: Multidimensional assessment of fatigue scale, MCS: Mental component score, PCS: Physical component score, PSQI: Pittsburgh sleep quality index, SF-36: Short form

Table 2. Clinical and demographic characteristics of patients with BD with good and bad sleep quality

Behçet's disease patients

		Good sleep quality (n=55)	Bad sleep quality (n=50)	p
Male		29 (52.7%)	35 (70%)	0.076
Age (years)		36.5±10.7	43.3±10.9	**0.000**
Smoking		15 (28.3%)	17 (34%)	0.670
Disease duration in years (mean ± SD)		7.1±5.3	10.7±7.7	**0.006**
Type of involvement				
Major organ		26 (49.1%)	17 (34.7%)	0.164
Mucocutaneous		27 (50.9%)	32 (65.3%)	
Immunosuppressive usage		20 (37%)	10 (20%)	0.082
BSAS (median, 25-75 percentile)		15 (5-34)	21 (11.5-35)	0.148
SF-36	PCS	46.3±10.4	40±9	**0.001**
	MCS	48±8.7	41.8±10.2	**0.001**
Anxiety		5 (9.1%)	14 (28%)	**0.021**
Depression		13 (23.6%)	18 (36%)	0.201
Fibromyalgia		7 (13%)	14 (28.6%)	0.055

BSAS: Behçet syndrome activity score, MCS: Mental component score, PCS: Physical component score, SD: Standard deviation

However, there was no correlation between PSQI score and doctor/patient global assessment (p>0.05). Multivariate logistic regression analysis revealed that increased age, MCS and MAF score statically significantly related to poor sleep quality (Table 3).

Fifty-nine (59.8%) of patients with BD had mucocutaneous and 43 (42.2%) had a major organ involvement. There was no difference between these two groups in terms of PSQI score, MAF score and the rate of depression.

PSQI include subgroup evaluation about subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Table 4 shows a subgroup evaluation of the index between the groups. Most parameters were disturbed for patients with BD compared with the control group.

Discussion

Our study results showed that BD had higher degree of poor sleep quality, depression, and fatigue scores with significantly lower QoL.

Our results support previous studies in the literature. Koca et al.[21] demonstrated higher PSQI scores in patients with BD from Turkey. Another study from Korea also reported decreased sleep quality for patients with BD.[8] Like our study, previous studies revealed that more than 40% of patients with BD have poor sleep quality.[8,22]

Senusi et al.[23] reported poor sleep quality in patients with BD. In this study, female patients with BD had worse sleep quality compared with males, opposite to our study, which showed no difference between gender groups in terms of sleep quality. This difference could be a result of increased fatigue in female patients as fatigue is closely correlated with poor sleep. In our study female and male patients with BD had similar fatigue scores. Unlike our study, Senusi et al.[23] showed no effect of age on sleep quality.

Our results also showed that patients with BD scored significantly higher in sub-components of PSQI with decreased subjective sleep quality-sleep duration, increased sleep latency-sleep disturbances- daytime dysfunction. Yazmalar et al.[22] reported similar disturbances in sleep characteristics for patients with BD.

Previous studies showed different results about the association between disease activity and sleep scores of patients with BD. Senusi et al.[23] and Koca et al.[21] showed a positive correlation between bad sleep quality and high disease activity.[21,23] In contrast to these studies our study like research from Korea, showed no association between sleep quality and disease activity.[8] These conflicting results may be explained by the challenges of evaluating disease activity of patients with BD because of its fluctuating clinical course and different tools were used in our research and the other studies. The only clinical finding correlated with lower sleep quality was genital ulcers in our study, complaining of one or more genital ulcers increased the risk of having poor sleep quality. Tascilar et al.[6] also reported a positive correlation between genital ulcers and wake before sleep, non-REM sleep latency and percentage of REM sleep.

One-fifth of patients with BD had fibromyalgia in our study and even it is not statically significant, patients with BD with poor sleep quality had increased fibromyalgia than patients with good sleep quality (Tables 1, 2). Previous studies showed increased fibromyalgia in patients with BD and increased central sensitization, which is disturbed in fibromyalgia.[24,25] Because of cross-sectional nature of the

Table 3. Logistic regression analysis for factors affecting poor sleep quality in patients with BD

	Multivariate analysis OR (95% CI)	p-value
Age	1.068 (1.023-1.114)	**0.003**
MAF	1.067 (1.031-1.104)	**0.000**
MCS	0.946 (0.899-0.996)	**0.033**

BD: Behçet's disease, CI: Confidence interval, MAF: Multidimensional assessment of fatigue scale, MCS: Mental component score, OR: Odds ratio

Table 4. Comparison of sleep quality components between groups

	BD	Healthy control	p
Subjective sleep quality	1 (0-3)	1 (0-3)	**0.001**
Sleep latency	1 (0-3)	0 (0-3)	**0.000**
Sleep duration	1 (0-3)	0 (0-3)	**0.008**
Habitual sleep efficiency	0 (0-3)	0 (0-3)	**0.062**
Sleep disturbances	1 (0-3)	1 (0-2)	**0.000**
Use of sleeping medication	0 (0-3)	0 (0-3)	**0.166**
Daytime dysfunction	1 (0-2)	0 (0-2)	**0.004**

All values are presented as medians (min-max), BD: Behçet disease

study, we could not conclude whether poor sleep quality is the cause or result of fibromyalgia in patients with BD. Previous studies searching for the frequency of fibromyalgia in patients with BD showed similar results to our study but the most patients with BD with fibromyalgia were females, unlike our study; 10% of our female patients with BD and 27% of male patients had fibromyalgia (p=0.046).[25,26]

Twenty-nine percentage of our patients with BD had depression. Previous studies have confirmed a higher prevalence of depression in patients with BD similar to other inflammatory rheumatic diseases such as RA and psoriasis.[7,27] Depression score and disease activity assessed with BSAS correlated, similar to the results reported by Melikoglu and Melikoglu[27] The interaction between physical and emotional health during rheumatic diseases is well-known and stressful life events can cause depression and relapse of BD. Stressful life events may precipitate relapses and may occur just before increased disease activity.[28]

An increased fatigue was present in patients with BD similar to other inflammatory diseases[29,30] and in our study, MAF score and bad sleep quality association was still statistically significant after regression analysis. Our study also revealed that mental, and physical well-being in patients with BD were decreased compared with healthy individuals. Moreover, patients with BD with poor sleep quality had decreased QoL scores although this correlation is only statically significant for MCS after multivariate regression analysis (Tables 2 and 3). A recent study showed that sleep quality is the most important predictor of patients with BD' self-rated wellness and another study found a deterioration in QoL for patients with BD with sleep disturbances and high disease activity. Our study showed an association between QoL and disease activity of patients, too.[5,8] This may suggest that patients' QoL can be eased by sustaining the low disease activity and using patient-reported measures such as patient-global, fatigue, MAF, and PSQI as a part of routine clinical practices.

Study Limitations

As the limitations of the study, patients with BD were from a hospital population and can minimally represent the full spectrum of BD in the community. Although we excluded all patients with active psychiatric disorder, we did not have a detailed psychiatric histories of the patients. Also, cross-sectional analysis of disease activity, MAF, PSQI, depression and anxiety evaluation can be affected by other potential influencers. The lack of data for obesity and cumulative steroid dosage, which can be a possible effector of sleep quality, is another limitation for our study.

Conclusion

Poor sleep quality and increased depression were detected among patients with BD compared with healthy persons. Poor sleep quality was affected by age, fatigue, and a lower mental component score of SF-36. As sleep is an important predictor of QoL, it may affect the patient's perception of the disease and expectations of treatment outcome. The patient reported measures can be used in routine clinical practice and treatment plans should also incorporate them.

Ethics

Ethics Committee Approval: The institutional review board of the Medical School approved the study (09.2012.202).

Informed Consent: All participants gave informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ö.P.K., A.A., B.I., F.A.O., H.D., Design: Ö.P.K., A.A., B.I., F.A.O., H.D., Data Collection or Processing: Ö.P.K., A.A., B.I., F.A.O., H.D., Analysis or Interpretation: Ö.P.K., A.A., B.I., F.A.O., H.D., Literature Search: Ö.P.K., A.A., B.I., F.A.O., H.D., Writing: Ö.P.K., A.A., B.I., F.A.O., H.D.

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References

1. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. N Engl J Med 1999;341:1284-91.

2. Ohno S, Ohguchi M, Hirose S, Matsuda H, Wakisaka A, Aizawa M. Close Association of HLA-Bw51 With Behçet's Disease. Arch Ophthalmol 1982;100:1455-58.

3. Stojanovich L. Stress and autoimmunity. Autoimmun Rev 2010;9:A271-6.

4. Kaneko F, Togachi A, Nomura E, et al. Role of Heat Shock Protein Derived from Streptococcus sanguinis in Behcet?s Disease. J Medical Microbiol Diagnosis 2012;03.

5. Masoumi M, Tabaraii R, Shakiba S, Shakeri M, Smiley A. Association of lifestyle elements with self-rated wellness and health status in patients with Behcet's disease. BMC Rheumatol 2020;4:49.

6. Tascilar NF, Tekin NS, Ankarali H, et al. Sleep disorders in Behcet's disease, and their relationship with fatigue and quality of life. J Sleep Res 2012;21:281-8.

7. Taner E, Coşar B, Burhanoğlu S, Calikoğlu E, Onder M, Arikan Z. Depression and anxiety in patients with Behçet's disease

compared with that in patients with psoriasis. Int J Dermatol 2007;46:1118-24.

8. Lee J, Kim SS, Jeong HJ, et al. Association of sleep quality in Behcet disease with disease activity, depression, and quality of life in Korean population. Korean J Intern Med 2017;32:352-9.

9. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's Disease. Lancet 19905;335:1078-80.

10. Yilmaz S, Simsek I, Cinar M, et al. Patient-driven assessment of disease activity in Behçet's syndrome: cross-cultural adaptation, reliability and validity of the Turkish version of the Behçet's Syndrome Activity Score. Clin Exp Rheumatol 2013;31(3 Suppl 77):77-83.

11. Koçyigit H, Aydemir O, Fisek G. Kısa Form-36 (KF-36)'nın Türkçe versiyonunun güvenilirliği ve geçerliliği. İlaç ve Tedavi Dergisi 1999;12:102-6.

12. Küçükdeveci AA, Sahin H, Ataman S, Griffiths B, Tennant A. Issues in cross-cultural validity: example from the adaptation, reliability, and validity testing of a Turkish version of the Stanford Health Assessment Questionnaire. Arthritis Rheum 2004;51:14-9.

13. Ware JE Jr, Kosinski M, Bayliss MS, McHorney CA, Rogers WH, Raczek A. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary of results from the Medical Outcomes Study. Med Care 1995;33(4 Suppl):AS264-79.

14. Bruce B, Fries JF. The Health Assessment Questionnaire (HAQ). Clin Exp Rheumatol 2005;23(Suppl 39):S14-8.

15. Multidimensional Assessment of Fatigue (MAF) User's Guide. . University of Washington. 2010;(updated 2012; cited 2012 13/1).

16. Aydemir O. Hastane anksiyete ve depresyon ölçeği Türkçe formunun geçerlilik ve güvenilirlik çalışması. Turk Psikiyatri Derg 1997;8:280-7.

17. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-70.

18. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken) 2010;62:600-10.

19. Buysse DJ, Reynolds CF, Monk TH, Hoch CC, Yeager AL, Kupfer DJ. Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). Sleep 1991;14:331-8.

20. Agargün MY, Kara H, Anlar O. The Validity and Reliability of the Pittsburgh Sleep Quality Index. Turk Psikiyatri Derg 1996;7:107-15.

21. Koca I, Savas E, Ozturk ZA, et al. The relationship between disease activity and depression and sleep quality in Behcet's disease patients. Clin Rheumatol 2015;34:1259-63.

22. Yazmalar L, Batmaz I, Mustafa A. et al. Sleep quality in patients with Behcet's disease. Int J Rheum Dis 2014;20:2062-9.

23. Senusi AA, Liu J, Bevec D, et al. Why are Behçet's disease patients always exhausted? Clin Exp Rheumatol 2018;36(6 Suppl 115):53-2.

24. Ayar K, Okmen BM, Altan L, Ozturk EK. Central sensitization and its relationship with health profile in Behcet's disease. Mod Rheumatol 2021;31:474-80.

25. Toprak M, Erden M, Alpayci M, et al. The frequency and effect of fibromyalgia in patients with Behcet's disease. Turk J Phys Med Rehabil 2017;63:160-4.

26. Jobanputra C, Richey RH, Nair J, Moots RJ, Goebel A. Fibromyalgia in Behçet's disease: a narrative review. Br J Pain 2017;11:97-101.

27. Melikoglu MA, Melikoglu M. The relationship between disease activity and depression in patients with Behcet disease and rheumatoid arthritis. Rheumatol Int 2010;30:941-6.

28. Koptagel-Ilal G, Tuncer O, Enbiyaoglu G, Bayramoğlu Z. A Psychosomatic İnvestigation of Behçet's Disease. Psychother Psychosom 1983;40:263-71.

29. Buyuktas D, Hatemi G, Yuksel-Findikoglu S, Ugurlu S, Yazici H, Yurdakul S. Fatigue is correlated with disease activity but not with the type of organ involvement in Behçet's syndrome: a comparative clinical survey. Clin Exp Rheumatol 2015;33(6 Suppl 94):S107-12.

30. Ilhan B, Can M, Alibaz-Oner F, et al. Fatigue in patients with Behçet's syndrome: relationship with quality of life, depression, anxiety, disability and disease activity. Int J Rheum Dis 2018;21:2139-45.