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# Prevalence of Restless Legs Syndrome among Psoriasis Patients and Association with Depression and Sleep Quality

## Psoriasis Hastalarında Huzursuz Bacak Sendromu Sıklığı ve Depresyon ve Uyku Kalitesi ile İlişkisi


## Abstract

**Objective:** Restless legs syndrome (RLS) is a chronic disorder characterized by an urge to move the legs. In the present study, we investigated the frequency of RLS in patients with psoriasis and tried to obtain the effects of RLS on sleep quality and psychiatric wellbeing.

**Methods:** A total of 114 consecutive psoriasis patients (60 women and 54 men) and 67 control subjects who attended the Department of Dermatology and Venereology were enrolled in the study. A diagnosis of RLS was made according to the criteria of the International RLS Study Group (IRLSSG), and severity was assessed using the IRLSSG severity scale. Sixty-seven of 114 patients answered the Turkish version of Beck Depression Inventory (BDI) and Pittsburgh Sleep Quality Index.

**Results:** We found a higher frequency of RLS in psoriasis patients (11.4%) compared to healthy controls (6.0%), but this prevalence has not reached a statistical significance (p=0.23). Body mass index, BDI score, and bad sleep quality were significantly higher in psoriasis patients compared to healthy controls.

**Conclusion:** Since presence of RLS worsens psoriasis patients' already bad quality of life, we suggest screening of patients for the presence of RLS, and directing them to a rheumatologist can improve their quality of life.


**Keywords:** Restless legs syndrome, psoriasis, depression, sleep quality, quality of life, psychiatric wellbeing


## Öz

**Amaç:** Huzursuz bacak sendromu (HBS), karşı konulamayan bacakları hareket ettirme ihtiyacı ile karakterize kronik bir hastalıktır. Çalışmamızda psoriasisli hastalarda HBS sıklığını saptamak ve HBS'nin uyku kalitesi ve duygu durum bozukluğu ile ilişkisini belirlemek amaçlandı.

**Yöntemler:** Deri ve Zührevi Hastalıklar Anabilim Dalımıza başvuran ardışık 114 psoriasis hastası (60 kadın ve 54 erkek) ve 67 sağlıklı kontrol çalışmamıza dahil edildi. HBS tanısı Uluslararası HBS Çalışma Grubu (UHBSÇG) tanı kriterlerine dayanılarak konuldu ve UHBSÇG şiddet skalası ile şiddeti hesaplandı. Beck Depresyon Ölçeği (BDÖ) ve Pittsburg Uyku Kalitesi indeksi 114 psoriasis hastasının 67'si ve tüm sağlıklı kontroller tarafından tamamlandı.

**Bulgular:** Çalışmamızda psoriasis hastalarında HBS (%11,4) sağlıklı kontrollere (%6,0) göre daha sık saptanmasına karşın, bu değer istatiksel anlamlılığa ulaşmadı (p=0,23). Vücut kitle indeksi, BDÖ skoru, kötü uyku kalitesi sağlıklı kontrollerle karşılaştırıldığında psoriasisli hastalarda daha yüksek sıklıkta izlendi.

**Sonuç:** HBS'nin varlığı psoriasisli hastaların mevcut kötü yaşam kalitesi üzerinde negatif etki yapmaktadır. Bu nedenle psoriasis hastalarının kontrollerde HBS varlığı açısından sorgulanması ve şüphelenilen olguların romatoloğa yönlendirilmesi hastaların yaşam kalitesini arttırabilir.


**Anahtar kelimeler:** Huzursuz bacak sendromu, psoriasis, depresyon, uyku kalitesi, yaşam kalitesi, duygu durum bozukluğu

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## Introduction

Restless legs syndrome (RLS) is a common neurological disorder characterized by an urge to move especially the legs (rarely also the arms) and peculiar, unpleasant sensations (paraesthesias) deep in the extremities (1). These sensations appear during periods of rest or inactivity, especially in the evening and at night, and are typically relieved by movement. In the general population, the prevalence of RLS varies between 5-15% (2,3). RLS onset mostly occurs in the forties and fifties (4). It is clearly shown that the prevalence of RLS increases in relation to age, and it is more common amongst women (5,6). There is no laboratory test for the diagnosis of RLS, and it is based on standardized clinical diagnostic criteria by the International RLS Study Group (IRLSSG) (7). Two subgroups of RLS phenotypes have been identified: primary (idiopathic) and secondary (symptomatic) RLS (8). Although patients have no underlying disease in primary RLS, secondary RLS is associated with another disease process (iron deficiency, pregnancy, kidney disease) or taking of substances/drugs. Many studies suggest that RLS might be related with rheumatologic diseases.

RLS is a major cause of insomnia and sleep disruption (9). In addition, sleep loss and fragmentation of sleep due to RLS has a major impact on health and daytime functioning (10). Poor restorative sleep has been connected with pain, fatigability, stress and disease activity in rheumatic disease population (11). Also a high prevalence of sleep disorders including RLS has been reported in rheumatic diseases. Patients with RLS had significantly higher depression and anxiety scores. The impairment of sleep because of RLS symptoms may cause distress and lead to psychiatric illness and decreased wellbeing (12).

Psoriasis is also a chronic multisystem disease of variable course with inflammatory process as other rheumatologic diseases. Due to its chronic inflammatory features, an increased frequency of RLS in patients with psoriasis is expected. Only two studies in the current literature examined RLS in psoriasis patients (13,14). In both studies a positive correlation between RLS and dermatology quality of life index scores was found indicating that RLS seems to have a significant impact on quality of life.

The relationship between RLS frequency and psoriasis has not been fully clarified. There are different results in the current literature. No study exists which investigates the relationship between RLS and sleep quality or depression in psoriasis patients. That's why our study was aimed to investigate the frequency of RLS in patients with psoriasis and tried to obtain the effects of RLS on sleep quality and psychiatric wellbeing.

## Materials and Methods

### Study Participants

Patients with psoriasis and/or psoriatic arthritis who were applied to the outpatient clinic of Dermatology and Venereology Department were recruited to the study. One hundred and fourteen consecutive, volunteer psoriasis patients were enrolled in the study. The demographic and clinical data of patients, including age, sex, duration of psoriasis, current therapy for psoriasis, body mass index (BMI), smoking and drinking habits (alcohol, tea and coffee use), concomitant diseases and drug use, concomitant psoriatic arthritis were recorded. Same dermatologist examined the patients to assess the severity of psoriasis with the psoriasis area severity index (PASI) which is the internationally accepted tool in measuring psoriasis disease activity in literature (15). All patients were also asked to answer the Turkish version of Beck depression inventory (BDI) and Pittsburg sleep quality index (PSQI) at the same day (16,17). Only 67 of 114 psoriasis patients gave the completed BDI and PSQI.

Sixty-seven healthy age- and sex-matched control volunteer subjects were recruited from the patients other than those with psoriasis and psoriatic arthritis whom visited the dermatology outpatient clinic during the specified study period.

Exclusion criteria (for patients and control subjects) were as follows;

1- Participants who cannot differentiate their locomotor system symptoms from RLS,

2- Participants whom has disease associted with secondary RLS [for example; multipl sclerosis, Parkinson's disease, polyneuropathy, lumbosacral radiculopaty, malignancy, chronic obstructive lung disease, amyloidosis, chronic renal failure, peripheral vascular disease, other rheumatologic disease like rheumatoid arthritis (RA), anclosing spondylitis, Behçet's disease, Crohn's disease, thyroid diseases, anemia, depression],

3- Participants whom has drug use associted with secondary RLS like antiepileptics, neuroleptics, calcium canal blokers, dopamin antagonists, antidepressants.

Control subjects were also assessed with the Turkish version of BDI and PSQI.

Patients comprised 60 women (52.6%) and 54 men (47.3%). The mean age was 45.2±15.0 years. The control group was composed of 67 individuals (40 women/27 men). The mean age of the control group was 43.3±12.4 years. The demographic and general clinical features of psoriasis patients and control subjects are shown in Table 1.

Both patients and control subjects completed a data collection interview for RLS by the same rheumatologist, including whether the patient/subject met the five essential diagnostic criteria for RLS and, if so, whether they had been previously diagnosed with RLS, taken medical attention for these symptoms, age onset and duration of RLS symptoms, frecuency of exacerbation periods at one week interval, severity of RLS symptoms according to visual analog scale (VAS), drug use for RLS before, family history for RLS. Ethics Committee approval (Akdeniz University Faculty of Medicine, Clinical Research Ethics Committee, Date: 07.01.2015, Number: 70904504/20, decision number: 6) was obtained and all participants gave written and verbal informed consent according to the Declaration of Helsinki.

### RLS Questionnaire

Diagnosis of RLS was established with using IRLSSG diagnostic criteria (7). All RLS positif subjects were also assessed for the severity of RLS using the IRLSSG rating scale which has been developed aiming to measure the severity of symptoms (18).

### Beck Depression Inventory

BDI which was created by Dr. Aaron T. Beck (16), is a tool used to measure the severity of depression with 21 multiple-choice questions. The lowest score for any question is 0, the highest score is 3.

### Pittsburg Sleep Quality Index

PSQI is a type of sleep disorder scale which examines sleep quality in the last 1 month and provides information about the severity of sleep disorder (17). Total score of sleep quality is accepted as well if total score is under 5. Turkish validity and reliability study of the scale was made by Agargün et al. (19) and internal consistency coefficient was reported as 0.80.

### Statistical Analysis

A preliminary estimate of sample size was based on RLS prevalence in rheumatologic diseases and in general population, for which a study with a type I error of 0.05 and a type II error of 0.2 would require approximately 48 patients per group with two sided significance testing. We planned to include 60 patients in this study to allow for dropouts and the possibility of requiring nonparametric tests for the skewed duration of stay data.

Continuous variables are presented as mean ± standard deviation, while categorical variables are given as percentages (%). The Kolmogorov-Smirnov test was used to verify the normality of the distribution of continuous variables. Statistical analysis of clinical data between two groups consisted of unpaired t-tests for parametric data, Mann Whitney U test analysis for nonparametric data and the chi-square/Fisher's exact test for categorical data. Analyses were performed with PASW 18 (SPSS/IBM, Chicago, IL, USA) software. Differences were considered statistically significant when the probability value (p) was 0.05.

## Results

Our study in which we investigated the frequency of RLS in patients with psoriasis, 114 patients with psoriasis and 67 healty control subjects were enrolled. General clinical features of psoriasis patients and controls are shown in Table 1. There were no significant differences in age, sex, smoking, life style, concomitant drug uses, concomitant diseases between psoriasis patients and healty controls. We found a higher frequency of RLS in our psoriasis patients (11.4%) compared to healthy controls (6.0%) but this prevalence hasn't reached to statistical significance (p=0.23). BMI, BDI score, bad sleep quality were significantly higher in psoriasis patients compared to healty controls. Two third of our psoriasis patients with RLS described that RLS symptoms occured after psoriasis. And control subjects have been found to use more frequent alcohol and coffee.

When psoriasis patients with RLS compared with psoriasis patients without RLS no significant differences were found with regard to sex, age, BMI, smoking and drinking habits,

**Table 1. General clinical features of psoriasis patients and controls**

| | Psoriasis patients | Controls | p value |
|---|---|---|---|
| n (Female/Male) | 114 (60/54) | 67 (40/27) | 0.36 |
| Age (mean ± SD) | 45.25±15.00 | 43.36±12.43 | 0.38 |
| BMI (mean ± SD) | 27.69±4.73 | 25.34±3.95 | <0.001 |
| Smoking n (%) | 44 (38.6) | 20 (29.9) | 0.24 |
| Alcohol n (%) | 6 (5.3) | 14 (20.9) | <0.001 |
| Overconsumption of coffee n (%) | 3 (2.6) | 8 (11.9) | 0.01 |
| Fulfilment of RLS criteria (diagnosis) n (%) | 13 (11.4) | 4 (6.0) | 0.23 |
| Duration of psoriasis (mean month ± SD) | 124.80±118.83 | - | - |
| PASI (mean ± SD) | 3.18±3.88 | - | - |
| Rheumatologic drug use n (%)<br>Topical n (%)<br>Systemic n (%)<br>Topical+systemic n (%) | 101 (88.6)<br>32 (31.6)<br>25 (24.7)<br>44 (43.5) | - | - |
| Duration of rheumatologic drug use (mean month ± SD) | 17.13±40.26 | - | - |
| Concominant psoriatic arthritis n (%) | 18 (15.8) | - | - |
| Beck depression inventory score γ(mean ± SD) | 13.61±9.85 | 6.64±5.00 | <0.001 |
| Pitssburg sleep quality index*, γ<br>Good sleep quality: n (%)<br>Bad sleep quality: n (%) | <br>21 (31.3)<br>46 (68.7) | <br>34 (50.7)<br>33 (49.2) | <0.05 |
| Pitssburg sleep quality index score γ(mean ± SD) | 5.97±3.41 | 4.91±3.31 | 0.06 |

SD: Standart deviation, BMI: Body mass index, RLS: Restless legs syndrome, PASI: Psoriasis area severity index, Alcohol: More than 2 days per week (ie at least 3 days) and at least one (50 cL) beer or a single rack or a full glass of wine drinkers grouped as "drinking", Overconsumption of coffee: Drinking more than two cup of coffee Daily, *: Total score of sleep quality is accepted as well if total score is under 5, γ: Total patient number was 67, n=67

life style, PASI, concomitant drug uses, BDI score, PSQI (Table 2). The disease duration was found to be shorter in psoriasis patients with RLS than others. Depression was shown to be more frequent in psoriasis patients with RLS (p=0.031). On the other hand the prevalence of hypertension was more frequent in psoriasis patients without RLS (p=0.015).

No significant difference were found between psoriasis/RLS patients and control/RLS subjects with regard to age, sex, BMI, clinical features of RLS, RLS severity score, BDI scores and PSQI.

## Discussion

We found a higher frequency of RLS (11.4%) in our psoriasis patients compared to healty controls (6.0%) but it wasn't statisticaly significant. This study is important that a few studies have investigated the frequency of RLS in psoriasis and there are different results in the current literature. Also there isn't any study which investigates the relationship between RLS and sleep quality or depression in psoriasis patients.

The reported prevalence of RLS in European countries ranges between 5% and 15%, whereas it is considerably low, 0.1-2.3%, in Asian countries (20). The prevalence of RLS was found to be 3.4% in the western Black Sea coast of Turkey (21). This result is similar to that (3.19%) found in the earlier study from Mediterranean coast of Turkey (22). The prevalence rate of control subjects in our study is a little higher than the prevalence rates reported in Turkey and Asian countries. Although small patient number in our study, this can be due to genetic and environmental differences.

The prevalence of RLS in rheumatologic diseases has been reported high compared to healty controls. RA is the most examined inflammatory disease and frequency of RLS in patients with RA range from 15% to 30% (23,24). Number of studies that examining the prevalence of RLS in chronic inflammatory connective tissue disease even more limited compared with RA (10,12-15). This association was thought to be related to inflammatory processes, iron deficiency, neurochemical predisposition arising from chronic pain, or neuropathies in rheumatologic diseases (24), although it is not certain.

Psoriasis can also be associated with RLS because of its certain rheumatologic features. Only two studies investigated RLS prevalence in psoriasis. Cicek et al. (13) found that RLS prevalence was not significantly increased in patients with psoriasis (18.0%) as compared to healthy individuals (10.8%). But recently in a larger German cohort, Schell et al. (14) found increased frequency of RLS in psoriasis patients (17%) compared to healty controls (4.0%) (p<0.01). Our findings also demonsrated that RLS is a common disorder, affected by 11.4% of psoriasis patients compared to 6.0% of healty controls although it was not significant. It can be due to small number of patients in our study.

**Table 2. Some of the characteristics of psoriasis patients with and without restless legs syndrome**

| | Psoriasis patients with RLS | Psoriasis patients without RLS | p value |
|---|---|---|---|
| n (Female/Male) | 13 (7/6) | 101 (53/48) | 0.93 |
| Age (mean ± SD) | 43.92±17.02 | 45.43±14.81 | 0.74 |
| BMI (mean ± SD) | 26.03±5.22 | 27.90±4.65 | 0.17 |
| Smoking n (%) | 3 (23.1) | 41 (40.6) | 0.22 |
| Alcohol n (%) | 1 (7.7) | 5 (5.0) | 0.53 |
| Overconsumption of coffee n (%) | 0 | 3 (3) | 0.99 |
| Duration of psoriasis (mean month ± SD) | 56.54±53.04 | 133.58±122.21 | 0.04 |
| PASI (mean ± SD) | 1.58±1.13 | 3.39±4.06 | 0.16 |
| Rheumatologic drug use n (%)<br>Topical n (%)<br>Systemic n (%)<br>Topical+systemic n (%) | <br>4 (36.3)<br>4 (36.3)<br>3 (27.2) | <br>28 (31.1)<br>21 (23.3)<br>41 (45.5) | ** |
| Duration of rheumatologic drug use (mean month ± SD) | 14.54±15.41 | 17.47±42.45 | 0.58 |
| Concominant psoriatic arthritis n (%) | 3 (23.1) | 15 (14.9) | 0.43 |
| Concominant diseases<br>Hypertansion n (%)<br>Depression n (%) | <br>1 (7.7)<br>3 (23.1) | <br>17 (16.8)<br>6 (5.9) | <br>0.015<br>0.031 |
| Beck depression score (mean ± SD) | 17.70±11.82 | 12.89±9.40 | 0.19 |
| Pitssburg sleep quality index score (mean ± SD) | 7.50±2.68 | 5.70±3.47 | 0.06 |
| Pitssburg sleep quality index*<br>Good sleep quality: n (%)<br>Bad sleep quality: n (%) | <br>1 (10)<br>9 (90) | <br>20 (35.1)<br>37 (64.9) | 0.15 |

SD: Standart deviation, BMI: Body mass index, RLS: Restless legs syndrome, PASI: Psoriasis area severity index, *: Total score of sleep quality is accepted as well if total score is under 5,

**: Insufficient sample

Two thirds of our psoriasis patients specified that RLS symptoms occurred after psoriasis. This can demonstrate that psoriasis disease process may be a risk factor for the development of RLS. Schell et al. (14) suggested that the chronic inflammation of the skin could influence RLS symptoms.

Psoriasis patients with RLS have shorter psoriasis disease duration than others (p=0.04). It can be due to increased rheumatologic drug use in long-term psoriasis patients. Suppression of RLS symptoms may caused by systemic anti-inflammatory, immunosupressive treatment for psoriasis. Additionally this finding demonstrates the necessity of informing psoriasis patients to RLS symptoms in the early stage. Increased recognition of RLS can lead us to cure this treatable problem.

The association of increased rates of primary sleep disorders seen in rheumatologic diseases, including RLS, is likely explained by rheumatologic diseases' chronic inflammatory features with numerous proinflammatory cytokines and other immunomodulatory changes (24). Sleep itself is generally divided into two main components of rapid eye movement (REM) and non REM (NREM) sleep. During the night, individuals have cycles between the various sleep stages and fluctuations in hormone and cytokine levels are detected (25). Some inflammatory mediators interleukin (IL)-1β and tumor necrosis factor (TNF-α) have a diurnal rhythm with elevated levels during sleep (26). And it has been previously reported that IL-4, IL-10, IL-13 and transforming growth factor (TGF)-β can interact to inhibit NREM sleep (25). Recent trials assessing subjective sleep outcomes showed benefit of immunomodulatory interventions (methotrexate, adalimumab) in RA patients (27). The use of immunomodulating medications for psoriasis is common like RA. In our study, psoriasis patients reported rheumatologic drug use 60.5% (n=69 patients). Patients were on traditional antipsoriatic drugs like methotrexate 40.4% (n=46) or cyclosporine 7.1% (n=8). Patients were using acitretin 9.7% (n=11), none of them were using the TNF-α antagonists or ustekinumab. This data shows that the majority of our psoriasis patients have moderate to severe psoriasis requiring systemic therapies. Systemic anti-inflammatory, immunosupressive treatment of patients may cause both suppression in psoriasis disease activity and symptoms of RLS by above-mentioned mechanisms. Also it is shown that psoriasis patients without RLS tended to have hypertension more frequent (p=0.015) (Table 2). This finding may be due to the positive effects of antihypertensive drugs on the symptoms of RLS (28).

RLS severity is expected to increase during exacerbation of rheumatologic diseases as a result of increased inflammatory cytokines. In a recently study it was shown that majority of patients reported that RLS severity shows an increase in the period of incline in Crohn's disease activity (29). Surprisingly, all 3 studies about psoriasis have shown no correlation between the PASI score and RLS symptoms, indicating that the severity of clinical manifestation of psoriasis does not seem to affect RLS (13,14).

We have detected that BMI, BDI score, PSQI were significantly higher in psoriasis patients compared to healty controls. Observation of this poor sleep quality and elevated depression scores in patients with psoriasis, and taken into consideration of its effects on quality of life and psychological state, psoriasis has important effects on daily life. Also psoriasis patients with RLS tended to have history of depression diagnosis (p=0.031) and more elevated BDI scores (p=0.19) although it wasn't statisticaly significant (Table 2). That could indicate coexistence of psoriasis and RLS increases negative psychological impact on individuals'.

We haven't found any difference with regard to obesity between RLS positive and negative patients and control subjects. But obesity was observed more frequently with psoriasis patients compared to control subjects as previously reported (30). This again showed that patients with psoriasis should be careful in terms of obesity and metabolic syndrome. BMI was found to be increased in psoriasis patients which also had bad sleep quality. So may be BMI has relation with sleep quality but not with RLS.

Since presence of RLS worsens psoriasis patients' already bad quality of life, we suggest screening patients for the presence of RLS and directing them to a rheumatologist can improve their quality of life.

## Conclusion

Current study have shown that psoriasis can accompany with RLS, depression and bad sleep quality. Evaluation of the patients by taking into account all these associations can be helpful to enhance patients' quality of life.

### *Ethics*

*Ethics Committee Approval: Akdeniz University Faculty of Medicine, Clinical Research Ethics Committee, Date: 07.01.2015, Number: 70904504/20, decision number: 6, Informed Consent: All participants gave written and verbal informed consent.*

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### *Authorship Contributions*

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