



# Restless Leg Syndrome in Hidradenitis Suppurativa Patients: A Cross-Sectional Study with Current Literature Review

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## Abstract

**Aim:** High frequencies of restless leg syndrome (RLS) have been reported in many dermatologic diseases like psoriasis and atopic dermatitis; however, its relationship with hidradenitis suppurativa (HS) is not clearly known. The aim of this study was to analyze the relationship between RLS and HS.

**Methods:** The cases of HS admitted to the dermatology clinic from February 2021 to May 2021 were included in this cross-sectional study. The study included HS patients as well as an age- and sex-matched healthy control group. The patients were evaluated with Hurley clinical staging. Body mass index (BMI) and waist circumference were noted. Laboratory tests were performed. A diagnosis and severity assessment of Restless legs syndrome were made using the International RLS Study Group (IRLSSG) criteria and the IRLSSG severity scale, respectively.

**Results:** A total of 40 patients with HS were enrolled in the study, with a control group of 99 healthy adults who were age and sex matched. The frequencies of RLS in the HS and control groups were 22.5% and 15.2%, respectively, and there was no statistically significant difference ( $p=0.43$ ). Restless leg syndrome was rated as "very severe" in 55.6% of HS patients compared to 33.3% in the control group. There was no statistically significant difference in RLS severity among the groups ( $p=0.57$ ).

**Conclusion:** There was no increase in the frequency of RLS in HS patients.

**Keywords:** Dermatology, hidradenitis suppurativa, restless leg syndrome

## Introduction

Restless legs syndrome (RLS) is a common nervous system disorder that causes unpleasant leg feelings that are difficult to describe and an intense need to move them (1). Recent literature proposes possible conditions whereby patients with some defined diseases could also have RLS. The overall quality of this research, however, restricts the proven relationship of RLS to only a few diseases, such as uremia and iron deficiency anemia (2).

There is some evidence in the literature that RLS frequency is increased in a few dermatologic diseases such as psoriasis, atopic dermatitis (AD), and chronic spontaneous urticaria (CSU) (3-6). Sensory nerve cells in

the skin respond to various stimuli, ranging from light touch to painful stimuli. The immune system and the neurological system share many characteristics. This has led to the discovery that nerve cells have some capabilities in common with innate immunity cells and can recognize infections and participate in innate immune responses. Soluble mediators from immune cells activate neurons, and soluble mediators from neurons can activate immune cells bidirectionally (7). The increased frequency of RLS in dermatologic diseases may be explained by this cutaneous neuro-immune interaction.

Although there are many studies pointing to sleep disturbance in hidradenitis suppurativa (HS) patients (8-

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10), there are no studies investigating the association of RLS in this patient group. The purpose of this study was to investigate the frequency and severity of RLS in HS patients, as well as the factors that influence it.

## Methods

### Compliance with Ethical Standards

The study was approved by the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital, Clinical Research Ethics Committee (decision date: 23.12.2020, approval number: 2020-250), and all the patients who took part in it provided their written consent.

### Study Design

Cases of HS admitted to the dermatology clinic from February 2021 to May 2021 were included in this cross-sectional study. The study included HS patients as well as an age- and sex-matched healthy control group. A clinical examination was performed after the patients' detailed histories were taken. Patients were evaluated with Hurley clinical staging. Body mass index (BMI) and waist circumferences were noted. Laboratory tests were performed. The International RLS Study Group (IRLSSG) criteria and IRLSSG severity scale were used to diagnose RLS and assess its severity.

### Assessment of restless leg syndrome

All patients with HS, as well as an age- and sex-matched healthy control group, were requested to fill out an RLS symptom questionnaire, which included four cardinal criteria for RLS as defined by the IRLSSG:

- Uncomfortable leg sensations that lead to a desire to move them,
- Symptom onset or worsening during periods of rest,
- Symptom relief can be achieved by movement, such as walking or stretching, at least during the activity.
- Symptoms that are worse in the evening or at night than they are during the day, or that only happen in the evening or at night (11).

The symptoms were further divided into four categories: mild (1-10 points), moderate (11-20), severe RLS (21-30), and extremely severe according to the IRLSSG severity scale (31-40) (12).

Exclusion criteria were psychiatric illnesses, neurologic diseases such as MS and Parkinson disease, dermatologic diseases other than HS, rheumatologic diseases, end-stage renal disease, and pregnancy.

## Results

A total of 40 HS patients and 99 age- and sex-matched healthy subjects were enrolled as a control group in the current study. The participants in the HS and control groups

were  $35.7 \pm 14.1$  and  $35.7 \pm 11.2$  years old, respectively. The percentages of male patients in the HS and control groups were 77.5% and 76.5%, respectively. Between the HS and control groups, there was no statistically significant difference in terms of demographic values. The presence of additional diseases like hyperlipidemia, hypertension, hypothyroidism, asthma, etc., and drug usage were statistically significantly higher in the HS group, as expected (Table 1).

The Hurley stages were distributed as follows: stage 1 in 14 patients, stage 2 in 12 patients, and stage 3 in 14 patients. The study found no statistically significant link between the Hurley phases and the presence of RLS in HS patients. Some information about HS patients is demonstrated in Table 2.

There was no statistically significant increase in RLS frequency and severity between the HS and control groups (Figures 1, 2).

In a group analysis, there was no statistically significant difference in age, BMI, waist circumference, age at diagnosis, laboratory data, or accompanying diseases between HS patients with and without RLS (Tables 3, 4).

## Discussion

Hidradenitis suppurativa is a chronic inflammatory illness marked by a range of skin lesions, such as deep nodules, draining tracts, abscesses, and fibrotic scars. These lesions are especially common in areas with a high concentration of apocrine glands, such as the axillary, groin, perianal, perineal, and inframammary regions (13).

Patients who are overweight or obese are more likely to get HS. Obesity results in a larger intertriginous surface area, which generates higher skin friction, increased sweat production and retention, and hormonal alterations that result in relative androgen excess, all of which are linked to HS. Obese people are more likely to develop metabolic syndrome, which is why it is more common in HS patients (14). The BMI and waist circumference of HS patients in this study were approximately 26 and 103, respectively, which are considered overweight.

There are publications showing that sex hormones may have an impact on the pathogenesis of HS. It's more common in women, and the age of onset is generally between puberty and menopause (14). In contrast to the literature, 77.5% of HS patients were male in our study, and the age range consisted of young patients, which did not comply with the above findings.

Hidradenitis suppurativa is one of the dermatological illnesses that has the most impact on one's quality of life (13). The severity of the disease, the number of flares, and the location of the lesion are the key factors that affect the quality of life. HS affects not only physical but also emotional and psychosocial beings (15).

The fact that it has such a negative impact on the quality of life could be attributed to its unpleasant symptoms. Patients' lives are made more difficult by HS lesions, which cause discomfort, itching, odor, and suppuration (16). Pain appears to be the most common and annoying symptom among HS patients, and it is

mentioned more frequently than other skin conditions (17). As in neuropathic pain, the pain is primarily described as shooting, itching, and burning (18). Pruritus is another HS symptom that is frequently neglected in the literature, although HS is not generally recognized as a pruritic disease (19).

**Table 1. Demographic variables of groups**

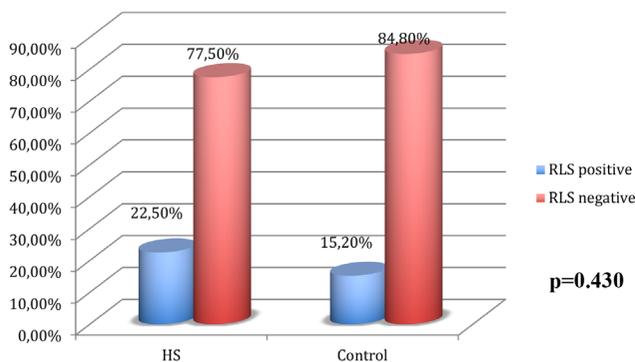
		HS	Control	
		Mean±SD (median)	Mean±SD (median)	p-value
<b>Age</b>		35.7±14.1 (33)	35.7±11.2 (35)	<sup>1</sup> 0.699
<b>Children number</b>		2.6±1.4 (2)	2.1±1.0 (2)	<sup>1</sup> 0.170
		<b>n (%)</b>	<b>n (%)</b>	
<b>Gender</b>	Male	31 (77.5%)	76 (76.5%)	<sup>2</sup> 0.8
	Female	9 (22.5%)	23 (23.5%)	
<b>Marriage status</b>	Married	18 (45%)	72 (72.7%)	<sup>3</sup> 0.002*
	Single	22 (55%)	27 (27.3%)	
<b>Having children</b>	Yes	20 (100%)	68 (94.4%)	<sup>4</sup> 0.573
	No	0 (0%)	4 (5.6%)	
<b>Other diseases</b>	Yes	22 (55%)	14 (14.1%)	<sup>2</sup> 0.000*
	No	18 (45%)	85 (85.9%)	
<b>Drug usage</b>	Yes	38 (100%)	16 (16.2%)	<sup>4</sup> 0.000*
	No	0 (0%)	83 (83.8%)	

In terms of demographic variables, there was no statistical difference between the groups (except marriage status). Additional diseases and drug usage were higher in the HS group than in the healthy controls, as expected.  
<sup>1</sup>Mann-Whitney U test, <sup>2</sup>Continuity (yates), <sup>3</sup>Chi-square test, <sup>4</sup>Fisher's Exact test, \*p<0.05, HS: Hydradenitis suppurativa, SD: Standard deviation, n: Number

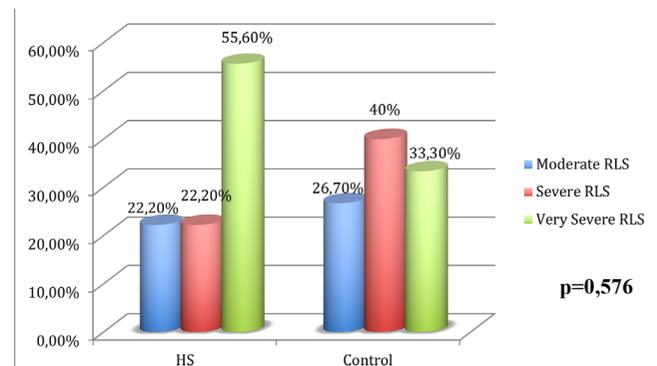
**Table 2. Some Information about the HS group**

	Min.-Max.	Mean±SD	Median
BMI	15.8-36.1	26.08±4.03	26.0
Waist circumference	80-139	103.16±14.14	101.5
Disease duration (year)	1-55	10.25±10.79	6
Age at diagnosis	12-45	24.35±8.15	23

Some characteristics of HS patients were mentioned.  
 BMI: Body mass index, Min.-Max.: Minimum-Maximum, SD: Standard deviation, HS: Hydradenitis suppurativa



**Figure 1.** The frequency of RLS between groups. There was no statistically significant difference in the frequency of RLS between HS and control group  
 Continuity (yates), HS: Hydradenitis suppurativa, RLS: Restless leg syndrome



**Figure 2.** The severity of RLS between groups. There was no statistically significant difference in the severity of RLS between HS and control group  
 Fisher-Freeman-Halton test, HS: Hydradenitis suppurativa, RLS: Restless leg syndrome

Restless leg syndrome, which is among a group of neurological diseases, has increased in several dermatologic diseases such as psoriasis, AD, and CSU, as reported in recent publications (3-6).

The RLS incidence has been observed previously in patients with psoriasis, but there were discrepancies in the outcome of these studies. While some of these studies found an increase in the rate of RLS, some studies did not find any association (20,21).

Many theories have been proposed in the literature to explain the higher frequency of RLS in patients with psoriasis.

Approximately 90% of the diseases associated with RLS appear to be of inflammatory or infectious origin (22).

Since psoriasis is also an inflammatory and autoimmune disease, increased RLS incidence seems logical from this perspective. Restless leg syndrome has also been linked to cardiovascular illness and diabetes mellitus, both of which are common among patients with psoriasis (23). Another possible link between RLS and psoriasis is iron deficiency, which is common in both disorders (24).

Restless leg syndrome is more common in patients with AD, especially in those with active disease (4). The reason for the high rate of RLS could not be explained precisely. But, there are some speculations in the literature about the pathogenesis of these disorders. According to some opinions, RLS symptoms may be confused with the symptoms of itching caused by AD. Clinical evaluation,

**Table 3. Distribution of RLS according to some variables**

	RLS		p-value
	Positive (n=9)	Negative (n=31)	
HS group	Mean±SD (median)	Mean±SD (median)	
Age	37.6±15.3 (40)	35.1±13.9 (32)	0.593
BMI	26.5±3.8 (26.3)	26.0±4.2 (26)	0.859
Waist circumference	101.3±11.7 (99)	103.7±15.0 (102)	0.823
Disease duration	9±6.7 (7)	10.6±11.7 (6)	0.897
Age at diagnosis	26.3±10.5 (25)	23.8±7.4 (22)	0.638
Hemoglobin	13.8±1.22 (12)	14.1±0.8 (13)	0.532
Neutrophil	14.3±21.1 (6.6)	6.7±3.2 (5.5)	0.317
Lymphocyte	3.2±0.6 (3.4)	3.0±1.1 (3)	0.342
CRP	18.4±18.7 (10)	17.9±38.7 (5.7)	0.064
HDL	38.6±9.1 (38)	45.5±12.5 (44)	0.149
LDL	109.6±35.9 (98)	120.2±40.1 (123)	0.391
Albumin	37.0±13.6 (43)	40.5±10.1 (43.9)	0.430
AST	52.7±104.2 (15)	20.3±7.8 (20)	0.744
ALT	21.1±13.9 (17)	24.6±16.7 (19)	0.492
Creatinin	0.72±0.1 (0.7)	0.63±0.2 (0.7)	0.924

In HS patients with and without RLS, there was no statistically significant difference in age, BMI, waist circumference, disease duration, blood values, chronic diseases, or anti-TNF use. Mann-Whitney U test, BMI: Body mass index, SD: Standard deviation, n: Number, HS: Hydradenitis suppurativa, RLS: Restless leg syndrome, CRP: C-reactive protein, HDL: High density lipoprotein, LDL: Low density lipoprotein, AST: Aspartate transaminase, ALT: Alanine aminotransferase

**Table 4. Distribution of RLS according to presence of some chronic diseases and anti-TNF use**

	RLS		p-value
	Positive (n=9)	Negative (n=31)	
HS group	n (%)	n (%)	
Diabetes mellitus	3 (33.3%)	4 (12.9%)	0.316
Hypertension	0 (0%)	4 (12.9%)	0.557
Anti-TNF use	2 (22.2%)	4 (12.9%)	0.602

In HS patients with and without RLS, there was no statistically significant difference in the presence of diabetes mellitus, hypertension and anti-TNF usage. Fisher's Exact test, n: Number, HS: Hydradenitis suppurativa, RLS: Restless leg syndrome

on the other hand, can easily distinguish this. Scratching relieves itching in AD. However, patients with RLS feel uncomfortable and unpleasant sensations in the legs that are relieved with movement (1,25). While the itching in AD can occur throughout the day, there may be a slight increase in the evening at rest. RLS symptoms, on the other hand, are usually felt in the evening or at night. Also, while AD symptoms can appear everywhere on the body or in a specific area, RLS symptoms are most commonly noticed in the legs (1,25).

There is evidence in the literature that the balance between the dopaminergic and noradrenergic systems in the brain is disturbed in patients with AD (25,26). Bupropion, a dopamine reuptake inhibitor, improves lesions of AD and psoriasis in individuals with severe and refractory disease, regardless of emotional circumstances. Although not fully clarified, the improvement of the balance in the dopaminergic system in the CNS may be a factor in the recovery of these lesions. However, other antidepressants may increase the symptoms of RLS by affecting the serotonin level in the nervous system (26,27). These theories may explain the increased frequency of RLS in patients with AD.

Crosstalk between the neurological and immune systems has been discovered in persistent AD, according to recent studies. Understanding the role of peripheral and central sensitization, as well as hypersensitization, in the chronicity and severity of itch in AD is important (28). The activation of central processes can also explain the higher incidence of RLS in active and long-term patients with AD.

Chronic spontaneous urticaria is another dermatological disorder associated with an increased prevalence of RLS. Urticarial pruritus can reduce the quality of sleep in people with RLS, as well as trigger and worsen the condition. Furthermore, RLS and CSU may share the same cause (5). Reports propose that CU may occur through interactions between the immune system and the central nervous system (29).

Pruritus has been discovered to be a possible risk factor for sleep disruption in various dermatoses (30,31). Pruritus was found to affect the quality of sleep in HS patients (8-10,32,33). The prevalence of RLS is estimated to be between 5% and 15% in the literature (34). In this study, 15.6% of healthy controls had RLS. Although the percentage was slightly higher in the HS group (22.5%), there was no statistically significant increase. Also, in patients with and without RLS, there was no difference in age, BMI, waist circumference, disease duration, blood values, chronic diseases, or anti-TNF use.

### Study Limitations

Our research is significant since it is the first to look into the frequency of RLS in patients with HS. Although

blood tests such as hemoglobin and renal function were performed in our study, the study's limitation is that iron, iron binding capacity, and ferritin values were not assessed. The study would have been more valuable if objective evaluation methods, such as polysomnographic studies of sleep disturbance in this patient group, had been used. The current study's other limitation could be attributed to the small number of participants. More research with a larger number of participants is needed to conclude if there is a link between HS and RLS.

### Conclusion

There is no increased frequency of RLS in HS patients as there is in other dermatologic problems like psoriasis, AD, and CSU. In terms of concomitant conditions, there was no difference between HS cases with and without RLS.

### Ethics

**Ethics Committee Approval:** The study was approved by the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital, Clinical Research Ethics Committee (decision date: 23.12.2020, approval number: 2020-250).

**Informed Consent:** All the patients who took part in it provided their written consent.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Concept: S.S.O., T.O.A., Design: S.S.O., T.O.A., Data Collection or Processing: T.O.A., Analysis or Interpretation: S.S.O., T.O.A., Literature Search: S.S.O., Writing: S.S.O., T.O.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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