


RESEARCH

Open Access



The relationship of the prevalence and severity of restless legs syndrome in primary Sjögren syndrome with insomnia status, anxiety, depression, and neuropathic pain

Meliha Kasapoğlu Aksoy^{1*} , Koray Ayar², Büşra Yeşil¹ and Tülay Dilara Hattatoğlu³

Abstract

Background and aims In this study, we aimed to compare the prevalence of restless legs syndrome (RLS) between primary Sjögren syndrome (PSS) patients and the healthy population and investigate the relationships between RLS and insomnia status, anxiety, depression, neuropathic pain, and lower extremity pain. Our case-control study, included 55 patients aged 18–65 who were diagnosed with PSS based on the 2016 ACR/EULAR criteria and 60 healthy controls aged 18–65. The pain levels of the participants were evaluated using the pain DETECT Questionnaire, the lower-extremity visual analog scale, and an algometer, all participants were screened for fibromyalgia syndrome, and their psychiatric parameters were evaluated with the Beck Depression Inventory and the Beck Anxiety Inventory. Insomnia status was assessed using the Insomnia Severity Index. The cases in the PSS group with and without restless legs syndrome were compared.

Results While the rate of RLS in the PSS group was 26.7%, that in the control group was found as 9%, and the difference between the two groups was significant ($p < 0.05$). The severity of RLS in the PSS group was found to be significantly higher in comparison to that in the control group ($p < 0.05$). The PSS group had significantly higher lower-extremity pain, fibromyalgia, insomnia, depression, anxiety, and pain scores, as well as a significantly higher mean number of painful points, than the control group ($p > 0.05$). In the results of the multivariate regression analysis, depression and insomnia scores were identified as independent predictors for the presence of RLS in PSS cases ($p < 0.05$).

Conclusions We found the prevalence and severity of restless legs syndrome higher in the primary Sjögren syndrome patients compared to the healthy participants in the control group. We identified depression and insomnia as independent predictors of the presence of restless legs syndrome in primary Sjögren syndrome cases.

Keywords Primary Sjögren syndrome, Restless legs syndrome, Pain, Insomnia, Depression

*Correspondence:

Meliha Kasapoğlu Aksoy
melihakasapoglu@hotmail.com

¹ Department of Physical Medicine and Rehabilitation, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey

² Department of Internal Medicine, Rheumatology Division, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey

³ Department of Internal Medicine, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

Background

Primary Sjögren syndrome (PSS) is a chronic, systemic, and autoimmune disease that is characterized by the inflammation and dysfunction of exocrine glands. While the main symptoms of the disease are dry eyes (xerophthalmia) and dry mouth (xerostomia), highly varying systemic symptoms may also be seen [1, 2]. At least a third of patients have systemic extra-glandular symptoms such as neurological, articular, pulmonary, and gastrointestinal involvements [2]. Nervous symptom involvement is a prominent symptom, and it has been known since the first definition of the disease by Dr. Henrik Sjögren in 1935. Nevertheless, highly different numbers varying in the range of 8.5–70% have been reported as the prevalence of neurological involvement [3, 4]. Neurological involvement in PSS is 4–30 times more prevalent in women [4].

Restless legs syndrome (RLS) is a chronic and progressive movement disorder that is also known as Willis-Ekbom disease and is characterized by abnormal sensations that arise from the urge or need to move one’s legs [5]. Today, regarding the pathophysiology of RLS, it has been proven that the dopaminergic system plays a significant role in the pathogenesis of the disease. Dopaminergic activity shows fluctuations that increase in the morning and decrease in the early hours of the night. It is thought that this change is in parallel with the circadian rhythm in RLS, and the lowered dopaminergic neurotransmission at night leads to symptoms [6, 7].

There is no single diagnostic test for RLS, and thus, the diagnosis is made based on clinical signs and some diagnostic criteria [5]. Differential diagnosis is not difficult as these diagnostic criteria are clear. Diagnostic signs for RLS were determined for the first time by the International Restless Legs Syndrome Study Group (IRLSSG)

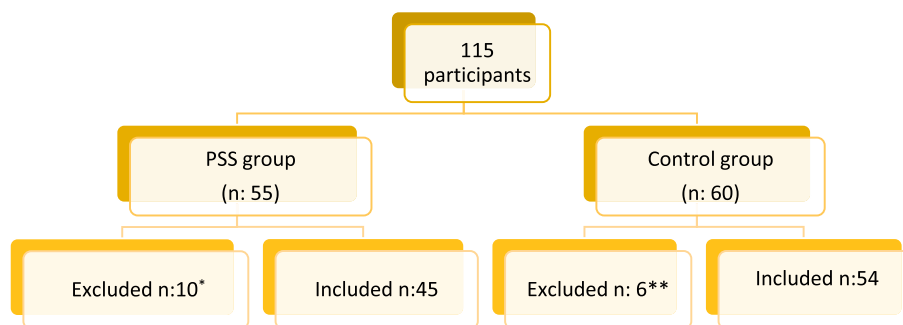
and published in 1995 [8]. After this, the criteria were turned into a review text by IRLSSG and published in 2003, and the latest revision was made in 2014 [9].

RLS is observed more frequently in some rheumatic diseases compared to the general population [10]. Patients with RLS may also experience extremity and joint pain. While pain used to be considered a complaint that excludes RLS, recent studies have reported that more than 50% of patients define pain as the primary component of their condition. Painful symptoms are observed more frequently in most patients diagnosed with RLS [3].

Although there are several studies on neurological symptoms in PSS, we did not encounter a study that examined parameters associated with RLS in PSS cases. In this study, we aimed to compare the prevalence of RLS between primary Sjögren syndrome patients and the healthy population and investigate the relationships between RLS and insomnia status, anxiety, depression, neuropathic pain, and lower extremity pain.

Methods

Our case-control study included 55 patients aged 18–65 who were diagnosed with PSS based on the 2016 ACR/EULAR criteria [11] and 60 healthy controls (hospital personnel) aged 18–65. The study excluded pregnant women, cancer patients, patients with another connective tissue disease in addition to PSS, multiple sclerosis patients, COPD patients, patients with heart failure and adrenal insufficiency, renal failure cases with GFR < 60 ml/min, anemia cases with Hgb < 11 g/dl in women and Hgb < 12 gr/dl in men, those with thyroid disorders, those with electrolyte disorders, those with vascular disorders of lower extremities, spinal stenosis cases, and cases diagnosed with polyneuropathy (Fig. 1). Local ethics committee approval was obtained to conduct the



*2 patient spinal stenosis, 3 patient anemia, 1 patient Rheumatoid arthritis, 2 patient varicose veins in the lower extremity, 1 patient polyneuropathy 1 patient radiculopathy)

**2 patient radiculopathy, 2 patient anemia, 1 patient multiple sclerosis, 1 patient polyneuropathy

Fig. 1 Flow diagram of the study

study, all participants were informed about the study in detail, and we obtained written consent form and all participants signed an informed consent form.

Among the 115 initially considered participants, 99 participants were found suitable for the study (Fig. 1). The demographic characteristics of the participants were recorded, and the diagnosis of RLS was made based on the IRLSSG criteria. The severity of RLS in the diagnosed cases was measured using the IRLSSG Rating Scale. The disease severity levels of the PSS patients were evaluated using ESSDAI (EULAR Sjögren's Syndrome Disease Activity Index) and ESSPRI (EULAR Sjögren's Syndrome Patient Reported Index), which are routinely used outpatient clinic tests. The pain levels of the participants were evaluated using the pain DETECT Questionnaire, the lower-extremity visual analog scale (VAS), and an algometer, all participants were screened for fibromyalgia syndrome (FMS), and their psychiatric parameters were evaluated with the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI). Insomnia status was assessed using the Insomnia Severity Index (ISI). The cases in the PSS group with and without RLS were compared.

Analysis parameters

Detecting fibromyalgia

The presence of fibromyalgia was examined based on the criteria of the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations Opportunities, and Networks (ACTTION) and the American Pain Society (APS) Pain Taxonomy (AAPT) criteria. According to these criteria, 9 painful body sites were defined (head, left arm, right arm, chest, abdomen, upper back and spine, lower back and spine including buttocks, left leg, and right leg). Fibromyalgia was classified based on the presence of pain for at least 3 months, with at least 6 painful body sites, and accompanying sleep disorders and/or fatigue [12].

ESSDAI (Sjögren's Syndrome Disease Activity Index)

ESSDAI is a disease activity index that was created in 2009 in a cohort of 702 clinical vignettes based on 96 actual patients. The scoring system was developed by the consensus of a large group of international experts from European and North American countries. ESSDAI is a systemic disease activity index and includes 12 domains (i.e., organ systems: cutaneous, respiratory, renal, articular, muscular, PNS, CNS, hematological, glandular, constitutional, lymphadenopathy, biological domains). Each domain is divided into 3–4 levels depending on the degree of disease activity that it refers to. The weights of each domain are obtained, using the PhGA of disease activity as the gold standard in a multiple regression

model. Before rating each domain, the physician is asked to rate only the manifestations related to the disease and avoid rating long-lasting clinical signs and exclude the rating of damage. The score of each domain indicates the level of activity multiplied by the domain weight. The possible final scores range between 0 and 123, where 0 indicates no disease activity. Preliminary data from the development study of the index showed that all disease activity scores had high sensitivity to change in cases whose disease activity had improved, and ESSDAI detects changes in disease activity more accurately compared to other indices [13].

ESSPRI (Sjögren's Syndrome Patient Reported Index)

ESSPRI was developed in 2011 in a multicentre international cohort of 230 patients [14]. The domains were selected based on previous data from the development of SSI and PROFAD, which included patient interviews. The pre-selected domains included dryness, pain, mental fatigue, and physical fatigue. The domains to be selected and the weight of each domain were determined from the patients' points of view, using a multiple linear regression model, where the patient's global assessment was the gold standard. ESSPRI uses numerical scales of 0 to 10, each scale for the assessment of one of the 3 domains: dryness, fatigue, and musculoskeletal pain. The weights of the domains are identical, and the average of the scores of the three domains gives the final score [14].

Pain DETECT Questionnaire (PD-Q)

Pain DETECT is a 9-item questionnaire that consists of seven sensory symptom items for pain that are graded from 0 = never to 5 = strongly, one temporal item on pain course and pattern graded from - 1 to + 1, and one spatial item on radiating pain status graded from 0 for non-radiating to + 2 for radiating pain. PD-Q was originally developed for people with low-back pain and showed good sensitivity (85%) and specificity (80%) in comparison to clinical diagnoses of predominantly nociceptive (e.g., visceral-pain) or neuropathic (e.g., postherpetic neuralgia) origins [15]. PD-Q classifies patients into different categories based on their total score on nine items: neuropathic pain (NeP) component is unlikely (≤ 12), inconclusive [8–13], and NeP component is likely (≥ 19). Most items use a 6-point scale, where higher scores indicate greater severity [16].

Lower-extremity visual analog scale (VAS)

VAS was used to determine the lower extremity pain severity of the participants. The meaning of numbers on a 10-cm line from 0 to 10 in VAS was explained to the participants [17].

Beck Depression Inventory (BDI)

This 21-item scale was used to assess the depressive symptoms of the participants. With response options varying from 0 to 3 for each item, the range of possible total scores on the scale is 0–63. BDI scores of 0–9 are considered no/minimal depression, scores of 10–18 indicate mild depression, 19–29 indicate moderate depression, and 30–63 indicate severe depression [18]. The validity and reliability of BDI in Turkish society were previously confirmed [19].

Beck Anxiety Inventory (BAI)

BAI is a self-assessment scale that was developed by Beck et al. [20] to measure the frequency of anxiety symptoms experienced by individuals. It is a 4-point (0–3) Likert-type scale consisting of 21 items. It was tested for validity and reliability in Turkey by Ulusoy et al. [21].

International Restless Legs Syndrome Rating Scale (IRLSRS)

IRLSRS determines the severity of RLS using 10 items. Each item is scored between 0 and 4, giving a maximum total scale score of 40. A score of 1–10 indicates mild RLS, 11–20 indicates moderate RLS, 21–30 indicates severe RLS, and 31–40 indicates highly severe RLS [9].

Insomnia Severity Index (ISI)

ISI is a measurement tool developed to evaluate the severity of insomnia and has high validity and reliability. It has seven items, each scored between 0 and 4. The scores that can be obtained from the scale vary between 0 and 28. A total score of 0–7 indicates the absence of insomnia, a score of 8–14 indicates sub-threshold insomnia, 15–21 indicates moderate insomnia, and 22–28 indicates severe insomnia [22]. The Turkish validity and reliability study of the scale was conducted by Boysan et al. [23].

Pain pressure threshold (PPT)

The PPT values of the participants were evaluated with a pressure algometer (Baseline® Dolorimeters, New York, USA, 2015). The measurements were made on the middle trapezius muscle by the same researcher under the same test conditions and room temperature and with the same test equipment. For the evaluations, a 1-cm² circular probe connected to a pressure device calibrated to Newton/cm² was used as the force application unit. Pressure was increased at a rate of 1 N/s until pain was detected by the participant. The test was stopped by the participant's "stop" command, and the value on the screen was recorded. Each measurement

was carried out three times, and the average of the three measurements was recorded as PPT.

Statistical analysis

The data analysis was performed by IBM SPSS 23.0 statistics software package. Descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min-max) were used to assess the study data. The Shapiro-Wilk test was used to check whether the data is normally distributed. Where the data showed normal distribution, *t* test was used. Otherwise, Wilcoxon test and Mann-Whitney *U* test were used to make intergroup comparisons. Chi-square test and Fisher's test were used to compare categorical data. The correlation between continuous variables with normal distribution was assessed using the Pearson correlation test, while the correlation between those without normal distribution was assessed using the Spearman correlation test. In order to determine the predictors of RLS in PSS patients, firstly possible predictive variables were analyzed with the enter method in the univariate model, and the predictors that were significant in the univariate model were analyzed with the forward likelihood ratio method in the multivariate model with logistic regression analysis. A *p* value of < 0.05 was considered statistically significant.

Results

The study included 45 patients diagnosed with PSS (47.67 ± 10.62) and 54 healthy individuals in the control group (50.22 ± 8.67). There was no statistically significant difference between the groups in terms of their distributions of age or sex (*p* > 0.05). While the rate of RLS in the PSS group was 26.7%, that in the control group was found as 9%, and the difference between the two groups was significant (*p* < 0.05). The severity of RLS in the PSS group was found to be significantly higher in comparison to that in the control group (*p* < 0.05) (Table 1).

The PSS group had significantly higher lower-extremity VAS, FMS, ISI, BDI, BDA, and PD-Q scores, as well as a significantly higher mean number of painful points, than the control group (*p* < 0.05).

In the comparison of the PSS patients who had RLS and those who did not have RLS, there was no significant difference in terms of age or sex between the two subgroups of PSS patients (*p* > 0.05). There was also no significant difference between the two subgroups in terms of their disease durations (*p* > 0.05). The PD-Q, lower-extremity VAS, BDI, BDA, and ISI scores were significantly higher in the subgroup with RLS (*p* < 0.05). While there was no significant difference between the two subgroups in terms of their mean ESSDAI total, ESSPRI total, ESSPRI dryness, or ESSPRI fatigue scores (*p* > 0.05), the subgroups had significantly different mean ESSPRI pain

Table 1 Demographic and disease-related characteristics of patients with primary Sjögren's syndrome and demographic data of healthy controls

	PSS (n = 45)		Control group (n = 54)		p value
Age (years)	47.67 ± 10.62	45 (29–71)	50.22 ± 8.67	52.50 (32–72)	0.149
Gender (female/male)	43 F (95.6%)/2 M (4.4%)		52 F (96%)/2 M (4%)		0.853
BMI (kg/m ²)					
RLS	12 (26.7%) 33 (73.3%)		5 (9%) 49 (91%)		0.022
RLS severity	1 patient mild RLS 6 patient moderate RLS 4 patient severe RLS 1 patient very severe RLS		1 patient mild RLS 3 patient moderate RLS 1 patient severe RLS		0.037
FMS	13 kişi FMS + 28.9% 32 kişi FMS-71.1%		5 kişi FMS + 9.3% 49 kişi FMS-90.7%		0.012
ISI	9.64 ± 6.06	8 (1–23)	6.44 ± 4.30	6 (1–23)	0.007
BDI	10.44 ± 8.15	9 (1–36)	7.61 ± 5.16	6 (0–23)	0.047
BAI	10.22 ± 7.84	10 (0–36)	7.28 ± 5.01	5 (0–24)	0.033
Lower extremity VAS	4 (0–8)		0 (0–8)		0.001
PDQ	7.71 ± 6.94	6 (0–23)	5.04 ± 4.17	5 (0–20)	0.099
Pain threshold right	9.29 ± 3.50	9 (3–18)	8.92 ± 3.57	9 (3–17)	0,816
Pain threshold left	9.06 ± 3.75	9 (2–19)	9.50 ± 3.19	10 (3–15)	0,370
Number of painful body sizes	4.04 ± 2.61	4 (0–9)	2 ± 1.94	1 (0–7)	< 0.001
ESSDAI	3.91 ± 1.85	4 (0–9)			
ESSPRI					
Mean	6.57 ± 1.79	7 (1.5–9)			
Dryness	6.22 ± 2.41	7 (0–9)			
Fatigue	6.96 ± 2.12	8 (1–9)			
Pain	6.36 ± 2.06	7 (1–9)			
Disease duration	3.49 ± 1.44	4 (1–6)			

PSS primary Sjögren's syndrome, BMI body mass index, RLS restless leg syndrome, FMS fibromyalgia syndrome, ISI Insomnia Severity Index, BDI Beck Depression Inventory, BAI Beck Anxiety Inventory, VAS visual analog scale, PDQ Pain Detect Questionnaire, ESSDAI EULAR Sjögren's Syndrome Disease Activity Index, ESSPRI EULAR Sjögren's Syndrome Patient Reported Index

subscale scores ($p > 0.05$) (Table 2). RLS presence did not differ significantly based on the drugs used by the patients ($p > 0.05$).

In the PSS group, RLS severity was found to be positively and significantly related to ISI, VAS, BDI, BDA, and ESSPRI pain scores ($p < 0.05$) (Table 3).

In the results of the multivariate regression analysis, BDI and ISI scores were identified as independent predictors for the presence of RLS in PSS cases ($p < 0.05$) (Table 4).

Discussion

In our study, we identified the prevalence of RLS in the PSS patients as 26.7%. The PSS patients in our study who were diagnosed with RLS had higher levels of anxiety, depression, lower extremity pain, neuropathic pain, and insomnia. We found that depression and insomnia were independent predictors of the presence of RLS in PSS cases.

Cognitive disorders, such as weakened memory and concentration problems, and sleep disorders are encountered more frequently in PSS cases [24]. It has been reported that anxiety and depression rates in PSS cases are higher compared to control groups in the same age group and RA patients [25]. In our study, we also found significantly higher rates of anxiety and depression among the PSS patients in comparison to the healthy controls. The pathophysiological mechanisms of these symptoms are not completely known. An underlying vasculitis case and response to chronic disease are proposed as possible mechanisms [3]. Symptoms such as pain, sleep disorders, and depression may contribute to the pathogenesis of cognitive dysfunctions [4, 26]. In this study, we found the rate of FMS presence, insomnia severity levels, and numbers of painful points significantly higher in the PSS patients than in the control group. On the other hand, there was no significant difference between the PSS and control groups regarding their algometer measurements.

Table 2 Comparison of data with and without RLS in patients with PSS

	PSS with RLS (12 patient)		PSS without RLS (33 patient)		<i>p</i> value
Age (years)	52.08 ± 11.05	51 (33–71)	46.06 ± 10.16	45 (29–71)	0.093
Gender (female/male)	12 F		31 F/2 M		0.771
Disease duration	3.67 ± 1.37	4 (1–5)	3.42 ± 1.48	4 (0–6)	0.623
Pain threshold right	8.34 ± 2.68	8.25 (4–13)	9.64 ± 3.73	9 (3–18)	0.278
Pain threshold left	8.38 ± 3.27	8 (4–15)	9.30 ± 3.93	10 (2–19)	0.470
Number of painful body sizes	5.17 ± 2.03	5.50 (1–7)	3.64 ± 2.70	3 (0–9)	0.066
FMS	5 FMS + 41.6% 7 FMS–%58.4		7 FMS + 21.21% 26 FMS–78.79%		0.060
BDI	15.17 ± 10.97	12.50 (1–42)	8.21 ± 6.91	6 (1–28)	0.016
BDA	14.50 ± 8.39	13 (4–31)	10.15 ± 8.43	8 (1–36)	0.009
Lower extremity VAS	5 (0–8)	4.50 ± 2.15	4 (0–7)	2.81 ± 2.32	0.034
PDQ	12.17 ± 5.55	12 (2–21)	6.09 ± 6.75	4 (0–23)	0.005
ISI	10 ± 4.88	9.50 (2–17)	8.42 ± 6.05	8 (1–23)	0.015
ESSDAI	4.08 ± 1.56	4 (2–7)	3.85 ± 1.97	4 (0–9)	0.712
ESSPRI					
Mean	7.48 ± 0.71	7.50 (6–8.5)	6.24 ± 1.95	6.50 (1.5–9)	0.055
Dryness	7.25 ± 1.48	7.50 (5–9)	5.85 ± 2.58	7 (0–9)	0.124
Fatigue	7.58 ± 1.56	8 (3–9)	6.73 ± 2.26	7 (1–9)	0.424
Pain	7.58 ± 0.99	8 (5–9)	5.91 ± 2.28	6 (1–9)	0.021

PSS primary Sjögren's syndrome, RLS restless leg syndrome, FMS fibromyalgia syndrome, ISI Insomnia Severity Index, BDI Beck Depression Inventory, BAI Beck Anxiety Inventory, VAS visual analog scale, PDQ Pain Detect Questionnaire, ESSDAI EULAR Sjögren's Syndrome Disease Activity Index, ESSPRI EULAR Sjögren's Syndrome Patient Reported Index

Table 3 Correlation between RLS and evaluation data

	ISI	FMS	VAS	BDI	BDA	PDQ	ESSDAI	ESSPRI mean	ESSPRI dryness	ESSPRI fatigue	ESSPRI pain
RLS severity											
<i>r</i>	0.346	0.250	0.342	0.375	0.417	0.437	0.068	0.275	0.219	0.098	0.354
<i>P</i>	0.020	0.097	0.021	0.011	0.004	0.003	0.657	0.067	0.148	0.521	0.017

PSS primary Sjögren's syndrome, RLS restless leg syndrome, FMS fibromyalgia syndrome, ISI Insomnia Severity Index, BDI Beck Depression Inventory, BAI Beck Anxiety Inventory, VAS visual analog scale, PDQ Pain Detect Questionnaire, ESSDAI EULAR Sjögren's Syndrome Disease Activity Index, ESSPRI EULAR Sjögren's Syndrome Patient Reported Index

RLS is one of the comorbidities that are seen in rheumatic diseases, and the sense of discomfort caused by RLS affects the person's activities of daily living negatively [10]. The exact pathophysiology of RLS is still not clear. It is usually encountered as an idiopathic condition. In an autopsy-based study, it was argued that the etiology of RLS may be connected to the modulation of transferrin receptors in the brain [26]. Radiographic imaging studies have also shown that changes in the dopaminergic receptors of the brain cause this disease [6]. Likewise, it was shown that low iron levels can lead to RLS [26]. We excluded patients with anaemia from our study. Some studies found mood disorders, reduced libido, and social isolation to be prevalent in patients with RLS, and a significant relationship was reported between RLS and depression [27]. The prevalence of RLS in chronic inflammatory diseases such as RA, Crohn's disease, Behçet's

disease, and SLE has been found higher in comparison to the healthy population. According to the literature review that we conducted for this study, one previous study showed an RLS rate of 24% in PSS cases [28], while another study reported this rate as 15.3% [29]. In our study, the rate of RLS in the PSS group was determined as 26.7%. Moreover, we found the severity of RLS in the PSS group to be higher in comparison to the severity of RLS in those with RLS in the control group.

A study that was conducted with RA patients revealed that the presence of RLS affected these patients' sleep quality, psychological health status, and activities of daily living negatively [30]. In our study, we observed that the presence of RLS had adverse effects on the PSS patients in terms of insomnia, pain, anxiety, and depression.

In another study where the prevalence of RLS was evaluated, it was seen that 90.8% of RA patients could distinguish

Table 4 Regression analysis

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Age, years	1.057	0.990–1.128	0.100			
DD	1.130	0.702–1.819	0.614			
ESSDAI	1.072	0.749–1.533	0.705			
Schirmer, mm	0.973	0.885–1.071	0.579			
WUSFR, ml	1.007	0.518–1.958	0.984			
SSA	0.357	0.077–1.652	0.188			
SSB	0.513	0.117–2.256	0.377			
RF	0.526	0.138–2.009	0.348			
FMS	3.714	0.910–15.154	0.067			
BAI	1.110	1.010–1.219	0.031			
BDI	1.142	1.030–1.266	0.012	1.143	1.02–1.28	0.021
ISI	1.138	1.011–1.282	0.032	1.132	0.997–1.285	0.056

OR odds ratio, CI confidence interval, DD disease duration, ESSDAI EULAR Sjögren's Syndrome Disease Activity Index, WUSFR whole unstimulated salivary flow rate, FMS fibromyalgia syndrome, BAI Beck Anxiety Inventory, BDI Beck Depression Inventory, ISI Insomnia Severity Index

RLS-related lower extremity symptoms from arthritis-related pain [31]. In our study, we found the lower extremity pain levels and neuropathic pain pattern rates in the PSS cases with RLS higher compared to the PSS cases without RLS. It was observed that the presence of RLS raised the perception of pain in PSS even further.

The low number of participants and the fact that this was a single-centre study may be listed as limitations of our study.

Conclusion

As a result of our study, we found the prevalence and severity of RLS higher in the PSS patients compared to the healthy participants in the control group. We identified depression and insomnia as independent predictors of the presence of RLS in PSS cases. Screening and treating depression and insomnia in PSS patients could further improve the quality of life of patients and may lead to positive results in the control of RLS, which is very common in these patients. Keeping the presence of RLS in these patients while planning their treatments may increase treatment success. Studies on this topic with larger samples are needed.

Abbreviations

RLS	Restless legs syndrome
PSS	Primary Sjögren syndrome
ACTTION	Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations Opportunities, and Networks
APS	American Pain Society
VAS	Visual analog scale
FMS	Fibromyalgia syndrome
BDI	Beck Depression Inventory
BAI	Beck Anxiety Inventory
ISI	Insomnia Severity Index
IRLSSG	International Restless Legs Syndrome Study Group
ESSDAI	Sjögren's Syndrome Disease Activity Index

ESSPRI	Sjögren's Syndrome Patient Reported Index)
PD-Q	Pain DETECT Questionnaire
IRLS	International Restless Legs Syndrome Rating Scale
PPT	Pain pressure threshold

Acknowledgements

Not applicable.

Authors' contributions

MKA contributed the idea, analyzed the data, and wrote the manuscript. KA have critically reviewed the manuscript and statistical analysis. BY and TDH contributed data collection and clinical assessment of the patients. All authors have read and approved the manuscript, and all authors have contributed significantly and are in agreement with the content of the manuscript.

Funding

The authors received no financial support for the research and/or authorship of this article.

Availability of data and materials

The data will be available if reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from institutional research committee (2011-KAEK-25 2021/02-14) and with the 1964 Helsinki Declaration and comparable ethical standards.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 30 December 2022 Accepted: 16 February 2023

Published online: 06 March 2023

References

1. Fox RI (2005) Sjögren's syndrome. *Lancet* 366:321–331

2. Vitali C, Bombardieri S, Jonsson R et al (2002) Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis* 61:554–558
3. Pavlakis PP, Alexopoulos H, Kosmidis ML et al (2012) Peripheral neuropathies in Sjögren's syndrome: a critical update on clinical features and pathogenetic mechanisms. *J Autoimmun* 39:27–33
4. Gono T, Kawaguchi Y, Katsumata Y et al (2011) Clinical manifestations of neurological involvement in primary Sjögren's syndrome. *Clin Rheumatol* 30:485–490
5. Smith JE, Tolson JM (2008) Recognition, diagnosis and treatment of restless legs syndrome. *J Am Acad Nurse Pract* 20(8):396–401
6. Michaud M, Soucy J-P, Chabli A, Lavigne G, Montplaisir J (2002) SPECT imaging of striatal pre- and postsynaptic dopaminergic status in restless legs syndrome with periodic leg movements in sleep. *J Neurol* 249(2):164–170
7. Earley CJ, Kuwabara H, Wong DF et al (2011) The dopamine transporter is decreased in the striatum of subjects with restless legs syndrome. *Sleep* 34:341–347
8. Sander HH, Eckeli AL, Costa Passos AD, Azevedo L, Fernandes do Prado LB, França Fernandes RM (2017) Prevalence and quality of life and sleep in children and adolescents with restless legs syndrome/ Willis-Ekbom disease. *Sleep Med* 30:204–209
9. Allen RP, Picchiotti DL, Garcia-Borreguero D et al (2014) Restless legs syndrome/ Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria-history, rationale, description, and significance. *Sleep Med* 15(8):860–873
10. Hening WA, Cainano CK (2008) Restless legs syndrome: a common disorder in patients with rheumatologic disorders. *Semin Arthritis Rheum* 38:55–62
11. Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM et al (2017) 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary Sjögren's syndrome: a consensus and data-driven methodology involving three international patient cohorts. *Ann Rheum Dis* 76(1):9–16
12. Arnold LM, Bennett RM, Crofford LJ, Dean LE, Clauw DJ, Goldenberg DL et al (2019) AAPT diagnostic criteria for fibromyalgia. *J Pain* 20(6):611–628
13. Seror R, Ravaud P, Bowman SJ et al (2010) EULAR Sjögren's syndrome disease activity index: development of a consensus systemic disease activity index for primary Sjögren's syndrome. *Ann Rheum Dis* 69(6):1103–1109
14. Seror R, Ravaud P, Mariette X et al (2011) EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI): development of a consensus patient index for primary Sjögren's syndrome. *Ann Rheum Dis* 70(6):968–972
15. Freynhagen R, Baron R, Gockel U, Tolle TR (2006) painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 22(10):1911–1920
16. Alkan H, Ardic F, Erdogan C, Sahin F, Sarsan A, Findikoglu G (2013) Turkish version of the painDETECT questionnaire in the assessment of neuropathic pain: a validity and reliability study. *Pain Med* 14(12):1933–1943
17. Huskisson EC (1974) Measurement of pain. *Lancet* 2:1127–1131
18. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961) An inventory for measuring depression. *Arch Gen Psychiatry* 4:561–571
19. Hisli N (1989) Beck depresyon anketinin üniversite öğrencileri için geçerliliği, güvenilirliği. *Psikoloji Dergisi* 7(23):3–13
20. Ulusoy M, Sahin NH, Erkmen H (1998) Turkish version of Beck Anxiety Inventory: psychometric properties. *J Cogn Psychother* 12(2):163–172
21. Beck AT, Epstein N, Brown G, Steer RA (1988) An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol* 56(6):893–897
22. Bastien CH, Vallières A, Morin CM (2001) Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med* 2(4):297–307
23. Boysan MG, Besiroglu L, Kalafat T (2010) Psychometric properties of the Insomnia Severity Index in Turkish sample. *Anatol J Psychiatry* 11(3):248–252
24. Chai J, Logigian EL (2010) Neurological manifestations of primary Sjögren's syndrome. *Curr Opin Neurol* 23:509–513
25. Fauchais AL, Magy L, Vidal E (2012) Central and peripheral neurological complications of primary Sjögren's syndrome. *Presse Med* 41:485–493
26. Connor JR, Boyer PJ, Menzies SL et al (2003) Neuropathological examination suggests impaired brain iron acquisition in restless legs syndrome. *Neurology* 61(3):304–309
27. Sevim S, Dogu O, Kaleagasi H, Aral M, Metin O, Camdeviren H (2004) Correlation of anxiety and depression symptoms in patients with restless legs syndrome: a population based survey. *J Neurol Neurosurg Psychiatry* 75:226–230
28. Gudbjornsson B, Broman JE, Hetta J, Hallgren R (1993) Sleep disturbances in patients with primary Sjögren's syndrome. *Br J Rheumatol* 32:1072–1076
29. Theander L, Strombeck B, Mandl T, Theander E (2010) Sleepiness or fatigue? Can we detect treatable causes of tiredness in primary Sjögren's syndrome? *Rheumatology (Oxford)* 49(6):1177–1183
30. Demir S, Küçük A, Altaş M, Cure E (2021) Restless leg syndrome and sleep disorders in patients with rheumatoid arthritis and its relation with anemia parameters. *Acta Medica (Hradec Králové)* 64(3):137–144
31. Taylor-Gjevne RM, Gjevne JA, Skomro R, Nair B (2009) Restless legs syndrome in a rheumatoid arthritis patient cohort. *J Clin Rheumatol* 15(1):12–15

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Submit your manuscript to a SpringerOpen® journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► [springeropen.com](https://www.springeropen.com)