RESEARCH

Prevalence and Associates of Restless Legs Syndrome in a Psychiatric Outpatient Clinic: A Single-Center Study

Nuryil Yilmaz[1], Burhanettin Cigdem[2]

[1] Psychiatry Clinic, Tepecik Education and Research Hospital, Izmir, Turkey
[2] Department of Neurology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

Abstract: : This study aims to investigate the prevalence of restless legs syndrome (RLS) in patients admitted to a psychiatry outpatient clinic and the association of RLS with patient characteristics. Four hundred and thirty consecutive patients who were admitted to the outpatient clinic of the Department of Psychiatry of Sivas Cumhuriyet University Education and Research Hospital were evaluated according to the RLS diagnostic criteria, and the severity of RLS in patients was assessed based on the International Restless Legs Syndrome Rating Scale. The prevalence of RLS in 430 consecutive patients was 19.1% (82/430). No difference was observed in the prevalence of psychiatric diagnoses. In the multivariable regression analysis, the history of RLS in first-degree relatives, the history of psychiatric disorder in the family, antidepressant medication use and substance use were determined to be independent predictors of RLS in psychiatric outpatients. Of note, 84.1% (69/13) of psychiatric outpatients with RLS versus 53.4% (186/162) of psychiatric outpatients without RLS had sleep disturbance. Restless legs syndrome is common among psychiatric outpatients. History of RLS in first-degree relatives, history of psychiatric disorder in the family, substance use and antidepressant medication use were found to be independent associates of RLS.

INTRODUCTION

Restless legs syndrome influences a considerable part of the population and leads to significant health problems, including insomnia, daytime sleepiness, and impaired quality of life[1]. Restless legs syndrome (RLS), which disturbs sleep, represents a sleep-related movement disorder. This syndrome is characterized by symptoms that are relieved by movements, those that increase at rest, and a desire to move legs even more in evenings or nights[2,3]. RLS can be either primary or secondary. RLS may develop secondary to iron deficiency anemia, pregnancy, renal insufficiency, dopaminergic neurotransmission disorder, and Parkinson's disease[4]. The prevalence of RLS in epidemiological studies is reported in a wide range of 3.9-14.3%[5-7]. This variation originates from the difference in the methodology of different studies and the implementation of surveys[5]. Previous studies have reported that RLS is associated with psychiatric disorders[8]. There are several studies, especially on the association of depression with RLS, and these studies have found a higher prevalence of RLS in those with depressive symptoms than in the overall population[2,9,10]. Furthermore, it has been reported that RLS is related to the use of tricyclic antidepressants, selective serotonin reuptake inhibitor (SSRI) group antidepressants, and dopamine antagonists[4,9,11,12]. Prevalence of RLS has not been evaluated specifically in psychiatric outpatients, though, prevalence in hospitalized patients were addressed in two small studies[13,14]. This research aimed to investigate the prevalence of RLS in patients, admitted to the psychiatry outpatient clinic, and the association of RLS with patient characteristics.

MATERIALS and METHODS

Participants: Consecutive patients who were admitted to the outpatient clinic of the Department of Psychiatry of Sivas Cumhuriyet University Education and Research Hospital between February 1, 2018, and April 30, 2018, were screened for their evaluation in terms of demographic data, the presence of psychiatric diagnoses, psychotropic medication, substance use and sleep disturbance. Psychiatric diagnoses were established by outpatient clinic psychiatrists, who were blinded to RLS assessment in accordance with the International Classification of Diseases-10 (ICD-10). The

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Corresponding Author:
Nuryil Yilmaz
E-mail; drnuryil@gmail.com
ORCID: 0000-0002-6229-9197
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exclusion criteria included being younger than 18 years of age or having a significant cognitive impairment to complete the questionnaire. Patients with recent (within 3 months) or index hospitalization, individuals with intellectual disability, dementia, and other significant cognitive impairment were excluded from the study. The *inclusion criteria* were signing informed consent and being older than 18 years.

Diagnosis of RLS

Four questions of the RLS diagnostic criteria questionnaire, determined by the International RLS Study Group (IRLSSG), were administered to all participants following the questions, used to determine their demographic characteristics. For the diagnosis of RLS, diagnostic criteria were established in 1995 by the International RLS Study Group and revised in 2003[15,16]. It was accepted that participants who responded as "yes" to all the following four questions had RLS. "1-An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs. 2- The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting. 3- The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues. 4- The urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night"[17].

All the subjects who received a positive diagnosis of RLS were asked to complete the International Restless Legs Syndrome Rating Scale (IRLSRS) to assess the severity of symptoms.

International Restless Legs Syndrome Rating Scale (IRLSRS)

The disease severity scale was developed by the International RLS Study Group in 2003 to evaluate the severity of RLS in patients with RLS symptoms. This scale comprises 10 questions, each of which is rated between 0-4. While the first five questions are directed at the severity of symptoms, the last five questions concern the effects of RLS on activities of daily living or quality of life. The total score reflects disease severity. The maximum score is 40, and a score of 1 to 10 is rated as mild, 11 to 20 as moderate, 21 to 30 as severe, and 31 to 40 as very severe disease[18]. Patients were also asked to evaluate sleep disturbance.

Approval for the study was obtained from the Local Ethics Committee for Non-Interventional Clinical Studies of Cumhuriyet University (Decision number: 2015-03/07).

Statistical Analysis

The sample size was calculated with a type I error of 0.005, type II error of 0.20 with an estimated 14% prevalence according to previous epidemiological data, and it was found that 393 patients were needed. Along with a 5% rejection rate, the minimum number was set to 413 outpatients. All data were recorded and then assessed by SPSS 22.0, registered institutional software. Parametric data were evaluated by the independent sample's t-test. Categorical data were evaluated by appropriate chi-square testing. A logistic regression analysis was obtained via Backward stepwise regression to predict the independent predictors of RLS. A p value$\leq$0.05 was accepted as significant.

RESULTS

Four hundred and fifty (n=450) consecutive patients who were admitted to the outpatient clinic of the Department of Psychiatry of Sivas Cumhuriyet University Education and Research Hospital between February 1, 2018, and April 30, 2018, were screened. Of the screened patients, 10 patients refused to participate in the study and were not referred to RLS assessment, and 10 patients were reported to have mental retardation, which precluded enrolment. Hence, there were 430 consecutive patients who accepted to participate in the study and were eligible according to the inclusion and exclusion criteria. The mean age of the 430 consecutive patients, admitted to the psychiatric outpatient clinic, was 33.3 ± 13.6 years, and there were 241 females and 189 males (F/M:241/189). The prevalence of RLS was found to be 19.1% (82/430) among the 430 consecutive patients, admitted to the outpatient clinic according to the addressed diagnostic criteria of RLS. According to the RLS severity rating scale, it was determined that 52.4% (43/82) of patients with RLS symptoms had mild-moderate symptoms. Depression was detected in 35.8% (154/430) of patients, and generalized anxiety disorder was detected in 30.5% (131/154) of patients. More than half of patients (59.5%, 256/430) reported significant sleep disturbance. The univariate comparison of the cohort with and without RLS is presented in Table 1.

The mean age of patients with RLS was not different from those without RLS (32.5±12.2 years versus. 33.5±13.9, p=0.512). Patients with and without RLS were found to be similar in terms of gender distribution (F/M: 52/30 vs. 189/159, p=0.135). No statistically significant difference was detected between those with and without RLS in terms of smoking and alcohol use (p = 0.278, p = 0.679). No significant difference was found in the prevalence of generalized anxiety disorder (34.1% vs. 29.6%), depressive disorder (39.1% vs. 35.1%), obsessive-compulsive disorder (6.1% vs. 4.3%), and schizophrenia (4.9% vs. 8.3%, p=0.74) in patients with and without RLS symptoms (See Table 1). It was found that 84.1% (69/13) of patients with RLS had sleep disturbance and 53.4% (186/162) of those without RLS had sleep disturbance (p<0.001) with a 1.574-fold increased risk for sleep disturbance among psychiatric outpatients with RLS compared to those without RLS (1.574, 95% CI: 1.374-1.803).

Parameters associated with RLS in the univariate analysis (Table 1) were included in multivariable logistic regression analysis via stepwise backward LR. Furthermore, history of RLS in first-degree relatives (p<0.001), history of psychiatric disorder in the family (p=0.038), antidepressant medication (p=0.029) and substance use (p=0.027) were noted to be independent predictors of RLS in psychiatric outpatients (Table 2).

DISCUSSION

Although RLS affects some part of the general population, there are many individuals who complain about having RLS symptoms but have not been diagnosed and treated yet[19]. The prevalence of RLS was found to range between 3.9 to 14.3% in epidemiological studies[5-7]. The prevalence of RLS in the present study was found to be 19.1%, and it was overall concordant with the previous literature. However, RLS was reported to be related to some psychiatric disorders in those reports[2,9,20]. It was noted that there was a relationship between some psychiatric disorders (especially depression) and RLS, regardless of antidepressant use[20]. The above-mentioned relationship may reflect a common pathophysiological subtype[20]. In this study, RLS frequency was overall lower than in some of the previous reports, and it was observed in 21.5% of patients with generalized anxiety disorder, 20.8% of patients with depressive disorder, 25% of patients with obsessive-compulsive disorder, and 12.1% of those with schizophrenia[2,9,20]. Differences in prevalence may simply be related to the age and/or characteristics of the selected population. In this research, the mean age was 33 years, which was lower than that in the study carried out by Auvinen P. et al.[9]. Generally, no statistically significant difference was detected between patients with and without RLS in terms of psychiatric diagnoses in this study in concordance with some reports[14,21].

Table 1. Comparison of psychiatric outpatients with and without RLS

		RLS		p
		Yes	No	
		Number (%)	Number (%)	
Age (years)		32.5±12.2	33.5±13.9	0.512
Gender	Female/Male	52/30 (63.4/36.6)	189/159 (54.3/45.7)	0.135*
Marital status	(married/single/other)	29/43/10 (35.4/52.4/12.2%)	141/179/27 (40.6/51.6/7.8%)	0.373
Educational status	(illiterate/primary/other)	3/23/31 (5.3/40.4/54.4%)	20/93/147 (7.7/35.8/56.5%)	0.709
Occupation	(unoccupied/student/self-employed/other)	23/35/5/19 (28/42.7/6.1/23.2%)	91/137/32/88 (26.1/39.4/9.2/25.3%)	0.769
Income	(low/middle/high)	18/61/3 (22/74.4/3.7%)	75/267/6 (21.6/76.7/1.7%)	0.538
Smoking	Yes/No	34/48 (41.5/58.5)	122/226 (35.1/64.9)	0.278
Alcohol	Yes/No	8/74 (9.8/90.2)	29/319 (8.3/91.7)	0.679
Substance use	Yes/No	3/79 (3.7/96.3)	2/346 (0.6/99.4)	0.019*
Antidepressant medication	Yes/No	42/40 (51.2/48.8)	127/221 (36.5/63.5)	0.014*
Antipyschotic medication	Yes/No	20/62 (24.4/75.6)	112/236 (32.2/67.8)	0.169*
Absence/ presence of psychiatric medication	Yes/No	30/52 (36.6/63.4)	143/205 (41.1/58.9)	0.454
History of RLS in first-degree relatives	Yes/No	11/71 (13.4/86.6)	1/347 (0.3/99.7)	<0.001*
Psychiatric diagnoses	Generalized anxiety disorder	28 (34.1)	103 (29.6)	0.740
	Depressive disorder	32 (39.0)	122 (35.1)	
	Obsessive-compulsive disorder	5 (6.1)	15 (4.3)	
	Schizophrenia	4 (4.9)	29 (8.3)	
	Posttraumatic stress disorder	0 (0.0)	3 (0.9)	
	Adjustment disorder	4 (4.9)	24 (6.9)	
	Bipolar disorder	5 (6.1)	38 (10.9)	
	Conversion disorder	2 (2.4)	3 (0.9)	
	Conduct disorder	1 (1.2)	7 (2.0)	
	Social phobia	1 (1.2)	4 (1.1)	
History of psychiatric disorder in the family	Yes/No	22/82 (26.8%)	48/348 (13.8%)	0.007*
Significant sleep disturbance	Yes/No	69/13 (84.1/15.9)	187/161 (53.7/46.3)	<0.001

RLS= Restless legs syndrome *parameters enrolled in multivariable regression at the first step

Table 2. Independent predictors of RLS in psychiatric outpatients

							95% C.I.for EXP(B)	
	B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Substance use	2.066	0.934	4.889	1	0.027	7.894	1.265	49.279
Antidepressant medication	0.574	0.264	4.739	1	0.029	1.776	1.059	2.978
History of RLS in first-degree relatives	3.828	1.060	13.035	1	0.000	45.951	5.753	367.027
History of psychiatric disorder in the family	0.670	0.322	4.321	1	0.038	1.954	1.039	3.676
Constant	1.570	0.712	4.863	1	0.027	4.805		

In a study of a single psychiatric ward in Lebanon, RLS was determined in 18% of hospitalized patients[14]. In a similar study in Lebanon, the prevalence of RLS in psychiatric hospitalized patients was also revealed to be 14.3%[13]. On the contrary, Hombali A et al. indicated the RLS prevalence as 14.8% among psychiatric outpatients, the majority of whom were young people[21]. It is remarkable that Hombali A et al. reported that RLS was less prevalent among the elderly compared to a younger group of psychiatric outpatients from different ethnicities[21]. Contrary to Hombali A et al., RLS was more frequently reported in women and the elderly in other studies[11,22]. No statistically significant difference was detected between patients with and without RLS in terms of age and gender in this study.

RLS was reported to cause deterioration in sleep quality or worsen the existing sleep disturbance[20]. In this study, sleep disturbances were also found in the majority of psychiatric outpatients with RLS, though, sleep disturbance was also common in psychiatric outpatients without RLS. In the study conducted by Talih et al. in 2018, a relationship was found between insomnia and RLS[13]. However, no relationship was revealed between smoking, alcohol consumption, and RLS in this study in concordance with previous literature[6,7,14]. Substance use was linked to RLS. However, since it was reported in few patients, it was difficult to achieve a definitive conclusion.

In a study examining the relationship between RLS and depression, it was revealed that moderate-to-severe RLS was more frequent in patients taking antidepressant medications[23]. A review paper conducted in 2018 mentioned that RLS was related to antidepressant, antipsychotic, and antiepileptic medications[24]. However, Dunvald AD et al. investigated the relationship between RLS and the prescription of selective serotonin reuptake inhibitors among RLS patients who were initiated RLS medication, and they reported no association between SSRI initiation and RLS[25]. However, in this study, although no further specific details were investigated, antidepressant medication use was not only related to RLS but was also an independent predictor of RLS in psychiatric outpatients.

This study has some limitations worth mentioning. The population was monocentric. Hence, single-center enrollment, particularly out of the tertiary care center, potentially precludes the overall generalization of the findings, even among the psychiatric outpatient population. Furthermore, although some antidepressants and antipsychotics are reported to be associated with RLS symptoms, thorough subclassification was not made in this study, and any potentially existing association might have been missed. It may be difficult to capture the association between psychiatric medication and RLS, particularly in patients with index or recent exacerbation. However, this study intentionally enrolled psychiatric outpatients, who were on stable therapy for at least 3 months, to decrease such an adverse influence. Of note, after psychiatric outpatient clinic visit, patients with RLS were referred to expert neurologist for RLS management.

Conclusion

In this study, one in five psychiatric outpatients had RLS, and history of RLS in first-degree relatives, history of psychiatric disorder in the family, substance use and antidepressant medication use were found to be independent associates of RLS.

Conflict of interest

The authors declare that they have no conflict of interest.

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