

Frequency, severity and risk factors for restless legs syndrome in healthcare personnel

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ABSTRACT

الأهداف: تقييم نسبة انتشار متلازمة الساق المتعلملة بين العاملين في مجال الصحة، بالإضافة إلى تقدير نسبة شدتها، وعوامل الخطر المرتبطة بها.

الطريقة: أُجريت هذه الدراسة الاستطلاعية في العيادة الخارجية لطب الأسرة والتابعة لمستشفى كلية ميرام الطبية، كونيا، تركيا. شملت الدراسة 354 من العاملين في مجال الصحة في المستشفى وذلك خلال الفترة من أكتوبر 2010م إلى يونيو 2011م. لقد قمنا باستخدام مقياس درجة متلازمة الساق المتعلملة من أجل تقييم مدى شدة المرض، كما أننا قمنا بعمل مجموعة من الفحوصات العصبية للمرضى الذين ثبتت إصابتهم بالمرض.

النتائج: لقد كان 277 مشارك من الإناث (78.2%). ولقد كانت النسبة الكلية لانتشار متلازمة الساق المتعلملة بين العاملين في مجال الصحة 15% (53) (16.9% من الذكور، و14.4% من الإناث) وذلك اعتماداً على المعايير الأربعة الأساسية. لم يكن للجنس ($p=0.726$) ولا للعمر ($p=0.197$) أي علاقة واضحة من الناحية الإحصائية بهذا المرض. وكانت درجة شدة متلازمة الساق المتعلملة لدى المرضى الذين ثبتت إصابتهم بالمرض كالتالي: 16% من المرضى كانت درجة مرضهم طفيفة (8)، 40% متوسطة (21)، 44% شديدة (24) وذلك اعتماداً على المقياس الذي وضعتة المجموعة العالمية لدراسة متلازمة الساق المتعلملة. ولقد كان لدى تقريباً 54.7% من 53 مريض ثبتت إصابتهم بهذه المتلازمة تاريخ أسري للإصابة بهذا المرض.

خاتمة: تعد متلازمة الساق المتعلملة من الأمراض التي يمكن علاجها، غير أنه عادة ما يتم الخطأ أو التأخر في تشخيصها عالمياً بين الأطباء. كما ويعد التاريخ الأسري بالإصابة بهذه المتلازمة ضرورياً خلال تشخيص المتلازمة.

Objective: To evaluate the frequency, severity, and risk factors for restless legs syndrome (RLS) in healthcare personnel.

Methods: This cross-sectional study was performed at the Outpatient Family Medicine Clinic of Meram Medical Faculty in Konya, Turkey and included 354 healthcare personnel who were working at the Meram Medical Faculty Hospital between October 2010 and June 2011. The International RLS (IRLS) rating scale was used to calculate RLS severity. The RLS symptoms positive patients were investigated for neurological examination.

Results: Of all the participants, 277 (78.2%) were female. The overall prevalence of RLS according to the 4 essential criteria in the participating healthcare personnel was 15% (n=53) (16.9% male, 14.4% female). Gender ($p=0.726$) and age ($p=0.197$) were not significantly related to RLS. According to the International Restless Legs Syndrome Study Group (IRLSSG) the severity scale for RLS, of the RLS positive patients, 16% were classified as mild (n=8), 40% as moderate (n=21), and 44% as severe (n=24). Approximately, 54.7% of 53 RLS patients had a positive family history of the disorder.

Conclusions: Restless leg syndrome is a treatable disorder; however, it is still widely misdiagnosed by physicians. The history of the patient and family is very important in the diagnosis of RLS.

Neurosciences 2012; Vol. 17 (3): 230-235

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Received 7th December 2011. Accepted 20th May 2012.

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Restless legs syndrome (RLS) is a common neurological sleep/wake disorder characterized by an irresistible desire to move the extremities associated with paresthesia/dysesthesia. These symptoms occur predominantly at rest and worsen at night, resulting in nocturnal insomnia, and chronic sleep deprivation.¹⁻³ The severity of the symptoms varies widely, ranging from occurring only occasionally in a stressful situation to nightly and severe, with almost total disruption of sleep.² Restless legs syndrome is characterized by uncomfortable and unpleasant sensations in the legs that appear at rest, with a typical circadian pattern, which induces an irresistible urge to move the legs. The symptoms are usually more prominent at bedtime or after 6 p.m.; only in severely affected patients do they start earlier or occur all day long.^{2,4} The RLS is usually (80-90%) associated with periodic leg movements during sleep (PLMS).^{5,6} Restless legs syndrome familial aggregation is frequent, accounting for up to 60-65% of reported cases; inheritance follows an autosomal dominant pattern in at least one third of familial cases.^{5,7,8} Some families show possible anticipation.⁷ Familial and sporadic RLS cases present similar signs, symptoms, and clinical course. The only differences between the 2 groups consist of a significantly earlier age of onset, and a more frequent worsening during pregnancy in patients with hereditary RLS.⁹ The same RLS symptoms may originate from reduced iron stores, folate, and B12 deficiency, neuropathy, renal failure, diabetes, pregnancy, carcinoma, amyloidosis, lesions of the lumbosacral plexus and possibly rheumatological diseases (secondary or symptomatic RLS forms).³ It is a common syndrome, the adult prevalence reported to range from 2-5% of the Caucasian population.¹⁰⁻¹⁴ The RLS symptoms worsen with increasing age and both genders are equally affected.³

Since the introduction of the 4 minimal criteria for RLS in 1995 by the International Restless Legs Syndrome Study Group, the number of published studies in RLS during the past 10 years has substantially increased.^{1,2} These studies have improved our knowledge of prevalences, risk factors, or outcomes of the disease at the population level, and provided a hypothesis on potential biological mechanisms. In this study, we aimed to evaluate the frequency and risk factors for restless legs syndrome in a special population, namely, healthcare personnel.

Methods. This cross-sectional study was conducted at the Outpatient Family Medicine Clinic of Meram Medical Faculty in Konya, Turkey between October 2010 and June 2011. The study population

comprised healthcare personnel who were working at Meram Medical Faculty Hospital, selected by cluster sampling. We included 354 individuals (78.7%) out of 450 healthcare personnel working at the Faculty Hospital during the study period. The rate of refusal to participate in the study was 31.3%. The study protocol was approved by the Ethics Committee of Meram Medical Faculty of Selcuk University. The participants were duly informed and written, and oral consent was obtained from volunteers according to the Principles of the Helsinki Declaration. All participants answered the questionnaire in a face-to-face interview.

The presence of RLS was diagnosed using internationally recognized criteria. Participants who responded positively to all 4 questions were diagnosed as having RLS. The RLS positive patients completed the IRLSSG questionnaire. We excluded pregnant women, those chronic neurological diseases (such as multiple sclerosis and Parkinson's disease), rheumatologic diseases, and all participants with a history of chronically painful conditions such as arthritis, neuropathy, or muscle pain. The RLS symptoms positive patients underwent a neurological examination by a physician experienced in RLS. The severity of RLS was assessed with the IRLSSG questionnaire.

The essential diagnostic criteria for RLS include: 1. An urge to move one's legs, usually accompanied or caused by an uncomfortable sensation in the legs. 2. The urge to move or unpleasant sensations beginning or worsening during periods of rest or inactivity. 3. The urge to move or unpleasant sensations that are either partially or totally relieved by movement. 4. The urge to move or unpleasant sensations that worsen in the evening or at night compared to during the day, or that occur only in the evening or night.²

In addition, we also researched RLS history of first-degree relatives by using standard supportive clinical features of RLS.^{2,8} The prevalence of RLS among first-degree relatives of people with RLS is 3-5 times greater than in people without RLS. The RLS positive patients completed the IRLSSG questionnaire. This questionnaire also included questions regarding the frequency of RLS. The IRLSSG severity scale for RLS (IRLS) is a 10-question scale that is validated to assess the severity of RLS symptoms and includes 5 items pertaining to symptom frequency and intensity, and 5 items addressing the impact of symptoms on aspects of daily living and sleep. Participants with IRLS scores of less than 10 were categorized as mild, 11-20 as moderate, 21-30 as severe, and 31 or greater as very severe.⁴

In all subjects, a fasting blood sample was taken in the morning after at least 10 hours fasting for analysis

of the following biochemical parameters using standard techniques: total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), and fasting blood glucose. In addition, hemogram, ferritin, folic acid, vitamin B12, and thyroid stimulating hormone (TSH) were examined. Diabetes was defined as fasting glycemia ≥ 126 mg/dL or treatment with insulin or hypoglycemic agents oral drugs (defined on the basis of the American Diabetes Association guidelines.¹⁵ Dyslipidemia (DLP) was defined as TC ≥ 200 mg/dL, or LDL-c ≥ 130 mg/dL, or HDL-c ≤ 40 mg/dL, or TG ≥ 150 mg/dL.¹⁶

The encoding and statistical analyses of the data were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 13.0. The minimum, maximum, mean, standard deviation, median, and percentages were used. To compare the statistical significance between groups, chi-square test and odds ratio were used and the significance level was taken as $p < 0.05$.

Results. Three hundred and fifty-four healthcare personnel were included in this study. Of all the participants, 77 (21.8%) were male, 277 (78.2%) were female, and the mean age was 29.8 ± 7.0 (median=30, minimum=19, maximum=45). Of the RLS positive healthcare personnel, 75.5% (n=40) were women, and all of the participants with RLS delineated uncomfortable and unpleasant sensations in the legs. Gender ($p=0.726$) and age ($p=0.197$) were not significantly related to RLS (Table 1). The overall prevalence of RLS according to the 4 essential criteria in the participating healthcare personnel was 15% (n=53) (16.9% male, 14.4% female). The mean IRLS score was 17.2 ± 6.7 . According to the IRLSSG severity scale for RLS (IRLS), of the RLS

positive patients, 16% were classified as mild (n=8), 40% moderate (n=21), and 44% severe (n=24). Among the patients with periodic limb movements (PLM) during wakefulness or sleep, the frequency of RLS was found to be 14.292 times more when compared with the RLS negative patients (odds ratio [OR]=14.292, 95% confidence interval [CI]: 7.310-27.944), and this difference was statistically significant ($\chi^2=77.838$, $p=0.000$).

As many as 66% of people with RLS reported disturbance of sleep onset and maintenance of sleep. Statistically, this rate was significantly higher in RLS positive patients than RLS negative healthcare personnel ($\chi^2=38.324$, $p=0.000$). The frequency of the disturbance of sleep onset and maintenance of sleep was found to be 6.538 times more when compared to the RLS negative patients (OR=6.538, 95% CI: 3.486-12.261). Approximately, 54.7% of 53 RLS patients had a positive family history of the disorder that is, at least one first-degree relative was affected with this condition. Roughly, a person with RLS is 9 times more likely to have another family member with RLS than someone without RLS. Statistically, this rate was significantly higher in RLS positive patients than RLS negative healthcare personnel (OR=9.489, 95% CI: 4.964-18.140, $\chi^2=55.149$, $p=0.000$) (Table 1).

Statistically, we found no difference between RLS and RLS negative healthcare personnel in TC, TG, HDL-c, LDL-c, fasting blood glucose, hemogram, ferritin, folic acid, vitamin B12, and TSH levels (Table 2). There was also no difference between RLS positive and RLS negative personnel in smoking status. The neurologic examination was normal in patients with RLS. Appropriate therapies for RLS (replacement of deficiency and dopamine agonists) were administered (especially to the moderate and severe categories), while some patients were followed without any treatment.

Table 1 - Comparison of age, gender, and family history between RLS positive and negative groups.

Parameters	RLS positive (n=53)	RLS negative (n=301)	Total	χ^2	P-value
	n (%)				
<i>Age</i>				1.662	0.197
≥ 30 age	28 (52.8)	127 (42.2)	155		
<30 age	25 (47.2)	174 (57.8)	199		
<i>Gender</i>				0.123	0.726
Male	13 (24.5)	64 (21.3)	77		
Female	40 (75.5)	237 (78.7)	277		
<i>Family history</i>				55.149	0.000
Yes	29 (54.7)	34 (11.3)	63		
No	24 (45.3)	267 (88.7)	291		

RLS - restless legs syndrome

Table 2 - Comparison of biochemical parameters between RLS positive and negative groups.

Parameters	RLS positive (n=53)		RLS negative (n=301)		Total	χ^2	P-value
	n (%)						
Fasting blood glucose (mg/dL)							
<100 (normal)	45	(85.0)	244	(81.0)	289	0.272	0.602
100-125 (impaired fasting glucose)	8	(15.0)	53	(17.9)	61		
≥126 mg/dl	---	(0.0)	4	(1.1)	4		
LDL-c (mg/dL)							
<130 (normal)	45	(85.7)	218	(72.2)	263	1.873	0.171
130-159 (borderline)	8	(14.3)	75	(25.2)	83		
160-189 (high)	---	---	8	(2.6)	8		
HDL-c (mg/dL)							
<40 (low)	23	(42.9)	124	(41.4)	147	0.000	1.000
≥40 (normal)	30	(57.1)	177	(58.6)	207		
T. cholesterol (mg/dL)							
<200 (normal)	39	(76.2)	226	(74.6)	265	0.270	0.603
200-239 (borderline)	14	(23.8)	60	(20.3)	74		
≥240 (high)	---	---	15	(5.1)	15		
Triglycerides (mg/dL)							
<150 (normal)	43	(81.0)	234	(77.8)	277	0.273	0.872
150-199 (borderline)	5	(9.5)	41	(13.5)	46		
≥200 (high)	5	(9.5)	26	(8.7)	31		
TSH (μIU/mL)							
<0.34	---	---	4	(1.4)	4	0.029	0.865
0.34-5.6	53	(100.0)	290	(96.4)	343		
≥5.6	---	---	7	(2.2)	7		
Folic acid (ng/mL)							
<2.33 (low)	---	---	11	(3.6)	11	1.244	0.265
2.33-17.24 (normal)	53	(100.0)	290	(96.4)	343		
≥17.24 (high)	---	---	---	---	---		
Ferritin (ng/mL)							
<11 (low)	8	(14.3)	86	(28.4)	92	1.425	0.233
11-306.8 (normal)	45	(85.7)	215	(71.6)	262		
Vitamin B12 (pg/mL)							
<126.5 (low)	3	(4.8)	15	(5.3)	18	0.451	0.798
126.5-505 (normal)	47	(90.5)	260	(86.0)	307		
≥505 (high)	3	(4.8)	26	(8.7)	29		
Hemoglobin (g/dL)							
<12.1 (low)	13	(23.8)	80	(26.5)	93	0.071	0.790
12.1-17.2 (normal)	40	(76.2)	221	(73.5)	261		
≥17.2 (high)	---	---	---	---	---		

RLS - restless legs syndrome, LDL-c - low-density lipoprotein cholesterol, HDL-c - high-density lipoprotein cholesterol, T. cholesterol - total cholesterol, TSH - thyroid stimulating hormone

Discussion. Before discussing the conclusions, the limitations of the study should be considered. This study was conducted in a medical faculty hospital with a small study group, which limits our ability to generalize the results to a general Turkish population; however, this sample helped us to determine the prevalence of RLS.

In BaHamam's study¹⁷ in 1303 adult Saudis attending primary health care, the prevalence of RLS was 5.2%, and was highest among participants between 45-60 years of age. The overall prevalence was equal between males and females; however, RLS was more prevalent in females older than 45 years compared to males in the same age group. However, the prevalence in our study was higher than the rate reported in this study.

Möller et al¹⁸ showed that out of all participating patients, 7704 (46.6%) suffered from unpleasant sensations in the legs, and 1758 (10.6%) were diagnosed with RLS according to the 4 essential clinical criteria. Merlino et al¹⁹ reported that 22 patients with type 2 diabetes (17.7%) were diagnosed as RLS positive in 124 individuals with diabetes. Micozkadioglu et al²⁰ reported that the prevalence of RLS was 4.7% in the hemodialysis patients in Baskent University School of Medicine, Ankara, Turkey. This rate was lower than our results. Kusbeci et al²¹ evaluated RLS prevalence in Medical School Students of Afyon Kocatepe University in Turkey and reported that the prevalence of RLS was 2.3%. This rate was also lower than our results.

Sahin et al²² reported that the incidence of RLS in 400 pregnant women was 19%, again higher than our results. In that study, snoring, apnea, and daytime fatigue were significantly higher in RLS pregnant women. Daytime sleepiness was higher in RLS pregnant women, but this was not statistically significant.

In our study, according to the IRLSSG severity scale for RLS (IRLS), of the RLS positive patients, 16% were classified as mild (n=8), 40% as moderate (n=21), and 44% as severe (n=24), and the mean IRLS score was 17.2 ± 6.7 . Merlino et al¹⁹ presented that based on IRLS, 31.8% patients were affected by mild, 54.5% by moderate, and 13.7% by severe/very severe RLS, in people with type 2 diabetes. Thirty-two percent of RLS positive patients reported a presence of RLS symptoms >3 nights per week. The age of onset of RLS was 60 ± 8.9 years. The mean IRLS score was 14.9 ± 5.5 . In this respect, these results were similar to our findings.

In research findings presented among patients with PLM during wakefulness or sleep, the prevalence of RLS was considerably higher (60.4%) than in the total population. In 1965, Lugaresi and colleagues²³ first documented the presence of PLM in patients with RLS. In a later study, Montplaisir et al⁵ evaluated 133 patients with RLS during one night of polysomnographic recording and found that 82.2% had a PLM. Our study documented that as many as 66% of people with RLS had the disturbance of sleep onset and maintenance of sleep. Restless legs syndrome presents 2 problems for sleep: initiating sleep, and maintaining sleep. The patient with moderate to severe RLS may sleep on average less than 5 hours per night, and may chronically have less sleep time than patients with almost any other persistent disorder of sleep. Moreover, the reduced sleep efficiency correlates with the reported clinical severity of RLS.² Crochard et al²⁴ reported that a diagnosis of RLS was assigned to 42.6% of patients with leg complaints, 35.5% of those with sleep complaints, and 54.9% of those with both complaints.

A variety of research studies have verified the clinical impression that approximately 50% of patients with RLS have a family history of the disorder. A person with RLS is 3-6 times more likely to have another family member with RLS than someone without RLS. More than 60% of cases of RLS are familial and are inherited in an autosomal dominant fashion with variable penetrance.¹² In our study, approximately, 54.7% of 53 RLS patients had a positive family history of the disorder. Yüksel et al²⁵ emphasized that 55% of patients had a positive family history. In Koc & Yelder's study²⁶ of 63 family members, 17 also had an RLS diagnosis. A similar study performed in Canada¹² showed that 80

out of 128 patients (63%) had a positive family history of RLS. In the Canadian study, 39% of all first-degree relatives were reported to have RLS. A study conducted in the United States⁸ revealed that more than 60% of 138 RLS patients had a positive family history of the disorder that is, at least one first-degree relative was affected with this condition. These results were similar to our findings.

We did not find any difference between RLS positive and RLS negative healthcare personnel for TC, TG, HDL-c, LDL-c, fasting blood glucose, hemogram, ferritin, folic acid, vitamin B12, and TSH levels. However, serum ferritin levels below 50 ng/mL have been associated with increased severity of RLS in adults.²⁷ In Frauscher's study,²⁸ almost one-third of all patients (31.1%) had ferritin levels <50 lg/l. There was an inverse correlation between RLS severity and ferritin levels. Patients with current augmentation had the lowest ferritin levels. In another study, in 5 (25%) patients the serum ferritin level was low (mean: 6.1ng/mL; N: 13-150ng/mL).²⁵

In conclusion, this survey revealed a high prevalence of RLS in 354 healthcare personnel. The overall prevalence of RLS according to the 4 essential criteria in the participating healthcare personnel was 15% (n=53). Of the RLS positive healthcare personnel, 75.5% (n=40) were women, and all the patients with RLS delineated uncomfortable and unpleasant sensations in the legs. Gender and age were not significantly related to RLS. Although the diagnosis of RLS does not require extensive investigations, RLS is still widely mis- or under-diagnosed. Our study showed that the history of the patient and family was very important in the diagnosis of RLS. In this regard, these findings shed light on the direction for future research.

Acknowledgments. *The authors acknowledge Sevdâ Gündüz and the Directors of Nursing of the Meram Medical Faculty for their support in collecting information. We also thank all of the participants.*

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