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ORIGINAL ARTICLE

Quality of life in patients with primary restless leg syndrome: community-based study

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Abstract Restless leg syndrome (RLS) is frequently associated with poor mental health and impaired quality of life (QoL), due to discomfort, pain, fatigue, inability to rest, sleep disturbances, and consequently, anxiety and depression. The aim of this study is to address this issue in a community-based cohort of patients with RLS. The present study is a sub-analysis of the community-based prevalence study. In this door-to-door survey, we identified according to four essential IRLSSG diagnostic criteria 107 people with RLS. Clinical characteristics of RLS, including QoL, were obtained from 94 subjects (88 %), who completed the Serbian translation of SF-36. The main finding of our study was that the severity of RLS, in particular frequency of symptoms, negatively influenced majority of the SF-36 domains. The severity of depressive and anxiety symptoms was negatively associated with all domains of SF-36. Age of participants significantly correlated with both physical and mental composite scores. In multivariate linear regression model, higher scores of Hamilton depression ($p = 0.001$) and anxiety ($p = 0.003$) Rating scales were the most significant negative contributors of the total SF-36 score in persons with RLS. Suggesting particular role of comorbid depression and anxiety, our results may have a practical implication in terms of different psychosocial treatment and support in addition to the regular therapeutic protocols in RLS patients.

Keywords Restless leg syndrome · IRLSSG diagnostic criteria · Quality of life · SF-36 · Anxiety · Depression

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Introduction

Restless legs syndrome (RLS; also known as Willis-Ekbom disorder) is a sensorimotor-related sleep disorder characterized by distressing deep sensations (tingling, creeping, crawling, burning or aching) in the limbs and irresistible urge to move the legs, often during the evening and nighttime [1, 2]. These symptoms frequently lead to a loss of sleep: more severely affected patients sleep less than 4–5 h per night and experience problems in performing daily activities [3]. Despite wide variations in severity of symptoms among patients [2], RLS in general is frequently associated with poor mental health and impaired quality of life (QoL), due to discomfort, pain, fatigue, inability to rest, sleep disturbances, and consequently, anxiety and depression [3]. Unfortunately, pattern of distribution according to the severity of RLS in general population has not been thoroughly investigated and potential factors that may correlate with severity of the disease are not fully highlighted.

Prevalence studies suggest that RLS affects between 5 and 10 % of the general population in European countries and USA [4, 5]. The International RLS Study Group (IRLS-SG) proposed a set of criteria that clearly defined symptoms of RLS and allowed its more uniform diagnosis worldwide [6]: (1) an urge to move the legs, usually accompanied by an uncomfortable sensation(s); (2) the

uncomfortable sensation(s) begins or worsens during periods of rest; (3) the unpleasant sensations are partially or totally relieved by walking/movement; and (4) the urge to move is greater in the evening or night than during the day. To exclude possible alternative diagnoses or "mimickers", the fifth criterion has been recently added that the symptoms cannot be accounted for as symptoms primary to another medical or behavioral condition [7, 8].

Little is known about the clinical and demographic features associated with the health-related quality of life (HRQoL) in patients with primary RLS [9–11]. RLS symptom severity, usually determined by frequency and severity of symptoms, may broadly range from mild, moderate, severe, to very severe [12]. Clinical series are biased due to the recruitment of the more severe cases with RLS. Therefore, the aim of this cross-sectional study is to address this issue in a community-based cohort of patients with RLS.

Patients and methods

The present study is a sub-analysis of the previously published community-based prevalence study conducted in the region of Sombor (Serbia) [5]. Shortly, between October 2011 and January 2012, a door-to-door survey was carried out to identify people with RLS. Face-to-face interviews were conducted by two specialized nurses who received additional training from neurological and epidemiological experts prior to the study. The study participants answered four specific questions comprising essential criteria for RLS according to the IRLSSG [13], in a brief questionnaire (validated Serbian version) that also collected demographic data. If all four questions answered positively, the respondent was regarded as positive (possible) RLS subject; otherwise, the respondent was considered negative. All four essential IRLSSG diagnostic criteria were met by 107 of 2,112 respondents (5.1 %). In the second step, positive RLS subjects were invited to the city hospital where the possible alternative diagnoses or "mimickers" were excluded after an interview and detailed examination by the movement disorders expert, with a particular emphasize on diabetes mellitus, renal insufficiency, and radicular lesions in the lumbosacral region.

Clinical characteristics of RLS, including participation in the QoL study, were obtained from 94 out of 107 subjects (88 %) who met diagnostic criteria for RLS (13 participants rejected additional examinations). The patients were included in the study after giving informed consent and filling out a comprehensive questionnaire designed for this study. The study was approved by the Ethical Committee of the School of Medicine, University of Belgrade.

Supplementary investigations performed in all 94 recruited subjects included magnetic resonance imaging (MRI) and/or computed tomography (CT) of the brain and cervical region, electromyoneurography and extensive laboratory analyses, including serum levels of glucose, renal and hepatic functions, iron, ferritin and transferrin. The severity of RLS symptoms occurring over 7 previous days was assessed by the 10-item IRLSSG rating scale (IRLSSG-RS) [12] and classified as mild, moderate, severe and very severe, based on scores from the IRLSSG-RS (mild: 0–10; moderate: 11–20; severe: 21–30; very severe: 31–40). The scale was validated and adapted for Serbian language. Depression and anxiety were assessed using the Hamilton Depression Rating Scale (HDRS) [14] and Hamilton Anxiety Rating Scale (HARS) [15], respectively.

All subjects completed the Serbian translation of SF-36 (http://www.qualitymetric.com SF36 Health Survey (original version) Language Recalls [accessed on 13/05/2006)], which was used as an outcome measure for the HR-QoL [16]. The attending physicians were available for questions and additional explanations. The SF-36 is a generic instrument that provides a profile assessment of HR- QoL in eight domains: physical functioning (PF), role functioning physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role functioning emotional (RE), and mental health (MH). Based on these eight domains, two summary scales have been constructed: the Physical Health Composite (PHC) and the Mental Health Composite (MHC). The total SF-36 score was also calculated. Scoring and the calculations were performed by using the original Ware's method [16]. Quality of life scores were presented as T scores (mean = 50; SD = 10), which were obtained by linear transformation of raw scores, that facilitates comparisons across the multiple subscales of the SF-36. The items can be summed to give scores ranging from 0 (worst possible health state) to 100 (best possible health state), i.e., higher values indicate better functioning and well-being.

Statistical analysis

Statistical analysis was performed with ANOVA and χ^2 depends on the normality of distribution. Pearson's correlation coefficient was used to study the relationship between the subscales of the SF-36 and different variables of interest (HDRS, HARS, age at onset, age, duration of disease and the IRLSSG-RS). Spearman rank correlation analysis was conducted to investigate relationships between the IRLSSG-RS severity score, frequency of symptoms and gender and both HDRS and HARS. The linear regression analysis was used to examine how the various variables contribute to the total SF-36 score. Statistical analysis was performed using SPSS software, version 17.0.

Results

Ninety-four subjects with RLS (67 females; 71.3 %) were included in the study (aged 57.9 ± 13.4 years; range 24–86 years). Considering disease severity, 9 patients (9.6 %) had mild, 46 patients (48.9 %) moderate, and 39 (41.5 %) severe and very severe symptoms. The most severely affected subjects were those with significantly more frequent symptoms ($p = 0.001$) (Table 1).

Significant positive correlation was obtained between the HDRS and the frequency of symptoms ($\rho = 0.357$; $p = 0.001$), the IRLLSSG Rating Scale scores ($\rho = 0.509$; $p = 0.001$), and female gender ($\rho = 0.296$; $p = 0.004$). Significant positive correlations were also observed between the HARS scores and the frequency of symptoms ($\rho = 0.386$; $p = 0.001$), the IRLLSSG Rating Scale scores ($\rho = 0.535$; $p = 0.001$); and female gender ($\rho = 0.296$; $p = 0.004$). Sleep disturbances, tiredness or daytime somnolence due to RLS, assessed by two IRLSSG Rating Scale items, were significantly more common among RLS sufferers with one or more episodes per week when compared to those with less than one episode of RLS per week (Table 2). Those with more frequent RLS symptoms also had significantly higher HDRS ($p = 0.001$) and HARS ($p = 0.002$) scores (Table 2).

Mean scores of the SF-36 questionnaire, as well as the influence of symptoms frequency on different SF 36 items, are presented on Table 3. Shortly, frequency of the RLS symptoms influenced all the SF-36 subdomains, except PF, RF, RE, and BP.

Gender, symptoms expression in hands, and time during the day when the symptoms occurred, did not influence QoL in our patients. Employment influences RF ($p = 0.014$), GH ($p = 0.003$), and PHC domains ($p = 0.002$), as well as the total score ($p = 0.014$). Family history influenced VT ($p = 0.028$), while adequate sleep influenced RF ($p = 0.059$) and RE ($p = 0.033$) domains. Treatment influenced MH scale ($p = 0.035$).

According to correlation analysis (Table 4), age of participants correlated with PF, RP, VT, MH, GH and PHC, as well as the total SF-36 score. The HDRS statistically significantly correlated with all domains, while the HARS correlated with all domains except BP. Statistically significant correlations are also observed between IRLSSG-RS and all domains of SF-36, except PF. Disease duration correlated only with PF and SF (Table 4).

Table 1 Restless leg severity score according to demographic and clinical characteristics of included subjects (mild: 0–10; moderate: 11–20; severe: 21–30; very severe: 31–40)

Variable	Severity score				*p*
	0–10 ($n = 9$)	11–20 ($n = 46$)	21–30 ($n = 33$)	34–40 ($n = 6$)	
Age groups (years)					
18–24	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0.877
25–34	1 (11.1)	3 (6.5)	1 (3.0)	0 (0.0)	
35–44	2 (22.2)	4 (8.7)	3 (9.1)	1 (16.7)	
45–54	2 (22.2)	7 (15.2)	9 (27.3)	0 (0.0)	
55–64	1 (11.1)	17 (37.0)	9 (27.3)	3 (49.9)	
>65	3 (33.3)	14 (30.4)	11 (33.3)	2 (33.4)	
Gender					
Males	4 (44.4)	14 (30.4)	7 (21.2)	2 (33.3)	0.547
Females	5 (55.6)	32 (69.6)	26 (78.8)	4 (66.7)	
Frequency of symptoms					
6–7 times per week	0 (0.0)	3 (6.6)	9 (27.3)	5 (83.3)	0.001
4–5 times per week	0 (0.0)	6 (13.0)	14 (42.4)	1 (16.7)	
2–3 times per week	0 (0.0)	14 (30.4)	8 (24.2)	0 (0.0)	
2–4 times per month	5 (55.6)	23 (50.0)	2 (6.1)	0 (0.0)	
1 time per month or rarely	4 (44.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Time of onset during the day					
At bedtime/night	4 (44.4)	39 (84.8)	27 (81.8)	4 (66.6)	0.103
At/or after 6 pm	4 (44.4)	4 (8.7)	3 (9.1)	1 (16.7)	
Before 6 pm	1 (11.2)	3 (6.5)	3 (9.1)	1 (16.7)	

Data presented as number of patients (%)

Table 2 Clinical characteristics of subjects according to the frequency of symptoms

Variable	Frequency of symptoms			*p*
	Total ($n = 94$)	≥1 per week ($n = 34$)	<1 per week ($n = 60$)	
How severe was your sleep disturbances due to your RLS symptoms? (IRLSSG-RS)[a]				
None	17 (18.1 %)	11 (32.4 %)	6 (10.0 %)	0.016
Mild	14 (14.9 %)	7 (20.6 %)	7 (11.7 %)	
Moderate	18 (19.1 %)	4 (11.8 %)	14 (23.3 %)	
Severe	30 (31.9 %)	10 (29.4 %)	20 (33.3 %)	
Very severe	15 (16.0 %)	2 (5.9 %)	13 (21.7 %)	
How severe was your tiredness or sleepiness during the day due to your RLS symptoms? (IRLSSG-RS)[a]				
None	32 (34.0 %)	18 (52.9 %)	14 (23.3 %)	0.001
Mild	25 (26.6 %)	11 (32.4 %)	14 (23.3 %)	
Moderate	25 (26.6 %)	5 (14.7 %)	20 (33.3 %)	
Severe	12 (12.8 %)	0 (0.0 %)	12 (20.0 %)	
Very severe	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
HDRS[b]	9.5 ± 6.5 (0–26)	6.7 ± 5.0 (0–20)	11.1 ± 6.7 (0–26)	0.001
HARS[b]	9.6 ± 6.3 (0–28)	7.0 ± 5.3 (1–19)	11.1 ± 6.4 (0–28)	0.002

IRLSSG-RS International RLS Study Group Rating Scale, *HDRS* Hamilton Depression Rating Scale, *HARS* Hamilton Anxiety Rating Scale

[a] Values presented as a number of patients (%)

[b] values presented as means ± SDs (range)

To determine factors statistically significantly associated with total quality of life in the persons with RLS, we performed univariate logistic regression analyses with the total SF-36 score as dependent variable, while independent variables were different demographic and clinical factors studied (Table 5). All variables univariately statistically significant ($p < 0.05$) entered in the multivariate logistic regression model. This analysis showed that higher scores of HDRS [standardized β coefficient = −0.443; 95 % confidence interval (CI), −1.939, −0.627; $p = 0.001$) and HARS (standardized β coefficient = −0.348; 95 % CI, −1.728, −0.363; $p = 0.003$] were the most significant negative contributors of the total SF-36 score in persons with RLS.

Discussion

The main finding of our study was that the severity of RLS, in particular frequency of symptoms, negatively influenced majority of the SF-36 domains, except PF, RF, and BP. The severity of depressive symptoms was negatively associated with all domains; the same was true for anxiety, with an exception for BP. Finally, age of participants significantly correlated with PF, RP, and RE domains, as well as both composite scores (Table 4). Our data are in accordance with the previous studies, suggesting that patients with more severe RLS symptoms have more severely impaired QoL [10, 17, 18]. As in our study, Abetz et al. [9] also found that increased RLS severity had a significant effect on all areas of functioning measured by the SF-36, with the exceptions of PF and general health, who did not discriminate between severity levels (Table 3). Winkelman et al. [19] conducted a large polysomnografic study and reveled that subjects with RLS had poorer HR-QoL (measured by the SF-36) in all physical domains, as well as in the Mental Health and Vitality domains. In a study that used the Restless Legs Syndrome Quality of Life questionnaire (RLS-QoL), which comprised social functioning, daily functioning, and emotional well-being, symptom severity significantly affected QoL [20].

There are several limitations of our study that make it difficult to compare our data with the data of other studies. First, this is the lack of standards for the SF-36 in the Serbian general population. For instance, Happe et al. [17] compared RLS patients with the age-matched general population using the EuroQoL (EQ-5D) and found considerably lower scores in the former group. In another study [18], comparison of the QoL of RLS patients with QoL of healthy controls, as well as patients with other chronic diseases (hypertension, diabetes type 2, and osteoarthritis in the knee) revealed that only patients with osteoarthritis were doing worse than RLS patients. Abetz et al. [9] also showed that RLS patients had significantly lower scores on all 8 scales of the SF-36 when compared with those suffering from hypertension, other cardiovascular conditions, diabetes mellitus or osteoarthritis. Second, we enrolled and personally examined participants from a community-based study prevalence study that used door-to-door survey. One may expect that the RLS symptoms in our cohort are less severe than in clinically based studies [17, 18]. Indeed, in our study, severe symptoms were present in about a third of patients, but only 6.5 % had very severe symptoms. Finally, like in few previous studies [4, 19, 21], we used the SF-36, while some other studies dealing with the QoL in RLS used different

Table 3 Influence of symptoms frequency on the SF-36 domains

Frequency of symptoms	Physical functioning	Role physical	Role emotional	Vitality	Mental Health	Social functioning	Bodily pain	General health	PHC	MHC	Total
6–7 times per week	66.1 ± 15.3	26.5 ± 43.7	62.7 ± 48.4	43.2 ± 29.0	59.1 ± 18.7	73.5 ± 29.3	50.9 ± 31.7	40.6 ± 14.5	47.1 ± 12.7	59.6 ± 25.8	53.1 ± 16.7
4–5 times per week	64.8 ± 11.0	42.9 ± 45.5	65.1 ± 47.7	40.2 ± 26.2	55.6 ± 24.1	65.5 ± 30.8	61.1 ± 29.1	39.8 ± 27.7	52.1 ± 18.2	56.6 ± 24.2	54.4 ± 20.8
2–3 times per week	57.8 ± 6.4	54.5 ± 44.7	83.3 ± 35.3	65.0 ± 26.3	74.9 ± 21.9	89.2 ± 19.8	61.6 ± 32.1	61.6 ± 20.3	58.9 ± 17.7	78.1 ± 22.3	68.5 ± 18.2
2–4 times per month	59.6 ± 14.9	54.2 ± 50.0	92.2 ± 25.8	56.3 ± 23.0	73.6 ± 13.0	87.9 ± 22.4	72.1 ± 29.4	62.7 ± 20.5	62.1 ± 16.2	77.5 ± 16.5	69.8 ± 15.3
≤1 time per month	55.6 ± 7.2	75.0 ± 50.0	75.0 ± 50.0	53.8 ± 25.0	74.0 ± 7.7	96.9 ± 6.3	81.3 ± 24.6	62.5 ± 16.5	68.6 ± 20.8	74.9 ± 21.6	71.8 ± 21.1
All patients	61.3 ± 12.6	47.6 ± 47.2	78.0 ± 40.2	52.3 ± 27.0	67.3 ± 20.5	80.1 ± 26.6	63.7 ± 30.7	53.3 ± 23.5	56.8 ± 17.5	69.6 ± 23.4	63.2 ± 19.0
p	0.135	0.198	0.063	0.017	0.002	0.005	0.148	0.001	0.020	0.002	0.003

Values presented as means ± SDs

PHC physical health composite, *MHC* mental health composite

questionnaires like the EQ-5D [17], the disease-specific RLS-QoL [20], or the visual analog scales [22].

In our study, the HDRS scores statistically significantly correlated with all the SF-36 domains, similar to the HARS and the IRLS, with the exception of BP. Cho et al. [18] identified depression, severity of symptoms and gender (females) as factors significantly associated with SF-36 scores in the RLS patients; the QoL patients was significantly worse in those with more severe depression. Happe et al. [17] also reported anxiety/depression among the main contributors of decreased QoL in RLS. Fatigue [23], insomnia [24, 25] and daytime somnolence [26], frequently observed in RLS, are also independent risk factors for depression. In patients with more frequent RLS patients, we observed significantly more common expression of sleep disturbances, tiredness or daytime somnolence (Table 2). In the same group of patients, the HDRS and HARS scores were higher and significantly positively correlated with the frequency of symptoms, disease severity and female gender. Abetz et al. [9] also found that depression and anxiety in RLS significantly positively correlated with these three variables. Therefore, in parallel with the treatment of basic RLS symptoms, identification and treatment of anxiety/depression may be beneficial approach in this disorder. As some other authors [9], we found that therapy for RLS influenced emotional well-being of patients. However, all current medications induce side effects that may reduce the extent to which QoL symptoms are improved (i.e. adverse effects further affect QoL) [27].

Age of our patients also correlated with several domains of the SF-36. It has been already shown that the older patients reported that RLS symptoms affected their daily functioning, impaired ability to perform tasks, had detrimental effects on cognitive functions, and led to the feelings of hopelessness, with irritability and short tempered behavior [20]. However, age at onset of RLS symptoms correlated with only with physical functioning. Despite hypothesis that early-onset RLS produced greater deficits in QoL than late-onset RLS, several studies failed to find influence of this variable on the QoL in RLS [9, 17].

As recently suggested by Kalloo et al. [27], we may also conclude in this community-based cohort that RLS has significant influence on patients QoL that "extends beyond sleep, affecting their social lives and emotional and psychological health". Suggesting particular role of comorbid depression and anxiety, our results may have a practical implication, i.e., that different psychosocial treatment and support could be added to the regular therapeutic protocols in RLS patients. Additionally, the severity of the disease should not also be underestimated in the planning of treatment approach. We used generic SF-36 instrument,

Table 4 Correlation analyses

	Physical functioning	Role physical	Role emotional	Vitality	Mental Health	Social functioning	Bodily pain	General health	PHC	MHC	Total
Actual age (years)											
r^a	0.502	−0.393	−0.078	−0.227	−0.205	−0.167	−0.055	0.294	−0.282	−0.191	−0.248
p	0.001	0.001	0.453	0.028	0.048	0.107	0.597	0.004	0.006	0.065	0.016
Age at onset (years)											
r^a	0.195	−0.245	−0.020	−0.095	−0.091	0.023	0.076	−0.191	−0.143	−0.049	−0.096
p	0.062	0.017	0.850	0.363	0.382	0.823	0.468	0.065	0.171	0.638	0.360
HDSR											
r^a	0.440	−0.520	−0.527	−0.611	−0.645	−0.667	−0.254	−0.530	−0.589	−0.733	−0.727
p	0.001	0.001	0.001	0.001	0.001	0.001	0.014	0.001	0.001	0.001	0.001
IRLSSG-RS											
r^a	0.187	−0.278	−0.300	−0.283	−0.322	−0.252	−0.211	−0.377	−0.355	−0.352	−0.382
p	0.073	0.007	0.003	0.006	0.002	0.014	0.041	0.001	0.001	0.001	0.001
Disease duration											
r^a	0.331	−0.137	−0.038	−0.121	−0.111	−0.212	−0.151	−0.097	−0.133	−0.136	−0.145
p	0.001	0.190	0.715	0.247	0.289	0.041	0.147	0.354	0.207	0.192	0.167
HARS											
r^a	0.388	−0.547	−0.515	−0.574	−0.618	−0.616	−0.187	−0.595	−0.602	−0.696	−0.077
p	0.001	0.001	0.001	0.001	0.001	0.001	0.071	0.001	0.001	0.001	0.001

HDRS Hamilton Depression Rating Scale, *IRLSSG-RS* International RLS Study Group Rating Scale, *HARS* Hamilton Anxiety Rating Scale, *PHC* physical health composite, *MHC* mental health composite

[a] Pearson's correlation coefficient

Table 5 Univariate and multivariate linear regression analyses (dependent variable: total SF-36 score)

Variable	Univariate analysis		Multivariate analysis	
	Standardized β coefficient (95 % CI)	*p*	Standardized β coefficient (95 % CI)	*p*
Gender	−0.183 (−16.345, 0.935)	0.080		
Age	−0.248 (−0.640, −0.066)	**0.016**		
Employment	0.160 (−0.754, 5.968)	0.127		
IRLSSG-RS	−0.381 (−1.456, −0.481)	**0.001**		
Frequency of symptoms	0.375 (2.927, 9.146)	**0.001**		
Duration of disease	−0.145 (−0.564, 0.099)	0.167		
Sleep disturbances	−0.287 (−6.878, −1.238)	**0.005**		
Tiredness or daytime somnolence due to RLS	−0.424 (−11.157, −4.285)	**0.001**		
Time during the day when the symptoms occurred	−0.188 (−12.014, 0.513)	0.071		
Symptoms expression in hands	0.213 (0.619, 26.685)	**0.040**		
HDRS	−0.727 (−2.544, −1.703)	**0.001**	−0.443 (−1.939, −0.628)	**0.001**
HARS	−0.707 (−2.577, −1.689)	**0.001**	−0.348 (−1.728, −0.363)	**0.003**
Treatment	0.126 (−3.585, 14.827)	0.228		

Bold values denote statistical significance

95 % CI 95 % confidence interval, *IRLSSG-RS* International RLS Study Group Rating Scale, *HDRS* Hamilton Depression Rating Scale, *HARS* Hamilton Anxiety Rating Scale

but further use of the disease-specific instruments for measuring specific problems in patients with RLS, as well as treatment effects, could be more useful.

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