



# The Impact of Restless Legs Syndrome on Quality of Life in Patients with Multiple Sclerosis

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## Abstract

**Objective:** This study aimed to examine the effect of restless legs syndrome (RLS) on quality of life in patients with multiple sclerosis (MS) using the MS Quality of Life Scale-54 (MSQOL-54).

**Materials and Methods:** A total of 80 patients (49 women and 31 men) were included in this study. The questionnaire was based on the International RLS Study Group diagnostic criteria for RLS. The Pittsburgh Sleep Quality Scale, Fatigue Severity Scale, and MSQOL-54 were used.

**Results:** RLS was significantly higher in patients with MS than in the healthy control group ( $p=0.001$ ). The MSQOL-54 scale mean values were significantly higher in patients with MS than in the healthy control group ( $p=0.000$ ). Poor sleep quality, and a statistically significant difference was observed between the two groups ( $p=0.007$ ). Patients with poor sleep quality had significantly lower mean MSQOL-54 values. A significant association was noted between poor sleep quality and RLS ( $p=0.023$ ). Moreover, chronic fatigue was significantly higher in the patient group ( $p=0.021$ ). In addition, chronic fatigue was significantly higher in patients with RLS ( $p=0.049$ ). In the patient group, no relationship was observed between mean values of the MSQOL-54 scale and the mean and RLS.

**Conclusion:** RLS was associated with poor sleep quality and chronic fatigue in patients with MS and may exert an indirect effect on quality of life; therefore, diagnosis and treatment are crucial.

**Keywords:** Fatigue, multiple sclerosis, quality of life, restless legs syndrome, sleep quality

## Introduction

Multiple sclerosis (MS), a chronic immune-related disease of the central nervous system (CNS), is characterized by inflammation, demyelination, and neurodegeneration and leads to considerable disability, especially in young adults (1). MS presents with various clinical symptoms, including nystagmus, dysarthria, intent tremors, optic neuritis, myelitis, and brain-cerebellum syndromes based on the location of demyelinated plaques in the CNS (2). Restless legs syndrome (RLS) is a common, chronic, multifactorial movement disorder characterized by an uncontrollable urge to move the legs and is often accompanied by uncomfortable or painful sensations, especially at night or during periods of rest (3).

RLS is particularly common in patients with MS, with studies showing a prevalence rate of 12.5–65.1%, which is significantly higher than that in the general population (4,5). RLS in patients

with MS is linked to several factors, including older age, longer disease duration, higher levels of disability, and the presence of spinal cord lesions, especially in the cervical region (6). In addition, patients with MS who have RLS often experience poorer sleep quality, increased daytime fatigue, and a higher risk of anxiety, depression, and neuropathic pain, which collectively affect the quality of life (7). Voxel-based lesion analysis identified associations between RLS and MS lesions in the subcortex of the left gyrus precentralis, which suggests that dysfunction in the efferent motor system due to cerebral lesions contributes to RLS in MS (8). Moreover, the role of iron metabolism and dopaminergic dysfunction is critical as low levels of alpha-synuclein, which is involved in dopamine receptor trafficking, have been observed in patients with MS who have RLS, potentially contributing to the pathogenesis of the syndrome. Furthermore, inflammatory demyelination, rather than axonal degeneration, appears to be the underlying

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mechanism, as evidenced by RLS symptoms coinciding with acute MS attacks (9).

This study aimed to determine the impact of RLS on quality of life in patients with MS using the MS Quality of Life Scale-54 (MSQOL-54).

## Materials and Methods

Patients aged 18-60 years who reported to the neurology outpatient clinic of Harran University Faculty of Medicine and were clinically and definitively diagnosed with MS according to the McDonald 2017 criteria and were in remission period were included in this study. A signed informed consent form was obtained from all patients. Ethics committee approval was obtained from Harran University Ethics Committee (decision no: 11, date: 09.09.2019).

Participants who had an MS attack within the last 3 months, who had received steroid treatment within the last 3 months, who had known systemic diseases such as connective tissue disease, and who were taking medications that may affect sleep cycles (such as benzodiazepines, modafinil, and melatonin) were excluded from the study. The control group comprised age- and sex-matched participants with no history of illness or drug use and normal physical and neurologic examinations. The study included 80 patients (49 women and 31 men). Neurologic examinations were performed for all patients, and disability status was determined for each patient using the Kurtzke Expanded Disability Status Scale. Participants' body mass index was calculated by dividing their body weight in kilograms by the square of their height in meters. The participants were interviewed using a preset standardized questionnaire to measure the prevalence of RLS. The questionnaire was based on the International RLS Study Group diagnostic criteria for RLS (10). The Pittsburgh Sleep Quality Scale was used to assess the sleep quality. According to this scale, a total score of  $\leq 5$  was considered as poor sleep quality and that of 6-21 as good sleep quality (11). The Fatigue Severity Scale that contained nine questions was used in patients with MS and the healthy control group. Each question was scored between 0 and 7, and the total score was averaged. A score of  $< 4$  was considered as no fatigue and that of  $> 4$  as severe fatigue syndrome (12). MSQOL-54, a multidimensional MS-specific health-related quality of life inventory that includes the generic Short Form-36 core items supplemented with 18 MS-targeted items, was applied to assess the quality of life. The scale comprises two sections, namely, physical and mental health, with higher scores indicating a better quality of life (13).

## Statistical Analysis

The Statistical Package for Social Sciences for Windows version 20.0 (SPSS, Chicago, IL, USA) was used for evaluation. For the comparison of measurement data between the two groups (patients with MS and the control group), Student's t-test was

used for normally distributed data, the Mann-Whitney U test for non-normally distributed data, and the chi-squared test for qualitative data. Data obtained via measurement were expressed as mean  $\pm$  standard deviation and those obtained via counting as number (%). The significance level was set as  $p < 0.05$ .

## Results

A total of 80 patients with MS and 55 healthy individuals were included in this study. The clinical and demographic characteristics of the patient and control groups are presented in Table 1. Of the patients with MS, 63 (78.80%) had relapsing-remitting MS and 17 (21.30%) had progressive MS.

RLS was significantly higher in patients with MS than in the healthy control group ( $p=0.001$ ). The MSQOL-54 scale mean values were significantly higher in patients with MS than in the healthy control group ( $p=0.000$ ). Totally, 56 (65.00%) patients in the patient group and 26 (17.6%) in the control group had poor sleep quality, and a statistically significant difference was observed between the two groups ( $p=0.007$ ). Patients with poor sleep quality had significantly lower mean MSQOL-54 values (mental  $p=0.006$ , physical  $p=0.014$ , total  $p=0.007$ ). RLS was present in 29 of the patients with poor sleep quality, which was significantly higher than that in the group with good sleep quality ( $p=0.023$ ). Chronic fatigue was significantly higher in the patient group than in the control group ( $p=0.021$ ). In addition, chronic fatigue was significantly higher in patients with RLS in the patient group ( $p=0.049$ ). In the patient group, no relationship was found between the mean values of the MSQOL-54 scale and the mean and RLS (Table 2).

## Discussion

RLS is more common in patients with MS than in the general population (4). Comparison of SF-36 scores of patients with RLS and the general population indicated that the disorder had a substantial impact on the patient's quality of life (14). In this study, the effect of the presence of RLS on the quality of life of patients diagnosed with MS was analyzed using MSQOL-54.

Consistent with the literature, in this study, it was observed that the rate of RLS was higher in patients with MS than in the control group. The presence of RLS in patients with MS was associated with several factors, including longer disease duration, higher levels of disability, and advanced age (15). However, there was no association between RLS and the clinical characteristics of the patients. Common terms that people with RLS used to describe their symptoms were "need to move", "crawling", "tingling", "restless", "cramping", "feeling like something is crawling inside", "pulling", "electric", "tension", "discomfort", "pain", and "itching" (16). The use of polysomnography might have increased the number of patients with RLS because some patients may describe their current clinic as MS-related pain.

**Table 1. Clinical and demographic characteristics of the patient and healthy control groups and comparison of MSQOL-54 scale mean values between groups**

	Patient n=80	Control n=55	p-value
<b>Gender (%)</b>			
Female	49 (61.20%)	36 (65.5%)	0.377
Male	31 (38.80%)	19 (34.5%)	
<b>Age (Mean ± SD)*</b>	36.71±10.66	36.49±9.37	0.899
<b>BMI (Mean ± SD)</b>	25.09±4.17	25.35±3.18	0.691
<b>RLS</b>	35 (43.80%)	9 (16.4%)	<b>0.001</b>
<b>MSQOL-physical</b>	58.51±19.52	69.86±17.25	<b>0.001</b>
<b>MSQOL-mental</b>	58.81±21.68	67.25±21.17	<b>0.026</b>
<b>MSQOL-total</b>	117.32±36.76	137.16±36.90	<b>0.004</b>
<b>Fatigue (%)</b>	43 (53.8%)	19 (34.5%)	<b>0.021</b>
<b>Poor sleep quality</b>	56 (65.00%)	26 (17.5%)	0.007

\*mean ± SD: Mean score ± Standard deviation, BMI: Body mass index, RLS: Restless legs syndrome, MSQOL: Multiple Sclerosis Quality of Life Scale

**Table 2. Quality of life of patients and control group**

	HBS positive (mean ± SD) n=35	HBS negative (mean ± SD) n=45	p-value
<b>MSQOL-physical</b>	53.9±14.9	59.0±23.01	0.282
<b>MSQOL-mental</b>	54.5±19.4	58.0±23.02	0.501
<b>MSQOL-total</b>	108.4±32.5	117.04±44.8	0.367

\*mean ± SD: Mean score ± Standard deviation, MSQOL: Multiple Sclerosis Quality of Life Scale

The quality of life was lower in patients with MS than in the control group, but it was not associated with RLS in this study. The severity of RLS symptoms was positively linked to poorer sleep quality, increased anxiety, and decreased cognition. Furthermore, poor sleep quality, a common problem in patients with MS, was independently associated with poor quality of life, and RLS exacerbated this problem by causing excessive daytime sleepiness and sleep disturbances (17,18). RLS in patients with MS was linked to increased sleep latency, decreased total sleep time, and a higher percentage of light sleep stages, which led to poorer sleep quality. This condition was also associated with increased fatigue and a higher risk of anxiety and depression, which further worsened the sleep quality and well-being (18,19). There was a relationship between poor sleep quality and the presence of RLS in patients with MS, but there was no association between poor sleep quality and decreased quality of life. Hence, it appears that RLS may indirectly reduce the quality of life by worsening the sleep quality and causing chronic fatigue.

### Study Limitation

The limitations of this study are the small number of patients, the lack of polysomnography, and the lack of evaluation according to the educational level and cognitive functioning of the patients.

### Conclusion

Overall, the coexistence of RLS and MS creates a compound burden that significantly impairs the quality of life of affected individuals, which emphasizes the need for comprehensive management strategies that consider both conditions simultaneously. The presence of RLS in patients with MS requires increased awareness and early diagnosis to improve their quality of life. Effective management of RLS can potentially alleviate the associated psychiatric comorbidities and sleep disturbances. Considering the impact of the disease on cognitive functions in patients with MS, studies should be conducted to ensure that such questionnaires are short, understandable, and comprehensive.

### Ethics

**Ethics Committee Approval:** Ethics committee approval was obtained from Harran University Ethics Committee (decision no: 11, date: 09.09.2019).

**Informed Consent:** A signed informed consent form was obtained from all patients.

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