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Research article

Factors Associated With Sleep Quality in Patients With Multiple Sclerosis

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Abstract: *Objective:* A limited number of studies with inconsistent results have assessed the factors associated with sleep quality in patients with multiple sclerosis (MS). This study aimed to evaluate sleep quality and to investigate the associations between sleep quality and demographic and health-related characteristics, anemia, fatigue and physical activity in Turkish patients with MS. *Methods:* A cross-sectional study was conducted in a sample of 102 patients with MS who were followed in a neurology outpatient clinic of a tertiary hospital in Turkey between March 2015 and November 2015. Data were collected by an information form, the Pittsburgh Sleep Quality Index, the Visual Analogue Scale for Fatigue and the short version of the International Physical Activity Questionnaire. Anemia was evaluated by measuring hemoglobin levels. Data analysis were performed using descriptive statistics, Mann-Whitney *U*-test, Kruskal-Wallis H test, Spearman's correlation coefficients and logistic regression analysis with backward stepwise elimination. *Results:* The mean global Pittsburgh Sleep Quality Index score was 5.98 ± 3.94, and 52.0% of the participants reported poor sleep quality. Twenty patients (19.6%) had anemia. Patients with higher fatigue were more likely to have poor sleep quality (adjusted Odds Ratio, 1.283; 95% confidence interval, 1.031–1.596, p = 0.026). *Conclusions:* Poor sleep quality was common in patients with MS and higher levels of fatigue predicted poorer sleep quality. A better understanding of risk factors related to sleep quality may facilitate effective interventions that improve health outcomes.

Keywords: anemia; fatigue; multiple sclerosis; physical activity; sleep quality

Abbreviations: Multiple sclerosis (MS); Pittsburgh Sleep Quality Index (PSQI); Visual Analogue Scale for Fatigue (VAS-F); Short version of the International Physical Activity Questionnaire (IPAQ-S)

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating, degenerative and disabling disease of the central nervous system that severely affects the quality of life of patients [1]. Sleep disorders are common in patients with MS. Studies have demonstrated that the prevalence of poor sleep quality ranges between 38.0% and 67.1% [2–6]. Investigators have suggested that sleep quality is an independent predictor of mental and physical status among this population [3–5].

However, a limited number of studies with inconsistent results have assessed the factors associated with sleep quality. Several studies have demonstrated that sleep quality in patients with MS is influenced by factors such as gender, the use of immunotherapy for the treatment of MS, psychological burden of disease [2], functional disability [4,7], comorbidity, pain due to MS [4], disease duration, anxiety, depression, motivation, mental fatigue [6], general fatigue [5,8,9], the presence of restless legs syndrome [3], physical activity [10] and health-related quality of life [7]. However, other studies have reported that gender, physical fatigue, general fatigue [6] and physical activity [11] have no effect on sleep quality of patients with MS.

On the other hand, the results of studies in different populations have indicated that the caregiver's presence, perceived health status [12] and anemia [13–15] influence sleep quality. To the best of our knowledge, the relationships between sleep quality and these variables have not been explored in patients with MS. Therefore, the purpose of this study was to evaluate sleep quality in patients with MS and to investigate the associations between sleep quality and demographic and health-related characteristics, anemia, fatigue and physical activity.

2. Materials and Methods

2.1. Study design, setting and sample

This cross-sectional study was conducted between March 2015 and November 2015. A convenience sample of patients with MS was recruited from a neurology outpatient clinic in a tertiary hospital in Turkey. Inclusion criteria were patients aged ≥ 18 years with a diagnosis of MS according to the McDonald's criteria for at least one month, those who were relaps-free for the past 30 days and able to communicate in Turkish. Exclusion criteria were severe comorbidity such as cancer, severe cardiopulmonary insufficiency or renal disease, cognitive impairment, major psychiatric disorder,

alcoholism, previously diagnosed sleep disorders such as obstructive sleep apnea syndrome, restless legs syndrome, and narcolepsy, pregnancy, lactation, working in the night shift, and clinically unstable condition. Of the 105 eligible patients, 102 (67.6% female) agreed to participate (response rate: 97.1%).

This study was reviewed and approved by the Hospital Ethical Committee. In addition, written informed consent was obtained from each participant before any data collection took place. Data were collected through face-to-face, structured interviews with the participants at the hospital and review of medical records.

2.2. Measures

2.2.1. Participant characteristics

A personal information form consisted of demographic (age, gender, marital status, employment status, education level, income level, living arrangement, smoking status, alcohol consumption, and the presence of a caregiver) and health-related characteristics (disease duration, comorbidity, perceived health status, functional disability, weight, height and hemoglobin value). Perceived health status was assessed on a 5-point Likert scale, ranging from 1 (very good) to 5 (very poor), and then self-rated health was categorized as poor (fair/poor/very poor) and good (good/very good). Functional disability was evaluated using the Kurtzke's Expanded Disability Status Scale score. The body mass index was calculated based on self-reported height and weight (kg/m²). Anemia was defined as hemoglobin values of < 12 g/dl in females and < 13 g/dl in males [16].

2.2.2. Sleep quality

The Turkish version of the Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality. It is composed of 24 items grouped into seven components: subjective sleep quality, sleep duration, sleep latency, sleep disturbances, habitual sleep efficiency, daytime dysfunction due to sleepiness, and the use of sleep medication. Each item is rated on a 4-point Likert scale (0 = not at all, 3 = three or more times a week), and a global PSQI score of ≥ 5 shows poor sleep quality. The scale had good internal consistency (Cronbach’s alpha = 0.80) [17]. Cronbach’s alpha coefficient of the PSQI was 0.82 in this study.

2.2.3. Fatigue

The Turkish version of the Visual Analogue Scale for Fatigue (VAS-F, 0–10 cm) was used to measure fatigue. The VAS-F is an 18-item instrument composed of two dimensions: fatigue and energy. Higher scores on the fatigue subscale and lower scores on the energy subscale reflect greater severity of fatigue. The authors reported acceptable internal consistency values for the VAS-F (Cronbach’s alpha: fatigue = 0.90; energy = 0.74; respectively) [18]. In this study, Cronbach’s alpha coefficients of the fatigue and energy subscales were 0.89, and 0.75, respectively.

2.2.4. Physical activity

The Turkish short version of the International Physical Activity Questionnaire (IPAQ-S) was used to assess physical activity. The metabolic equivalent of task (MET)-minutes/week was determined for each participant (duration x frequency x MET intensity). The physical activity level was categorized as follows: low < 600 MET-min/week, moderate = 600–3,000 MET-min/week, and high > 3,000 MET-min/week [19].

2.3. Data analysis

All statistical analyses were calculated with the SPSS (version 15.0; SPSS Inc., Chicago, IL, USA). Descriptive statistics for all data in this study were computed. Bivariate associations of demographic and health-related variables with sleep quality were evaluated. The Mann-Whitney *U*-test was used to compare the parameters of the two groups; while the Kruskal-Wallis H test was used to examine differences between the three groups. Spearman's correlation coefficients were calculated to investigate the associations between the study variables. Univariate and multivariate logistic regression analyses were conducted to identify factors associated with poor sleep quality. Firstly, significant variables after bivariate analysis were entered into univariate logistic regression analysis. Then, all variables with a p value < 0.20 in the univariate analysis were included in the multivariate logistic regression analysis with backward stepwise selection. The categorical variables in the multivariate regression model were cigarette smoking, comorbidity, self-rated health, and the level of physical activity, and the continuous variables were the VAS-F fatigue and energy subscale scores, as well as the total IPAQ-S score. Multicollinearity was eliminated by using the variance inflation factor and tolerance values for the variables in the model before multivariate analysis. The highest variance inflation factor was 2.57 and the lowest tolerance value was 0.39 in this study. The tests showed that there was no multicollinearity problem in the model (tolerance > 0.20, and variance inflation factor < 10) [20]. The Hosmer and Lemeshow test was used to evaluate the goodness-of-fit of the final model. A p value of < 0.05 was considered as statistically significant.

2.4. Sample size

The sample size was calculated according to the number of independent variables in the multiple model. The necessary sample size should be at least 10 times the number of independent variables [20]. A total of seven independent variables were included in the multivariate regression model; hence, the minimum sample size required for the study was 70. One hundred and two patients were enrolled in the study.

3. Results

3.1. Participant characteristics

Table 1. Descriptions of participant characteristics, the presence of anemia and the level of physical activity and comparison of the global PSQI scores by these variables (N = 102).

Variables	N (%)	PSQI M (SD)	χ^2 *or z*†	*p*
Gender				
Female	69 (67.6)	5.67 (4.01)	$z = -1.36$	0.175
Male	33 (32.4)	6.64 (3.76)		
Marital status				
Married	72 (70.6)	6.44 (4.07)	$z = -1.73$	0.084
Unmarried	30 (29.4)	4.89 (3.42)		
Education level				
Literate/primary school (5 y)	24 (23.5)	6.97 (3.73)	$z = -1.55$	0.120
Secondary school or greater (≥ 6 y)	78 (76.5)	5.68 (3.97)		
Employment status				
Working	41 (40.2)	5.63 (3.57)	$z = -0.46$	0.643
Not working	61 (59.8)	6.22 (4.18)		
Income level				
Adequate	41 (40.2)	5.66 (4.10)	$\chi^2 = 4.06$	0.131
Moderate	46 (45.1)	5.83 (4.11)		
Inadequate	15 (14.7)	7.33 (2.66)		
Living arrangement				
Living with family	93 (91.2)	6.08 (4.03)	$z = -0.42$	0.675
Living alone	9 (8.8)	4.99 (2.74)		
Smoking history				
Never smoked/former smoker	31 (30.4)	7.16 (3.93)	$z = -2.24$	0.025
Current smoker	71 (69.6)	5.47 (3.86)		
Caregiver				
Present	71 (69.6)	5.99 (4.22)	$z = -0.38$	0.705
Absent	31 (30.4)	5.97 (3.26)		
Comorbidity				
Yes	24 (23.5)	7.63 (4.03)	$z = -2.34$	0.019
No	78 (76.5)	5.48 (3.79)		
Self-rated health				
Good	50 (49.0)	4.97 (3.64)	$z = -2.54$	0.011
Poor	52 (51.0)	6.95 (4.00)		
Anemia				
Present	20 (19.6)	5.56 (4.12)	$z = -0.70$	0.486
Absent	82 (80.4)	6.23 (4.28)		
Level of physical activity				
Low	39 (38.2)	7.04 (3.75)	$z = -2.49$	0.013
Moderate/High	63 (61.7)	5.33 (3.94)		

Note. PSQI, Pittsburgh Sleep Quality Index.

† Group differences were measured by Mann-Whitney *U*-tests, except for income level (Kruskal-Wallis H test, χ^2).

Tables 1 and 2 show the demographic and health-related characteristics of the study sample. The mean age of the study group was 36.93 ± 10.50 years, and the median duration of disease was 60 years. Ninety patients (88.2%) had relapsing remitting MS and 23.5% had a comorbid condition (37.5% hypertension, 16.7% diabetes, and 45.8% other). As shown in Table 1, anemia was present in 19.6% of the participants. The level of physical activity was found as high in 2.9%, moderate in 58.8% and low in 38.2% of the patients with MS.

Table 2. Means, standard deviations, ranges, medians and comparison of the global PSQI scores by various parameters (N = 102).

				PSQI	
Variables	Mean (SD)	Range	Median	*r*†	*p*
Age (years)	36.93 (10.50)	19–75	37.00	0.11	0.286
Disease duration (months)	71.51 (59.23)	1–300	60.00	0.12	0.232
Body mass index (kg/m²)	24.13 (4.65)	16.14–43.37	23.31	0.12	0.234
Hemoglobin (g/dl)	13.45 (1.74)	9.70–17.50	13.40	0.13	0.268
EDSS	1.84 (2.03)	0–8	1.25	0.18	0.071
VAS-F fatigue	3.86 (2.42)	0–10	3.85	0.39	< 0.001
VAS-F energy	5.24 (2.75)	0–10	5.20	−0.32	0.001
IPAQ-S (MET-min/week)	962.42 (853.45)	0.00–4692.00	693.00	−0.32	0.001

Note. PSQI, Pittsburgh Sleep Quality Index; EDSS, Expanded Disability Status Scale; VAS-F, Visual Analogue Scale for Fatigue; IPAQ-S, Short version of the International Physical Activity Questionnaire.

† Spearman's correlation coefficient was used to calculate *p* values.

3.2. Sleep quality and comparison of its by participant characteristics, the presence of anemia and physical activity

As seen in Table 3, the mean global PSQI score was 5.98 ± 3.94, and 52.0% of the participants (n = 53) reported poor sleep quality (global PSQI≥ 5). The use of sleep medication had the lowest mean score (0.47 ± 1.07), while daily sleep latency had the highest mean score (1.20 ± 1.04) among the PSQI components.

The results of the Mann-Whitney U-test showed that the global PSQI scores were higher in patients who never smoked or who quit smoking (z = −2.24; p = 0.025), those who had a comorbidity (z = −2.34; p = 0.019), those who had poor self-rated health (z = −2.54; p = 0.011) and patients with low levels of physical activity (z = −2.49; p = 0.013) (Table 1). Spearman's correlation coefficients also demonstrated a significant positive correlation between the global PSQI score and the VAS-F fatigue subscale score (r = 0.39; p < 0.001), as well as negative correlations with the VAS-F energy subscale score (r = −0.32; p = 0.001) and the total IPAQ-S score (r = −0.32; p = 0.001) (Table 2).

Table 3. Mean scores, standard deviations, ranges and medians for the Pittsburgh Sleep Quality Index (N = 102).

Variables	Mean (SD)	Range	Median
Global score	5.98 (3.94)	0.00–17.11	5.28
Component			
Sleep latency	1.20 (1.04)	0.00–3.00	1.00
Subjective sleep quality	1.05 (0.87)	0.00–3.00	1.00
Sleep duration	0.91 (1.05)	0.00–3.00	1.00
Sleep disturbance	0.81 (0.57)	0.00–2.11	0.78
Habitual sleep efficiency	0.77 (1.07)	0.00–3.00	0.00
Daytime dysfunction	0.77 (0.94)	0.00–3.00	0.00
Use of sleep medication	0.47 (1.07)	0.00–3.00	0.00

3.3. Factors associated with sleep quality

The univariate analyses showed that poor sleep quality was associated with not smoking/former smoking, the presence of a comorbidity, poor self-rated health, low levels of physical activity, higher scores on the VAS-F fatigue subscale and lower scores on the VAS-F energy subscale and the total IPAQ-S. As seen in Table 4, the multivariate logistic regression analysis indicated that higher VAS-F fatigue subscale scores were associated with increased likelihood of poor sleep quality (adjusted Odds Ratio [OR], 1.283; 95% confidence interval [Cl], 1.031–1.596, $p = 0.026$). In addition, lower IPAQ-S scores were associated with poor sleep quality ($p = 0.027$), however, the OR value with a 95% Cl very close to 1 indicated the low distinctive power of this variable (OR, 0.999; 95% Cl, 0.999–1.000). The final multivariate regression model that included only fatigue explained 29.7% of the variation in poor sleep quality ($R^2 = 0.297$). The Hosmer and Lemeshow test demonstrated that the final model fitted the data well ($\chi^2 = 6.252$, degrees of freedom [df] = 8, $p = 0.619$).

Table 4. Effects of various variables on poor sleep quality of patients based on multivariate logistic regression analysis (N = 102).

Risk factors	Adjusted OR	95% Cl	*p*
VAS-F fatigue	1.283†	1.031–1.596	0.026
IPAQ-S	0.999†	0.999–1.000	0.027

Note. OR, Odds Ratio; CI, Confidence Interval. This table includes only the final model as determined by the multivariate analysis with backward elimination.

† Adjusted for cigarette smoking, comorbidity, self-rated health, the level of physical activity, the VAS-F fatigue and energy subscale scores, and the total IPAQ-S score.

4. Discussion

This paper highlights the importance of identification of the factors associated with sleep quality to provide appropriate interventions in patients with MS. Poor sleep quality was common (52.0%) in patients with MS as reported in other studies [2–6]. Therefore, health care providers should take into account the evaluation of sleep quality when implementing care for patients with MS.

Higher levels of fatigue in patients with MS predicted poorer sleep quality. This result shows that fatigue is an independent and modifiable risk factor for poor sleep quality in patients with MS, and it is consistent with previous studies [8,9]. In this context, the removal of fatigue is especially recommended to improve sleep quality. Sleep quality is often associated with fatigue, and the link seems to be bidirectional. Poor sleep quality leads to fatigue in this population, which in turn contributes to poor sleep quality [2,5,9,10]. On the other hand, many factors, such as elevated levels of inflammatory cytokines, lesions in the brain, and immunomodulating therapies used for MS adversely affect both sleep quality and fatigue [8]. Further research is required to determine the causes of this association.

In the multivariate model, poor sleep quality was not influenced by physical activity. Our finding is congruent with Pilutti et al.'s study [11], reporting that the lifestyle physical activity intervention had not any significant effect on sleep quality among patients with MS. However, Motl et al. [10] found that poor sleep quality was associated with lower levels of physical activity in patients with MS (assessed with the Godin Leisure-Time Exercise Questionnaire, and the IPAQ-S). They emphasized that sleep quality may "be more strongly associated with physical activity under conditions of severe, but not minimal, fatigue" [10, p. 410]. We did not find any other study which dealt with these two variables together in this patient group. Additional research is needed to elucidate the relationships between sleep quality and physical activity.

This study had several limitations due to its cross-sectional design, the relatively small number of patients, the possible effects of the excluded patients, and potential recall bias. The cross-sectional design does not allow the determination of cause-and-effect relationships between the study variables. In addition, potential confounding factors associated with sleep quality, including sleep disorders, psychological problems, diet, medications used, and the environment were not evaluated in the current study and may have influenced the results. Therefore, the results of this study cannot be generalized to all Turkish patients with MS. Longitudinal studies with larger samples are needed to confirm our findings and to explore causal mechanisms underlying the relationships between the variables.

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Conflict of Interest

The authors declare no conflicts of interest in this paper.

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