

## Research Paper

## Fatigue Severity and Sleep Disorders Among Patients With Multiple Sclerosis: A Cross-sectional Study From Iran

Mohammad-Hasan Imani-Nasab<sup>1</sup>, Nasrin Galehdar<sup>1\*</sup>, Fatemeh Almasi Moghadam<sup>2</sup>

1. Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran.
2. Student Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran.



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## ABSTRACT

**Background and Purpose:** Multiple sclerosis (MS) is the most prevalent autoimmune chronic disease globally. The current study was conducted to determine the relationship between fatigue severity and circadian rhythm sleep disorders among Iranian MS patients.

**Materials and Methods:** The statistical population of this cross-sectional study included MS patients who were members of the MS Association in Khorramabad City, southwestern Iran. The sample size included 64 MS patients who met the inclusion criteria for the study and were selected through a simple random method. The study data were collected using a demographic questionnaire, fatigue severity scale (FSS), and Pittsburgh sleep quality index (PSQI). The obtained data were analyzed using SPSS software, version 18 through the independent t-test and Pearson correlation test. The significance level was considered to be <0.05.

**Results:** Fatigue severity of 53% and 47% of studied patients were severe and weak, respectively. The mean scores of men's fatigue severity and sleep disorders were significantly more than women's ( $P=0.01$ ,  $P=0.03$ , respectively). The Pearson correlation coefficient between circadian rhythm sleep disorders and fatigue severity scores was 0.33, which was significant ( $P=0.008$ ).

**Conclusion:** Sleep disorders and fatigue severity in the studied patients can be outcomes of MS or whether there is a cause-and-effect relationship between them. So, the sleep disorder aggravates the fatigue severity. If this relationship is confirmed in a randomized clinical trial, it can help reduce the fatigue severity in MS patients by treating sleep disorders.

**Keywords:** Multiple sclerosis, Fatigue, Sleep disorders, Iran

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### \* Corresponding Author:

**Nasrin Galehdar, PhD.**

**Address:** Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran.

**Tel:** +98 (916) 3611417

**E-mail:** [galehdar.n@lums.ac.ir](mailto:galehdar.n@lums.ac.ir)

## 1. Introduction

**M**ultiple sclerosis (MS) is one of the central nervous system's prevalent inflammatory and chronic autoimmune diseases [1], mainly in mature young women. The initiating speed and symptoms' appearance depend on the involvement location and the size of the lesions [2]. The possibility of having MS exists in all individuals and all ages [3]. MS has involved more than 2.5 million individuals in the world. MS is more prevalent in white people [4]. The prevalence of MS in women is three times that of men [5]. The prevalence of this disease in Iran is 50 in every 100000 individuals [6]. After trauma, this disease is one of the principal reasons for disabilities in youth and middle age groups. MS symptoms are varied and mainly develop silently and slowly [7]. The prevalent symptoms include fatigue, sleep disorders, walking disorders, urinary system disorders, bladder dysfunction, pain, sensing problems, diplopia, cognition disorders, and tremor [8].

Fatigue and sleep disorders are the most disabling and prevalent symptoms of MS disease [9]. Fatigue is the lack of adequate physical and mental energy that disrupts the activities of daily living [10, 11]. This symptom causes devastating effects on daily performance, physical activities, occupational and social roles, and the reduction of quality of life among MS patients [12]. If left untreated, fatigue can worsen, or other disease symptoms may intensify [13-15]. Environmental and central fatigue was experienced in 75% to 95 % of MS patients. Almost half of the patients feel that when they get tired, other symptoms are intensified [8, 16].

Sleep disorders or insomnia have been considered an epidemic issue [17]. Many studies have reported fatigue and sleep disorders as the prevalent outcomes of MS disease. Such adverse effects can affect patients' health and limit their daily activities [18-20]. More than 50% of MS patients have sleep disorders and low sleep quality [21]. Some studies have reported a significant positive relationship between sleep disorders and fatigue severity in MS patients, but the degree of correlation between them has varied from weak to strong [22-24]. Sleep disorder causes patients to feel exhausted; thus, it negatively affects their concentration and excessive irritability [25]. Considering the increasing prevalence of MS and the relationship between its negative outcomes, the current study was conducted to determine the relationship between fatigue severity and circadian rhythm sleep disorders among Iranian MS patients.

## 2. Materials and Methods

The statistical population of this cross-sectional study included all patients who were members of the MS Association in Khorramabad City, Iran (395), in 2019. MS was confirmed by a neurologist using an expanded disability status scale (EDSS). Considering  $\alpha=0.05$ ,  $d=0.2$ , and  $s=1$ , the sample size was 97 [24] (Equation 1).

$$1. n = \left( \frac{z_{1-\alpha/2} \cdot s}{d} \right)^2 \approx 97$$

Estimated samples were selected using systematic random sampling from the list of registered patients among the MS Association in Khorramabad. The inclusion criteria were as follows: lacking sleep apnea, asthma, restless legs syndrome, metabolic and rheumatoid diseases, cardiopulmonary diseases in classes 3 and 4, severe anxiety and depression, and not being addicted to drugs. The exclusion criteria were as follows: lacking the tendency to continue the cooperation and not completing the questionnaire. The study data were collected using a questionnaire, including demographic data, fatigue severity scale (FSS), and Pittsburgh sleep quality index (PSQI). The time and place of filling out the questionnaires were determined according to the patient's views.

The fatigue severity was revealed using 9 questions. A score of 1 for each question meant "completely disagree". and 5 meant "completely agree". The cut-off point for fatigue severity is 32; a score of less than 32 is considered mild chronic fatigue and more severe. The validity and reliability of the Persian version of this scale have been tested and confirmed [26].

The sleep quality was measured using the PSQI in 7 subscales of mental quality sleep, having a delay in sleeping, sleep duration, sleep restitution, sleep disorders, using soporific medicines, and daily activity disorders. The validity and reliability of the Persian version of this questionnaire have been confirmed [27]. Every question received a score of 0 to 3; 0 means not having any problems in the previous month, and a score of 3 means having a problem in the last week at least 3 times. The sum of the scores of 7 subscales shows the total score of patients' sleep quality.

The obtained data were analyzed using SPSS software, version 18. We used descriptive and analytical statistical tests such as Mean $\pm$ SD, independent sample t-test, and Pearson correlation. The significance level was considered to be equal to or less than 0.05.

### 3. Results

The response rate was about 66%. The studied patients included 18 men (28.1%) and 46 women (71.9%). The Mean±SD age of men was 37.6.93, and 35.028.76 years for women. The Mean±SD duration of the disease was 5.8±4.5 years. The patients' EDSS score was 1.96±1.08. The Mean±SD fatigue severity score in men (35.88±6.95) was significantly more than in women (29.45±9.25) ( $P=0.01$ ). There were no significant differences between the mean fatigue severity scores of patients who have used soporific medicine and those who have not.

The Pearson correlation coefficient between age and fatigue severity was not statistically significant ( $P=0.35$ ). Data analysis shows that 34 patients (53%) had severe, and 30 (47%) had mild chronic fatigue. The fatigue status severity in terms of gender and use of sleep medication has been provided in [Table 1](#).

Patients' sleep disorders in terms of their gender are presented in [Table 2](#).

The mean sleep disorder scores of patients in terms of gender and use of sleep medication are provided in [Table 3](#).

The results indicated that the Mean±SD sleep disorders score in men (7.83±3.75) was significantly more than in women (5.21±2.69) ( $P=0.03$ ). Moreover, the mean sleep disorders score of patients using soporific medicine (8.09±3.59) was significantly more than patients not using it (5.5±2.98) ( $P=0.014$ ).

The Pearson correlation coefficient between age and the mean score of sleep disorders among patients using soporific medicine was 0.11, which was not statistically significant ( $P=0.4$ ).

Given the categorization of the total score of sleep disorders from weak (more than 5) and good (less than or equal to 5), the gender and use of sleep-inducing medicine have been presented in [Table 4](#).

The Pearson correlation coefficient between the mean score of sleep disorders and fatigue severity (0.33) was statistically significant ( $P=0.008$ ); as the severity of fatigue increased, the score of sleep disorders increased and vice versa. The amount of this correlation was  $r=0.11$ ,  $P=0.67$  in men and  $r=0.35$ ,  $P=0.018$  in women, showing that this medium positive correlation was significant in women but insignificant in men.

### 4. Discussion

This study aimed to determine the relationship between fatigue severity and sleep disorders in patients with MS. The studied patients had sleep disorders. Some studies have reported sleep disorders as the most critical complications [22, 28-30]. In a descriptive study in Iran, Razazian et al. (2014) reported the existence of sleep disorders in MS patients to be 3 times more than healthy individuals [31]. Vitkova et al. also said sleep disorders exist in all MS patients [12].

According to the results, sleep disorders in the studied men were significantly more than in women. In Pokryszko-Dragan et al.'s (2013-Poland) study, no relationships were reported among the gender with sleep disorders [32].

There was no significant correlation between age and sleep disorders. In Pokryszko-Dragan et al.'s (2013-Poland) study, no relationships were reported among the age with sleep disorders [32]. However, in Motaharizhad et al.'s (2016-Iran) study, sleep disorders of the studied patients increased with age [24].

**Table 1.** Fatigue severity of studied patients in terms of gender and taking sleep medication

Variables		No. (%)	
		Chronic Fatigue Severity	
		Mild	Severe
Gender	Female	25(39.1)	21(32.8)
	Male	5(7.8)	13(20.3)
Taking sleep medication	Take	3(4.7)	8(12.5)
	Not take	27(42.2)	26(40.6)

**Table 2.** Status of sleep disorders of patients in terms of gender

Subscales of Sleep Quality	Status	No. (%)		
		Female	Male	Total
Subjective sleep quality	Does not have	7(10.9)	4(6.3)	11(17.2)
	Medium	35(54.7)	8(12.5)	43(67.2)
	Seriously	3(4.6)	4(6.3)	7(10.9)
	Very serious	1(1.6)	2(3.1)	3(4.7)
Sleep latency	Does not have	11(17.5)	1(1.6)	12(19.1)
	Medium	13(20.6)	3(4.8)	16(25.4)
	Seriously	15(23.8)	10(15.9)	25(39.7)
	Very serious	6(9.5)	4(6.3)	10(15.9)
Sleep duration	Does not have	24(37.5)	3(4.7)	27(42.2)
	Medium	10(15.6)	10(15.6)	20(31.2)
	Seriously	9(14.1)	1(1.6)	10(15.7)
	Very serious	3(4.6)	4(6.3)	7(10.9)
Habitual sleep efficiency	Does not have	42(66.7)	14(22.2)	56(88.9)
	Medium	3(4.8)	2(3.2)	5(8.0)
	Seriously	0(0)	1(1.6)	1(1.6)
	Very serious	0(0)	1(1.6)	1(1.6)
Sleep disturbances	Does not have	9(14.1)	2(3.1)	11(17.2)
	Medium	31(48.4)	10(15.6)	41(64)
	Seriously	6(9.4)	5(7.8)	11(17.2)
	Very serious	0(0)	1(1.6)	1(1.6)
The use of sleep medication	Does not have	37(58.8)	13(20.3)	50(78.1)
	Medium	3(4.7)	1(1.6)	4(6.3)
	Seriously	2(3.1)	3(4.7)	5(7.8)
	Very serious	4(6.3)	1(1.6)	5(7.8)
Daytime dysfunction over the last month	Does not have	22(34.4)	8(12.5)	30(46.9)
	Medium	15(23.4)	2(3.1)	17(26.5)
	Seriously	9(14.1)	6(9.4)	15(23.5)
	Very serious	0(0)	2(3.1)	2(3.1)

**Table 3.** The mean scores of sleep disorders in terms of gender and use of soporific medicine

Variables		Mean±SD	P*
Gender	Female	5.21±2.69	0.003
	Male	7.83±3.75	
Soporific Medicine	Take	8.09±3.59	0.014
	Don't take	5.50±2.98	

\*The independent sample t-test

**Table 4.** Quality of sleep among studied patients in terms of gender and soporific medicine

Variables		Sleep Quality, No. (%)		
		Weak	Good	Total
Gender	Female	20(31.3)	26(40.6)	46(71.9)
	Male	13(20.3)	5(7.8)	18(28.1)
Taking soporific medicine	Take	9(14.1)	2(3.1)	11(17.2)
	Don't take	13(37.5)	29(45.3)	53(82.8)

The current study showed a weak positive correlation between patients' sleep quality and fatigue severity, significant in women. In Strober's study (2015), sleep disorders predicted a 70% variance in fatigue severity [33]. A significant relationship was reported between sleep disorders and fatigue severity in MS patients [9, 22, 23]. In Motaharinezhad et al.'s (2016) study, a moderate and significant relationship was obtained between sleep disorders and fatigue severity [24]. Furthermore, Veauthier et al.'s (2011) study showed a significant relationship between sleep disorders and fatigue severity [34]. Braley et al. (2014) also proved in their research that sleep disorders intensified fatigue severity among MS patients [35]. Veauthier et al. (2014) considered a significant relationship between sleep disorders and fatigue severity [17]. Other studies confirmed these findings, as well [29, 30]. Based on the results, patients who did not use soporific medicines had fewer sleep disorders than others. Also, other studies reported a significant relationship between sleep disorders and the use of soporific medication [36, 37]. Study Limitations

Difficult access to some patients and patients' early exhaustion were limitations of the study. So, the response rate in the present study was relatively low. Generalizing the results to the statistical population should be done with caution.

## 5. Conclusion

According to the current study results, MS is accompanied by various sleep disorders, such as circadian rhythm sleep disorder and fatigue. The correlation between the severity of fatigue and sleep disorders can provide new causal clues about these two complaints among MS patients. Maybe the role of demyelination lesions of the nervous system, such as the optic nerve and hypothalamus, in the pathogenesis of both disorders, including MS or sleep disorders. Since fatigue and sleep disorders can have a cyclical relationship and reduce one's health level, detecting these complaints in patients is necessary. It can help in programming and presenting services to minimize these two complaints. Although several studies have investigated the relationship between these two outcomes of MS, there is little evidence from Iran. Therefore, studying the relationship between these outcomes seems necessary to accurately estimate their correlation and design stronger studies. Also, the results of the present study are useful for developing knowledge and explaining the care needs of this group of patients.

## Ethical Considerations

### Compliance with ethical guidelines

Ethics Committee approval was obtained (Ethical Code: IR.LUMS.REC.1397.051).

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### Authors contributions

All authors equally contributed to preparing this article.

### Conflict of interest

The authors declared no conflict of interest.

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