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Original Research Article.

Insomnia and Disability Severity Among Multiple Sclerosis Patients in Saudi Arabia

Mohammed Saeed Alqahtani[1], Mohammed Saeed Alahmari[1], Shahad Sahem Alkhashrami[1], Leen Abdulmohsin Sarhan[1], Muhannad Ali Asiri[1], Noof Mofareh Alamri[1], Abdullmgeed Abdullah Asiri[1], Reem Ali Alqahtani[1], Adel Ali Alfaifi[1], Adel Ali Alhazzani[1,2]

[1]MBBS, College of Medicine, King Khalid University, Abha, Saudi Arabia.
[2]MBBS, MD, FRCPC, FAAN, Neurology section,
King Abdulaziz Medical City, National Guard Health Affairs, Riyadh, Saudi Arabia.

ABSTRACT

Background: Sleep disturbance is common among MS patients. Patients are in a vicious circle where both their physical and mental state may depend on and lead to these sleep disorders and many health problems like physic disability. In the current study, we aim to assess the Insomnia and disability severity among MS patients.

Methodology: This study was conducted among a sample of 598 MS patients resident in five regions in Saudi Arabia and aged between 15 and 60 years old. To assess participants' demographic characteristics, disease related factors, detected depression and medication adherence and their association with the insomnia and the disability severity, this survey was conducted among consenting participants by a self-administered questionnaire that involves four validated scores (ISI, PDDS, PHQ-9 and Morisky score). We used SPSS version 22 to analyze the data by applying Chi-square test and one way ANOVA tests.

Results: Respondents were female (64,2%), the mean age at the time of diagnosis was 26,1(±7,9) years old and the mean disease duration was of 6,7 (±6,2) years. Among respondents, 23,1% were suffering from moderate to severe insomnia, 11,4% were suffering from advanced disability and 50,5% from major depression, while, 59,9% had low adherence to MS treatment. Overall, demographic and the rest of studied variables were significantly associated with the level of insomnia and the level of disability.

Conclusion: Awareness programs should be conducted in order improve patients quality of life and to prevent physical and mental health problems known as frequent in MS population.

Key Words: Insomnia, Multiple Sclerosis, Disability, Saudi Arabia.

***Correspondence to:**

Mohammed Saeed Alqahtani, MBBS,
King Khalid Univeristy,
Abha, Saudi Arabia.

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INTRODUCTION

Multiple sclerosis is considered an active and degenerative autoimmune inflammatory disease that attacks the central nervous system (brain, spinal cord and optic nerves).[1-3] It begins in the young adult[4] (around 30 years, two women for a man) and often evolves in two periods.[5,6] In the first years, often in relapses interrupted by periods of remission: we speak about remitting forms. After a very variable time, or sometimes immediately when the disease occurs at a later age, the evolution becomes progressive. Multiple sclerosis targets myelin[7], a protective sheath of nerve fibers, causing phenomena of inflammation/deterioration and subsequent repair, resulting in lesions known as "plates", scattered within the central nervous system. Since myelin is essential to the propagation of nerve impulses, this explains the appearance of neurological signs when it is impaired. If it is only slightly deteriorated, the impulse is transmitted without too many interruptions. On the other hand, if the deterioration is significant and the myelin is replaced by scar tissue, the influx can be completely blocked, and the nerve fibers may themselves be altered.

Symptoms vary depending on the affected area[8], hence the unpredictable nature of the disease for a particular person, which can be manifested by the following symptoms: extreme fatigue, incoordination, weakness, tingling, sensitivity disorders, bladder disorders (incontinence), sexual problems, pain or cognitive and psycho-affective disorders (difficulty concentrating, memory, depression, less emotional control) that are not rare, especially after a long evolution. The disease also has financial and physical implications including sleep disorders.

Sleep disorders do not constitute an isolated fact, one study found that nearly half (40%) of people with multiple sclerosis were at risk of suffering from these disorders.[9]

The most common sleep disorders in multiple sclerosis patients are insomnia at the top of the troubles, nocturnal leg spasms, narcolepsy, paradoxical sleep disorder and sleep respiratory disorders.[10]

Sleep disorders are not a direct result of the disease; they are a consequence of the symptoms of multiple sclerosis[10], like pain, spasms and frequent nocturnal urination (nocturia). Depression is also a common cause of sleep disorders; it must therefore be sought and treated. In addition, in the treatment of multiple sclerosis, corticosteroids can disrupt sleep.

Insomnia can go as far as chronic insomnia[11], which is the most prevalent sleep disorder in multiple sclerosis (MS) with deleterious consequences on the quality of life of patients.

Depressive syndrome, is by far the most frequent psychopathological disorder in M patients, with a frequency up to 79% of a population of MS.[12,13] Depression sometimes could occur very early in multiple sclerosis and may concern about 50% of patients. The prevalence appears to be higher than in other equivalent diseases, potentially explained by immune perturbations or more likely by brain lesions.[12]

There is still no cure for multiple sclerosis[14], but a number of treatments are used or being tested with increasing effectiveness in reducing the frequency and severity of relapses, delay the transition to the progressive phase and the emergence of disabling symptoms. Reeducation and rehabilitation also have a central role in the treatment of symptoms, prevention of loss of autonomy and some complications, comfort of life.

METHODS

The survey comprised a sample of 598 MS patients resident in Saudi Arabia aged between 15 and 60 years old.

Measures

The study MS patients have responded to self-administered questionnaire including questions concerning socio-demographic data and data related to the disease (duration of the disease, number of admissions, age at time of diagnosis, first symptoms at onset of diagnosis, number of attacks in the last 2 years, family history of MS, consanguinity between parents, number of family members having MS…), the study included also four validated questionnaires to assess: insomnia severity (Insomnia Severity index)[15], severity of the disability (PDDS score)[16], depression (Patient Health Questionnaire: PHQ-9)[17] and medical adherence (MORISKY scale).[18] Statistical Analysis was performed using SPSS (version 22); we used Chi-square test and the One way ANOVA to study the relation between variables. P-values ≤ 0.05 were considered as statistically significant. In term of ethical considerations, before agreeing to participate in the study, patient's confidentiality and anonymity were ensured; also, participants were sufficiently informed about the study and its purpose and were given the right to refuse the involvement in the study.

RESULTS

Our study included 598 patient aged between 15 and 60 years old with a mean age of 32.4 (± 8.5) years old. The majority of subjects (64.2%) were female, and most than the half of them (51.8%) were married. Almost all participants (88%) were Saudi. The majority of subjects (63.2%) had a bachelor qualification and were workers (44.5%). Less than half of participants (43.5%) had a monthly income less than 3000 SR and more than quarter of participants were living in southern region (Table 1).

Overall, from table 2 the mean duration of the MS disease was 6,6 (±4,8) years old and the reported mean age at time of diagnosis was 26,1 (±7,9) years old. The surveyed patients reported suffering from about two attacks (±2) in the last two years and that they were using MS medications for a mean duration of 1.7 (±3.07) years. The majority of studied subjects (39.1%) had no admission in the last year; By far the majority of patients (90.3%) did not have family history of MS. Most patients (63.9%) reported no consanguinity relation between their parents

The great majority of participants (80.3%) had no one of their family diagnosed with MS. Almost three quarters of respondents (72.6%) have not been diagnosed with depression before and 82% were not using antidepressant drugs.

Insomnia Severity

Table 3 summarizes results of the ISI score calculation, in fact, the majority of participants (39,1%) were not detected as having significant insomnia, while 37,8% were likely to have subthreshold insomnia, while 23,1% were screened positive for moderate or severe insomnia.

Relation with Socio-Demographic Factors

Insomnia severity was not found significantly associated with age or nationality, but the gender was found significantly associated insomnia severity, in fact, women with MS likely to have moderate or severe insomnia were by far more frequent than men with MS (66% vs 34%) and (89,5% vs 10,5%), (p=0,004).

Marital status was found significantly associated with insomnia severity (p=0,022), where moderate insomnia was more frequent among single patients (52%), while, severe insomnia was more frequent among married patients (57.9%).

Educational level is strongly significantly associated with insomnia severity (p=0,000), where most participants screened positive for severe insomnia had bachelor degree (68.4%). Our results revealed that work was significantly associated with insomnia severity (p=0,006), where most patients likely to have moderate to severe depression were non workers (54%, and 52.6% respectively). Work place wad found significantly associated with insomnia severity (p=0,000), in fact, more than half of participants screened positive for severe insomnia (52,6%) were non worker followed by patients working in private sector (21.1%). Monthly income was found significantly associated with insomnia severity (p=0,000), in fact, most participants screened positive for moderate or severe insomnia were earning less than 3000 SR per month (66% and 47.4% respectively).Region of residence was not found significantly associated with insomnia severity (p=0,059).

Relation with Factors Related to the Disease

The number of admission during the last year was significantly associated with the insomnia severity (p=0,000). Most patients likely to have severe insomnia were not admitted (26.3%) or admitted for once in the last year (26.3%). No significant association was found between the insomnia severity and the fact of having family history of MS (p=0,128). Parents consanguinity was found significantly associated with insomnia severity (p=0,000), where 31% of patients with first degree had no clinically significant insomnia and 31% had moderate insomnia,

while almost half of patients with second degree consanguinity had no clinically significant insomnia. Table 4 shows, patients screened positive for moderate or severe depression had significantly longer duration of MS disease (respectively 8,2 and 7,1 years, p=0,019), also patients detected with severe insomnia had significantly the oldest age at time of diagnosis (27,158, p=0,003) and the highest number of attacks in the last two years (3 attacks, p=0,000), we also found that the more the duration of drug use is longer the more the insomnia is likely to be severe (p=0,000).

Table 1: Demographics of the studied patients

CHARACTERISTICS	PATIENTS (N=598)	
Mean age ± S. D. (years) [range]	**32,4± 8,5**	
	Frequency	**Percent (%)**
Gender		
Male	214	35,8
Female	384	64,2
Marital status		
Single	250	41,81
Married	310	51,84
Divorced	36	6,02
Widower	2	0,33
Nationality		
Saudi	520	87,96
Non Saudi	78	13,04
Educational level		
Illiterate	4	0,67
Primary	12	2,01
Intermediate	28	4,68
Secondary	140	23,41
Bachelor	378	63,21
Advanced studies	36	6,02
Work		
Does not work	238	39,8
Working	266	44,48
Student	94	15,72
Work place		
Education	128	21,41
Health sector	38	6,35
Government employee	70	11,71
Private sector	70	11,71
Free business	10	1,67
Retired	20	3,34
I do not work	262	43,81
Monthly income		
Less than 3000 SR	260	43,48
From 3001-6000	76	12,71
From 6001-10000	130	21,74
More than 10000	132	22,07
Region		
Southern	170	28,43
Middle	150	25,08
East	114	19,06
North	28	4,69
West	136	22,74

Table 2: Factors related to MS disease

	Descriptive Statistics				
	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
The duration of the disease (MS)	598	0,3	30	6,6	4,8
Age at time of diagnosis	598	0	56	26,1	7,92
Numbers of attacks in last 2 years	598	0	14	1,9	1,960
Duration of drug use	598	0	24	1,7	3,07
CHARACTERISTICS					**PATIENTS (N=598)**
Number of admissions during the last year [n (%)]					
0					234 (39,13)
1					162 (27,09)
2					90 (15,05)
3					42 (7,02)
4					16 (2,68)
5					16 (2,68)
More than 5					38 (6,35)

Do you have family history of MS [n (%)]	
Yes	58 (9,70)
No	540 (90,30)
Consanguinity between parents [n (%)]	
No	382 (63,88)
First degree	116 (19,40)
Second degree	100 (16,72)
How many member of your family have MS [n (%)]	
0	480 (80,27)
1	76 (12,71)
2	24 (4,02)
3	10 (1,67)
4	2 (0,33)
6	4 (0,67)
7	2 (0;33)
Did have been diagnosed by depression before?	
Yes	164 (27,42)
No	434 (72,58)
Did you use antidepressant drugs?	
Yes	108 (18,06)
No	490 (81,94)

Table 3: Insomnia severity categories

Insomnia Severity Index	Frequency	Percent (%)
No Clinically Significant Insomnia	234	39,1
Subthreshold Insomnia	226	37,8
Moderate Severity	100	16,7
Severe	38	6,4
Total	598	100,0

Table 4: Insomnia severity and clinical variables .

		N	Mean	Std. Deviation	p-value
The duration of the disease (MS)	**No Clinically Significant Insomnia**	234	6,883	7,9803	0,019
	Subthreshold Insomnia	226	5,894	4,4280	
	Moderate Severity	100	8,200	5,5922	
	Severe	38	7,105	3,9166	
	Total	598	6,744	6,2471	
Age at time of diagnosis	**No Clinically Significant Insomnia**	234	26,094	7,2289	0,003
	Subthreshold Insomnia	226	27,053	8,5248	
	Moderate Severity	100	23,580	7,6912	
	Severe	38	27,158	7,6848	
	Total	598	26,104	7,9204	
Numbers of attacks in last 2 years	**No Clinically Significant Insomnia**	234	1,598	1,7036	0,000
	Subthreshold Insomnia	226	2,062	2,0277	
	Moderate Severity	100	1,840	2,2235	
	Severe	38	2,947	1,9023	
	Total	598	1,900	1,9602	
Duration of drug use	**No Clinically Significant Insomnia**	234	1,397	2,6881	0,000
	Subthreshold Insomnia	226	1,544	2,4587	
	Moderate Severity	100	1,978	4,0264	
	Severe	38	3,768	4,5878	
	Total	598	1,701	3,0695	

Table 5: Disability severity categories

PDDS / EDSS score	Frequency	Percent (%)
Mild (0-2)	318	53,2
Moderate (3-5)	212	35,5
Severe (6-8)	68	11,4
Total	598	100,0

p-value=0,002

Disability Among MS Patients

Based on PDDS score in table 5, more than half of MS patients (36,8%) had mild disability, followed by moderate disability (35.5%) followed by severe disability (11.4%).

Relation of Insomnia with the PDDS Score

Table 6 shows the insomnia severity levels is found significantly associated with the disability levels (p=0,002). Patients screened positive for higher disability were likely to have mostly no clinically significant insomnia to subthreshold insomnia.

Depressoin and Treatment Adherence Morisky Scales

From table 7, Using the PHQ-9, about half of participants (49.5%) were revealed likely to have minimal depression symptoms, followed by almost quarter of patients (24.7%) with MS who showed possible mild major depression, followed by 15.1% of

patients who were likely to have moderate major depression and 10.7% of respondents who were likely to suffer from severe major depression. Refer to MMAS-8 score, more than half of participants (59.9%) were likely to have low treatment adherence, followed by 30.4% of respondents who were likely to show moderate medication adherence and by only 9.7% of respondents who were likely to highly adhere to their treatment.

Relation of Insomnia with the Depression and Treatment Adherence

The insomnia severity levels were significantly associated with the depression levels (p=0,000). Most patients screened positive for severe insomnia were likely to have severe major depression (42.1%).

The insomnia severity levels were significantly associated with treatment adherence (p=0,010). Almost the three quarters of patients screened positive for severe insomnia reported low adherence to medication (73.7%) followed by moderate adherence (15.8%) and high adherence (10.5%).

Depression and medication adherence were found significantly associated (p=0,002). Patients likely to suffer from moderately severe or severe major depression were mostly low adherent to their treatment.

Table 6: PDDS score * Insomnia Severity Index Crosstabulation

			Insomnia Severity Index				Total
			No Clinically Significant Insomnia	Subthreshold Insomnia	Moderate Severity	Severe	
PDDS score	Mild	Count	146	118	38	16	318
		% within PDDS score	45,9%	37,1%	11,9%	5,0%	100,0%
		% within Insomnia Severity Index	62,4%	52,2%	38,0%	42,1%	53,2%
	Moderate	Count	70	78	46	18	212
		% within PDDS score	33,0%	36,8%	21,7%	8,5%	100,0%
		% within Insomnia Severity Index	29,9%	34,5%	46,0%	47,4%	35,5%
	Severe	Count	18	30	16	4	68
		% within PDDS score	26,5%	44,1%	23,5%	5,9%	100,0%
		% within Insomnia Severity Index	7,7%	13,3%	16,0%	10,5%	11,4%
Total		Count	234	226	100	38	598
		% within PDDS score	39,1%	37,8%	16,7%	6,4%	100,0%
		% within Insomnia Severity Index	100,0%	100,0%	100,0%	100,0%	100,0%

p-value=0,002

Table 7: Depressoin and treatment adherence Morisky scales

Severity depression score	Frequency	Percent
Minimal symtoms	296	49,5
Major depression, mild	148	24,7
Major depression, moderately severe	90	15,1
Major depression, severe	64	10,7
Total	598	100,0
MMAS-8	**Frequency**	**Percent**
Low	358	59,9
Medium	182	30,4
High	58	9,7
Total	598	100,0

DISCUSSION

Our study was conducted to explore the insomnia severity among the selected MS patients. We were also interested in assessing the disability and the depression occurrence in MS patients and the medication adherence among them.

In the literature, lack of sleep was reported as a common problem during multiple sclerosis[19,20] and more frequent than among healthy individuals.[20-22] The insomnia severity assessment using the ISI allowed us to identify about quarter of patients (23.1%) with moderate to severe insomnia. Also in order to evaluate the sleep disorders among a sample of 240 patients, Montserrat González-Platas et al.[21] used the Insomnia Severity Index, where they founded lower rate of patients screened positive for moderate or severe insomnia (12.6%) and about 10% suffering from sleepiness based on the ESS. Besides, counter to our results, Steven D. Brass et al.[22] reported higher prevalence of possible moderate to severe insomnia of about 32 % counted among a population of 11400 studied patients with MS, whereas patients in whom physicians actually diagnosed insomnia were estimated to be 10.6%. In previous study, the researchers were also interested in evaluating the overall sleep disorders among the MS surveyed patients, they noted that: about 60% were sleeping <7 hours/night which is less than recommended, that over half of subjects had sleep latency > 30 minutes which is more than recommended and that patients that mentioned daytime drowsiness were about 30%. In terms of insomnia, another study[23] revealed that a high rate of MS patients (40%) suffer from it.

Our findings revealed statistically significant association of the sleep disorder severity categories with socio-demographic factors such as gender, marital status, educational level, work, work place and the monthly income. In fact, we found far higher rate of severe insomnia among female patients compared with men; findings of the study also showed that severe insomnia was mostly common

among married patients, patients with bachelor degree, not working ones and those owing less than 3000 SR. However, no statistically significantly association was observed with age, nationality, and region of residency. Based on the Medical Outcomes Study Sleep (MOSS), AM Bamer et al.[24] reported that sleep troubles were more frequent among women with MS disease compared to men with MS.

Insomnia severity score categories were also found significantly associated with factors related to the MS disease like the duration of the disease, the age at time of the diagnosis, the number of attacks in the last two years and the duration of drug use. Patients with moderately severe and severe insomnia have been experiencing the MS disease since the mean age of 24 and 27 years old and for about eight and seven years respectively. Patients with moderately severe and severe insomnia have also been exposed to meanly two to three attacks in the last two years and were consuming MS medication for a mean duration of two to four years respectively.

In the current study, the depression severity score and the medication adherence were found statistically significantly associated with the severity of insomnia, where most patients detected with major severe depression were suffering from moderate insomnia and where most chronic illness patients likely to suffer from severe insomnia (42%) were likely to have severe major depression; in addition, moderate or severe insomnia were by far more frequent among patients with low medication adherence.

In general, Daniel J. Buysse, MD et al.[25] showed that insomnia that lasts more than two weeks predicts major depressive syndrome (MDS) among young adults and that MDS could predict the insomnia. Specifically among patients with MS, many authors[20,26] reported that sleep disorders are not isolated symptoms, they suggested that many factors could disturb the sleep quality including depression and that insomnia could also lead to depression.

In our study, we used the PDDS score to evaluate the disability severity among participants. We found that disability severity was statistically strongly related to the insomnia severity. Most patients identified as having severe insomnia were screened positive to have mild disability, while moderate insomnia is most likely to be observed among MS patients with probable gait disability. On the other hand, patients supposed to have higher PDDS score and using late cane, bilateral support, wheelchair scooter or even bedridden were at most likely to suffer from subthreshold insomnia. Refer to the EDSS score, Montserrat González-Platas et al.[21] predicated that severely disabled MS patients were likely to suffer from lower sleep quality compared with those experiencing mild disability.

Low respect of the treatment adherence was also found significantly associated with physical disability and with the severity of depression occurrence in our study. In concordance with our results Gina Remington et al.[27] underlined the importance of medication adherence in the decrease of reaching disability levels and the risk of serious relapse.[28] Findings of a previous study[29] showed thatthe lack of treatment adherence was revealed to be related with several psychological difficulties including anxiety, memory troubles and depression… among patients with MS who could suffer five times more than patients with psychiatric problems and who don't adhere to their DMTs.

CONCLUSION

Sleep disorders are common among patients with MS. In our study, using the ISI score, severe insomnia was detected among a minority of participants also the PDDs score allowed us to identify that the majority of patients were suffering from mild disability. Most demographic factors as well as the depression severity and the treatment adherence were significantly associated with insomnia and disability severity levels. To improve their physical, mental and overall quality of life, Ms patients should be supported, awarded, treated and well educated.

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