

# Frequency of obsessive-compulsive disorder in patients with multiple sclerosis: A cross-sectional study

Mohsen Foroughipour<sup>1</sup>, Fatemeh Behdani<sup>2</sup>, Paria Hebrani<sup>3</sup>, Majid Nabizadeh Marvast<sup>4</sup>, Fereshte Esmatinia<sup>5</sup>, Amir Akhavanrezayat<sup>6</sup>.

<sup>1</sup>Associate Professor, Department of Neurology, School of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran.

<sup>2</sup>Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Ibn-e-Sina Hospital, School of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran. <sup>3</sup>Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Ibn-e-Sina Hospital, School of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran. <sup>4</sup>Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Ibn-e-Sina Hospital, School of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran.

<sup>5</sup>Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Ibn-e-Sina Hospital, School of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran. <sup>6</sup>Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Ibn-e-Sina Hospital, School of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran.

**Background:** Obsessive compulsive disorder has been reported in patients with multiple sclerosis (MS). Obsessive compulsive disorder (OCD) is a kind of anxiety disorder characterized by a combination of repetitive thoughts and repetitive behaviors for reducing anxiety. We aimed to investigate the frequency of OCD in patients with MS. **Materials and Methods:** 112 patients with multiple sclerosis participated in this study. Demographic data were obtained through using patients' medical records. MS clinical subtypes, the duration of disease and neurological signs were determined. The Kurtzke Expanded Disability Status Scale (EDSS) was used to quantify disability in MS, which was confirmed by psychiatrist through using DSM-IV criteria for OCD. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to rate the severity of OCD. Data analysis was performed by SPSS for Windows software (version 15.0) and Chi-square test and Exact test were used for analyzing data. **Results:** The frequency of OCD in patients with MS was 16.1%. The OCD was significantly correlated with a higher EDSS score ( $X^2 = 86.515, P = 0.0001$ ). OCD was also significantly correlated with the duration of disease, phenotypic subgroup, cranial nerve involvement, cerebellar, autonomic, sensory and motor nerve involvement. **Conclusions:** OCD might be considered in quantifying disability of patients with MS. It might be suggested that all the patients with MS to be screened for OCD.

**Key words:** Obsessive compulsive disorder, multiple sclerosis, Frequency

## INTRODUCTION

Obsessive compulsive disorder (OCD) is an anxiety disorder characterized by a combination of obsession, i.e. repetitive thoughts or images caused by severe anxiety and compulsion that is repetitive behaviors for reducing anxiety. OCD prevalence is 1-3 % among adults and pediatric population.<sup>[1]</sup> In Iran, the prevalence of OCD is 8.87%, and it is more common among the persons residing in urban regions and the ones who have a positive OCD among their families.<sup>[2]</sup> Comorbidity of OCD with depression and anxiety disorders is very common.<sup>[3,4]</sup>

The exact etiology of OCD is unknown, but it is believed that serotonin neurotransmitter may play a role in pathogenesis of OCD.<sup>[5]</sup> Gene deletions have been reported in animal models with symptoms similar

to OCD. In patients with OCD, brain dysfunction has been also have a role in pathogenesis of OCD.<sup>[11]</sup>

Multiple sclerosis (MS) is an autoimmune disorder characterized by the destruction of myelin in central nervous system. The peak prevalence is between ages 20 and 40 and it is twice more common in women than in men. Sensory dysfunction of the limbs is the most common clinical symptom in these patients.<sup>[12]</sup> In some areas, prevalence of MS is rising.<sup>[13,14]</sup> MS has 4 phenotypes: relapsing-remitting, primary progressive, progressive relapsing and secondary progressive.<sup>[12]</sup> The exact etiology of MS is unknown, but it is believed that MS is the result of interaction between genes and the environment.<sup>[15]</sup> The two most important environmental factors are viral infections and ultraviolet B radiation exposure.<sup>[16,17]</sup> Furthermore, MS exacerbation is

**Address for correspondence:** : Mrs. Fatemeh Behdani, Psychiatry and Behavioral Sciences Research Center, Ibn-e-Sina Hospital, Faculty of Medicine, Associate professor of psychiatry, Mashhad University of Medical Sciences, Mashhad, Iran. E-mail: behdanif@mums.ac.ir

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associated with stressful life.<sup>[18]</sup> The best diagnostic test for MS is MRI, but it is not specific for MS.<sup>[19]</sup>

Comorbidity of MS and psychiatric disorders have been documented. Depression is the most common mental disorder in MS.<sup>[20]</sup> Other psychiatric disorders include: bipolar disorder, pseudo-bulbar affect, anxiety, personality changes, cognitive disorders, acoustic hallucinations, binge eating and impulse control disorders.<sup>[21-24]</sup>

OCD has been reported in patients with multiple sclerosis.<sup>[23,25-29]</sup> In some previous studies, the prevalence of OCD in multiple sclerosis was 8.6%. The etiology of OCD in multiple sclerosis is unknown, but some researchers believe that OCD is the result of disruption of the functional connection between cortical-cortical and/or cortical-subcortical brain regions.<sup>[29]</sup> It has been reported that the patients with brain-white matter abnormalities due to multiple sclerosis, cerebrovascular diseases, and paraneoplastic leucoencephalopathy may develop OCD symptoms.<sup>[28]</sup> Autoimmunity may play a role in pathogenesis of OCD in multiple sclerosis. Researchers have shown a link between OCD and autoimmunity.<sup>[30]</sup> Anti-brain antibodies have been reported in patients with OCD.<sup>[31]</sup>

For more clarification of the relationship between OCD and multiple sclerosis, we aimed to investigate the frequency of OCD in a group of patients with multiple sclerosis.

## MATERIALS AND METHODS

### Subjects

112 consecutive known cases of multiple sclerosis participated in this study whose disease was diagnosed during the year 2008 at outpatient MS clinic in GHAEM hospital (Mashhad, Iran). Patients with serious neurological or psychiatric diseases such as epilepsy, drug abuse, mental retardation, psychosis, depression, anxiety, etc...and patients who did not accept to join the study were excluded from the study. Our Institutional Ethics Committee also approved our research project. An informed consent was obtained from the patients participating in the study or from their parents. Demographic data including age, gender, educational level, and marriage status were collected through using patients' medical records. Definite diagnosis of MS was made by neurologist using Mc Donald criteria.<sup>[32]</sup> Clinical manifestations including MS clinical subtypes (relapsing-remitting, primary progressive, progressive relapsing and secondary progressive), the duration of disease, neurological signs such as, cortical dysfunction, cranial nerve involvement, cerebellar involvement, and sensory, motor or autonomic nerve involvement. The drugs used by the patients were determined.

### Scales

The Kurtzke Expanded Disability Status Scale (EDSS) was used to quantify the disability in multiple sclerosis.<sup>[33]</sup> Firstly, the patients screened for OCD symptoms by psychiatrist, she also ruled out depression and anxiety in these patients; and the OCD was confirmed through using DSM-IV criteria for OCD. The family history of OCD was determined by psychiatrist via asking the patient and by additional information supplied by others (parents). Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to rate the severity of OCD symptoms where a score between 8 and 15 was mild, between 16 and 23 was moderate, between 24 and 31 was severe, and between 32 and 40 was very severe.<sup>[34]</sup> For this purpose, a check list was prepared by psychiatrist and it was completed during an interview with the patient. An example of this check list was illustrated in Figure 1. Target symptoms were determined and the score was calculated for each patient. Then, the relationship between OCD and

### Statistical analysis

Data analysis was performed by SPSS for Windows software (version 15.0) and Chi-square test and the Exact test were used for data analysis. The  $P$  value  $\leq 0.05$  was considered statistically significant.

## RESULTS

A total of 112 patients participated in this study (25% male and 75% female and female/male ratio: 2.29). Mean age was 31.9 (range: 14-48 years). 25.9% of the patients had bachelor degree or higher, and 73.2% of all patients were married. Demographic data and clinico-pathological profiles were illustrated in Table 1.

OCD was confirmed in 18 patients out of 112 patients (16.1%). Only 9 patients had a positive family history for OCD. According to the exact test results, EDSS score was  $\geq 3$  in 10 patients out 18 patients with OCD. OCD was significantly correlated with a higher EDSS score ( $X^2 = 86.515$ ,  $P = 0.0001$ ). The predominant phenotype was relapsing-remitting (95.5%), and there was no case of progressive relapsing phenotype. Exact test analysis showed an association between OCD and phenotypic subgroups in patients with multiple sclerosis ( $X^2 = 8.970$ ,  $P = 0.029$ ). Duration of the disease was  $\geq 10$  years in 7 patients (6.3%) with multiple sclerosis. The OCD was significantly correlated with the duration of disease in patients with multiple sclerosis (According to Exact test:  $X^2 = 9.135$ ,  $P = 0.033$ ). There was also a significant correlation between OCD and cranial nerve involvement (according to Chi-square test:  $X^2 = 6.531$ ,  $P = 0.011$ ), cerebellar involvement (according to Chi-square test:  $X^2 = 19.390$ ,  $P = 0.0001$ ) and sensory nerve involvement (according to Chi-square test:  $X^2 = 11.593$ ,  $P = 0.001$ ). All of the patients with OCD had

**Table 1: Demographic data and clinico pathological profiles**

	number
Gender	
Male	28
Female	84
Age	
<30	53
>=30	59
Education	
Junior high school or less	35
High school diploma	48
Bachelor degree or above	29
Marriage status	
Single	30
Married	82
Family history of OCD	
Positive	9
Negative	103
OCD	
Positive	18
Negative	94
Duration of MS	
<1 year	11
1-5 years	72
5-10 years	22
>=10 years	7
Phenotype of MS	
Relapsing-remitting	107
Primary progressive	1
Secondary progressive	4
Progressive relapsing	0
The drug was used by the patient	
Synovex	82
Avonex	24
Betaferon	6
Cortical dysfunction	
Positive	83
Negative	29
Cranial nerve involvement	
Positive	39
Negative	73
Cerebellar involvement	
Positive	47
Negative	65
Sensory nerve involvement	
Positive	27
Negative	85
Motor nerve involvement	
Positive	51
Negative	61
Autonomic nerve involvement	
Positive	60
Negative	52
MRI findings	
Supra+infra tentorial plaques	93
Supra tentorial	19

OCD: Obsessive compulsive disorder; MS: Multiple sclerosis

**Table 2: The relationship between OCD and other variables**

	OCD		P value
	Positive	Negative	
Gender			
Male	4	24	0.766
Female	14	70	
Education			
Junior high school or less	8	27	0.415
High school diploma	6	42	
Bachelor degree or above	4	25	
Marriage status			
Single	3	27	0.290
Married	15	67	
Family history of OCD			
Positive	1	8	1
Negative	17	86	
Duration of MS			
<1 year	1	10	0.033
1-5 years	9	93	
5-10 years	8	14	
>=10 years	0	7	
Phenotype of MS			
Relapsing-remitting	15	92	0.029
Primary progressive	1	0	
Secondary progressive	2	2	
Progressive relapsing	0	0	
The drug was used by the patient			
Synovex	11	71	0.358
Avonex	6	18	
Betaferon	1	5	
Cortical dysfunction			
Positive	6	23	0.432
Negative	12	71	
Cranial nerve involvement			
Positive	11	28	0.011
Negative	7	66	
Cerebellar involvement			
Positive	16	31	0.0001
Negative	2	63	
Sensory nerve involvement			
Positive	10	17	0.001
Negative	8	77	
Motor nerve involvement			
Positive	18	33	0.0001
Negative	0	61	
Autonomic nerve involvement			
Positive	18	42	0.0001
Negative	0	52	
MRI findings			
Supra+infra tentorial plaques	17	76	0.159
Supra tentorial plaques only	1	18	

OCD: Obsessive compulsive disorder; MS: Multiple sclerosis; the results are expressed as number. Data were analyzed by Fisher exact and Chi-Square tests

also autonomic nerve involvement (according to Chi-square test:  $X^2 = 18.587$ ,  $P = 0.0001$ ) and motor nerve involvement (according to Chi-square test:  $X^2 = 25.652$ ,  $P = 0.0001$ ).

**Table 3: The relationship between OCD and EDSS scores**

Kurtzke Expanded Disability Status Scale (EDSS) core	Obsessive-Compulsive Disorder (OCD)		P value
	Positive	Negative	
0	1	35	0.0001 exact test
1	2	22	
1.5	2	8	
2	1	18	
2.5	2	1	
3	6	10	
4	3	0	
5	1	0	

OCD: Obsessive Compulsive Disorder; MS: Multiple sclerosis; the results are expressed as number

Only 9 patients had a positive family history for OCD, but according to Chi-square test results, there was no statistically significant correlation between OCD and family history. There was also no statistically significant correlation between OCD and demographic variables including age, gender, educational level, and marriage status.

Most commonly, the patients used the SYNOVEX for treatment of MS, but according to the Exact test results, the type of drug that was used by the patient had no statistically significant correlation with OCD. Cortical dysfunction was observed in 74.1% of the patients, but there was no association between OCD and cortical dysfunction. The relationship between OCD and other variables was illustrated in Table 2.

OCD was confirmed in 18 patients out of 112, and severe symptoms were found in 4.7% of these patients. According to EDSS scale, there was an association between the severity of MS and OCD in these patients ( $X^2 = 86.515, P = 0.0001$ ).

The relationship between OCD and EDSS scores was summarized in Table 3.

## DISCUSSION

This study was performed on 112 patients with multiple sclerosis. In this cross-sectional study, the prevalence of OCD in patients with multiple sclerosis was determined.

In our study, the prevalence of OCD in patients with multiple sclerosis is 16.1% that is higher than the prevalence of OCD in general population.<sup>[35]</sup> Assarian *et al.* measured the prevalence of OCD among 293 Iranian high school students. In their study, the prevalence of OCD was 8.87%.<sup>[2]</sup> The prevalence of OCD in Beiske *et al.* study was reported to be 19.3%, which is close to our findings.<sup>[36]</sup>

In Korostil *et al.* study that was performed on 140

consecutive cases of MS, the prevalence of obsessive compulsive disorder was 8.6%.<sup>[27]</sup> In Feinstein *et al.* study, the percentage of OCD in 150 patients with multiple sclerosis was 15.8%.<sup>[37]</sup> The differences in prevalence may partially be due to the cultural factors and the area that the patients live<sup>[2]</sup> or the drug beta interferon that has been reported to raise anxiety disorders prevalence in patients with MS.<sup>[35]</sup> In chronic usage, the drug beta interferon may cause mood alterations and anxiety attacks.<sup>[38]</sup> In our study, the patients did not differ in ethnicity. In contrast to Feinstein *et al.*'s findings,<sup>[37]</sup> in our study, there was an association between OCD and the duration of disease, phenotypic subgroups and with a higher EDSS score that describes patient's reaction to a debilitating disorder. In our study, the OCD was significantly correlated with cranial nerve involvement, cerebellar involvement, autonomic nerve involvement, and motor and sensory nerve involvement. These findings are compatible with the previous reports of brain dysfunction in patients with OCD. Kalatzis *et al.*, have shown that the OCD patients have abnormalities at the prefrontal and temporo-central brain regions.<sup>[7]</sup> In another study, pathological changes were found at different locations in patients with OCD.<sup>[8-10]</sup> But, it is not clear if OCD was induced by neurological dysfunction as a stressor or it was a separate disease. Furthermore, it is believed that cerebral lesions in periventricular white matter, *caudate nuclei* and deep subcortical white matter can simulate OCD symptoms.<sup>[39]</sup>

In our study, there was no statistically significant correlation between OCD and a positive family history of OCD, which is consistent with Aouizerate *et al.* study.<sup>[33]</sup> Assarian *et al.* have shown a positive family history of OCD among the first or second degree relatives.<sup>[2]</sup>

In our study, there was no statistically significant correlation between OCD and demographic variables including age, gender, educational level, and marriage status in patients with multiple sclerosis. In epidemiological studies, OCD was slightly more common in women, but the difference was not statistically significant and there was no statistically significant correlation between OCD and socio-demographic status of the patients.<sup>[40]</sup>

Collectively, our study aimed at investigating the prevalence of OCD in patients with multiple sclerosis.

The OCD was significantly correlated with the duration of disease, phenotypic subgroup, cranial nerve involvement, cerebellar involvement, autonomic nerve involvement, and sensory and motor nerve involvement as well as with a higher EDSS score. Our findings suggest that, in addition to functional disability and motor dysfunction, other factors including obsessive compulsive disorder should

be considered in quantifying disability of the patients with multiple sclerosis. But more investigations are mandatory because of limitations of our study including small sample size and other limitations of a cross-sectional study, in general, that this kind of study can not establish causality.

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