## Original article

# The Prevalence of Depression in Multiple Sclerosis Patients Who Referred to the Multiple Sclerosis Society of Yazd, Iran

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**Abstract**

**Background:** Multiple sclerosis (MS) is a central nervous disease that may cause disability. Depression is very common in MS which has a negative impact on quality of life and cognitive status. This study was designed to determine the prevalence of depression in MS patients, to assess the association of neuropsychological, demographic factors and clinical features of it.

**Methods:** This study was performed on 220 patients. A questionnaire was completed by patients and Beck Depression Inventory (BDI-II) test was used to evaluate the severity of depression.

**Results:** 81.3% of patients had depression based on the cutoff point of 13. A significant relationship was found between gender, treatment duration, motion disability, Cerebellar and pyramidal symptoms and severity of depression,also between history of depression and prevalence of it. The prevalence of depression was more in age group of 20-40. No significant association was found between the duration of disease and severity of depression and demonstrated an inverse relationship between depression severity and level of education.

**Conclusion:** We conclude, future studies should use a structured interview based on the DSM to assess patients' mood.

***Keywords:*** *Multiple sclerosis; prevalence; Depression; neuropsychological; interview*

## Introduction

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) such as brain and spinal cord that will cause permanent disability. (1-3) Studies declared a major increase in prevalence and incidence of MS in Iran (4-7). Iran is one of the most known areas for MS in Asia-Pacific region. (4-7) The myelin sheath acts as a protective covering that surrounds damaged nerve cells in MS. This damaged nerve cover can lead nerve signals to slow down or stop. The reason of nerve damage is inflammation that occurs along any area of the brain, spinal cord, and optic nerve. In fact, what causes this to happen is not exactly known. It seems that virus or gene defect, or both, could be the cause of injury. Moreover, environmental factors play a role in pathology of MS [8].People who have a family history of MS or live in the part where MS is more common, are slightly more prone to get MS [8). Multiple sclerosis (MS) affects women more than men and is often diagnosed between ages 20 and 40, though it can occur at any age. (8)

The existence of psychiatric symptoms in multiple sclerosis has been known since the time Charcot gave the first detailed clinicopathological description of "disseminated sclerosis" in his lectures at the Salpêtrière hospital in the nineteenth century. (9) Among the psychiatric symptoms noted by Charcot were pathological laughing, weeping, and mania, euphoria, hallucinations, and depression. In fact, Charcot's patient was described as experiencing a fit of *lypemania* (or severe depression), with hallucinations and paranoia. (10). The estimated prevalence of Depression (about 50%) is more common in MS than in other chronic diseases or neurological disorders. The etiology of depression in MS is likely multifactorial such as brain lesions, psychosocial losses, and/or immune dysregulation. Studies show that the relationship between depression and immune dysregulation in MS is unidirectional, with immune dysregulation causing depression (11). Therefore, depression is much more prevalent in people with MS than in the general population. Reports on the rate of suicide in MS vary greatly, but it seems that there is at least a slightly increased risk of suicide in the MS patients. Some indicators of depression in MS include: difficult sleeping, staying asleep, early morning waking, changing appetite, weight gain, weight loss, and loss of interest in things. Depression responds well to medical treatment, and counseling. In fact, depression is treatable so that treatment plays an important role in improving the quality of life for patients and their families(12). Other mood disorders are also more common in these patients. Anxiety occurs about 5.1% in general population, while it is almost 18.8% in MS population. Panic, Bi-polar, and Obsessive Compulsive disorders are also increased in MS and, Mood changesinpatients withMSis important andshouldreportthem tothe physician (12).

According to epidemiologic studies, among MS patients, 22%-54% have a lifetime risk of major depression. The relationship between depression and disability in MS has been investigated revealing a contentious relation between the two (13). Although there is a concern that interferon-β mayleadto depression, though itis declining(14). One of the questions about depression is existence of the lesions in specific areas of the central nervous system in the MS Patients. Response to this question has particular relevance for understanding and treating depression in patients with MS. It is also important to understand the complex relation that exists between biological and psychosocial factors in the genesis of depression(15). Therefore, a wide number of studies were performed that investigated the relationship between depression and CNS lesion. Imaging studies to date vary widely in both their design and rigour. However, according to the evidence, there is an association between depression in MS with greater neuropathology in the left anterior temporal/parietal regions, though, there is a need for further research on this question. Recent advances in our understanding of the neuropsychology, neuropathology and neuroimaging of depression, show that it may soon occur Moreover, it is not clear if depression is a result of the lesions in any particular brain regions in MS patients (15).

Depression may be independent of the disease, may be a reaction to the disease, or may be directly related to the lesions of the disease. Depression in MS seems to be the result of complex interaction between biological, demographic, functional, and psychological factors but the nature of this interaction and their influence on depression is still controversial.(16, 17) Neuropsychological functioning and other potential factors were shown to be associated with depressive symptoms of MS in a number of previous studies including disability, duration of illness, celibacy, stress, education, social support, age, income, fatigue, and cognitive status (18). However, depressive symptoms remain undiagnosed and are not treated in a quarter of MS patients (19).

Multiple Sclerosis patients also have depression (20**)** , because:

- Depression may be the result of a difficult situation or stress. Understanding how having MS, while it can to be a potential reason for progressing to permanent disability that it can lead to depression.
- Depression may be caused by MS which may damage the myelin sheath that surrounds nerves and transmit affecting mood signals.
- Depression may be caused by side effects of some drugs used to treat MS, such as steroids or interferon.

Depression is very common in multiple sclerosis patients. In fact, symptoms of depression severe enough to require medical intervention affect up to half of all people with MS at some point during their illness (20). Although the moderate to high prevalence of depression in MS is well established, little attention has been paid to the prevalence as well as neuropsychological determinants of depression in a community-based sample of Iranian MS patients. Moreover, the extent of their antidepressant use has also absorbed little attention. Considering the increasing prevalence of MS in Iran, importance of early detection and treatment of depression in this disease, this study was performed to determine the prevalence of depression among Iranian population as well as to assess the association of neuropsychological factors and other

demographic and clinical features of MS with depression (18).

**Method**

This cross-sectional study was performed on 220 patients with multiple sclerosis (MS) that referred to Multiple Sclerosis Society of Yazd (YMSS), Iran. The study protocol was approved by the Research Committee of the Shahid Sadoughi University of Medical Sciences and was conducted in accordance with the Declaration of Helsinki. All patients lived in Yazd, a province in center of Iran. Patients with a clinically confirmed diagnosis of MRI finding were arrived in this study. Inclusion criteria in this study were every patient with diagnosis of MS that referred to YMSS. Exclusion criteria were the patients with any other medical diseases, severe cognitive impairment and who did not consent to participate in this study.

Out of the total 360 patients, (from the membership listing of YMSS) 103 Patients did not consent to participate in this study, were excluded and 37 patients had severe cognitive disorder, thus, 220 patients were finally included in the study. After obtaining the informed consent, a questionnaire was completed by patients containing their demographic and clinical characteristics, including age, sex, educational status, and disease duration, and movement ability, disability in movement (Using a cane or wheelchair or Walker), interferon use duration and previous history of depression. The second edition of Beck Depression Inventory (BDI-II) created by Aaron T. Beck was validated and standardized in order to be applied in this study (18) which includes a 21 question multiple-choice self-report inventory, one of the most widely used tools for measuring the severity of depression. BDI consists of 21 items, each answered on a scale of 0 to 3 goals. Based on the cut-off point of 13, the results were divided into: minimal depression: 0-13, mild depression: 14-19, moderate depression: 20-28 and severe depression: 29-63. In addition, more severe depressive symptoms were indicated with higher scores. (21)

**Statistical Analysis**

After data collection, statistical analyses were performed using statistical package for the social sciences (spss), version 18.0. Continuous variables are presented as mean ± standard deviation or number (%). Independent samples t-test, chi square test and ANOVA with a 90 % power, were used. The significance level was considered as “p value ≤0.05” in this study.

**Results**

After obtaining the informed consent and meeting inclusion criteria, 220 out of 360 patients were enrolled in this study. Patients with severe cognitive impairment (37 patients) and patients, who did not consent to participate in this study (103 patients), were excluded from this study. Among 220 enrolled patients, 69 (31.4 %) were males and 151 (68.6 %) were females, with a female predilection (F: M=2.18). The average age of the study population was 33.68 ± 9.36. The patients were classified into three age groups: 19 patients (8.6%) were less than 20 years, 154 (70%) were between 20-40 years and 47 (21.4%) above 40 years. The mean duration of disease was 52.98 ± 42.74 months, and the mean duration of treatment with interferon was 38.09± 30.01 months. 24.1% of patients had a past history of depression. Based on the cut-off point of 13 on the Beck Depression Inventory, 81.3% of patients had different degrees of depression: 24.7% mild, 44.7% moderate and 11.9% severe depression. The mean score of the BDI-II was 31.19 ± 14.5 as well. In this study, a significant relationship was found between gender and severity of depression. (PV=0. 04), so that the prevalence of severe depression in men was 20.3%, whereas that of women was 8%. Based on chi-square test, the prevalence of depression more in age group of 20-40, more than any other age group (70%), the 75 patients of this group (48.4%) had severe depression. According to PV = 0.04, there was a significant relationship between age and depression. No significant association was found between the duration of disease and severity of depression, as the median of duration of MS in patients with severe depression and mild depression was 48 and 30 months respectively (PV=0. 16). Median of duration of treatment with interferon in patients with moderate depression and mild depression was 36 and 22 months respectively. The duration of treatment with interferon and severity of depression had a significant relationship (PV=0. 02). In this study, the prevalence of depression was 22.6% in patients with a past history of depression, whereas it was 8.4% in patients without history of depression (PV=. 001). This study demonstrated an inverse relationship between depression severity and level of education (PV=0. 08). This research also indicated that statistically through Sensory, sphincteral, brain stem, Cerebellar and pyramidal symptoms only Cerebellar and pyramidal symptoms had a significant correlation with increasing severity of depression, respectively, with PV =0. 03 and PV=0. 04. Moreover, prevalence of severe depression in MS patients with motion disability (movement with walker or wheelchair and so on) was 40% and in patients with the ability to move without help was 7.9% (PV=0. 01).

**Discussion**

The main objectiveof thisstudy was “the assessment of the prevalence of depression in

patients with multiple sclerosis referred to the MS Society of Yazd. Consistent with previous studies (16), our findings demonstrated a higher prevalence of depression symptoms in MS patients than in normal population. Moreover, the highest prevalence belonged to the moderate depression.

Clinically,depressionisa syndromewithsymptoms ofa mood disorderand a numberofcognitive, physical andpsychological disorders. In fact, it involves a vegetative state that canlead tosignificantimpairmentsinthe ability ofthe individual. Although thediagnosis ofdepression inthe sidetestwas a clinical diagnosis, ourstudy was based on BeckDepressionInventory to determine thedegree of depression [20].

In this study, the prevalence of significant depression in MS was 81.3 %, while this result in Mattioli et al.'s study was 25% in Italian MS patients (17), which was lower than what we reported. Our prevalence of depression in MS patients were much higher than the general population and also those reported in earlier studies (19, 22, 23). Moreover, consistent with previous studies, the moderate intensity was the most common form of depression (15, 16, 24). The prevalence of depression in the Iranian general population is reported from 4.1 % (33) to 43.55% (25). Modabernia et al. (2008) found that 23 % of people living in Rasht, the capital city of Guilan province, had a BDI-II score over 15 and 9.5 % suffered from depressive disorders based on semi-structured psychiatric interview (DSMIV-TR) (25).

It seems that high prevalence of depression in our study population than another study might be due to the use of various diagnostic or screening tools for the diagnosis of depression or the use of different cutoff points for screen tools. Other possible explanations for this could be related to study design or population sampling, as well as the lack of adequate studies, appropriate interventions, and on time standardized treatment.

The prevalence of MS in our study sample was two times more in females than in males. In addition, MS prevalence in the age group of 20-40 years was more, which was in line with previous studies (18). Given that the average start of the depression is about age 40 and 50% of the cases up to this age manifest the depression symptoms, (26) high prevalence of depression in this age group can be caused by these two factors.

In this study 75.9% of MS patients were reported not to have any history of depression, though severity of depression in MS patients with previous history of depression was more, while the McGuigan and his co-worker (29) reported that 35.8 % of MS patients with no previous history of depression or use of antidepressant drugs, manifested mild to severe symptoms of depression. A possible explanation is that patients who had the previous history of mood disorders prior to enrollment were not excluded. Therefore, further research is needed to examine the prevalence of depression in MS patients who were undiagnosed or not treated.According to the MS (as the stress), and side effects of drugs used in MS can cause a recurrence or worsening of depression, this result is not farfetched. By minimizing the potential causes, we will be able to better detect depressed patients at higher risks for remaining undiagnosed and consequently untreated.

After adjustment for potential confounding covariates of depression, education levels and duration of disease (MS), no significant correlation with depression was observed, but older age showed strong association with severity of depression in our MS patients (27, 28). As a matter of fact, unlike most previous studies (27, 28), older age was associated with severity of depression. This could be due to different cultural issues, poor coping strategies in patients with a lower academic status, educational level, and more severity of disability among older people. The relationship of depression with disease-related variables such as disease duration (22, 28, 29) is a matter of conflict in different studies. This might be explained by the fact that patients with similar disease duration may have different course of disease and various relapse rates. In addition, spinal cord and cerebral lesions have different effects on severity of physical disability and each of these will have different impacts on mood disorders (18). This study also indicated that statistically through Sensory, sphincteral, brain stem, Cerebellar and pyramidal symptoms only Cerebellar and pyramidal symptoms had a significant correlation with increasing severity of depression. It seems that these symptoms have a greater impact on the severity of depression in patients with MS, though according to the role of pyramidal and the cerebellar system in motor control and cognitive processes, these results are controversial.

The results of this study revealed a high correlation between the degree of disability and severity of depression. In these patients, in line with the similar studies, due to the decreased ability to perform daily activities and frustration, severity of depression was increased.Due to the high prevalence of depression in MS patients and the effect of depression on the treatment and prognosis of this disease, patients need to be aware of the warning signs of depression [20]. Physicians should also periodically review these symptoms in MS patients.

In the end, it should be mentioned that the treatment of depression as well as improvement of mental health are not less important than curing

MS and thus, preventing progression of symptoms and MS patients with depression warning signs should be psychiatric consultation and on early standardized intervention.

**Conclusion**

According to this fact that some MS symptoms overlap with cognitive and biological signs of depression, for diagnosis of depression, further studies in the assessment of mood with a structured interview based on DSM are recommended.

**Limitations**

It is clear that the patients referred to YMSS are not a representative sample of those with MS living in Iran, but it was a limitation of this study and we try to note this on the title of the study.

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