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# THE PREVALENCE OF DEPRESSION IN MULTIPLE SCLEROSIS PATIENTS AND ITS RELATIONSHIP WITH SOME DEMOGRAPHIC AND CLINICAL VARIABLES IN AHVAZ GOLESTAN HOSPITAL

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## ABSTRACT

**Introduction:** The prevalence of depression in MS patients is significantly higher than this amount in general population or patients with general medical conditions except MS. Due to the high prevalence of depression in MS patients, its importance in quality of life and improvement of patients, its association with suicide and the possibility of effect on the duration of illness, depression in these patients was strongly studied. This study was designed to determine the prevalence and effective factors in depression in MS patients. **Material and Method:** This study was cross-sectional and descriptive-analytic that was performed on 230 patients referred to the MS association of Ahvaz Golestan Hospital in 2017. The patients are analyzed by demographic questionnaire, Beck depression test and modified Fatigue Impact Scale (MFIS) questionnaire. Finally, all analyses were performed using SPSS software version 20. **Results:** The frequency of MS type indicated that 208 subjects (90.4%) had RRMS and other types of MS were reported in 22 patients (9.6%). The average time of the disease was 4.34 ± 4.01% and the mean fatigue was 22.25 ± 20.02%. 110 (47.8%) patients did not have depression, 51 subjects (22.2%) had mild to moderate depression, 40 subjects (17.4%) had moderate to severe depression and 29 (12.6%) had severe depression. In general, 120 (52.2%) patients had depression. **Conclusion:** In general, more than half of MS patients had depression that was not associated with gender but depression increases in MS patient with increasing age, marital status, low level of literacy, other types of MS except PRMS, increased duration of illness and increased fatigue.

**KEYWORDS:** Depression, Multiple Sclerosis, Beck depression test, Modified Fatigue Impact Scale.

## INTRODUCTION

Multiple Sclerosis (MS) is a chronic autoimmune disease of the central nervous system characterized by the emergence of dispersed demyelinated regions - most of the regions around the veins - with reactive gliosis, axonal and neuronal degeneration. These lesions are created in the white and gray matter of the brain and the spinal cord and in the optic nerve. The central multi-focal dysfunction is characterized by involvement of different parts of the central nervous system at different times and in the event of rejection of other causes.[1,2] Early symptoms generally start before the age of 55, the maximum incidence is between the ages of 40 and 20 and women are almost twice as likely to become infected. In addition, the highest onset age in women is about 5 years earlier than men. Furthermore, about half of the patients develop mild to moderate degrees of disability after 10 years of onset of symptoms.[3,4] The spread of the disease varies between 150-2 per 100,000 people depending on the country and population, which affects nearly one million people in the world. The onset cases during the childhood include 2-5% of all patients. During the last decade, the prevalence and incidence of MS in the population of Iran increased significantly and the ratio of female to male was reported to be about 1.8-3.6. According to a recent study, the prevalence of MS in Iran is twice as high as in neighboring countries and its prevalence is different in different geographical regions of Iran. The prevalence of major depression varies throughout the life of MS patients, ranging from 19- 54% depending on the sample population and diagnostic criteria used, with an estimated 16% annual prevalence and significant outbreak of significant clinical symptoms of depression with a frequency of 50%. Obviously, the prevalence of depression in MS patients is significantly higher than in the general population or in patients with general medical conditions other than MS.[5,6] It seems that several factors contribute to depression in MS

patients; including psychosocial factors (such as helplessness, uncertainty, loss of recreational activities, weak coping skills and stress), fatigue, cognitive impairment and complications Side effects are medications. The reported risk factors include sex, age below 35 years, the family history of major depression and high levels of stress. Moderating factors, especially interferon beta, are known to cause depression symptoms. However, the relationship between depression of these patients and all its variables is not well known.[7,8] In a number of previous studies, the relationship between neuropsychiatric activity and other potential factors including disability, duration of illness, abstraction, stress, education level, social support, age, income, fatigue and cognitive status with symptoms of depression in multiple sclerosis was shown.[9] Depression in MS patients has serious consequences because it is the most important factor in thinking and suicidal ideation. The obtained data showed that suicide is a significant cause of mortality in these patients determining the importance of this issue.[10] Due to the high prevalence of depression in MS patients, its importance in quality of life and improvement of patients, its association with suicide and the possibility of effect on the duration of illness, depression in these patients was strongly studied. Although depression develops after the onset of multiple sclerosis, the studies showed that it is highly treatable.[11] Based on the above-mentioned factors, due to the different rates of depression in MS patients in different articles, different results of the findings regarding the demographic and clinical factors involved in depression in these patients, the need for further study in this field and Also, due to the importance of depression, preventable and curable disease, and since depression reduces treatment in chronic patients and has a devastating economic and cultural impact in the community, this study was designed to determine the prevalence and effective factors in depression in MS patients.

## MATERIAL AND METHODS

This study was cross-sectional and descriptive-analytic that was performed on 230 patients referred to the MS association of Ahvaz Golestan Hospital in 2017. A total of 230 patients with multiple sclerosis were studied by convenience sampling in case of willingness and having the inclusion criteria. Exclusion criteria included patients with previous history of psychiatric disorders, substance abuse and alcohol abuse, antidepressant drugs, cognitive impairment, mental retardation and chronic diseases (diabetes, hypertension, thyroid disease and cerebrovascular accidents). The patients older than 18 years of age were examined.

Firstly, the patients were analyzed by demographic questionnaire, Beck depression test and modified Fatigue Impact Scale (MFIS) questionnaire. Beck Depression Inventory (BDI) was a tool for assessing depression. The subjects had to respond to 21 questions according to their feelings last week. Each answer had 0-3 points to determine the amount of depression in a person. The individuals with scores of 0 to 9 were not depressed, scores ranging from 10 to 18 represented mild to moderate depression, scores of 19 to 29 showed the subjects with moderate to severe depression, and the scores 30-63 belonged to people with severe depression. The Persian version of BDI was used in our study (Pearson correlation coefficient for Persian version of BDI-II and ATQ (self-concept questionnaire) was 0.77 indicating a strong correlation between two criteria for depression). The modified fatigue impact scale assessed the effects of fatigue on patient's quality of life. This questionnaire contained 21 questions. Each answer was scored from 0-4, the score of 0 was the absence of a problem, and the score of 4 showed a severe problem. Finally, the overall score was between 0-84, when higher scores represented a greater disruption to quality of life due to fatigue. The reliability of the questionnaires was evaluated using the Cronbach's alpha coefficient (acceptable and recommended alpha $\geq 0.7$) as 0.84 for the MFIS questionnaire and 0.87 for the Beck Depression Inventory.[12,13] At the end of data collection, the mean and standard deviations in quantitative variables and the frequency and percentages in qualitative variables were used to describe the data. For data analysis as one- variable, t-test and chi-square test were used and for data analysis as multivariate, logistic regression was used. All analyses were performed using SPSS software version 20.

## RESULTS

The results of this study showed that the mean age of patients was 34.31 ± 8.99 years. In addition, 54 (23.5%) patients were male and 176 (76.5%) patients were female. Among these subjects, 74 (32.2%) patients were single, 150 (65.2%) subjects were married, 5 (2. 2%) subjects were divorced and one (0.4%) subject was widow. The subjects were divided into non-married and married categories for a better analysis. Thus, 80 (34.8%) subjects were non-married and 150 subjects (65.2%) were married. Surveying the level of education of patients showed that 49 (21.3%) patients were under diploma, 79 (34.3%) subjects had diploma, 24 (10.4%) subjects had an associate degree, 70 (30.4%) subjects had bachelor degree and 8 (3.5%) subjects were above the bachelor's degree. In order to better analyze the data, the individuals were divided into three groups of under diploma, diploma, and higher diploma. Accordingly, 49 (21.3%) subjects were under diploma, 79 (34.3%) subjects were diploma and 102 (44.3%) subjects were higher diploma. Regarding the MS type, 208 (90.4%) patients had RRMS, 4 (1.7%) patients had SPMS and 2 (0.9%) patients had PRMS. To better analyze the data, the individuals were divided into two types of RRMS and other MS types, including PPMS, SPMS and PRMS, based on their type of disease. This means that 208 (90.4%) patients had RRMS and 22 9.6%) patients had the other MS types. The average duration of illness was 4.34 ± 4.01%. In addition, the average fatigue rate of patients was 22.25 ± 20.02%. It should be noted that 218

(94.8%) patients received interferon beta during treatment and 12 (5.2%) patients did not receive interferon beta.

110 (47.8%) patients did not have depression, 51 (22.2%) patients had mild to moderate depression, 40 (17.4%) patients had moderate to severe depression, and 29 (12.6%) patients had severe depression. In order to better analyze the data, the individuals were divided into two groups of patients without depression and patients with depression. According to this, 110 (47.8%) patients did not have depression and 120 (52.2%) patients had depression (Table 1).

**One- variable analysis**

The incidence of depression in women is 1.017 times that of men, which is not statistically significant (P = 0/957). For ten years increase in age, the possibility of developing depression in patients is 1.58 (P = 0/004). In addition, the risk of depression in married patients was 1.82 times higher than that of non-married patients (P=0/033). The chance of having depression in patients under diploma was 41.4 times higher than that of the patients with higher diploma. This difference was statistically significant (P<0/001). The chance of having depression in patients with a diploma was 1.45 times higher than that of higher diploma (P=0/152). In addition, the risk of depression in the patients under diploma was 2.86% higher than that of patients with diploma (P=0/009). The risk of depression in patients with other types of MS was 6.7% higher than the RRMS patients (P=0/003). The analysis of the results showed that the risk of developing depression in patients was equal to 1.32 (1.80 times for a 2-year increase during the disease). (P=0/047) per one year of increase (-value=0/047) per two years of increase. In addition, the risk of depression was doubled by 2.41 for 20 units of patient fatigue (P<0/001). The risk of developing depression in patients receiving interferon beta was 1.10 times (P=0/877) (Table 2).

**Multivariate analysis**

By controlling other variables, the risk of depression in female patients was 1.16 times that of male patients. This difference was not statistically significant (P=0/685). By controlling other variables for one year, the age of patients increased the risk of depression by 0.999. This difference was not statistically significant (per one year of increase P=0/979). By controlling other variables, the risk of having depression in married patients was 1.521 times that of single patients. This difference was not statistically significant (P=0/228). By controlling other variables, the risk of developing depression in patients under diploma was 3.09 times higher than those with diploma. This difference was statistically significant (P=0/012). By controlling other variables, the risk of developing depression in patients with diploma was 1.37 times higher than those with higher diploma. This difference was not statistically significant (P=0/343). By controlling other variables, the risk of depression in patients with other types of MS was 3.42% times higher in RRMS patients which were not statistically significant (P=0/089). By controlling other variables for one unit of increase during the disease, the risk of developing depression in patients was 1.26. This difference was not statistically significant (P=0/16). By controlling other variables for one unit of increase in the patient's fatigue, the risk of developing depression in patients was 1.039 times. This difference was statistically significant (P<0/001). By controlling other variables, the risk of depression in patients receiving interferon was 1.937 times that of patients who did not receive interferon beta. This difference was not statistically significant (P=0/37)(Table 3).

**Table 1. Patient's characterizations.**

| | | |
|---|---|---|
| **Age (M±SD)** | | 34/31 ± 8/99 |
| **duration of illness(M±SD)** | | 4/34 ± 4/01 |
| **fatigue rate(M±SD)** | | 22/25± 20/02 |
| **Gender (n/%)** | **Male** | (5/23%) 54 |
| | **Female** | 176 (76/5) |
| **Marital Status (n/%)** | **Single** | 80 (% 34/8) |
| | **Married** | 150 (% 65/2) |
| **Education Level (n/%)** | **<Diploma** | 49 (% 21/3) |
| | **Diploma** | 79 (% 34/3) |
| | **> Diploma** | 102 (% 44/3) |
| **Type of MS (n/%)** | **RRMS** | 208 (% 90/4) |
| | **Other than RRMS** | 22 (% 9/6) |
| **Interphone beta (n/%)** | **yes** | 218 (% 94/8) |
| | **No** | 12 (% 5/2) |
| **Depression (n/%)** | **yes** | 120 (% 52/2) |
| | **No** | 110 (% 47/8) |

**Table 2. Table 3. One- variable analysis. 1: per 10 years of increase, 2: per one unit of increase, 3: per 20 units of increase**

| Variable | | Depression | | Or | 95%CI | P-Value |
|---|---|---|---|---|---|---|
| | | Yes | No | | | |
| Age (M±SD) [1] | | 35/99±9/40 | 32/47±8/17 | 1/58 | 1/54,1/63 | 0/004 |
| duration of illness(M±SD)[2] | | 4/74±3/77 | 3/91±4/24 | 1/315 | 1/004,1/722 | 0/047 |
| fatigue rate(M±SD)[3] | | 22±29/33 | 14/09±14/54 | 2.41 | 2/37.2/45 | <0.001 |
| Gender (n/%) | Female | %52/3)92 | (%47/7)84 | 1/017 | 0/55,1/87 | 0/957 |
| | Male | (%51/9)28 | (%48/1)26 | | | |
| Marital Status (n/%) | Married | (%57/3)86 | (%42/7)64 | 1/82 | 1/05,3/15 | 0/033 |
| | Single | (%42/5)34 | (%57/5)46 | | | |
| Education Level (n/%) | <Diploma | (%75/5)37 | (%24/5)12 | 4/41 | 2/06,9/43 | <0/001 |
| | Diploma | (%51/9)41 | (%48/1)38 | 1/54 | 0/85,2/79 | 0/152 |
| | > Diploma | (%41/2)42 | (%58/8)60 | | | |
| Type of MS (n/%) | Other than RRMS | (%86/4)19 | (%13/6)3 | 6/71 | 1/93,23/36 | 0/003 |
| | RRMS | (%48/6)101 | (%51/4)107 | | | |
| Interphone beta (n/%) | yes | (%52/3)114 | 104(%47/7) | 1/10 | 0/34,3/51 | 0/877 |
| | No | (%50) 6 | (%50 ) 6 | | | |

**Table 3. Multivariate analysis. 1: per one year of increase, 2: per one unit of increase, 3: per one unit of increase**

| Variable | | OR | 95%CI | P-Value |
|---|---|---|---|---|
| Age (M±SD) [1] | | 0/999 | 0/959,1/042 | 0/979 |
| duration of illness(M±SD) [2] | | 1/26 | 0/913,1/738 | 0/16 |
| fatigue rate(M±SD)[3] | | 1/039 | 1/02,1/058 | <0/001 |
| Gender (n/%) | Male | | | |
| | Female | 1/16 | 0/57,2/34 | 0/685 |
| Marital Status (n/%) | Single | | | |
| | Married | 1/521 | 0/769,3/005 | 0/228 |
| Education Level (n/%) | <Diploma | 3/09 | 1/28,7/49 | 0/012 |
| | Diploma | 1/37 | 0/71,2/65 | 0/343 |
| | > Diploma | | | |
| Type of MS (n/%) | RRMS | | | |
| | Other than RRMS | 3/42 | 0/83,14/12 | 0/089 |
| Interphone beta (n/%) | yes | 1/937 | 0/456,8/233 | 0/37 |
| | No | | | |

## DISCUSSION AND CONCLUSION

In this study, the multiple sclerosis patients referred to the MS association of Ahvaz Golestan Hospital in 2017 were evaluated by convenience sampling method. The majority of patients, 208 (90.4%), 4 (1.7%) RRMS, 16 (7%) SPMS, and 2 (0.9%) PRMS were studied by cross sectional study of Khadijeh Mohammadi et al (6) entitled as the prevalence and risk factors for depression in women with MS, that 74.8% patients had RRMS and 25.2% had SPMS and PPMS. A cross-sectional study by Kinsinger et al.[14] examined the relationship between depression, fatigue, subjective cognitive impairment and obstructive psychoeducational function in MS patients in a randomized clinical trial in 127 patients in 2010. This study reported that 61.3% patients had RRMS and 38.7% had the other types of MS and was not consistent with the study of Khadijeh Mohammadi et al.[6] The average fatigue rate of patients was 22.25 ± 20.2%, with a mean fatigue score (mean MFIS score of 8.18 ± 5.29) and was consistent with the study by Mahsa Ghajarzadeh et al[12] entitled "Fatigue, depression and Sleep disturbances in Iranian patients with MS, which was performed in 100 patients in 2012 in Tehran. The prevalence of depression was not statistically significant. And by controlling other variables, this difference was not statistically significant as it was consistent with previous studies. In the study of Cauchy Jones[15] et al entitled A Great Study of Anxiety and Depression Evaluation in MS Patients: A Survey through the UK Registry Portal", 7786 patients were examined in 2011. The findings showed that male depression score were higher than that of women.

The chance of having depression in married patients was 1.829 times that of non-married patients, which was statistically significant (P = 0.033). However, it was not statistically significant by controlling other variables (OR = 1/521, P = 0.228) which was consistent with previous studies. in a cross-sectional study by K. L Taylor et al.[16], lifestyle, demographic factors and drugs associated with the risk of depression in an international sample of MS patients in 2459 patients in 2014 were reviewed and the results showed that those who were divorced or widowed had 1.7 tomes of chance for having depression compared to married ones. The chance of having depression in patients under diploma was 4.41 times higher than that of the patients with diploma. This

difference was statistically significant (P <0/001) by controlling other variables, this difference was statistically significant (OR = 3/09, P = 0/012). The risk of being depressed in patients with diploma was 1.44 times higher than those with higher diploma. This difference was not statistically significant (P = 152.1) and with other variables control, this difference was not statistically significant (OR = 1/37, P = 0/343). In addition, the risk of depression in patients under diploma was 2.86% higher than those with diploma. This difference was statistically significant (P = 0.009). The results of previous studies showed a significant relationship between education and depression in multiple sclerosis patients, so that patients with lower education have a higher chance of having depression. However, the results of the study by Feinstein et al.[17], Entitled "Disturbing imaging impairment in depressed MS patients" in 62 MS patients in 2009, showed no significant relationship between depression and education level. The risk of depression in patients with other types of MS was 6.71 times higher than those of RRMS patients. This difference was statistically significant (P = 0.003). The results of the study by K. L Taylor et al,[16]., showed a significant correlation between depression and type of illness in 2459 patients in 2014, so that the risk of depression in PRMS patients was about 2.5 times as much as RRMS patients. Similarly, K. H. Jones et al[15] found that for both genders, SPMS men and women were more depressed than other types of MS. In a cross-sectional study by Fariba Askari et al[18] entitled "Anxiety in MS: its relation to disability, depression, type of disease and sex", 180 patients were examined in 2012 in Tehran. The results showed that patients with SPMS type had significantly higher BDI and BAI scores.

For one year of increase during the disease, the risk of developing depression in patients was 1.32 times (1.80 times for a 2-year increase in the duration of illness), which was statistically significant. The findings of the study showed no significant relationship between the incidence of depression and the duration of the disease. However, the study of Khadijeh Mohammadi et al.[6], showed a significant relationship between depression and the duration of the disease. In addition, a cross-sectional study by K. L Taylor et al[16] showed that there is 1.4% significant increase in the chance of depression for one year of increase in the elapsed time of the disease.

The risk of developing depression increased by 2.41% for the 20 units of fatigue, which is statistically significant (P <0/001). By controlling other variables, this difference was statistically significant (OR = 1/039, P <0/001) which was consistent with previous studies.

The risk of depression in patients receiving interferon beta was 1.10 times, but this difference was not statistically significant (P). This difference was not statistically significant by controlling other variables (OR = 1/937, P = 0/37). The study of K. L Taylor[16] showed that receiving interferon was associated with a higher risk of depression. In addition, Also, Fragoso et al[19] in the study of severe depression, thoughts and attempts at suicide while using interferon beta in MS patients, described 11 patients with severe depression and thought or attempted suicide while receiving beta-interferon beta. In a cross-sectional study by Tsivgoulis et al[20], the relationship between EDSS and anxiety and depression in outpatients MS in 2006 in 86 RRMS patients was examined but did not show a significant relationship between interferon therapy and BDI score. Kim et al[21] in a cross-sectional study examined the levels of depression and interferon treatment in MS patients in 694 patients in 2012 and the results showed that there was no significant relationship between depression levels and interferon therapy.

The results of this study and the review of other studies showed that in general, more than half of MS patients had depression that was not related to gender, but depression in MS patients increased with increasing age, marital status, low level of literacy, other types of MS except PRMS, increasing the duration of the disease, and increasing fatigue.

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