

## Anxiety in Patients with Multiple Sclerosis: Association with Disability, Depression, Disease Type and Sex

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**Abstract-** The aim of the current study was to evaluate anxiety in patients with multiple sclerosis (MS) and factors which are associated with this symptom. Eighty totals of 180 patients with MS were enrolled in this cross-sectional study. They were asked to answer the valid and reliable Persian version of the Beck depression inventory (BDI) and Beck anxiety inventory (BAI) questionnaires. Demographic characteristics (sex and age), duration of the disease, disease course and Kurtzke Expanded Disability Status Scale (EDSS) were recorded for all participants. Mean BDI was  $17.5 \pm 11.4$  in patients while mean BAI was  $17.7 \pm 12.5$  in all participants, respectively. Mean BDI and BAI were not statistically different between male and female participants. Patients with higher levels of disability (higher EDSS) had significant higher BDI and BAI scores and there was significant positive correlation between EDSS and BDI and BAI scores ( $\rho=0.42$ ,  $P<0.001$ ,  $\rho=0.35$ ,  $P<0.001$ ). Patients with SP (Secondary progressive) type of disease had significant higher BDI and BAI score. Multiple linear regression analysis showed that depression and disability level were independent predictors of anxiety in patients. Anxiety and factors which are related with this symptom should be considered in MS patients.

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### Introduction

Multiple sclerosis (MS) is an inflammatory, chronic and progressive disease of central nervous system which is more prevalent in women than men (1). MS is one of the most causes of disability all over the world which affects physical, emotional, cognitive and social aspects of patient's lives (2,3). Most patients suffer from mood difficulties especially depression although the exact reason of depression in such patients is not definitely clear (4,5).

Anxiety is another mood problem which has been evaluated not as much in patients with MS. Its prevalence is reported between 14%-41% in such patients (6,7) which could reduce the quality of life, worsen clinical symptoms and influence general health (7).

The exact cause of anxiety in MS is not clear and

debates remain if anxiety in such patients is because of disease course such as site of lesions, duration of disease, type of the disease or it is the reaction to disease occurrence (8). Previous studies showed that history of depression, higher level of disability, higher level of stress, alcohol use and suicide attempt are associated with anxiety experience in MS patients (6,8).

Focus on treating depression and anxiety in MS patients is important as they could affect the quality of life and general health of patients.

The goal of this study was to evaluate anxiety in patients with MS and factors which are associated with this symptom.

### Materials and Methods

A total of 180 clinically definite MS patients (according to MC Donald) who referred to MS clinic of

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Sina Hospital (affiliated to Tehran University of Medical Sciences) were enrolled in this cross-sectional study.

All participants were asked to fill informed consent forms before study entrance.

Exclusion criteria were: active MS and corticosteroids treatment during last four weeks.

Demographic characteristics (sex and age), duration of the disease and disease course [Relapsing Remitting (RR), Primary Progressive (PP), Secondary Progressive (SP), Progressive Relapsing (PR)] were extracted from patients medical files.

All patients were examined by an expert neurologist to obtain Kurtzke Expanded Disability Status Scale (EDSS).

All participants filled valid and reliable Persian version of BDI (Beck depression Inventory) and Beck Anxiety Inventory (BAI) questionnaires (9, 10).

The BDI consists of 21 questions which are answered by the participants according to their feelings over the last week. Each item is scored from 0 to 3 to decide the participant's level of depression. Those with total scores between 0 and 9 are not recognized as depressed, scores between 10 and 18 are indicative of mild to moderate depression, scores between 19 and 29 indicate moderate to severe depression, and scores between 30 and 63 are defined as severe depression (9).

The BAI includes 21 self-reported questions which will be scored from 0 to 3 by ordinal scaling system. Individuals with total scores between 0 and 7 are recognized as minimal anxious, scores between 8 and 15 are indicative of mild anxiety, scores between 16 and 25 indicate moderate anxiety, and scores between 26 and 63 are defined as severe anxiety (10).

All data were analyzed using SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA). Continuous variables compared by means of independent sample t-test or ANOVA tests, and Fisher's exact test was used to compare categorical variables. Correlation coefficient (Pearson or Spearman) applied to assess the association between variables. Multiple regression analysis was used to calculate the predictive value of EDSS, BDI, age, type of disease, and sex for the anxiety score in patients. P-value less than 0.05 was considered as significant.

## Results

Number of eighty out of 180 MS patients was enrolled in this cross-sectional study between August and November 2012. Demographic characteristics are presented in table 1.

Mean BDI was  $17.5 \pm 11.4$  in patients while mean BAI was  $17.7 \pm 12.5$  in all participants, respectively.

Forty eight (26.7%) had BAI score between 0-7, 38 (21.1%) had BAI score between 8-15, 44 (24.4%) had BAI score between 16-25 and 50 (27.8%) had BAI between 26-63.

Mean BDI and BAI were not statistically different between a male and female ones (Table 2).

**Table 1. Demographic characteristics of all patients**

	Patients
Age(mean $\pm$ SD)	32.4 $\pm$ 8.7
Sex (F/M)	(151/29)
Marital status	
Single	60
Married	117
Divorced	3
Disease duration (mean $\pm$ SD)	5.7 $\pm$ 4.3 (years)
EDSS (median)	2
Type of disease	
RR	142 (78.9%)
SP	38 (21.1%)

RR=Relapsing Remitting; SP=Secondary progressive

**Table 2. Mean BDI and BAI in different sex groups of patients**

	Female	Male	P value
BDI	17.7 $\pm$ 11.8	16.2 $\pm$ 9.4	0.5
BAI	18.2 $\pm$ 13.1	14.7 $\pm$ 8.5	0.06

Patients with higher levels of disability (higher EDSS) had significant higher BDI and BAI scores (Table3).

There was significant positive correlation between EDSS and BDI and BAI scores ( $\rho=0.42$ ,  $P<0.001$ ,  $\rho=0.35$ ,  $P<0.001$ ).

Participants with higher BDI scores had significant higher EDSS and BAI score, too (Table 4).

**Table 3. Mean BDI and BAI in patients with different EDSS**

EDSS	0-2 N=95	2.5-4 N=31	4.5-6.5 N=41	6.5-8 N=13	P value
BDI	13.6 $\pm$ 11.3	18.4 $\pm$ 8.1	23.4 $\pm$ 10.9	24.2 $\pm$ 10.2	<0.001
BAI	14 $\pm$ 11.7	17.9 $\pm$ 9.6	25 $\pm$ 13.6	21.4 $\pm$ 10.5	<0.001

**Table 4. Mean BAI score in participants with no, mild, moderate and severe depression**

BDI	0-9 N=51	10-18(mild) N=51	19-29(moderate) N=51	30-63(severe) N=27	P value
EDSS (median)	1	2	3	5.5	<0.001
BAI	6.5±5.7	16.3±10.4	24.1±11.4	29.2±9.8	<0.001

We found significant positive correlation between BDI and BAI scores in patients ( $r=0.66, P<0.001$ ).

Mean BDI score was  $15.6 \pm 10.9$  in patients with RR type of disease and  $24.4 \pm 10.8$  in patients with SP type of MS disease ( $P<0.001$ ) while mean BAI score was  $16.1 \pm 11.8$  and  $23.7 \pm 13.5$  in patients with RR and SP types of MS ( $P=0.001$ ).

Multiple linear regression analysis showed that depression and disability level are independent predictors of anxiety in patients.

**Table 5. Multiple linear regression analysis between BAI score and other variables**

	B	95% CI	P. value
BDI	0.61	(0.53 -0.8)	0.001
EDSS	0.38	(1 -3.3)	<0.001
Age	0.02	(-0.45 -0.4)	0.7
Sex	0.09	(.048 -10.2)	0.09
Type of disease	-0.02	(-5.1 -7.1)	0.7

## Discussion

Current results showed that the depression is a good predictor of anxiety in patients with MS and anxiety in such patients is related to the level of disability. Authors also found that patients with EDSS between 6.5-8 had higher scores of depression and anxiety than other EDSS groups. In addition, positive correlation was considered between EDSS and depression and anxiety scores.

This finding is consistent with findings of a previous study (8).

Garfield and Lincoln evaluated 157 MS patients and found that MS patients with a higher level of disability and depression had a higher level of anxiety (8).

On the other hand, some other studies supported no association between disability and anxiety in patients with MS (11-13). Beiske *et al.*, evaluated 140 MS patients with median EDSS of 4 and found that anxiety is associated with lower disability (11). By evaluating newly diagnosed MS patients, Janssens *et al.*, reported that the anxiety did not change over time along with changes in disability level in such patients (13).

Present results also showed that scores of BDI and BAI questionnaires did not differ significantly between men and women which is consistent with Dahl *et al.*, results who reported that men had more anxiety symptoms than women although, this difference was not

statistically significant (14).

In Garfield and Lincoln study, women were more anxious than men (8). Also, Beiske *et al.*, reported that women with MS were more anxious and depressed than women in the general population (11).

We also found that patients with severe depression had higher BAI score, and significant positive correlation was detected between BDI and BAI scores.

Depression is the most common mood disorder in MS with prevalence near 50% in such patients (15). The exact cause of depression in MS is not obvious, but changes in immune and nervous systems or living with a chronic disabling disease could be considered. The authors found significant positive association between BDI score and EDSS, which can be indicative that level of disability influences patient's mood. This could be due to difficulties resulted from the disease course such as reduced daily activities, sleep disturbances, fatigue, and pain (5).

This finding is not consistent with findings of Dahl *et al.*, They evaluated 172 patients with MS and reported no association between EDSS and anxiety neither depression (14) such as Silva *et al.*, (15).

Experiencing co-morbid depression with anxiety among MS patients had been reported in previous studies (8, 6) similar to the general population. As experience of anxiety predates experience of depression e, it is important to consider these psychological problems, because patients with co-morbid psychological problems are at risk of more quality of life impairment, reduced functional activity and increased risk of suicidal attempt (16,17).

In a Canadian study, authors stated that the anxiety is common in MS patients but it is disregarded and under-treated in such patients (6).

Considering psychological problems in patients with MS and applying appropriate treatment is an essential issue. As depression and anxiety are closely related to each other, treatment of depression could reduce anxiety and other psychological problems in such patients. Evidences show that the depression predicts disease progression in MS and treatment of depression will result in a reduction of pro-inflammatory cytokines and gadolinium-enhanced lesions on MRI (Magnetic resonance Imaging (18,19).

Anxiety and factors such as depression that are

associated with this symptom and level of disability should be considered in MS patients.

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