

The Relation between Fatigue Severity with Psychological Symptoms and Quality of Life in Multiple Sclerosis

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Article information	Abstract
<p>Article history: Received: 21 Oct 2011 Accepted: 22 Dec 2011 Available online: 16 Oct 2012</p> <p>Keywords: Multiple Sclerosis Fatigue Severity Depression Anxiety Stress Quality of Life</p> <p>*Corresponding author at: Department of Psychology, University of Guilan, Rasht, Iran E-mail: maisam.salehpoor@yahoo.com</p>	<p>Background: Fatigue is one of the most common and disabling symptoms of multiple sclerosis (MS) disease. Since fatigue can cause a great deal of problems it create can cause a variety of psychological symptoms particularly depression, anxiety and stress as well, that quality of daily lives, endanger. Thus, the objective of this study was to determine the relation between fatigue severity and psychological symptoms and quality of life in patients with MS.</p> <p>Materials and Methods: In this descriptive-correlational study, 76 patients with MS with a mean age of 34.02 ± 9.42 (16-58 year), a member of Guilan province MS association, were selected consecutively. At first, all patients completed the questionnaire of demographic information, and then they were evaluated by the Fatigue Severity Scale (Fatigue Severity Scale), depression, anxiety, Stress Scale (depression, anxiety, stress scale-21) and Quality of Life questionnaire (Short Form-36).</p> <p>Results: Correlational analyses indicated a significant association between fatigue severity and patient's age, depression, anxiety and stress ($p < 0.05$) and quality of life ($p < 0.01$), While there were no significant relations between fatigue severity and duration of MS. The results of multiple stepwise regression analysis showed that only the factor of quality of life as a selected variable in final model could explain 27% of the shared variance of fatigue severity results ($p = 0.002$).</p> <p>Conclusion: The findings showed that regardless of other variables, the levels of quality of life are predictor of fatigue severity in patients with MS. Therefore it is suggested in these patients psychotherapy based on improvement of quality of life for decrease of the levels of fatigue be set as the central aim of psychological interventions.</p> <p>Copyright © 2012 Zahedan University of Medical Sciences. All rights reserved.</p>

Introduction

Multiple Sclerosis (MS) is a neurological degenerative disease which is also chronic and progressive and is resulted from demyelination in Central Nervous System (CNS) [1]. From pathology point of view, MS is specified through inflammation and sclerosis (hardening of tissue) in numerous areas of white matter in CNS [2]. This disease is one of the reasons for disability in youth and middle aged people and mainly prevalent in ages between 20-40 years [3]. There is a little understanding as to the exact reason of the disease and the treatment is also unknown. But the most important factors stated to be involved, include immune system, genetics and environmental factors [2, 4, 5].

Meanwhile, fatigue is one of the most prevalent and debilitating symptoms in MS which still little is known about the reason. Fatigue is defined as "subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities" [6]. About 92% of those patients with MS, complain from fatigue and more than two third of them describe it as the most disturbing symptom [7]. One study showed the fatigue is the most prevalent symptom of MS

which is more prevalent than other symptoms such as movement problems, muscular spasm and Weakness and endangers routine daily activities of the individual [6]. Moreover, the chronic nature of the disease, having no prognosis and certain treatment in addition to engaging people in young ages, causes various psychological symptoms in patients, among which depression, anxiety and stress are the most common [8].

Depression is the most current psychological disorder in MS which appears as a noteworthy source of morbid and attenuation. Thus, its emersion and treatment are of most importance [9]. It should be remembered that, chronic and unpredictable course of the disease implying continuous adjustments of the patient's sense of self. These adjustments are crucial to accept the progressive limitations imposed by MS, to perceive and adapt to the resulting family and social demands, to deal with unpleasant self-injectable medications and to handle with the generalized pressure of frequent reports about new potentially more effective medications. In fact, anxiety is also common among them and maybe these disorders have remarkable role in high prevalent of fatigue in MS

patients. Yet, stress is a widespread symptom which in MS studies is considered as a potential enhancing disease factor or as a factor of its relapse. Currently, stress is considered some kind of change in an individual's life, the "stressor", which requires readjustments that surpass the ability of coping, and leads to psychological or biological harm. So, according to different researches, since these patients are more and in significant way subject to unusual stress and experience more stressful events of the life, it seems that increase of stress in them is accompanied by more intense fatigue [10].

In parallel to recent psychological problems, as far as MS involves people in their best efficiency age, it imposes irrecoverable psychological, economical and social effects on the patient [11], in a way that those patients, confront with psycho-social and physical challenges such as experiencing unpleasant and unpredictable symptoms, hard therapeutic regimes and side effects of drugs, increasing physical disability levels in one hand, and vanishing life targets, income, relationships and entertaining activities in addition to the daily life assignments, on the other hand [1].

In addition, MS patients subjectively describe their feeling of fatigue as "washed out," "exhausted," or "lacking in energy" and say that fatigue has prevented revival of physical function, they easily become bored, it interferes their physical performance and social responsibilities, causes them frequent problems and it becomes worse by heat. Also, it has been shown that fatigue is the main reason of MS Patients, to be unable to do their employment duties. Besides these overt limitations, fatigue in MS has been shown to be associated with lowered positive affects, psychological distress, and a sense of loss of control [12].

It could be thought that the aforementioned problems are becoming decreasing factors of quality of life in these patients and downfall of it. Da Sliva et al, have acknowledged in their study that level of anxiety and depression in MS Patients has been considerably higher in comparison to those healthy under experience [13]. Moreover, considering connection of psychological symptoms and fatigue severity in MS Patients, Bol et al, declared that in comparison to the other chronic diseases, depression is more prevalent in MS which makes these patients more prone to fatigue [7].

Ketelslegers et al, also comparing two groups of children patients with MS as well as demyelination inflammation, to the aim of comparison between fatigues and determining connection it with depression, discovered that frequent fatigue occurred more in MS Children. Meanwhile, fatigue and depression were connected to each other in these patients [14]. In a one year study upon 23 women stricken by MS, the findings showed that 85% of MS exacerbations were related to stressful life events of the past 6 weeks [15]. When we pay attention to the fact that, fatigue occurs mostly at time exacerbation of the disease [16], we confirm that stress naturally has a role in outbreak of fatigue in MS Patients.

Generally, considering these data and ascendant fatigue process resulted from various psychological crisis and

decrease in quality of life level, paying attention to the infrastructural factors causing it, first, could maximize our level of understanding in this field and second, paves the way for right planning, so that, different experts (such as neurologist, psychologist, psychiatrist, etc) could increase contrast and compatibility level of patients to these matters, which these matters by themselves guarantee the necessity of research in this field. In the end, despite there has been various researches done in relation to the MS Patients, but few of them has dealt with psychological symptoms (depression, anxiety, and stress) and quality of life level in relation to perceived fatigue severity in this patients. So, the main aim of this paper is to provide more extensive information regarding changeability of fatigue severity in MS Patients in connection to psychological symptoms and quality of life level.

Materials and Methods

Present research was taken place in descriptive-sectional method and of correlation type which was conducted upon MS patients who were under supervision of MS society of Guilan province in 2010. 76 patients were chosen via consecutive sampling to go under study. Those criteria as to the entrance to the research were to be patient by MS according McDonald criteria [2] and the diagnosis being confirmed by a neurologist.

Exist of MS disease as the clinical symptoms and characteristics of the patient and exist of lesion clinical evidence in two places or more in CNS. To prove the aforementioned, paraclinical measures including magnetic resonance Imaging (MRI), called potential and examination of cerebrospinal fluid (CSF) have been used and those patients having recorded files in MS society, have been taking confirmed diagnosis according above cited findings.

Those criteria causing emersion from study consisted of acute MS disease attack, co-existence of another debilitating disease with MS and severe cognitive problems to the extent that the patients could not fill out the questionnaire or answering to the questioner. Questionnaires were filled out by the patients themselves and in case they were of low education, all questions were read to them and their verbal answer documented in related fields of the questionnaire.

Information gathering was done through questionnaire and scale, consisting of two parts: one including demographic information and another was regarding examination of fatigue severity and evaluation of psychological symptoms and life quality of the MS patients. Those MS Patients having entrance criteria to the present research were referring to the Center upon being called. In primary discussion with patient individual and his/her family or entourage, some explanation was made as to the reason and method of doing this study and taking their consent, the patients were assured of confidentiality of their information; additionally, they were promised that not taking part in this research, should have no outcome on behalf of the Society.

Those under research firstly, filled out demographical questionnaire including age, gender, education, marital status, employment status, duration, and other information related the disease and then scales & questionnaire was filled out under supervision of a psychologist. Fatigue Severity Scale (FSS): The same was used to evaluate fatigue severity of the MS patients. This tool was made by a neurologist named Lauren Krupp in 1989 to evaluate fatigue in MS patients [17].

This is a valid scale for measurement of fatigue severity in MS patients. Through this tool, overall fatigue is evaluated quickly in a way that the resulted score is completely proportionate to scale and fatigue severity of the patient, does not make him/her more fatigue, and is understandable by all patients and 98% of the patients could answer the questions without help. This scale consists of 9 questions, five of which evaluates quality of fatigue and three of them are for measuring physical-subjective fatigue and reviewing fatigue results affecting social situation of the individual. The last question makes comparison between fatigue severity and other symptoms indicated in MS stricken person. Each item in this scale is grading from 1 to 7. Score 1, means that the individual is strongly opposed to it and score 7, shows the person completely agrees with it. Total score is resulted from dividing sums of scores by 9, which the result is fluctuating between 1-7 and 7 shows highest fatigue and 1 shows lack of fatigue [18]. This instrument has had criterion validity and high internal consistency coefficient. Krupp et al. reported its criterion validity as 68% and the internal consistency coefficient as 88% [19]. In Iran, we have reviewed its reliability also. In recent study, internal consistency of FSS scale items was equal to 96%, calculating Cronbach's alpha coefficient, which indicated that all items in above scale are evaluating one notion. Moreover, Interclass Correlation Coefficient (ICC) test which was used to evaluate relative repeatability of Persian version of this tool in test frequencies was equal to 93% which shows appropriate repeatability of Persian version of FSS. Overall result showed that we could use the tool to examine fatigue severity and impact of different treatments on the person patient with MS [20].

Depression, Anxiety, and Stress Scale (DASS-21): This tool designed by Lovibond & Lovibond was used to evaluate negative sentimental moods in depression, anxiety and stress of patients. Scale consists of 21 questions, within which every 7 questions are respectively used to evaluate depression, anxiety and stress. The instrument is designed as Likert Scale having alternatives such as none, low, average, and high. The least score related to each question is zero and the highest score is three [21].

Validity of the scale in Iran was reviewed by Jokar & Samani, reporting retrial scores of 0.80, 0.76 and 0.77 respectively for depression, anxiety and stress scales and Cronbach's alpha coefficient for depression, anxiety and stress, respectively as 0.81, 0.74, and 0.78. An overall results of the study shows sufficiency of the scale for the usage in Iran [22].

Short Form Health Survey Questionnaire (SF-36): This questionnaire was designed by Ware et al, in order to evaluate quality of life [23]. The questionnaire consists of 36 questions which evaluates life quality according 8 sub-scales relating to physical and psychological health. These 8 sub-scales include: physical functioning, role limitations due to physical health, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and mental health. Each question takes from 1 to 100 scores and each criterion is estimated through totalizing questions' scores and determining the average. In this questionnaire, the more the score be near to 100, quality of life is better. Reliability and validity of it was examined by Faghihi & Asghari Moghaddam, through two separate studies upon students of Shahed University. In first study, 404 male and female students completed the questionnaire and in order to review "retest coefficients of sub-scales", in a time interval of one week, the same questionnaire was given to 120 students (60 male and 60 female) from the same first group. The results showed reliability and favorable internal consistency of all sub-scales of the questionnaire under study (retest coefficients of sub-scales were between 0.43 to 0.79 and Cronbach's alpha coefficient varied from 0.70 to 0.85). In second study, validity of "health questionnaire" was examined through execution of it upon two healthy (48 persons) and patients (81 persons) groups. Comparison has been made between scores of two healthy and patient groups regarding all sub-scales of the questionnaire. There has been significant statistical difference in all sub-scales between two groups of healthy and patients. Findings of the two studies were indicative of acceptable validity and reliability regarding questionnaire SF-36 in Iranian adult samples [24].

In order to describe data in present study, use have been made of descriptive statistics indexes such as percentage, frequency, mean and range. To show information and data, different tables have been used. In inferential statistics section, we have used correlation analysis to review connection hypotheses and to prediction criterion variable (fatigue severity) from predictor variables (depression, anxiety, stress and quality of life), we have got help from "stepwise multiple linear regression statistical method" via SPSS-16. Finally, from results of these statistical analysis including Standard Error Estimation, Beta coefficients (β), p values, and Significant Levels, we extracted Prediction Model of Fatigue Severity on the basis of psychological symptoms and quality of life.

Results

As a whole, 76 MS patients (22 male and 54 female) supervised by MS society of Guilan Province, participated in this research and evaluation has been made as to their fatigue severity, psychological symptoms and quality of life. Most participants under experiment in this research were female which according to consecutive method of sampling shows the number and more references of women to MS society of Guilan. Meanwhile, marital status of patients indicates that 4 of them were divorced

(3.5%), 16 persons were single (21.1%), and 56 of them were married (73.7%). Yet, only one of them was illiterate (3.1%) which his information was completed with the assistance of interviewer and family members; 25 of patients have had academic education (32.8%) and 38 were of high school education (50%). As far as occupation of the patients is concerned, 32 (42.1%) were housewives (of course due to more female patients in sample group), 16 persons were jobless because of retirement, disablement and unemployment (to be fired or finding no work), and 21 of them had a job (27.6%). Moreover, there were just 7 people studying at the time. In terms of number of outbreak of attacks, only 4 patients have had no record of it (5.3%), but 27 persons (35.5%) have had record of more than three attacks and in total, 45 people (59.2%) have had between 1 – 3 attacks as their record. In the meantime, considering number of hospitalization, 33 have not had the experiment (43.4%), 28 of them have been hospitalized one time (36.8%), and 13 patients have experienced it between 2-3 times (17.1%). Eventually, it was recognized that only 2 patients (%2.6) have been hospitalized more than 3 times.

As you may see, patients are of mean ages (34.02±9.42) which holds out those subjects to experiment were mostly in youth ages. Mean education of subjects in terms of year was (11.7±3.49). This makes it appear that most of the patients have been in high school range. Aside, mean level of depression and anxiety of the patients was respectively (6.24±4.16) and (5.6±3.62) which both has shown levels less than average. Besides, stress level of the patients also has become (8.34±3.7) which somehow signifies high level of stress of them in their group. Mean quality of life of the patients was (49.79±23.61) which in reality refers to average quality of life of those under experiment and at last, the mean fatigue severity in present research was (4.65±1.91). This score shows fatigue to be more than average in MS Patients (Table 1).

In table 2, we observe a significant relation between psychological variables (depression, anxiety and stress) and quality of life with fatigue severity ($p=0.001$); in the way that the patient’s age, higher morbid symptoms (positive correlation) and lower quality of life level

(negative correlation) was accompanied with more fatigue severity. While, no significant linkage existed between fatigue severity and duration of MS disease.

According to table 3, stepwise multiple regressions just selected the quality of life factor as a chosen variable to prediction fatigue severity in final model. This variable by itself 29% has explained common variance regarding results of fatigue severity ($p=0.002$).

Discussion

Upon findings of present research, each of reviewed factors had significant relation to fatigue severity in patients (Table 2). But, when prediction value of these factors was evaluated in stepwise regression analysis, only it was quality of life which appeared as a chosen significant forecasting variable for fatigue severity (Table 3). These findings shows that other demographic factors (such as age and education level) or biomedical (like duration) and psychological (e.g. depression, anxiety and stress) may just be indirectly related to fatigue severity through their relation with chosen variable of quality of life in regression analysis. Though this chosen variable explains medium share of fatigue severity variance (0.267), but the important thing is that each of psychological factors such as depression, anxiety and stress by themselves, did not appear as significant predictor of fatigue severity. In fact, although results of the research indicated that depression, anxiety and stress are of no value for prediction, but it has been recognized that there is a significant relation between fatigue severity and depression (0.44), anxiety (0.46), and stress (0.42), (Table 2).

Table 1. Description of basic variables in the research

Variables	Mean±SD	R
Age(yr)	34.02±9.42	16-58
Education(in terms of year)	11.7±3.49	0-19
Duration(in terms of month)	56.88±55.91	1-384
Depression	6.24±4.16	0-21
Anxiety	5.6±3.62	0-20
Stress	8.34±3.7	2-21
Quality of life	49.79±23.61	3.33-96.25
Fatigue severity	4.65±1.91	1-7

Table 2. Correlation coefficient matrix between variables in the sample as a whole (N=76)

Variables	1	2	3	4	5	6	7
Age(yr)	1						
Duration	0.42**	1					
Depression	0.31**	0.23**	1				
Anxiety	0.19	0.04	0.66**	1			
Stress	-0.24*	0.04	0.82**	0.75**	1		
Quality of life	-0.40*	-0.11	-0.69**	-0.63**	-0.62**	1	
Fatigue severity	0.27*	-0.10	0.44*	0.46*	0.42*	-0.54**	1

* $p < 0.05$, ** $p < 0.01$

Table 3. Stepwise multiple regression analysis to prediction fatigue severity

Variables	Indexes			
Selected Variable	B Coefficient	t	Sig	Tolerance
Quality of life	-0.54	-3.35	0.002	1.000
Model Summary	$R^2 = 0.29$, $SE_E = 0.0001$, $F = 11.2$, $p < 0.002$			

Formerly, also in parallel to these findings, there have been some confirmations as to the relation of fatigue and depression [14]. In this context, Voss et al. have also concluded from their study that physicians should be sensitive to the complaints such as excitability and sadness in MS Patients, even if criterion symptoms are not considered for official psychological diagnosis [25].

According to Ziemssen the reason is structural changes happening in brain of those patients with MS which causes its biological deterioration and may play a role in their depression. For example, in a study done via MRI, it was shown that there is a relation between depression and anxiety symptoms with the disease symptoms in MRI images of 95 MS Patients. In confirmation of this study, another research explained that severity of psychological symptoms i.e. depression, anxiety and stress is weakly related to right anterior area lesion and extensively related to right temporal area atrophy [26]. These data make the researchers believe that maybe not being able to forecast fatigue severity upon psychological symptoms in this research is stemmed from existence of unknown brain lesions which has not been recognized at the time of MS diagnosis through MRI or CT scan, so, in the same research also psychological test has not been able to evaluate and measure it. Although, Cathebras et al. [27] along with Fuhrer & Wessely [28] have found in their studies upon those patients under primary care that fatigue in MS patients is of no specific sensitivity as to the recognition of depression. Besides, primary surveys on MS Patients have had no relation found between fatigue and depression or there has been a modest correlation there between [29].

Meanwhile, one of the principles of published statement by International Gathering of Researchers, as further clarity of stress impact on MS says that, supporting evidences regarding hypothesis of relation between stressful life-events and MS relapses (which are followed by ascending process of fatigue) are not conclusive [30]. In fact, these results are contrary to the findings of present research. To explain the results, we may cite that even if upon former findings [7, 13, 14, 31], MS Patients are experiencing higher level of psychological symptoms such as depression, anxiety and stress and potentially could be stricken by anxiety and mood disorders, but since these symptoms are usually playing role in individual and social behaviors of these people and most of the patients report them as immediate psychological situation of their physical disease and its complications, triple scores of (depression, anxiety and stress) resulting from DASS-21 test could not significantly explain variability of fatigue severity scores in these patients. On the other hand and at the same time, different studies through different methods also, confirmed what resulted from relation of quality of life and fatigue severity in this research. Instantly, Benedict et al [32] and Yozbatiran et al [33], each in their studies realized that MS Patients confront with low or damaged quality of life and disorders in physical aspect of it. Moreover, Pitton-Vouyovitch et al. [31], have founded that fatigue has

considerable impact on any and each of scales of quality of life on SF-36 and this is why more fatigue is related to disorder in quality of life. Since fatigue is the most debilitating symptom in MS Patients, its impacts on daily life of the patients is clearly observable in a way that upon reviews performed by Glanz, lack of energy, unwell feeling, restrictions in doing voluntary movements, preventing from physical pressure tolerance and working as well as social role performance limitations, are all among problems arising in relation to quality of life in MS Patients and make it moving downfall [34].

In different studies, fatigue and physical disability are found to be strong predictors of quality of life in such a way that relation between fatigue and damaged quality of life in MS patients became prominent in one study [26]. In fact, quality of life variable is probably appeared as a significant predictor of fatigue severity because of role of physical factors, social performance and vitality in addition to performance of emotional role and improved level of psychological health, which seems clearer interpretation of this relationship, needs more research in future.

The study and findings, clearly showed existence of a medium relationship between fatigue severity and psychological symptoms (depression, anxiety and stress) and quality of life of MS Patients. So, for these group of patients, it seems rational to propose some kind of rehabilitation and therapeutic interventions (such as self care programs upon Orem pattern, water therapy, energy maintenance techniques as well as psychotherapies on the basis of improvement of quality of life) in order to minimize fatigue and disability of them and concentrate on effective psychological factors (e.g. negative psychological factors, how to manage psychological stressors) on the basis of cognitive-behavioral approach and promotion of their quality of life levels.

The reason is that results from researches indicate mutual relationship existing between those methods like energy maintenance techniques, exercise, behavioral interactions and psychological interventions with MS symptoms [35, 36]. This is why, considering main finding of the present research (i.e. role of quality of life as a significant predictor of fatigue severity), there is a need for identifying and making decisions as to debilitating problems control of stricken people and lifting their quality of life on behalf of therapy team. From the point of the view that, medical methods also are of little influence on quality of life, naturally, performing psychotherapy programs stemmed from requirements of these patients and based upon self-care principles, would have better and positive results.

Meanwhile, such programs are safe and comfortable and the receptivity of patient becomes better. Besides, considering that psychotherapy on the basis of quality of life improvement is a low cost non-pharmacologic and non-invasive method to improve quality level of life, we may propose these kind of psychotherapies which could be spread through training, following and supporting the patient or even his/her family, to be a part of therapeutic

protocol of MS Patients and totally alongside with medical programs, psychological interventions be applied to improve quality of life.

It should be noticed that, we did not refer to the role of medicals consumed by the patients, in this research, so, samples under study have not been equal; this may have been effective in outbreak of those symptoms under review. Meanwhile, findings of this research have no capability to be generalized to other chronic diseases similar to MS. It should be also mentioned that, due to sampling constraints, non-availability and non-cooperation of some of patients, nearly numerable samples were used in this research. Moreover, this evaluation is limited to statistical society of Guilan province and caution should be made in generalization of results to other societies.

Finally, all data from the current research are self-reporting which may call increase probability of bias and distortion of answers within various tools. Any way, we should consider that role of psychological symptoms and quality of life is only available and ponderable through self-reporting tools.

On the basis of mentioned limitations, we propose that future researches be performed using more samples, possibility of more accurate evaluation of variables and more generalization feasibility. Meanwhile, in these kinds of researches advantage could be made of other psychological variables (e.g. coping styles and personality patterns). Eventually, emphasize should be made upon imposing scientific & clinical enlightenments extracted from findings of this research that could play a role in decrease of fatigue severity and negative psychological symptoms or increase of level of quality of life in MS Patients.

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As a whole, the results of the present research showed that fatigue severity has tangible relationship with psychological symptoms (depression, anxiety and stress) and also quality of life in MS patients, but quality of life factor (29%) has provided possibility of forecasting fatigue severity as the only selected variable. Achieving these results, makes outstanding the potential importance of psychological interventions in confronting psychological problems and increasing level of life quality of these people in order to decrease fatigue severity, to the aim of revival and maximize awareness of both patients and therapists.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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