

Psychosocial and Medical Determinants of Health-related Quality of Life in Patients with Relapsing-Remitting Multiple Sclerosis

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ABSTRACT

Introduction: Relapsing-remitting multiple sclerosis is a debilitating neurological disease accompanied with adverse consequences for quality of life. The purpose of this study was to investigate the role of relapsing-remitting multiple sclerosis on psychological, disease-related, socioeconomic, and demographic determinants of health-related quality of life of patients.

Methods: In this cross-sectional descriptive study, 193 patients with relapsing-remitting multiple sclerosis were selected by compliance sampling method among the patients who attended the Iranian Multiple Sclerosis Association in Tehran from March 2014 to July 2014; and they completed the Multiple Sclerosis Quality of Life Questionnaire, the Depression Anxiety and Stress Scales, and the Socio-demographical Questionnaire. Then, a hierarchical multiple regression analysis with the stepwise method is used for data analysis by the PASW-18.

Results: According to the findings, in model 1, low socioeconomic status (SES) had a negative coefficient ($\beta = -0.30$, $p < 0.01$), and treatment

history had a positive coefficient ($\beta = 0.22$, $p < 0.01$). In model 2, while all variables of model 1 were controlled, depression had a negative coefficient ($\beta = -0.26$, $p < 0.05$), while disorder severity of multiple sclerosis had positive coefficients in lower level ($\beta = 0.35$, $p < 0.001$), moderate level ($\beta = 0.23$, $p < 0.01$), and severe level ($\beta = 0.22$, $p < 0.01$). Other studied variables in model 1, and stress and anxiety in model 2 were not predicted in terms of the quality of life ($p > 0.05$).

Conclusion: Unfavorable SES, lack of effective treatment history, higher depression, and signs and symptoms severity of multiple sclerosis significantly predict decreased health-related quality of life in patients with relapsing-remitting multiple sclerosis. Thus, it is consequential to emphasize the value of tailored intervention for attending to these factors in the treatment and rehabilitation agendas for improvement of health-related quality of life in relapsing-remitting multiple sclerosis.

Keywords: Quality of life, depression, psychosocial, multiple sclerosis

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INTRODUCTION

Multiple Sclerosis (MS) is a debilitating neurological condition described worldwide as lesions of myelin sheaths condensing the neurons of the brain, spinal cord, and optic nerve, bringing about the temporary or progressive symptoms, morbidity and dysfunction (1, 2). Correspondingly, MS as a partially prevalent neurological disease is the one of the leading agents of morbidity and mortality from neurological conditions in Iran (3). MS has major consequences for health-related quality of life (HRQOL). Furthermore, relapsing-remitting multiple sclerosis (RRMS) is the most common form of MS (1). While the HRQOL in patients with RRMS is expected as poorer than healthy people, it is also more unfavorable than other chronic diseases, like diabetes or epilepsy (4, 5). HRQOL as a multidimensional concept points out to functional dimensions, productivity affairs, and subjective understanding of the health status in patients with MS (1, 4). In recent times, researchers concentrated on HRQOL as the main outcome measure in MS because the fact that this concept is related to the extensive impact of MS, and might point out

unclear disease burdens (6). Adverse psychosocial and demographic factors deteriorate the quality of life in patients with MS. Recognizing the influential agents on HRQOL may help us improve therapeutic capacities, and strengthen the suitable quality of life in the patients with MS (4, 6).

Some psychosocial and medical factors impact on HRQOL in patients with RRMS. Social and demographic determinants, physical impairment, psychological factors, especially depression, cognitive shortages, longer disease course and chronic fatigue, medication for modifying the disease symptoms and pain are all related to the deficient quality of life in patients with MS (7–10). In separate studies, depression and psychological factors (8, 11), economic burden and financial costs for treatment (1, 12), disease characteristics such as disease progression, disease severity, and related disability (13) predicted HRQOL in patients with MS. In a recent study, Yamout et al. (1) concluded that the HRQOL in patients with MS is affected by physical disability, neighborhood factors, social support, depression,

literacy, employment and socioeconomic status (SES), fatigue, and religious beliefs.

Psychological distress related factors including depression, anxiety, and stress separately or together have an impact on deteriorating the HRQOL in patients with MS (14, 15). Glanz et al. (16) showed that depression, anxiety and other negative emotions have influences in an adverse manner on HRQOL and work productivity in recurring MS. Among the socio-demographic factors, male gender (17), functional disability, fatigue and lower socioeconomic status (1, 18, 19), lower degree of literacy (18, 20), unstable marriage status (1, 21), and higher age (7, 18) dramatically have deteriorating impacts on quality of life in MS patients. On the other hand, Flensner et al. (18) suggested that male gender, the high level of literacy, lower age, and lower emotional distress were the major contributing factors for better HRQOL.

Apart from the psychosocial influences on the health-related QOL in patients with MS, disease characteristics and therapeutic factors also have an influential impact on the quality of life in these patients (22, 23). In the previous studies, quality of life in patients with MS were affected by disease duration, disease progression, and medications that prescribed for managing the pain and disease symptoms (10, 24).

Astonishingly, there are no studies that have simultaneously and comprehensively evaluated the role of the various socio-demographic and socioeconomic factors, psychological agents, clinical correlates, and therapeutic factors in the prediction of the HRQOL in patients with MS in Iran. It is fundamental to increase the knowledge of the major psychological, disease-related, socioeconomic, and demographic factors in HRQOL in men and women with RRMS. So, with regard to the necessity of programming and implementation of the tailored treatments for patients with relapsing-remitting multiple sclerosis (RRMS), this study aimed to investigate influential psychosocial and medical factors on HRQOL in patients with RRMS via multidimensional determinants including psychological, disease-related, socioeconomic, and demographic factors.

METHODS

In this cross-sectional descriptive study, the statistical population was the patients with MS who attended the Iranian Multiple Sclerosis Association in Tehran from Mar 2014 to July 2014. During the 5-month period, 193 patients with MS whom their age ranged from 21 to 62 with a mean age of 38.13 ± 9.67 were selected by compliance sampling method and included the study. The diagnosis of RRMS was based on the revised criteria by Milo & Miller (25), and formally diagnostic examinations of therapeutic neurologist whom the patients referred at least for twelve months. The sample included a most common clinical type of MS that is RRMS's course. This cross-sectional study aimed to predict the quality of life in certain groups of patients with MS who meet the inclusion criteria. According to the correlational research design and predictions of the quality of life based on blocks of variables in patients with RRMS, lack of the comparison in the groups or subgroups of patients, and the specification of the inclusion and exclusion criteria for entry to the study, there was no need to select a control group or a counterpart. Therefore, a control group or a counterpart was not selected in this study. Inclusion criteria of patients were; active involvement in the study and entirely responding to the scales with at least one-year history of the MS, stable clinical conditions in the interviewing process, and presently attending the clinic of the Iranian Multiple Sclerosis Association for routine follow-up or managing the acute episode of the disease. On the other hand, exclusion criteria were flare-up of disease and hospitalization in the study course, the ongoing and concurrent severe psychiatric disorders (such as schizophrenia, bipolar disorder, borderline personality disorder, substance use), mental deterioration, extremely severe symptoms of

depression and anxiety (depression score of DASS-21 > 28, and anxiety score of DASS-21 > 20), comorbid serious medical conditions, at least 10 episodes of disease intensification, and receiving the psychosocial and health-promoting interventions in the past six months. The ongoing and concurrent severe psychiatric disorders were assessed by psychiatric diagnosis, and mental deterioration by the Mini-Mental State Examination (MMSE score < 24). In this study, the role of psychosocial and medical factors in the quality of life in patients with RRMS was assessed without severe comorbid psychiatric disorders. A diagnosed psychiatric comorbidity with inability and dysfunction, and the ongoing acute episode of psychiatric disorders that require tailored treatment such as psychotic disorders and substance use deteriorate the HRQOL, and lack of control for these disorders in the cross-sectional studies can lead to bias. Due to the lack of a control group in this study and consistent with the previous studies (8, 9, 15, 18), excluding the severe psychiatric disorders in the study bring about more accurate results. Moreover, acute and extremely severe depression and anxiety, and taking the depressive or anxious medications were excluded in this study to obtain more refined results. Among the 220 participants, 11 cases were excluded because of incomplete answers to the study measures, and the other 16 cases in terms of inclusion and exclusion criteria were omitted from the study. Thus, the final sample was 193 participants.

The research was approved by Review Board of the Postgraduate Research Committee on Semnan Researches & Sciences University. The research plan was established upon ethical frameworks and outlines of the Ethics Committee. With regard to the research ethics (Declaration of Helsinki), all participants completed the informed consent form at the onset of the study.

Participants completed the Multiple Sclerosis Quality of Life Questionnaire (MSQOL-54), the Depression, Anxiety and Stress Scales (DASS-21), and the Socio-demographical and Medical Information Questionnaire.

The MSQOL-54 tool is used to measure the quality of life in the MS patients. It is a MS-specific instrument to measure the quality of life in these patients (1). It includes questions from the SF-36 Health Survey Questionnaire with supplemental specific MS items for an entire 54 items, and was proven appropriate for the social and cultural setting of diverse societies (26). The MSQOL-54 is used to extract three separate outcome measures with amounts between 0 and 100. Investigated outcome variables were: 1) total quality of life; 2) physical health mixed score (PHCS); and 3) mental health mixed score (MHCS). This instrument has internal consistency and excellent test-retest reliability, and evidence confirming its construct and content validity (27). Furthermore, inter-rater consistency (0.91, 0.99 and 0.95) and test-retest reliability (0.80, 0.87 and 0.95) is measured two times (6–8 weeks apart), and indicated suitable consistency for total MSQOL-54, PHCS, and MHCS, respectively (1). The MSQOL-54 questionnaire with Cronbach's alpha 0.96 has the excellent structural characteristic in a Persian version, and it is a valid and reliable instrument that is used for assessing the impact of MS on the Quality of Life (28).

Depression, anxiety and stress manifestations are assessed using a self-administered scale of the Depression, Anxiety and Stress Scales-21 item (DASS-21). Each of the three sections; (DASS-D), Anxiety (DASS-A), and Stress (DASS-S) has 7 items. Each item includes a statement and four small response options to demonstrate symptom severity. Participants are asked to appraise their experience on each section over the past seven days on a four-point severity scale ranging from 0 to 3. Afterwards, scores for each scale are added up and according to the DASS-21 manual classified as normal symptoms, mild symptoms, moderate symptoms, severe symptoms, and extremely severe symptoms (29). In order to yield identical scores to the total DASS-42, the entire score of each section is multiplied by 2 and extended from 0 to 42 (29). The DASS-21 has proven to have

excellent internal consistency with Cronbach's alpha higher than 0.92 (30). This scale has good psychometric properties in Iranian samples (31).

Socio-demographical and Medical Information Questionnaire is constructed by investigators and used for obtaining social, demographic, and medical variables. Social and demographic sections included gender, age, marriage status, socioeconomic status, and literacy. A medical section included onset and disease duration, treatment type (simple and routine treatment for the disease symptom management, or complicated treatment for controlling the serious complication of RRMS), history of concurrent severe psychiatric disorders, history of concomitant medical conditions, kind and dose of medication, and history of previous psychosocial interventions. In addition, medical section is included for daily dysfunction due to disease intensification, social support status during the disease course, and psychosocial aspects of medications and therapeutic specific factors (preceding hospitalization, therapeutic adherence, and response to medicinal treatment). Socio-demographic and medical data is obtained by self-reported procedure and refer to the Medical Records.

After sampling completion and clarification of the aim and procedure of the study, the participants are encouraged to answer the measures. In some cases, in this survey, completed measurements are received in the later session due to mental status, settings of administration, timing, and conditions of these participants. All authors have had identical participation in planning the study design, study accomplishment, analysis of data and manuscript writing.

Statistical Analysis

Descriptive statistics including frequency and percent, mean and standard deviation, and afterwards a hierarchical multiple regression analysis (stepwise method) is used for data analysis by applying of the PASW-18 to assess predictors of HRQOL in patients with MS. The hierarchical regression analysis is the valid statistical method for evaluation of the predictive relationships among various predictors, and one continual criterion variable in medical studies including symptoms and outcomes of MS (32). The selection of variables in the multiple

regression model was based on hierarchical analyses (stepwise method) and controlling the variables in the regression model. In the first block, background and demographic factors were examined, and in the second block by controlling the effect of background and demographic factors, the role of depression, anxiety, stress, and disease severity was evaluated on the HRQOL. The rationale for this work was controlling the effects of covariates, and assessing the effects of specific predictors without dependence on the influence of others. Background and demographic factors are selected for entry as a block 1 because those are conceptually related, and block 1 is theoretically prior to block 2. In addition, these variables were included in the regression model as a block 1 because these were objective, relatively affordable variables to measure and had good enough predictive power in the literature without the entrance of subsequent subjective variables such as depression and disease severity. Furthermore, depression, anxiety, stress, and disease severity have had greater theoretical linkage, and were more theoretically prominent for the quality of life. Therefore, depression, anxiety, stress, and disease severity are entered last at block 2 to consider whether these important and theoretically related predictors add the prediction of the HRQOL in the regression model.

RESULTS

The age spectrum of participants expanded from 21 to 62 years old (mean age 38.13 ± 9.67). Disease duration varied in the range of 2 to 23 with mean 7.96 ± 3.66 years. Among 193 participants in the study, 68 (35.2%) patients were male, and 125 (64.8%) patients were female. Furthermore, 53 (27.5%) participants had lower socioeconomic status, 107 (55.4%) participants had a moderate socioeconomic status, and 33 (17.1%) participants have a higher socioeconomic status. Seventy-six of these patients were single (39.4%), and 117 patients were married (60.6%). According to the literacy level, 28 participants were illiterate or had elementary education (14.5%), 21 participants were in guidance level (10.9%), 58 participants had diplomas (30.1%), 24 participants were graduates (12.4%), 43 cases of them were in bachelor level (22.3%), and the remaining 19 cases were in master of art level or beyond (9.8%). Finally,

Table 1. Correlation matrix, mean and SD between predictors and criterion variable (N=193)

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. QoL																		
2. Age	-0.04																	
3. Gender (male)	-0.13*	0.12**																
4. Literacy (Diploma or Higher)	0.13*	-0.25**	0.02															
5. Marriage (Single)	-0.16*	-0.29**	0.06	-0.01														
6. LSES	-0.18**	0.16**	0.04	-0.08	0.037													
7. MSES	0.04	-0.20**	0.04	-0.01	-0.036	-0.76**												
8. SOMHIS	0.04	0.13*	-0.07	-0.09	0.036	0.02	-0.04											
9. PSYCHIS	0.01	0.11	-0.05	-0.04	0.056	0.10	-0.01	0.30**										
10. DISDUR	-0.05	0.40**	0.01	-0.08	-0.036	0.04	-0.09	0.00	0.07									
11. TRETHIS	0.21**	0.04	-0.09	-0.01	-0.053	0.04	-0.03	0.20**	0.27**	0.05								
12. TRETYP	-0.03	-0.06	-0.02	0.00	0.059	0.07	-0.09	0.07	0.14*	0.13*	0.21**							
13. stress	-0.57**	0.02	0.02	-0.01	-0.087	0.12*	0.01	-0.02	0.05	-0.05	-0.13*	-0.01						
14. Anxiety	-0.50**	0.09	0.04	-0.03	-0.088	0.16*	-0.05	0.02	0.10	-0.05	-0.20**	-0.05	0.73**					
15. Depression	-0.61**	0.07	0.08	-0.05	-0.077	0.17**	-0.05	-0.03	0.03	-0.02	-0.10	0.00	0.89**	0.70**				
16. LSVRT	0.35**	-0.04	0.02	-0.02	-0.080	-0.03	0.00	-0.10	-0.15*	0.06	0.01	-0.04	-0.25**	-0.21**	-0.31**			
17. MSVRT	0.08	0.02	0.07	0.04	0.057	-0.11	0.04	0.05	0.15*	-0.01	0.05	0.03	-0.11	-0.08	-0.10	-0.32**		
18. SEVRT	-0.11	-0.05	-0.11	0.01	0.011	0.04	-0.04	0.00	-0.02	-0.04	-0.02	-0.02	0.18**	0.16*	0.19**	-0.33**	-0.49**	
Mean	149.54	38.25	0.34	0.43	0.32	0.17	0.73	0.34	0.26	8.59	0.40	0.37	18.00	15.44	16.18	0.17	0.32	0.33
SD	29.41	10.12	0.47	0.50	0.47	0.38	0.44	0.47	0.44	4.71	0.49	0.48	4.48	3.66	4.78	0.38	0.47	0.47

Note: LSES=Low socioeconomic status; MSES=Moderate socioeconomic status; SOMHIS=Somatic disorder history; PSYCHIS=psychiatry disorders history; DISDUR=disorder duration; TRETHIS=Treatment history; TRETYP=Treatment type; LSVRT=low severity of multiple sclerosis; MSVRT=Moderate severity of multiple sclerosis; SEVRT=Sever of multiple sclerosis *P<0.05, **P<0.01

Table 2. Summary of hierarchical regression analyses predicting quality of life (N=193)

Model		β	R^2	Adjusted R^2	F change	df1	df2
1	Age	-0.03					
	Gender	-0.08*					
	Literacy	0.10*					
	Marriage	-0.13*					
	LSES	-0.30**					
	MSES	-0.18					
	SOMHIS	0.00					
	PSYCHIS	-0.00					
	DISDUR	-0.04					
	TRETHIS	0.22**					
TRETTYP	-0.07						
Block 1	–		0.14	0.09	2.69	11	181
2	Stress	-0.16					
	Anxiety	-0.13					
	Depression	-0.26*					
	LSVRT	0.35***					
	MSVRT	0.23**					
	SEVRT	0.22**					
Block2	–		0.53	0.48	23.77	6	175

Note: LSES=Low socioeconomic status; MSES=Moderate socioeconomic status; SOMHIS=Somatic disorder history; PSYCHIS=psychiatry disorders history; DISDUR=disorder duration; TRETHIS=Treatment history; TRETTYP=Treatment type; LSVRT=low severity of multiple sclerosis; MSVRT=Moderate severity of multiple sclerosis; SEVRT=Severity of multiple sclerosis

* $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$

in terms of treatment type, 118 participants were receiving simple and routine treatment (61.1%) only for disease symptom management, and another 75 patients were receiving the complicated treatment (38.9%) for extra symptom management for controlling the serious complication of RRMS.

Before the data analysis with the regression model, initial analyses are performed about probable violation of the assumptions of normality and homoscedasticity, collinearity, multicollinearity, and linearity in the regression analysis. The results indicated no violation in accord with these statistics. Collinearity Statistics including Tolerance with amounts 0.46 to 1, Variance Inflation Factor (VIF) between 1 and 1.54, and the Durbin-Watson Index for rejecting the assumptions of residual correlation with the amount of 1.92, all showed that the assumptions of linear regression analysis is established. Correlation matrix and mean \pm SD among the predictors and the criterion variable is shown in Table 1.

In terms of associations among variables (Table 1), the correlation coefficients among stress, anxiety, depression, and severity of the disorder (lower, moderate, severe) with HRQOL in patients with RRMS were $r = -0.57$, $P < 0.01$; $r = -0.50$, $P < 0.01$; $r = -0.61$, $P < 0.01$; $r = 0.35$, $P < 0.01$; $r = 0.08$, $P > 0.05$ and $r = -0.11$, $P > 0.05$ respectively.

The hierarchical multiple regression analysis is used to examine the contribution of the severity of the disorder (lower, moderate, severe), stress, anxiety, and depression on the quality of life. In addition, treatment type, gender, marital status, literacy, somatic disease history, psychological disease history, disease duration, treatment history, age, and socioeconomic status are included in the model (Table 2). Categorical variables are considered dummy variables in the analysis.

For testing the predictive role of psychosocial and medical factors on HRQOL in patients with RRMS, treatment type, gender, marital status, literacy, somatic disease history, psychological disease history, disease duration, treatment history, age, and socioeconomic status are entered

in model 1. These variables collectively explain 14% of the variance of quality of life in patients with RRMS ($R^2 = 0.14$). Then, the severity of the disorder (low, moderate, severe), stress, anxiety, and depression are entered as main predictors in the analysis in model 2. The findings are shown in model 2, all variables explain about 53% of the variance of quality of life in patients with RRMS ($R^2_{\text{change}} = 0.37$).

In model 1, low SES had a negative coefficient ($\beta = -0.30$, $p < 0.01$), while treatment history had a positive coefficient ($\beta = 0.22$, $p < 0.01$); other variables had no significant relations. In model 2, while we controlled all the variables in model 1, depression had a negative coefficient ($\beta = -0.26$, $p < 0.05$), while severity disorder of MS had positive coefficients in every three levels: lower level ($\beta = 0.35$, $p < 0.001$), moderate level ($\beta = 0.23$, $p < 0.01$) and severe level ($\beta = 0.22$, $p < 0.01$), although the coefficients of beta reduced gradually as severity of the disorder of MS increased (Table 2).

DISCUSSION

According to model 1, the results of this study in prediction of HRQOL in patients with RRMS demonstrate that HRQOL for these patients was significantly influenced by low SES and treatment history; and other psychosocial and medical variables, including age, gender, literacy, marriage status, moderate socioeconomic status, somatic disorder history, psychiatry disorders history, disorder duration, and treatment type had no significant relations with HRQOL in patients with RRMS. While all variables in model 1 are controlled, the results of this study in model 2 demonstrated that HRQOL in these patients is significantly influenced by depression and severity of MS in every three levels of lower, moderate, and severe.

The obtained significant results in this study were consistent with previous findings. In previous studies, lower socioeconomic status had an influential impact on quality of life in patients with MS (19, 33). According to Papuč and Stelmasiak (19), low socioeconomic conditions via increasing the therapeutic costs and psychosocial burden of disease,

may have negative impact on HRQOL in these patients. Similarly, Yamout et al. (1) concluded that lower socioeconomic status predicted the diminished quality of life. Moreover, it can be concluded that poor socioeconomic status somewhat conceals the psychosocial aspects of quality of life dimensions. So, changes in employment status and deterioration in SES by means of progression of disease are the main factors that reduce HRQOL for patients with RRMS. Furthermore, in previous studies, longer and effective treatment history after MS diagnosis was related to increased HRQOL because of hindering the deteriorating changes of disease processes (34–36). Wiendl and Meuth (35) claimed that longtime highly-efficient immune therapies can decrease disability and deterioration in patients with RRMS. In fact, provided early and long-term treatment, especially the most effective therapies for RRMS results in the best consequences of HRQOL.

Interestingly, mainly inconsistent with previous studies (1, 10, 14, 21, 37), age, gender, literacy, marriage status, somatic disorder history, psychiatry disorders history, disorder duration, and treatment type did not have any significant effect on the HRQOL. Papuč and Stelmasiak (19), and Hadgkiss et al. (37) concluded that MS patients with higher age have more deteriorated quality of life than younger ones. Results about gender effects on HRQOL among MS patients were disputable. Casetta et al. (17) concluded that the impact of MS disability on HRQOL was higher for male than female concerning physical performance, social performance, vitality, mental health, and emotional well-being. On the other hand, Casetta et al. (17) concluded that female and male patients with MS don't differ in HRQOL. Marrie et al. (20) stated that higher health literacy is correlated to favorable quality of life in patients with MS. In contrast, one study by Papuč and Stelmasiak (19) revealed that married MS patients with good marital status in comparison with single ones who are without social support have appropriate quality of life. In a systematic review, Marrie et al. (38) concluded that histories of medical and psychiatric disorders or comorbid conditions with RRMS were the leading factors for persistent disability, and deteriorated HRQOL. In addition, incongruously, Hadgkiss et al. (37) and Łabuz-Roszak et al. (10) showed that longer duration of disease reduced the quality of life, and resulted in adverse outcomes. As mentioned before in literature (4, 14), the continuation of MS as a progressive, periodic, and deteriorating neurological disorder is inevitably accompanied by the unfavorable quality of life. The results about the effects of treatment type on the HRQOL in patients with MS are controversial. In one consistent research, Abolfazli et al. (23) revealed that treatment with interferon beta (IFNB) including Avonex or Cinnovex did not influence on HRQOL in patients with MS during a one-year treatment. But, inconsistent with this study, Damal et al. (39) stated that various drug therapies such as interferons, immunomodulation, monoclonal antibodies, glatiramer acetate and dimethyl fumarate have different effects on outcomes of RRMS disease.

Totally, it can be said that in the model 1, low SES and treatment history have significant relations with HRQOL because of these variables pertaining to the main social and structural factors, and disease management than other variables that are studied in this model. Furthermore, it can be claimed that most factors in this model do not predict HRQOL, unlike the most other studies, due to lower sample size, socio-cultural differences in medication adherence, special issues related to study design, different methodology to the other studies, study inclusion and exclusion criteria, and interference of other major predictors in this model such as SES and treatment history.

Similar to the previous investigations (1, 11, 16, 40), depression was strictly correlated with the HRQOL in patients with RRMS. According to the literature, comorbid depression and MS was related to the deteriorated quality of life (5, 16). In separate studies, Glanz et al. (16) and Fernández-Muñoz et al. (8) mentioned that depression deteriorates

HRQOL in patients with MS. Therefore, patients with lower depression had better HRQOL than those with elevated depression. There are some explanations for these outcomes. Depression is a common psychiatric sign in neurological conditions that impact the consequences of these disorders. This result implies that the clinician ordinarily has to assess, treat and consult the patients with MS for depression.

Inconsistent with previous studies (14, 16), anxiety and stress do not have significant relations with HRQOL in this study. Kern et al. (14) showed that diverse psychological distress; including chronic stress, anxiety, and emotional tension have an important impact on diminished HRQOL in patients with MS. Probably, this incompatible result occurred due to the inclusion of depression as a main correlating factor of MS in the model 2. In fact, it is claimed that anxiety and stress loss has effects on HRQOL whereas these variables are accompanied by the depression in the model.

As a last result, the severity of MS in every three levels of low, moderate and severe had significant correlations with HRQOL in patients with RRMS. This finding was consistent with preceding studies (41, 42). This result is supported by Williams et al. (42) who reasoned that symptoms' severity in RRMS has a strong association with HRQOL, and should be taken into account in therapeutic decisions and evaluation of therapeutic outcomes.

This study identified four important factors in deteriorated HRQOL in patients with RRMS: 1) the background and demographic factor (unfavorable socioeconomic situation), 2) the therapeutic factor (absence of effective treatment), 3) psychological factor (more depression), and 4) disease characteristic (higher severity of clinical symptoms). According to the controlling factors affecting the HRQOL in patients with RRMS by excluding the identified influential factors on the quality of life, it would be worthwhile to identify these factors collectively reduce HRQOL in patients with RRMS. These results are new announcements in this statistical population, and are specific findings on this topic. Therefore, these findings imply on careful consideration about socioeconomic status, treatment history, depression, and severity of MS for better management of RRMS consequences. The interpretation that can be extracted from these findings is that patients with low socioeconomic status, decreased treatment history, increased depression, and severity of MS by extending of vulnerability to psychosocial aspects of MS are susceptible to HRQOL deterioration. Thus, initial screening and permanent assessment during the treatment and follow-up for HRQOL promotion are necessary for this group of RRMS patients.

For the better implementing of these outcomes, this study is the initial investigation that aims to find the associations between psychosocial and medical determinants such as psychological, disease-related, socioeconomic, and demographic factors with HRQOL in one Iranian sample with MS. Nonetheless, the results of this study should be interpreted from the perspective of several shortcomings. The cross-sectional design with compliance sampling, gathering data with self-reported instruments, excluding patients with severe psychiatric disorders, the absence of clinical measurement, and small sampling were drawbacks and restrict the generalization of study findings. On account of applicable considerations, we included those of RRMS outpatients with common conditions while inpatients were excluded and this issue might have an impact on the results. Hence, future investigations about inpatients may reveal important realities. In this study, a control group was not included. It is suggested that in subsequent studies, a control group composed of other chronic diseases or healthy people may be used to control for confounders. Finally, as suggested by other authors (43, 44), considering the major determinants of HRQOL in the patient with RRMS can help us to plan valid randomized clinical trials in promoting

the HRQOL and making life better for these patients.

Regarding the new and important results of the study, among studied psychosocial and medical factors of low SES, treatment history, depression, and severity of MS has a consequential role in the prediction of HRQOL in patients with RRMS. Eventually, we can draw the conclusion that unfavorable socioeconomic status, the absence of effective treatment history, elevated depression, and main signs and symptoms might make patients with RRMS more susceptible for decreased HRQOL. Thus, these main factors should be considered during planning and implementation of tailored treatments for improvement of HRQOL in RRMS. Interventions that aim to these factors have the capability to improve HRQOL among RRMS patients. As well, the recognition and management of psychosocial correlates of quality of life in these patients could be more noticeable.

Ethics Committee Approval: Semnan Researches & Sciences University (IRANDOC: 2275318, 21/01/1395)

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