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**Research Article**

# The relationship between treatment adherence and depression in multiple sclerosis(MS) patients;The moderating role of sleep quality

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**Abstract**

**Objective:** This research was conducted to study the role of sleep quality moderators in the relationship between depression and treatment compliance.

**Method:** The research design was descriptive and correlational, and the research population included all patients with multiple sclerosis living in Tehran. 229 subjects with Multiple Sclerosis were selected in a convenient method, and they were asked to answer Morinsky's treatment compliance, Petersburg sleep quality, and Beck's depression questionnaires using the pencil and paper method.

**Results:** Evidence of the predictive role of depressive symptoms for poor adherence to treatment in patients with multiple sclerosis was found. In addition, evidence of the predictive role of sleep quality in treatment adherence was found, but its mediating role in the relationship between depression and treatment adherence was not found.

**Conclusion:** The findings indicated the importance of depression symptoms and sleep quality in the treatment compliance of multiple sclerosis patients. Considering the importance of treatment compliance in the prognosis of the disease, it is suggested that doctors consider this issue to formulate treatment plans to target cognitive and emotional problems parallel to the main treatment of the disease and thereby increase treatment compliance.

**Keywords:** Treatment Compliance, Depression, Multiple Sclerosis, Sleep Quality.

# Extended Abstract


**Background and Objectives**

The primary objective of this research was to investigate the moderating role of sleep quality in the relationship between depression and treatment compliance among patients diagnosed with Multiple Sclerosis (MS). Multiple Sclerosis is a chronic illness that affects the central nervous system, leading to a wide range of physical and cognitive challenges. Due to the progressive nature of the disease, treatment compliance becomes a critical factor in managing its symptoms and improving patients' quality of life. Depression, a common co-occurring condition in MS patients, is known to negatively impact the patient's ability to adhere to treatment regimens. Furthermore, sleep disturbances are frequently reported by MS patients, and poor sleep quality is linked to both depression and treatment non-compliance. Therefore, this study aimed to explore whether sleep quality could moderate the relationship between depression and treatment compliance in MS patients.

**Materials and Methods**

A descriptive and correlational research design was employed for this study, which sought to examine the relationships between depression, sleep quality, and treatment compliance. The study's sample included 229 patients diagnosed with MS, all of whom were living in Tehran, Iran. Participants were selected using a convenience sampling method from several outpatient clinics and rehabilitation centers. The inclusion criteria required patients to have been diagnosed with MS by a neurologist, and the exclusion criteria ruled out individuals with other severe psychiatric disorders or neurological diseases unrelated to MS.

Data collection was done using three standardized self-report questionnaires:

1. Morinsky's Treatment Compliance Scale (MTCS): This scale measures the extent to which patients adhere to prescribed treatment regimens.
2. Pittsburgh Sleep Quality Index (PSQI): This index is used to assess the overall quality of sleep, including factors such as sleep duration, disturbances, and the presence of sleep-related disorders.
3. Beck's Depression Inventory (BDI): The BDI is a widely used tool for measuring the severity of depressive symptoms in individuals.

The participants were asked to complete the questionnaires using a paper-and-pencil method, with the assistance of trained research assistants to ensure accurate data collection. The responses were scored and analyzed to examine the relationship between depression, sleep quality, and treatment compliance.

**Results**

The analysis revealed several important findings. First, depressive symptoms were found to be a significant predictor of poor treatment compliance. MS patients who reported higher levels of depressive symptoms tended to have lower adherence to their prescribed treatment regimens. This finding is consistent with previous research, which has shown that depression in chronic illness can decrease a patient's motivation to follow medical recommendations, potentially exacerbating the condition.

Second, the quality of sleep was also found to have a significant predictive role in treatment adherence. Patients who reported poor sleep quality were more likely to have low treatment compliance. This highlights the importance of sleep in the overall well-being and functioning of MS patients. Poor sleep is often associated with increased fatigue, cognitive impairment, and emotional distress, all of which can interfere with the ability to consistently follow treatment protocols. However, the study did not find evidence supporting the hypothesis that sleep quality serves as a mediator in the relationship between depression and treatment compliance. In other words, while both depression and sleep quality independently predicted treatment adherence, sleep quality did not significantly explain the link between depression and non-compliance. This suggests that although sleep disturbances and depression are related to treatment adherence, other factors may be at play in explaining the connection between depression and compliance.

The results also indicated that while depressive symptoms and sleep quality individually contributed to treatment non-compliance, they did not have a combined or interactive effect that would suggest a more complex relationship. The lack of a moderating effect of sleep quality on the depression-treatment adherence relationship may indicate that depression's impact on treatment compliance is primarily driven by other psychological or social factors, such as cognitive distortions, lack of social support, or poor disease understanding.

**Discussion and Conclusion**

The findings of this study underscore the significant role that both depression and sleep quality play in the treatment adherence of MS patients. Depressive symptoms were found to negatively impact treatment compliance, suggesting that interventions aimed at reducing depressive symptoms may improve adherence to treatment regimens. Given that treatment adherence is crucial for managing MS and improving patient outcomes, healthcare providers should consider integrating psychological support, such as cognitive-behavioral therapy (CBT) or other forms of mental health care, into the treatment plan for MS patients.

Furthermore, the study highlights the importance of sleep quality in the overall treatment compliance process. As poor sleep quality was found to independently predict lower treatment adherence, healthcare providers should also address sleep disturbances as part of the comprehensive care for MS patients. Interventions aimed at improving sleep quality, such as cognitive behavioral therapy for insomnia (CBT-I) or pharmacological treatments for sleep disorders, could potentially enhance patients' ability to adhere to treatment.

Although the hypothesis that sleep quality moderates the relationship between depression and treatment compliance was not supported, the study contributes to our understanding of the complex interplay between these factors. The lack of a moderating effect suggests that future research should explore other potential mediators or moderators, such as cognitive factors, social support, or disease-related factors, that may better explain the relationship between depression and treatment compliance.

In conclusion, the findings of this study have significant implications for clinical practice. Considering the high prevalence of depression and sleep disturbances in MS patients, healthcare providers should adopt a holistic approach to care that addresses both the emotional and physiological aspects of the disease. By improving mental health and sleep quality, clinicians can help enhance treatment compliance and, ultimately, improve the overall quality of life for MS patients. Future research should continue to explore the complex relationships between psychological factors, sleep, and treatment adherence to further refine interventions that can optimize patient outcomes in chronic illness management.

## Introdution

Adherence to long-term treatment can be challenging for those suffering from a chronic disease such as multiple sclerosis. In a widely cited report, the World Health Organization (WHO) stated that only 50% of patients adhere to treatment recommendations. (De Geest & Sabaté, 2003). It is thought that if patients are better able to adhere to treatment regimens for chronic diseases, this will have a higher impact on health outcomes than other treatment advances. Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system that affects more than 2.8 million people worldwide (Walton et al., 2020). MS is characterized by demyelination, inflammation, and neurodegeneration of the brain and spinal cord, which can lead to significant cognitive and physical disability. Based on the course of the disease, different types of MS affect the prognosis and treatment options. Relapsing-remitting MS (RRMS) is the most common form of the disease and accounts for approximately 80-85% of initial diagnoses (McGinley, Goldschmidt, & Rae-Grant, 2021). RRMS is characterized by periods of illness and disability known as relapses, followed by remission.

The clinical course of MS is highly variable, and collaborative decision-making regarding treatment is

essential for effective patient care. Multiple sclerosis remains an incurable disease, and the goal of drug treatment is to reduce debilitating symptoms, slow progression, and protect quality of life. A review of 24 studies that examined treatment adherence in MS found that adherence to disease-modifying drug therapy can be poor, ranging from 41 to 88 percent (Menzin et al., 2013). Although efficacy and compliance vary among different DMD options, and personal preference may be key, adherence is universally poor (Liu, Liao, Wen, & Zhang, 2021). Therefore, in chronic diseases, following the treatment instructions is very important, which is influenced by many factors.

Researchers have found that factors such as old age, female gender, smoking, history of other physical diseases, and cognitive problems affect patients' treatment compliance (Kim, 2009; Kugler, Vlaminck, Haverich, & Maes, 2005; Moist et al., 2008). In addition to all the mentioned factors, two psycho-social factors of depression and perceived low social support from others were also mentioned as the most important predictors of non-compliance with treatment (Karamanidou, Clatworthy, Weinman, & Horne, 2008; Taskapan et al., 2005). Cognitive and emotional difficulties associated with MS are associated with difficulty managing independent activities of daily living, poorer occupational status, and reduced quality of life (Benedict et al., 2005). These cognitive and emotional problems can affect the disease to the extent that they even affect adherence to the treatment. One of the factors affecting adherence to recommended treatments is the emotional state of the MS patient (Alosaimi et al., 2017; Bruce, Hancock, Arnett, & Lynch, 2010).

Patients diagnosed with depression or anxiety are five times more likely to have trouble following a prescribed medication regimen. The prevalence of depression in MS patients has been estimated from 23.7% (Marrie et al., 2015) to 38% (Henry et al., 2019). Such conditions can affect the treatment of primary diseases such as Multiple Sclerosis. A meta-analysis by Fiest et al. showed that both pharmacological treatments and psychological interventions are beneficial in controlling depressive symptoms and also have an effect on the cognitive functions of people with multiple sclerosis (Fiest et al., 2016). The results of various research have shown that the presence of secondary problems, such as depression, affects the prognosis of treatment; in most cases, depression is associated with reduced recovery (Kołtuniuk & Rosińczuk, 2021).

Various studies have reported that the quality of sleep is among the things that are affected by multiple sclerosis (Amtmann, Bamer, Kim, Chung, & Salem, 2018; Hare, Crangle, Carney, & Hart, 2019; Lublin et al. al., 2020). Sleep disturbance is one of the most common symptoms reported among people with MS and can significantly reduce quality of life (Merlino et al., 2009). Significantly, sleep problems affect up to 90% of people with MS and are characterized by subjective feelings of restlessness, lethargy, or tiredness. Insomnia in MS is one of the main factors of unemployment, early retirement, and disability in this population. The assessment and treatment of MS-related sleep problems are particularly challenging because of their multidimensional presentation (e.g., physiological, cognitive, and behavioral). Its inherently subjective nature and overlap with other symptoms and comorbidities make it difficult to study (Veauthier et al., 2013). Sleep disorder—a general term that encompasses a wide range of sleep problems, symptoms, and diagnoses—is also common in people with MS. More than 50% of people with MS have reported sleep disorders or dissatisfaction with it (Beran, Ainley, & Holland, 2008; Côté et al., 2013). Sleep disorders are more common in people with MS compared to the general population and include insomnia, sleep-disordered breathing, restless leg syndrome, and narcolepsy (Brass, Li, & Auerbach, 2014; Čarnická et al.,

2015). ). Such conditions affect the compliance rate of the disease.

Studies have shown that acceptance and compliance are often less than optimal in patients with MS, and such conditions endanger the recovery of the disease, and if another problem coexists with the disease, treatment compliance is less (Sawyer et al. ., 2011; Weaver & Grunstein, 2010) sleep problem is one of these factors that affects treatment adherence and may consistently predict non-adherence to treatment (Crawford, Espie, Bartlett, & Grunstein, 2014; Hiensch, Nandedkar, & Feinsilver, 2016; Weaver & Sawyer, 2010). Considering such conditions, the question arises whether sleep quality problems moderate the relationship between depression and treatment compliance in multiple sclerosis patients or not.

## Method

This research was descriptive and correlational. The statistical population of the study consisted of all patients with multiple sclerosis who lived in Tehran in 1400. After examining and estimating the total number of affected people, the total number of samples was 240 people with multiple sclerosis by considering the average power of 0.8 and the significance level of 0.05 using APIM-POWER software. To enter the research, each of the subjects had to meet conditions that included getting an official diagnosis from a doctor for having multiple sclerosis, 6 months had passed since this diagnosis, and being literate in reading and writing; in addition, the subjects must be in the age range of 20. They were up to 50 years old and had no medical problems that could be diagnosed by a doctor. After checking the inclusion and exclusion criteria, the subjects were determined. The sample was selected in a non-random and available way. Before the research, information about the research was provided to the subjects, and ethical principles such as the freedom to participate and the right to leave the research during the implementation were explained to the subjects. The paper-pencil method was used to perform the test.

The duration of answering the questions was 15 to 60 minutes, considering the conditions of the subjects (2 times that of a healthy person). Questionnaires filled in less than 15 or more than 60 minutes were discarded as outliers. If the subjects did not answer more than 10% of the questions, they were excluded from the study. Finally, 229 questionnaires remained. In addition, before starting the research and sampling, the code of ethics was obtained from the ethics committee in biological research at Shahid Beheshti University.

To implement this, the pencil-paper method was used. Eligible subjects were invited to participate in the research. In addition, the questionnaire included a consent form (representation of research objectives and confidentiality of participants' information) for participating in the study and step-by-step instructions, and in all stages of ethical principles (confidentiality of participants' information, participation in the research without the need to mention names and surnames, etc.) was fully observed. After collecting the data, the data of 229 subjects entered the analysis process. The descriptive data, such as the mean and standard deviation of the main variables and their different dimensions, were calculated using SPSS software version 24. The data of the inferential section were also analyzed using the same software after confirming the assumptions through Pearson's correlation and hierarchical regression. The participants were asked to answer the questionnaires unassisted. Also, in the guidelines of the questionnaires' instructions, it was mentioned that participants should avoid writing their names. The research code of ethics was obtained from the Shahid Beheshti University Ethics Committee under the number IR.SBU.REC.1400.018.

And finally, the subjects were asked to answer the questionnaires without mentioning their names. The following questionnaires were used to collect data.

***1.Morisky therapy adherence questionnaire:*** Moriski's treatment adherence questionnaire has eight questions, seven of which have two points (yes = zero, no = one point), one question has five points (never = zero, rarely = one, sometimes = two, often = three, always = four), and a person who has scored six or higher in this test is considered to have good adherence to treatment (Tan, Patel, & Chang, 2014). In other words, after adding up the points, a score of less than 6 means weak compliance, a score of 6 or 7 means moderate compliance, and a score of 8 equals full compliance (Lair et al., 2012). The Moriski questionnaire was translated by Negarande et al. in 2013, and its validity and reliability were confirmed in Farsi (Qashlaq et al., 2012). The internal reliability of the questionnaire was calculated using Cronbach's alpha in research of 0.81 (Dianti, Mansour, Nejad, & Taghdasi, 2019). Its validity and finality were measured by Koshiar et al. (2012) in Iran, and its Cronbach's alpha coefficient was reported as 68%.

***2.Beck depression inventory (BDI-II):*** The revised form of the Beck depression questionnaire was developed to measure the severity of depression, and compared to its original form, it is more consistent with the fourth edition of the DSM (Jackson, 2016). In addition, all elements of depression that are considered based on Beck's cognitive theory of depression have been discussed in the second edition of this questionnaire. This questionnaire, like its first edition, consists of 21 items and measures the physical, cognitive, and behavioral symptoms of depression. Each item includes four options that are scored from 0 to 3 and determine different degrees of severity of depression symptoms. The maximum score in this questionnaire is 63, and the minimum score is 0. The cutoff points for diagnosing depression in this test are as follows: 0 to 13 = minor depression, 14 to 19 = mild depression, 20 to 28 = moderate depression, and 29 to 63 = severe depression. Beck, Steer, and Brown (2000) have reported the internal consistency of this questionnaire to be 0.73 to 0.92, with an average of 0.86 and an alpha coefficient of 0.86 for the patient group and 0.81 for the non-patient group (Lasa, Iosu Mateus, Vazquez-Barcoro, Diez-Manrique, and Davrik, 2000). The investigations carried out in the field of reliability of this test inform about the appropriate reliability of this test. Grath (1990) reported a retest reliability of 0.48 to 0.86, depending on the time interval between the retest and the type of society (Shafer, 2015).

***3.Petersburg Sleep Quality Questionnaire:*** The Petersburg Sleep Quality Questionnaire is one of the best tools designed and built to measure sleep quality. This questionnaire was developed in 1989 at the Pittsburgh Psychiatric Institute by Dr. Boyce and his colleagues. The Petersburg Sleep Quality Questionnaire has nine main questions, but because question 5 contains 10 sub-questions, the whole questionnaire contains 19 items, which are scored on a 4-point Likert scale from 0 to 3. Dr. Boyce and colleagues (1989) obtained the internal consistency of this questionnaire using Cronbach's alpha of 0.83. In the Iranian version of the Petersburg questionnaire, a reliability of 0.89 and a validity of 0.86 have been obtained (Ehtshamzadeh and Marashi, 2019). In general, a score higher than five on this questionnaire means poor sleep quality (Bois et al., 1989). This index was designed by Boyce et al. with a sensitivity of 89.6%, a specificity of 86.5%, and a validity of 0.88% in 1989. This questionnaire is also a valid tool in Iran, and its validity and reliability have been investigated in various research (Hossein Abadi et al., 2017). Its validity and reliability have been

determined as R=0.88 and R=0.84, respectively, through retesting.

## Results

In the first step, the findings were analyzed descriptively. The results showed that 53% of the participants in this research were in the age group of 30 to 40 years, 24% in the age group of 40 to 50 years, and 22% in the age group of 20 to 30 years. In addition, 59% of the participants in this research were married, and 41% were single. It should be noted that due to the design of only two options for this descriptive variable, it is assumed that divorced or widowed people are among single people. On the other hand, 75.1% of the subjects were female, and 24.9% of the subjects were male. The subjects were also examined in terms of education, and the results showed that 39.7% of the participants had a bachelor's degree, 34.5% had a diploma, 21% had a master's degree, and 4.8% had a doctorate. The subjects were also examined for their history of multiple sclerosis. 68% of people under 10 years old, 29% of people between 10 and 20 years old, and 3% of people over 20 years old had a history of receiving an official diagnosis of multiple sclerosis. The second step was to examine research findings in terms of inferential statistics. To use parametric methods, it is necessary to check the specific assumptions of each test. To check the relationship, Pearson's correlation was used, and before using Pearson's correlation, Smirnov's K-S test was used to check the normality of clinical data distribution. And the results indicated that this test was not significant ($p>0.01$). On the other hand, the skewness and elongation indices were also checked, and the amount of the above indices was in the range of $+1 > x > -1$, so the assumption of normality of the data was confirmed. After confirming the assumption of normality, Pearson's correlation was used to check the relationship, and its results are shown in Table 1.

**Table 1-** Correlation matrix of clinical data

| | 1 | 2 | 3 |
|---|---|---|---|
| Treatment adherence | 1 | | |
| Depression | 309/0- | 1 | |
| Sleep quality | 26/0- | 39/0 | 1 |

The findings are statistically significant at the 0.05 level.

The findings in Table 1 show evidence of the relationship between treatment compliance with depression and sleep quality. This relationship was negative for treatment adherence with depression and negative for sleep quality with treatment adherence, and, therefore, it can be argued that the increase in depression scores is associated with a decrease in treatment adherence; on the other hand, the relationship between treatment adherence and sleep quality is direct, and it seems that the increase in the score in the quality scale Sleep, which is associated with increased sleep quality, is associated with increased treatment compliance. To investigate the moderating role of executive functions in the relationship between treatment adherence and depression, stepwise regression analysis was used. To use regression

analysis, its presuppositions were checked, and after confirming the normality of the distribution of clinical data, the multicollinearity index of predictor variables was checked. In examining the indices of special values, Status index, and variance ratio, large numbers were not observed in the analysis of predictor variables. The VIF index is less than 2 for each dimension. Therefore, it can be concluded that there is no multiple co-collinearity between the predictor variables included in the model, and this assumption was confirmed. The results of this assumption are listed in Table 2.

**Table 2-** Examining the presence/absence of multiple collinearity between variables

| | Unstandardized coefficient | | standardized coefficient | t | sig | Collinear statistic | |
|---|---|---|---|---|---|---|---|
| | Std | B | B | | | Endurance index | VIF |
| constant | 64/1 | 35/2 | - | 12/3 | 01/0 | - | - |
| Depression | 24/0 | 43/1 | 56/0 | 76/5 | 01/0 | 67/0 | 98/0 |
| Sleep quality | 18/0 | 22/0 | 45/0 | 21/3 | 03/0 | 84/0 | 17/1 |

The findings are statistically significant at the 0.05 level.

According to Table 2, the tolerance statistics for both variables are close to one, which indicates the absence of colinearity between the variables. The assumption related to the independence of errors was also examined using the Durbin-Watson test, and the results confirmed this assumption.

To investigate the role of the moderator, stepwise regression was used, and in the case that the relationship between the first and second variables changed significantly by adding the third variable, the third variable was selected as the moderator. To investigate the hypothesis of the moderating role of executive functions in the relationship between treatment adherence and depression, the variables were analyzed by stepwise regression. In the present study, the findings supported the moderating effect of executive functions in the relationship between depression and adherence to treatment. Therefore, in line with the suggestion of Baron and Kenny (1986), in each linear hierarchical regression analysis design, in the first order, the predictor variable (depression), in the second order, the moderating variable (executive functions), and in the third order, the interaction between the predictor variable and the moderating variable were entered into the equation. In other words, in line with the logic proposed by Baron and Kenny (1986), before analyzing the data, the dispersion pattern between the depression variable and executive functions was tested based on the change in the quantitative measures of the treatment adherence variable.

The results in this section showed that the relationship between depression variables and adherence to treatment based on changes in executive functions was linear. To determine the presence or absence of interaction between depression variables and sleep quality in predicting treatment adherence, a hierarchical regression analysis was used. Therefore, in the first order, the depression variable, in the second order, the

sleep quality variable, and in the third order, the interaction between depression and sleep quality were entered into the regression equation. The results are shown in Table 3.

**Table 3-** Stepwise regression analysis to predict treatment adherence through depression and interaction between sleep quality variables

| Model | variable | B | Beta | t | sig |
|---|---|---|---|---|---|
| 1 | constant | 24/9 | | 06/34 | 01/0 |
| | depression | 16/0- | 30/0- | 90/4- | 01/0 |
| 2 | constant | 00/11 | | 04/17- | 01/0 |
| | Depression | 034/0- | 16/0- | 85/20- | 03/0 |
| | Sleep quality | 03/0- | 04/0 | 71/0 | 04/0 |
| 3 | constant | 89/10 | | 37/15 | 01/0 |
| | Depression | 031/0- | 139/0- | 37/1- | 17/0 |
| | Sleep quality | 01/0 | 01/0 | 11/0 | 91/0 |
| | Depression /Sleep quality | 01/0- | 12/0- | 68/0- | 49/0 |

The findings are statistically significant at the 0.05 level.

The moderating role of the variable of executive functions for depression and adherence to treatment was calculated using the hierarchical regression method. In the first step, the beta value of depression on adherence to treatment was calculated, and the obtained coefficient was negatively significant ($P < 0.05$, Beta -0.30). This result shows that depression is a negative predictor of treatment compliance. In the second step, the variable of executive functions is also included in the regression equation, and its regression coefficient is significant (Beta=0.04, $P<0.05$). This result shows that sleep quality is a predictor of treatment compliance. In the third step, the interaction of depression and executive functions is also entered into the equation, and it is observed that the interaction is not significant ($P>0.05$, -0.12), meaning that there is no moderating effect. As a result, the sleep quality subscales were included in the study and are listed in Table 4.

**Table 4-** Statistical indices and results of regression analysis related to the moderating role of subscales of executive functions in the relationship between depression and treatment adherence.

| | coeff | SE | t | sig |
|---|---|---|---|---|
| Constant | 82/11 | 77/0 | 28/15 | 01/0 |
| Depression | 46/0- | 01/0 | 63/2- | 01/0 |
| Subjective quality of sleep | 33/0 | 17/0 | 95/2 | 05/0 |
| Delay in falling asleep | 20/0 | 17/0 | 22/1 | 22/0 |
| Sleep duration | 24/0 | 16/0 | 15/10 | 03/0 |

| | | | | |
|---|---|---|---|---|
| Sleep efficiency | 09/0- | 15/0 | 61/0- | 53/0 |
| Sleep disorders | 07/0 | 28/0 | 27/0 | 78/0 |
| Sleeping medicine | 03/0- | 14/0 | 22/0- | 82/0 |
| Daily dysfunction | 37/0- | 20/0- | 87/2- | 04/0 |

Table 4 examines the significance of sleep quality and depression subscales and their relationship with treatment adherence. The results of this table showed that depression will still be able to predict treatment adherence ($p<0.01$). Therefore, evidence of decreased adherence to therapy was found in multiple sclerosis patients with worsening depression. On the other hand, evidence showed that daily dysfunction was a negative predictor of adherence to treatment, and sleep duration and mental quality of sleep were positive predictors of adherence to therapy.

## Discussion and Conclusion

The present study was conducted to investigate the role of sleep quality moderators in the relationship between treatment adherence and depression symptoms in multiple sclerosis (MS) patients. The findings of the research indicated that depression is a predictor of treatment compliance in patients with multiple sclerosis. The evidence showed that with the increase in scores in patients, the rate of adherence to treatment decreases. In line with our research findings, Ahrari et al. (2014) showed that with the exacerbation of depression symptoms in patients, the treatment compliance rate decreases (Ahrari, Tougian Chaharsoghi, Basiri Moghadam, Khodadoost, & Mohtsham, 2015). In another study, Omrani Fard et al. (2015) examined the relationship between the severity of depression and the rate of treatment adherence. In their research, they showed that the degree of patient compliance with treatment depends to a large extent on the severity of depression, however, high anxiety was associated with greater treatment compliance. They considered it necessary to pay more attention and focus on the treatment of depression along with the treatment of the main disease (Omrani Fard et al., 2017). In another study, Khalili, Eslami, Farajzadegan, and Hassanzadeh (2013) examined the relationship between psychosocial factors and treatment compliance behaviors of patients. In their research, they showed that there was no relationship between the examined psycho-social factors and the overall treatment compliance behaviors, but a significant relationship was observed between these factors and the behavioral subscales. In this study, Khalili and colleagues concluded that people's understanding of therapeutic behaviors is a factor that affects the relationship between treatment adherence and depression (Fateme Khalili, Ahmad Ali Eslami, Ziba Farajzadegan, & Akbar Hassanzadeh, 2013).

In other words, a person's perception of therapeutic behaviors affects the relationship between depression and treatment compliance. Therefore, it seems that the person's perception that the treatment changes the person's prognosis and finally determines the person's disease in the future has been considered important. In their research, Naderi, Sekaki, and Hafazi (1402) showed that depression is related to treatment adherence, but this relationship is mediated by the quality of the disease. In other words, the stage of the disease that a person is in determines the degree of treatment compliance. In such a way that when a person has reached the stage of the disease that becomes worse day by day, the level of adherence to treatment decreases (Sakaki, Naderi, & Hafez, 2023). The research findings of Carlos et al. (2023) also indicated that the presence of mental disorders in a person, especially mood disorders, is associated with poor adherence to treatment in patients with chronic

disorders. Therefore, it is concluded that depression has an inverse relationship with treatment compliance; however, the condition in which the patient is located and the person's perception of treatment measures have an effect on treatment compliance.

The moderating role of sleep disorders was also investigated. The results showed that sleep quality in general has a relatively weak relationship with treatment compliance, and the examination of sleep quality subscales indicated that daily sleep problems, sleep cycles, and daily function loss were related to treatment compliance. Everyday problems and functional decline were negative predictors of treatment compliance, and patients with high scores in daily challenges and potential functional decline reported poor therapeutic compliance, and in cases where the subjects reported regularity in sleep periods. They reported that their treatment compliance rate also increased, and under conditions where there was no daily sleep routine, patients reported that they had low treatment compliance. Of course, these cases have been examined in the context of correlation, and no causal relationship should be inferred. Marta Dittmer et al. (2021) showed in their research that sleep problems in patients with chronic diseases predicted a poor prognosis in addition to poor adherence to treatment. In their study, they considered the relationship between illness and sleep to be a two-way relationship, and the aggravation of one will affect the other. In line with our research findings, the report of the World Health Organization (2019) also indicated that sleep problems, if they appear with another disease, will affect the treatment of the main disease. The research findings of Reimer and Fleming (2003), Richer, Milnes, and Aqualens (1997), and Vitkova et al. (2016) also showed that sleep problems affect treatment adherence, in line with our findings. Fatahzadeh Ardalani and his colleagues (2020) also pointed out that MS disease is inherently associated with sleep problems, and trying to treat patients with MS without paying attention to sleep problems is associated with failure, so it is recommended to Paying attention to the problems of multiple sclerosis should also pay attention to the quality of sleep of the patients.

Finally, it can be concluded that mood disorders and problems related to the quality of sleep are associated with poor treatment compliance in MS patients; such conditions can affect the recovery of the disease, and it is necessary to improve the quality of sleep and mood problems.

**Contribution of authors**

Each of the authors had an equal share in the implementation, editing, and writing the article. The article was taken from the research conducted in the Psychology Department of the Faculty of Educational Sciences and Psychology of Shahid Beheshti University.

**Conflict of interest**

This article was done at the personal expense of the authors and has no conflict of interest.

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