

The effect of social support, depression, and illness perception on treatment adherence in patients with multiple sclerosis

Derya GIRGIN¹, Zeynep TOSUN², Nilda TURGUT³, Sibel GULER⁴

¹ Neurology Clinic, Tekirdağ Namik Kemal University Hospital, Tekirdağ, Turkey.

² Department of Nursing, Tekirdağ Namik Kemal University Health College, Tekirdağ, Turkey.

³ Department of Neurology, School of Medicine, Tekirdağ Namik Kemal University, Tekirdağ, Turkey.

⁴ Department of Neurology, School of Medicine, Trakya University, Edirne, Turkey.

Corresponding Author: Zeynep Tosun

E-mail: ztosun@nku.edu.tr

Submitted: 21.01.2022

Accepted: 05.04.2022

ABSTRACT

Objective: This study was planned to determine the treatment adherence levels of multiple sclerosis (MS) patients and the factors affecting treatment adherence.

Patients and Methods: This descriptive and cross-sectional study was conducted with 211 people with MS. Data for this study was obtained through face-to-face interviews with MS patients who presented at the neurology outpatient clinics of two university hospitals between April and October 2018. The “Morisky, Green, and Levine Adherence Scale”, “Beck Depression Inventory”, “Multidimensional Perceived Social Support Scale”, and the “Illness Perception Scale” were used in data collection.

Results: The mean age of the sample was 40.03±10.82, and 70.1% were female. Treatment adherence was not good in half of the patients (51.7%). Patients with good adherence were found to have higher Multidimensional Perceived Social Support Scale scores ($p<0.01$) and lower Beck Depression Inventory scores ($p<0.01$). The illness perceptions of the patients regarding MS did not affect treatment adherence ($p>0.05$).

Conclusion: Treatment adherence was insufficient in half of the MS patients. According to our findings, ensuring more cooperation with the families of patients, which constitute the strongest source of social support, increasing treatment adherence can be suggested as well as screening patients with regard to depressive symptomatology during follow-up.

Keywords: Multiple sclerosis, Treatment adherence, Social support, Depression, Illness perception

1. INTRODUCTION

Multiple Sclerosis (MS) is the most widespread chronic neurological disorder causing disability among young adults, and it is estimated to affect 2.2 million people worldwide with a prevalence of 33 per hundred thousand [1]. MS prevalence has been calculated to be between 19 and 288 per hundred thousand in Turkey [2-5]. In recent years, the incidence of the disease has been increasing, especially among women [6].

Although, full recovery from MS is not possible today, medical treatment is important with regard to decreasing disability and slowing down progression. Obtaining the expected result from these medicines applied in differing forms is only possible through regular and continuous use of the medicines, in other terms, ensuring “treatment adherence” [7,8].

The fatigue and weariness brought about by long term use of medicines in chronic diseases is one of the most important obstacles for treatment adherence. Alongside this, problems that may vary with the disease and the medicine used may affect treatment adherence. The frequency and method of medication application, the logistical difficulties of obtaining medicine depending on social security status or place of residence, and regulations regarding the funding of medicine can also be listed as factors affecting treatment adaptation in MS, just as in any other chronic disease. In addition to those problems, the severity of the disease, emerging cognitive problems, and depressive mood in MS all make continuing treatment more difficult, and factors such as fear of injection, injection area reactions, and side effects of medications can affect treatment

How to cite this article: Girgin D, Tosun Z, Turgut N, Guler S. The effect of social support, depression, and illness perception on treatment adherence in patients with multiple sclerosis. *Marmara Med J* 2022; 35 (3): 323-329, doi: 10.5472/marumj.1192560

satisfaction. Additionally, the treatment of MS being directed towards delaying poor prognosis and an insufficient perception of medicine efficiency can affect patient motivation negatively in MS in a manner differing from most chronic diseases [8-10].

The factors affecting treatment satisfaction in MS change alongside changing treatment options, changing treatment satisfaction levels in turn affect medication adherence, and a need to periodically evaluate medication adherence thus arises.

Treatment adaptation in MS is a multidimensional concept, and it is difficult to evaluate. While treatment adherence can be promptly evaluated using measurable objective parameters such as blood sugar, blood pressure, or HbA1C levels in other chronic diseases, there are no measurable parameters indicating treatment adherence in MS. Thus, the treatment adherence levels of individuals with MS can only be evaluated using standardized scales.

The aim of this study was to evaluate the attitudes of MS patients regarding medication adherence using standardized evaluation tools and to examine the effect of certain factors discussed in a small number of studies such as perceived social support and illness perception on treatment adherence. The findings of the study may contribute to planning efforts to increase treatment adherence.

2. PATIENTS and METHODS

This study was conducted as a cross-sectional research. Data for the study was obtained through face-to-face interviews with patients who presented at the neurology outpatient clinics of two university hospitals in the cities of Edirne and Tekirdag between April and October 2018.

Patients were invited to the study consecutively according to the time of admission to the outpatient clinic. Two hundred eleven patients who were 18 years of age or above, had been receiving treatment for MS for at least 6 months, had no communication problems, and signed the informed consent form were included in the study.

Data Collection Tools

Data were collected by use of a patient information form including socio-demographic, disease and treatment related characteristics of the patients, which was developed by the researchers. Also the four-item "Morisky, Green, and Levine Adherence Scale (MGLS)", the "Beck Depression Inventory (BDI)", the "Multidimensional Perceived Social Support Scale (MPSS)", and the "Revised Illness Perception Scale (RIPS)" were used for data collection.

The Morisky, Green, and Levine Adherence Scale (MGLS)

This scale was developed by Morisky, Green, and Levine [11]. The scale consists of four closed ended items with two choices each. The questions are answered as "yes" or "no". Adherence was classified as high if all four questions were answered as "no", moderate if one or two questions were answered as "yes", and

low if more than two questions were answered as "yes". Patients with moderate or low adherence were considered non-adherent [11]. In this study, the Cronbach alpha coefficient of the scale was calculated to be 0.829.

The Revised Illness Perception Questionnaire (IPQ-R)

The scale was developed by Weinmann et al. [12] and revised by Moss-Morris et al. [13]. The revised illness perception questionnaire (IPQ-R) was tested for the validity and reliability in Turkish by Kocaman et al. [14]. The IPQ-R consists of three sub-dimensions: illness identity, illness perception, and causes of the illness. The illness identity is questioned through 14 items, illness perception is questioned through 38 items, and the causes of the illness are questioned through 18 items. The identity of the illness is determined by asking the patients whether they have experienced the symptoms on the scale and whether they find these symptoms related to the illness. In the identity of the disease, each experienced and associated symptom is scored as "1". The illness perception comprises seven dimensions: timeline acute/chronic, timeline cyclical, consequences, personal control, treatment control, illness coherence, and emotional representations. The causes of the illness are sub divided into psychological characteristics, immune disorders, external risk factors, and accident/luck. Illness perception and the causes dimensions of the illness are evaluated with a 5-point Likert scale [13]. In our study, the Cronbach's alpha value of the illness perception dimension of the scale was calculated as 0.672.

The Multidimensional Scale of Perceived Social Support (MSPSS)

This scale was developed by Zimet et al. [15]. and tested for validity and reliability in Turkish by Eker et al. in 1995 [16]. The scale was revised for its cultural adaptation [17]. The scale consists of four items each in the family, friends, and significant other categories, for a total of 12 items. The scores that can be attained from the scale vary between 12 and 84, and higher scores indicate higher perceived social support. In this study, the Cronbach alpha value of the scale was found to be 0.897.

The Beck Depression Inventory (BDI)

This scale was developed to measure the bodily, emotional, cognitive, and motivational symptoms seen during depression [18]. There are 21 symptom categories in the scale, each scored between 0 and 3. The total depression score is obtained by the sum of these scores. Higher total scores indicate higher levels of depressive symptomology. The validity and reliability study of the Turkish form of the scale was performed by Hisli [19]. In this study, the Cronbach alpha value of the scale was found to be 0.919.

Local ethical board permission from Namık Kemal University, School of Medicine was taken before the study (Decision number: 2018/51/03/24). The volunteers who participated in the study were informed of the aim of the study by the researcher and gave consent. The principles of the Helsinki Declaration were upheld throughout the study.

Statistical Analysis

The SPSS (IBM, v.21,0) package program was used for statistical analyses. Descriptive statistical methods (numbers-percentages, mean, median, minimum and maximum) were used in the evaluation of study data. The internal consistency analyses of the scales used in the study were performed using the Cronbach alpha coefficient. The difference between nominal variables was determined using the Chi-square test. Since, Kolmogorov Smirnov test showed that data did not comply with normal distribution, the difference between continuous variables was calculated using Mann Whitney U or Kruskal Wallis test. The level of statistical significance was taken as $p < 0.05$.

3. RESULTS

The mean age of the 211 individuals with MS who constituted the sample was 40.03 ± 10.82 , and 70.1% were female. In 88.2% of the patients ($n=186$), the clinical type of the disease was Relapsing-Remitting Multiple Sclerosis (RRMS). The mean time from diagnosis in patients was calculated as 8.05 ± 6.29 years. More than half of the patients (54.3%) were using subcutaneous (SC) medications. 68.7% of the patients considered their treatment schedule as easy regarding the frequency and type of application (Table I).

Table I. The effect of clinical variables on treatment adherence

Variables	All groups	Perfect (high) adherence (MGLS=0)	Insufficient (medium and low) adherence (MGLS=1-4)	P-Value
Age, year				
Mean±SD	40.03±11.11	39.16±10.46	39.39±11.55	0.514 ^a
Median (Min-Max)	40.0 (18.0-71.0)	40.0 (20.0-69.0)	40.0 (18.0-71.0)	
Gender				
Female, n (%)	148 (70.1)	73 (49.3)	75 (50.7)	0.387 ^b
Male, n (%)	63 (29.1)	29 (46)	34 (54)	
MS type				
RRMS, n (%)	186 (88.2)	91 (48.9)	95 (51.1)	0.402 ^b
SPMS/PPMS, n (%)	25 (11.8)	11 (44.0)	14 (56.0)	
Disease duration, year				
Mean±SD	8.05±6.29	6.45±5.11	8.72±6.70	0.052 ^a
Median (Min-Max)	5.0 (0.6-29.0)	5.0 (0.6-20.0)	7.0 (1.0-29.0)	
Relapses within last year				
Mean±SD	0.89±0.99	0.87±0.94	0.92±1.08	0.932 ^a
Median (Min-Max)	1.0 (0.0-5.0)	1.0 (0.0-5.0)	1.0 (0.0-5.0)	
Attendance at outpatient clinic				
Regular, n (%)	200 (94.8)	100 (50)	100 (50)	0.038 ^{ab}
Irregular, n (%)	11 (5.2)	2 (18.2)	9 (81.8)	
Number of outpatient clinic visit (last year)				
Mean±SD	5.37±3.32	5.30±3.37	5.51±3.47	0.245 ^a
Median (Min-Max)	4.0 (0.0-12.0)	4.0 (0.0-12.0)	4.0 (1.0-12.0)	
Hospitalization for MS				
Yes, n (%)	193 (91.5)	88 (45.6)	105 (54.4)	0.008 ^{**b}
No, n (%)	18 (8.5)	14 (77.8)	4 (22.2)	
Route of medication administration				
Oral, n (%)	87 (41.2)	43 (49.4)	44 (50.6)	0.451 ^b
Parenteral, n (%)	124 (58.8)	59 (47.6)	65 (52.4)	
Frequency of s.c.injection				
3-4 times a week, n (%)	95 (82.6)	37 (38.9)	58 (61.1)	0.011 ^{ab}
Once a week, n (%)	20 (17.4)	14 (70.0)	6 (30.0)	
Person applying s.c. injection				
Self-injection, n (%)	88 (77.2)	39 (44.3)	49 (55.7)	0.938 ^c
By someone else, n (%)	19 (16.7)	9 (47.4)	10 (52.6)	
Changeable, n (%)	7 (6.1)	3 (42.9)	4 (57.1)	
Perception of treatment program				
Complicated, n (%)	66 (31.3)	26 (34.9)	40 (60.6)	0.054 ^b
Simple, n (%)	145 (68.7)	76 (48.3)	69 (51.7)	
The last major treatment change, year				
Mean±SD	3.79±3.76	3.18±3.29	4.35±4.20	0.048 ^{*a}
Median (Min-Max)	2.0 (0.0-20.0)	2.0 (0.0-19.0)	3.00 (0.5-20)	

* $p < 0.05$; ** $p < 0.01$; SD: Standart deviation; Min: Minimum; Max: Maximum; MGLS: Morisky, Green, and Levine Adherence Scale; ^aMann-Whitney U test; ^bChi-square test; ^cFisher chi-square test;

Treatment adherence was not good in half of the patients (51.7%) (Fig. 1). The mean score of the MS patients from the MGLS was 0.78 ± 0.90 .

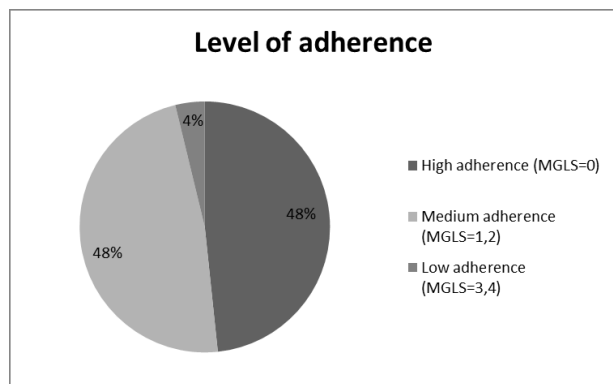


Figure 1. The patients' level of adherence; MGLS: Morisky, Green, and Levine Adherence Scale

Treatment adherence did not vary according to age or sex among the patients, and neither was it affected by type of MS, disease duration, number of attacks, number of outpatient clinic visit, route of medication administration, person applying the SC injection, or perception of difficulty in the treatment program. The application frequency of SC injections, on the other hand, was seen to be an important variable in treatment adherence ($p < 0.05$). Patients with poor adherence were found to miss out on their outpatient clinic visit more compared to patients with good adherence, and have to be hospitalized more ($p < 0.05$), (Table I).

Multiple sclerosis patients with poor treatment adherence stated forgetfulness (46%) to be the most important reason behind this situation (Fig 2).

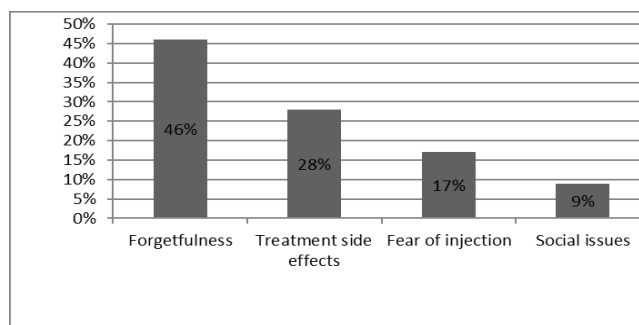


Figure 2. Causes of non-adherence to treatment ;Note:More than one reason has been chosen

In the illness perception evaluation, the MS patients were found to complain most about fatigue (87.2%), and hold psychological reasons responsible for the presence of their disease (Not included in Tables).

The effect of illness perception on treatment adherence among MS patients could not be shown ($p > 0.05$). The strongest source of social support among the MS patients was "family". Patients with good treatment adherence had higher MSPSS scores ($p < 0.01$) and lower BDI scores ($p < 0.01$), (Table II).

Table II. Depression, social support, and illness perception according to treatment adherence

	All groups	High adherence (MGLS=0) n=102	Medium adherence (MGLS=1-2) n=101	Low adherence (MGLS=3-4) n=8	P Value
IPQ-R					
Consequences					
Mean±SD	19.06±5.26	18.49±5.11	19.73±5.22	18.00±7.19	0.211 ^d
Median (Min-Max)	19.0(6.0-30.0)	18.0(6.0-30.0)	2.0(9.0-29.0)	18.5(10.0-30.0)	
Timelineacute/chronic					
Mean±SD	22.56±4.75	22.45±4.55	22.89±4.76	19.87±7.03	0.315 ^d
Median (Min-Max)	23.0(6.0-30.0)	22.5(11.0-30.0)	24.0(6.0-30.0)	21.5(10.0-30.0)	
Personal control					
Mean±SD	20.19±3.82	19.84±3.76	20.56±3.96	20.12±3.44	0.567 ^d
Median (Min-Max)	20.0(10.0-30.0)	20.0(10.0-27.0)	21.0(10.0-30.0)	20.0(16.0-27.0)	
Treatment control					
Mean±SD	17.82±3.89	17.96±3.88	17.85±3.75	15.87±5.51	0.634 ^d
Median (Min-Max)	18.0(7.0-25.0)	18.0(8.0-25.0)	18.0(7.0-25.0)	17.0(7.0-23.0)	
Illness coherence					
Mean±SD	17.31±4.07	17.45±4.09	17.11±4.00	18.00±4.95	0.745 ^d
Median (Min-Max)	17.0(7.0-25.0)	17.0(7.0-25.0)	17.0(9.0-25.0)	18.0(9.0-25.0)	
Timelincyclical					
Mean±SD	13.78±3.46	13.59±3.67	13.93±3.29	14.25±3.05	0.677 ^d
Median (Min-Max)	14.0(4.0-20.0)	14.0(4.0-20.0)	14.0(4.0-20.0)	15.5(7.0-16.0)	
Emotional representations					
Mean±SD	18.91±5.71	19.05±5.73	18.90±5.68	17.37±6.30	0.629 ^d
Median (Min-Max)	20.0(6.0-30.0)	19.0(6.0-30.0)	20.0(6.0-29.0)	16.5(10.0-30.0)	

Table II. (Continued)

MSPSS					
MSPSS total					
Mean±SD	64.79±16.53	69.52±14.20	60.48±17.33	58.87±19.18	0.000** ^d
Median (Min-Max)	69.0 (18.0-84.0)	74.0 (27.0-84.0)	61.0 (18.0-84.0)	61.5 (36.0-81.0)	
MSPSS-FA					
Mean±SD	24.87±4.76	25.68±4.16	24.01±5.12	25.25±6.25	0.007** ^d
Median (Min-Max)	27.0 (5.0-28.0)	28.0 (7.0-28.0)	26.0 (5.0-28.0)	28.0 (10.0-28.0)	
MSPSS-FR					
Mean±SD	20.65±7.28	22.40±6.36	19.15±7.61	17.37±9.41	0.002** ^d
Median (Min-Max)	23.0 (4.0-28.0)	25.0 (6.0-28.0)	21.0 (4.0-28.0)	19.5 (4.0-28.0)	
MSPSS-SO					
Mean±SD	19.20±8.13	21.37±7.23	17.25±8.42	16.25±8.90	0.001** ^d
Median (Min-Max)	21.0 (4.0-28.0)	24.0 (4.0-28.0)	17.0 (4.0-28.0)	19.0 (4.0-28.0)	
BDI					
BDI score					
Mean±SD	13.10±10.28	9.00±8.74	16.73±10.40	20.33±3.77	0.003** ^d
Median (Min-Max)	11.0 (0.0-42.0)	7.5 (0.0-42.0)	17.0 (0.0-41.0)	19.0 (17.0-25.0)	

* $p < 0.05$; ** $p < 0.01$; SD: Standard deviation; Min: Minimum; Max: Maximum; ^aKruskal-Wallis Test; ^bThe difference was between patients with high adherence and medium adherence according to Tukey's post hoc analysis; MGLS: Morisky, Green, and Levine Adherence Scale; MSPSS: Multidimensional Scale of Perceived Social Support; MSPSS-FA: MSPSS Family; MSPSS-FR: MSPSS Friends; MSPSS-SO: MSPSS Significant Other; BDI: Beck Depression Inventory; IPQ-R: Revised Illness Perception Questionnaire

4. DISCUSSION

Adherence with treatment is important in slowing the progression of MS and improving the patient's quality of life, and therefore factors that may affect adherence should be investigated.

In our study, 48.3% of the individuals with MS were seen to exhibit good treatment adherence. While only patients receiving parenteral treatments are included in some studies evaluating treatment adherence, other studies include all administration methods including oral and parenteral administration in a manner similar to our study. In a study conducted with 198 patients in Turkey using the Multiple Sclerosis Treatment Adherence Questionnaire, 59.6% of the patients were found to adhere to their disease-modifying therapy. In that particular study, oral medication adherence was not evaluated [10]. In another study conducted in the Turkish society with 219 MS patients, the facts that SC interferon treatments were skipped four times a month, glatiramer acetate treatments were skipped six times a month, and IM interferon treatments skipped once a month were considered poor treatment adherence by the authors. In that particular study, while 53% of the RRMS group and 52% of the SPMS group had good treatment adherence, 24.9% of the patients completely abandoned their treatments [9]. In a multinational evaluation, 75% of 2648 MS patients receiving SC and IM treatments were found to have good treatment adherence [20], while 71% of 157 MS patients receiving oral and/or parenteral treatments were found to have good treatment adherence in a study conducted in Spain [21], and 48% of 188 patients receiving immune modulators were found to have good treatment adherence in a study conducted in Brazil [22].

The difference in the methods of evaluating treatment adherence may be held responsible for the variance in results to a degree. For example, although 3.8% of the patients were categorized as having poor treatment adherence and 47.9% were categorized

as having medium treatment adherence according to the MGLS in our study, 27.5% of the patients answered "yes" when the researchers asked the question "Do you think you have poor treatment adherence?" As it can be seen from this example, the use of standardized evaluation scales can contribute to more objective and comparable results.

The effects of MS type, disease duration, number of attacks, outpatient clinic visit frequency, the person performing the SC injection, or the perceived difficulty of the treatment schedule of the patient on treatment adherence could not be shown in this study. While Rio et al., did report higher rates of low treatment adherence among SPMS patients [23], most studies could not find a relationship between treatment adherence and type of MS [9,10,21]. Treatment adherence in subcutaneously administered medications has been found to be lower compared to medications administered orally or through IV infusion [24]. In our study, while whether the medication was administered through oral or parenteral means did not affect treatment adherence, the frequency of SC injections did. Treatment adherence was better among those receiving weekly SC injections compared to those receiving 3-4 SC injections a week.

Our results Show that patients who missed their outpatient clinic visits were found to have low treatment adherence. The importance of regular outpatient clinic attendance for treatment adherence has been previously emphasized in the literature [22,25]. Since, the reasons behind missing outpatient clinic visits and having poor treatment adherence may overlap, questioning the reasons behind missing outpatient clinic appointments may contribute to increasing treatment adherence.

In our study, patients hospitalized were shown to have lower treatment adherence, and this finding was interpreted as low treatment adherence negatively affecting disease progression.

The cost of inpatient treatment to the health care system is another important dimension of low treatment adherence.

In this study, 46% of the patients stated forgetfulness to be the primary reason behind poor treatment adherence. Forgetfulness has been shown as an important reason behind low treatment adherence in MS in the literature as well [10,20,21,26]. A third of MS patients experience injection related problems such as exasperation caused by long term injection applications, pain in the injection area, injection related anxiety, and skin reactions [20]. In our study, 28% of the patients stated that they experienced treatment adherence difficulties because of the side effects of medications.

Treatment adherence among MS patients is a multifactorial concept. The chronic nature of the disease, the prognosis of the disease, variances in disease progression all constitute the component of illness perception [12,13]. It is known that MS patients who accept their disease are better in terms of adherence to treatment [27]. Illness perception was considered as a predictor for treatment adherence. However, illness perception was found not to affect treatment adherence among MS patients in this study.

Social support is very important in coping with chronic diseases and ensuring treatment adherence. In our study, the importance of social support for treatment adherence among MS patients was shown. While the strongest source of social support for our sample was "family", the weakest source was "significant others". In another study examining the role of social support among MS patients in Turkey, family was found to be the strongest source of social support [28]. The importance given to the MSPSS components of social support, namely family, friends, and significant others, may vary from society to society. For example, support from friends was found to be a more effective type of social support compared to familial support in a study conducted with MS patients in the USA [29].

Comorbid conditions that are considered basic factors affecting treatment adherence, such as depression, can be found among substantial number of patients as a result of MS and/or its treatment [24,30-32]. The effect of depression on treatment adherence is unclear. Although, some studies have reported depression to not affect treatment adherence [7,8], depressive symptomology was shown to negatively affect treatment adherence in our study, in a manner similar to the study by Higuera et al. [24].

Limitations

The fact that the results of this study conducted in two centers cannot be generalized to all MS patients constitutes the limitation of this study.

5. CONCLUSION

Half of the MS individuals in the study (52%) did not have good treatment adherence. Treatment adherence should be evaluated using standardized evaluation tools during patient follow up and the reasons behind poor treatment adherence should

be explored. Since, forgetfulness was stated to be the most important reason behind poor treatment adherence, considering the cognitive disruption in individuals with MS, planning should be performed to ensure the patients do not forget taking medications on time. More cooperation with families, which constitute the strongest source of social support in the treatment process, should be achieved. Since, depression is an important factor in the treatment adherence of MS patients, screening tools should be used for the early detection of depressive symptoms. Various precautions should be taken to ensure regular outpatient clinic visits to increase treatment adherence. The treatment adherence of patients should be comprehensively evaluated in cases of frequent hospitalizations.

Acknowledgments

The authors thank all the patients and their care givers who took the time to participate in this study.

Compliance with Ethical Standards

Ethical Approval: Local ethical board permission was taken from Namık Kemal University, School of Medicine before the study (Decision number: 2018/51/03/24). The volunteers who participated in the study were informed of the aim of the study by the researcher and gave consent. The principles of the Helsinki Declaration were upheld throughout the study. In order to use the MGLS, permission was taken from Donald E. Morisky through e-mail.

Financial support: This research received no specific grant from any funding agency in the public, commercial, or non-profit sectors.

Conflict of Interest Statement: There is no conflict of interest.

Authors' Contributions: DG, ZT, NT and SG: Concept, DG and ZT: Design, ZT, NT, SG: Supervision, DG and ZT: Data Collection and/ or processing, DG and ZT: Analysis and / or interpretation, DG and ZT: Literature search, DG and ZT: Writing, ZT, NT and SG: Critical review. All authors read and approved the final version of the article.

REFERENCES

- [1] GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019; 18:459-80. doi:10.1016/S1474-4422(18)30499-X
- [2] Celik Y, Birgili O, Yılmaz H, et al. Prevalence of multiple sclerosis in the metropolitan area of Edirne City, Turkey. *Balkan Med J* 2011; 28:193-6 doi: 10.5174/tutfd.2010.04089.0
- [3] Türk Börü Ü, Duman A, Kulualp AŞ, et al. Multiple sclerosis prevalence study: The comparison of 3 coastal cities, located in the black sea and mediterranean regions of Turkey. *Medicine (Baltimore)* 2018;97:e12856. doi:10.1097/MD.000.000.0000012856
- [4] Akdemir N, Terzi M, Arslan N, Onar M. Prevalence of multiple sclerosis in the Middle Black Sea Region of Turkey

- and demographic characteristics of patients. *Noro Psikiyatrs Ars* 2017;54:11-4. doi:10.5152/npa.2016.12451
- [5] Gökçe ŞF, Çiğdem B, Nemmezi Karaca S, et al. Prevalence of multiple sclerosis in an urban population of Sivas province in Turkey. *Turk J Med Sci* 2019;49:288-94. doi:10.3906/sag-1808-112
- [6] Magyari M, Sorensen PS. The changing course of multiple sclerosis: rising incidence, change in geographic distribution, disease course, and prognosis. *Curr Opin Neurol* 2019;32:320-26. doi:10.1097/WCO.000.000.0000000695
- [7] McKay KA, Tremlett H, Patten SB, et al. Determinants of non-adherence to disease-modifying therapies in multiple sclerosis: A cross-Canada prospective study. *Mult Scler* 2017;23:588-96. doi:10.1177/135.245.8516657440
- [8] Hao J, Pitcavage J, Jones JB, Hoegerl C, Graham J. Measuring adherence and outcomes in the treatment of patients with multiple sclerosis. *J Am Osteopath Assoc* 2017;117:737-47. doi:10.7556/jaoa.2017.145
- [9] Köşkderehoğlu A, Gedizlioğlu M, Ortan P, Öcek Ö. Evaluation of the adherence to immunomodulatory treatment in patients with multiple sclerosis. *Noro Psikiyatrs Ars* 2015;52:376-9. doi:10.5152/npa.2015.8825
- [10] Erbay Ö, Usta Yeşilbalkan Ö, Yüceyar N. Factors affecting the adherence to disease-modifying therapy in patients with multiple sclerosis. *J Neurosci Nurs* 2018;50:291-7. doi:10.1097/JNN.000.000.0000000395
- [11] Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67-74. doi:10.1097/00005.650.198601000-00007
- [12] Weinman J, Petrie K, Moss-Morris R, Horne R. The illness perception questionnaire: a new method for assessing the cognitive representation of illness. *Psychol Health* 1996; 11:431-45. doi: 10.1080/088.704.49608400270
- [13] Moss-Morris R, Weinman J, Petrie K, et al. The revised illness perception questionnaire (IPQ-R). *Psychol Health* 2002;17:1-16. doi:10.1080/088.704.40290001494
- [14] Kocaman N, Ozkan M, Armay Z, Ozkan S. The reliability and the validity study of Turkish adaptation of the revised Illness Perception Questionnaire. *Anatolian Journal of Psychiatry* 2007; 8:271-280.
- [15] Zimet GD, Dahlem NW, Zimet SG, Farley GK. The Multidimensional Scale of Perceived Social Support. *J Pers Assess* 1988; 52 :30-41. doi:10.1207/s15327752jpa5201_2
- [16] Eker D, Arkar H. Perceived social support: psychometric properties of the MSPSS in normal and pathological groups in a developing country. *Soc Psychiatry Psychiatr Epidemiol* 1995;30:121-6. doi:10.1007/BF00802040
- [17] Eker D, Arkar H, Yaldız H. Factorial structure, validity, and reliability of revised form of the Multidimensional Scale of Perceived Social Support. *Türk Psikiyatri Dergisi* 2001; 12: 17-25.
- [18] Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561-71. doi:10.1001/archpsyc.1961.017.10120031004
- [19] Hisli N. Use of the Beck Depression Inventory with Turkish university students: reliability, validity and factor analysis. *J Psychol* 1989;3:3-13.
- [20] Devonshire V, Lapiere Y, Macdonell R, et al. The Global Adherence Project (GAP): a multicenter observational study on adherence to disease-modifying therapies in patients with relapsing-remitting multiple sclerosis. *Eur J Neurol* 2011;18:69-77. doi:10.1111/j.1468-1331.2010.03110.x
- [21] MorilloVerdugo R, Ramírez Herráiz E, Fernández-Del Olmo R, et al. Adherence to disease-modifying treatments in patients with multiple sclerosis in Spain. *Patient Prefer Adherence* 2019;13:261-72. doi:10.2147/PPA.S187983
- [22] Câmara NAAC, Gondim APS. Factors associated with adherence to immunomodulator treatment in people with multiple sclerosis. *Braz J Pharm Sci* 2017;53:e16132. doi.org/10.1590/s2175.979.0201700.011.6132
- [23] Río J, Porcel J, Téllez N, et al. Factors related with treatment adherence to interferon beta and glatiramer acetate therapy in multiple sclerosis. *Mult Scler* 2005;11:306-9. doi:10.1191/135.245.8505ms1173oa
- [24] Higuera L, Carlin CS, Anderson S. Adherence to disease-modifying therapies for multiple sclerosis. *J Manag Care Spec Pharm* 2016;22:1394-401. doi:10.18553/jmcp.2016.22.12.1394
- [25] Gromisch ES, Turner AP, Leipertz SL, et al. Who is not coming to clinic? A predictive model of excessive missed appointments in persons with multiple sclerosis. *Mult Scler Relat Disord* 2020;38:101513. doi:10.1016/j.msard.2019.101513
- [26] Ožura A, Kovač L, Sega S. Adherence to disease-modifying therapies and attitudes regarding disease in patients with multiple sclerosis. *Clin Neurol Neurosurg* 2013;115 Suppl1:S6-S11. doi:10.1016/j.clineuro.2013.09.013
- [27] Kołtuniuk A, Rosińczuk J. The levels of depression, anxiety, acceptance of illness, and medication adherence in patients with multiple sclerosis –descriptive and correlational study. *Int J Med Sci* 2021;18:216-25. doi:10.7150/ijms.51172
- [28] Zengin O, Erbay E, Yıldırım B, Altındag O. Quality of life, coping, and social support in patients with multiple sclerosis: A pilot study. *Turk J Neurol* 2017; 23:211-8.
- [29] Kasser SL, Kosma M. Social cognitive factors, physical activity, and mobility impairment in adults with multiple sclerosis. *Behav Med* 2018;44:306-13. doi:10.1080/08964.289.2017.1368441
- [30] Soyuer F, Unalan D, Mirza M. Depressive symptoms in multiple sclerosis and the association with sociodemographic factors and functional status. *Turk J Neurol* 2010;16:31-5.
- [31] Bilgi E, Ozdemir HH, Bulut S. Determining the frequency of depression and cognitive dysfunction in patients with multiple sclerosis. *TJN* 2013; 19:11-4.
- [32] Gottberg K, Einarsson U, Fredrikson S, et al. A population-based study of depressive symptoms in multiple sclerosis in Stockholm county: association with functioning and sense of coherence. *J Neurol Neurosurg Psychiatry* 2007;78:60-5. doi:10.1136/jnnp.2006.090654