Ann Med Res 2021;28(6):1241-6

Annals of Medical Research

DOI: 10.5455/annalsmedres.2021.01.105

Original Article

Comparative study of multiple sclerosis patients based on distance from the advanced health center

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Abstract

Aim: There are several reasons for presenting to a hospital for multiple sclerosis (MS), a neurodegenerative disorder. We aimed to determine how distance affects presentation by patients with MS to an advanced health center in Malatya, Turkey.

Materials and Methods: The study was performed on 109 patients at the Neurology Department of Inonu University Hospital in 2017. The patients were divided into group-1, who lived in Malatya, and group-2, who live in the upstate region. Demographic and clinical data were analyzed retrospectively from medical records. Chi-square tests, independent sample T-tests, and Mann–Whitney U-tests were used to analyze the data.

Results: The duration of the disease was longer among patients who lived in Malatya. In terms of mean expanded disability status scale scores, patients who lived in Malatya had higher scores and patients who lived upstate exhibited more clinical complaints. Among patients who lived upstate, there were more motor problems, vertigo, cognitive impairment, psychiatric disturbances, and visits for blood tests.

Conclusion: Distance affected admission to MS outpatient clinics. We should be more careful in terms of attack when assessing the reasons of patients present from outside the province. More meaningful results can be obtained by following more patients for longer periods.

Keywords: Demyelination; multiple sclerosis; neurodegenerative diseases

INTRODUCTION

Multiple sclerosis (MS) is a degenerative autoimmune central nervous system disease characterized by demyelination, inflammation, and loss of axons (1). MS affects more than 2.8 million people worldwide (2,3). It is three times more common in females than males (4). Although it generally occurs between the age of 20 and 50, it can occur in younger and older patients (4). Immunological, environmental, and genetic factors play roles in the etiology (5-7). There is a complicated relationship between environmental factors and genetics (8). Viral infections, genes encoding the T cell receptor, and human leukocyte antigen (HLA II) are thought to be involved in the pathogenesis (8). The clinical signs and symptoms of the patients vary widely. The most common class of complaint is sensory symptoms (9). Associated complaints include motor and visual function problems, symptoms referable to the brainstem, cerebellar complaints, bladder dysfunction, sexual dysfunction, sleep disorders, spasticity, fatigue, epileptic seizures, and gastrointestinal symptoms (10,11).

These symptoms can occur in the context of acute attacks or can be chronic complaints. An accurate assessment of complaints determines the treatment process. As is known, MS is a neurodegenerative disease that causes disability. Many MS patients cannot easily access the hospital. Access difficulties stem from economic, social, and transportation problems. For this reason, it is essential to evaluate the distance from the health center of the MS patient when investigating patient complaints. In this study, we determined the effect of geographical distance on an advanced health center for presentation reasons

MATERIALS and METHODS

The Ethics Committee approved this clinical trial of Inonu University (decision number of 2017/13-14, June 2017). The study was carried out with patients who presented to the MS outpatient clinic of Turgut Ozal Medical Center

Received: 04.02.2021 **Accepted:** 05.03.2021 **Available online:** 25.06.2021
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between 01.06.2016–01.06.2017, the medical faculty of Inonu University. This was a retrospective study of a population of 654 patients who were examined at the Neurology Department of Inonu University Turgut Ozal Medical Center. The minimum sample size to be reached was 59 based on an analysis assuming 80% power and 95% confidence intervals. Per McDonald 2010 criteria, 109 patients diagnosed with MS were involved in the study. A systematic sampling method was used to select the sample. Patients were included in the research according to the following criteria: >18 years of age; and diagnosis of MS conforming to McDonald 2010 diagnostic criteria.

The patient information form used for the examination included demographic and clinical information. Patients are categorized into two groups based on demographic information. Group 1 were patients who presented from the city of Malatya, while group 2 were those who presented from upstate. There were 48 women and 21 men in group 1 and 28 women and 12 men in group 2.

Demographic information included age, gender, birthplace, living environment, residence (rural or urban), and marital status. Clinical information included duration of disease, the number of presentations in 1 year, whether a clinical complaint was documented, presence of visual complaint, brainstem symptoms, speech disorder, sensory or motor complaints, bladder dysfunction, loss of balance, walking disorder, vertigo, pain, spasticity, psychiatric complaints, cognitive disorder, sexual dysfunction, application for blood tests, medical board report request, applications for magnetic resonance imaging, applications for monthly pulse steroid treatment, and other clinical complaints (fatigue, constipation, nausea, vomiting, chest pain, and menstrual irregularity). We also evaluated types of preventive treatment, expanded disability status scales (EDSS), and disease types.

Clinical progression was evaluated throughout the following period, and the patients were classified as having primary progressive multiple sclerosis (PPMS), secondary progressive multiple sclerosis (SPMS), and relapsing-remitting multiple sclerosis (RRMS). We also recorded EDSS scores of the patients, which were calculated at the most recent visit.

Statistical Analysis

The SPSS 17.0 software package (SPSS Inc., Chicago, IL, USA) was used to evaluate data and analyze descriptive statistics (frequency, mean, SD). The Kolmogorov–Smirnov test was used to assess the distribution of data. Descriptive statistics were used for demographic variables. Independent sample T-tests (parametric test) and Mann–Whitney U-tests (nonparametric test) were used to analyze the continuous variables. The chi-square test was also used for categorical variables when comparing clinical data between the groups. The level of significance was accepted as $p<0.05$.

RESULTS

Sociodemographic and clinical characteristics of 109 MS patients are displayed in Table 1. While 69 patients lived in the city of Malatya, others lived upstate. The average age of patients was 34.88 ± 10.42. The patients were 69.7% female and 30.3%, male.

In the 2nd group, the disease duration was significantly shorter, the number of patient applications was lower, and there were many more visits for clinical complaints.

Motor complaints, vertigo, cognitive complaints, and psychiatric complaints were significantly higher in group-2 (Table 2).

Table 3 shows other reasons than clinical complaints. The most frequent application reason for clinical complaint in group-2 was to obtain a blood test.

Table 4 shows the EDSS scores. Scores in group-2 were significantly lower. There was a weak correlation between the groups and the EDSS scores. The distribution of EDSS scores of all patients according to groups is given in Figure 1. The range of EDSS scores was wider, and the average was higher in group-1.

Table 1. Sociodemographic and clinical characteristics of patients

	Group 1	Group 2	p
Age (Year ± SD)	35.84± 10.35	33.23±10.47	0.200
Gender (Female/Male, %)	48/21 (69.6/30.4)	28/12 (70/30)	0.570
Period of Disease (Month ± SD)	75.12±68.88	45.60±36.96	0.014
The Number of Application	4.09±3.27	3.53±2.36	0.340
Marital Status (Married /Single, %)	51/18 (73.90/26.10)	23/17 (57.50/42.50)	0.060
Inhabitation (Urban/Rural, %)	61/8 (88.40/11.60)	21/19 (52.50/47.50)	≤0.001
Clinical Complaint On Application (+/-, %)	44/25 (63.80/36.20)	34/6 (85/15)	0.014
RRMS, n(%)	59 (85.5)	35 (87.5)	
PPMS, n(%)	3 (4.3)	2 (5)	0.890
SPMS, n(%)	7 (10.1)	3 (7.5)	

+: available, -:none, SD: Standard Deviation. Chi square and independent sample t test were performed

Table 2. Clinical complaints analysis of patients who applied to MS outpatient clinic

	Group 1 n/%	Group 2 n/%	p
Vision complaint (+, %)	5/(7.2)	7/(17.5)	0.093
Brainstem complaint (+, %)	2/(2.9)	1/(2.5)	0.697
Sensory complaints in the upper extremities (+, %)	9/(13)	8/(20)	0.240
Sensory complaints in the lower extremities (+, %)	9/(13)	10/(25)	0.094
Sensory complaints in both of upper and lower extremities (+, %)	7/(10.1)	9/(22.5)	0.072
Motor complaints in the upper extremities (+, %)	1/(1.4)	6/(15)	**0.010**
Motor complaints in the lower extremities (+, %)	5/(7.2)	8/(20)	**0.049**
Motor complaints in both of upper and lower extremities (+, %)	2/(2.9)	6/(15)	**0.027**
Urinary incontinence (+, %)	5/(7.2)	6/(15)	0.167
Loss of balance (+, %)	3/(4.3)	4/(10)	0.222
Walking disorder (+, %)	5/(7.2)	4/(10)	0.433
Vertigo (+, %)	2/(2.9)	8/(20)	**0.005**
Pain (+, %)	8/(11.6)	6/(15)	0.408
Spasticity (+, %)	1/(1.4)	2/(5)	0.303
Cognitive complaints (+, %)	1/(1.4)	7/(17.5)	**0.004**
Psychiatric complaints (+, %)	2/(2.9)	11/(27.5)	**≤0.001**
Single dose steroid treatment (+, %)	3/(4.3)	3/(7.5)	0.386
Sexual dysfunction (+, %)	1/(1.4)	4/(10)	0.060
Other complaints (+, %)	9/(13)	12/(30)	**0.029**
Total	**69**	**40**	

+: available, chi-square test was performed

Table 3. Reasons for non-clinical complaints of patients admitted to multiple sclerosis outpatient clinic

Reason of application	Group 1 n/%	Group 2 n/%	p
Blood tests (+, %)	39/(56.5)	31/(77.5)	0.046
Radiological imaging (+, %)	50/(72.5)	28/(70)	0.470
Treatment change (+, %)	8/(11.6)	3/(7.5)	0.370
Medical board report (+, %)	1/(1.4)	3/(7.5)	0.139

+ : available, chi-square test was performed

Table 4. EDSS comparison by groups

	EDSS		Eta	p
	X±Std	Median		
Group 1	2.52±1.40	2.0	0.282	**0.002**
Group 2	1.72±1.18	2.0		

Std: Standard Deviation, Mann Whitney U test was performed

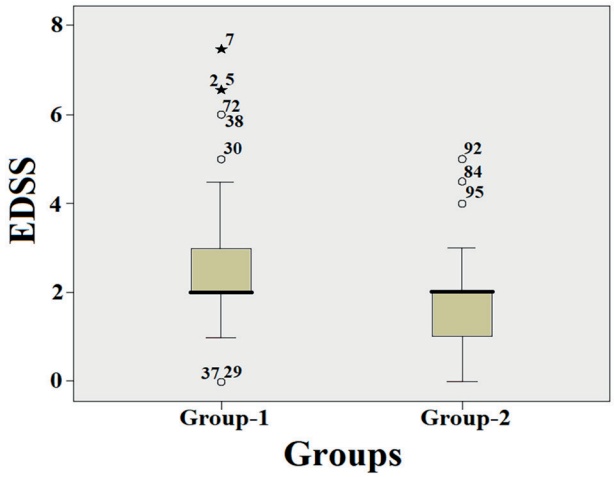

Figure 1. EDSS distribution of patients by groups

DISCUSSION

MS is a chronic inflammatory disease caused by demyelination of the central nervous system (1). The disease usually affects the young-adult age group (4). The incidence of disease in the female is higher than male (4).

The etiopathogenesis of the disease is multifactorial. The disease interacts with environmental, genetic, and autoimmune mechanisms (5-7).

We used McDonald diagnostic criteria to diagnose MS. History, neurological examination, magnetic resonance imaging, blood tests, cerebrospinal fluid (CSF) tests, and evoked potentials are used for diagnosis. Treatment is according to the type of presentation: treatment of acute attacks, preventive treatment, or symptomatic treatment. During the treatment of attacks, intravenous methylprednisolone is used. Preventive therapy is either immunomodulatory or immunosuppressive. There are various approaches for symptomatic treatment. Clinical signs and symptoms vary widely (8).

Comparative results showed that the patients who lived upstate had shorter durations of disease than those who lived in Malatya. The duration of disease in patients living in Malatya was 75.1 ± 68.8 months. For those living upstate, it was 45.6 ± 36.9 months. This difference was statistically significant (p:0.014). This difference may be related to delayed presentation due to the distance to the MS outpatient clinic. In a study performed in the upper Fırat region in 2011, 121 MS patients were studied in terms of clinical and demographic characteristics. The average duration of disease was 96 ± 70.8 months (12). The reason for the higher duration of the disease may be differences in the patient population.

In the present study, the average age of patients living in Malatya was 35.84 ± 10.35, while the average age of patients who lived upstate was 33.23 ± 10.47. These values were not statistically significant. Similar results were obtained in terms of patients' average age; Bulut et al. studied the clinical and demographic characteristics of the 121 patients who were followed up with diagnoses of MS in the upper Fırat region (12). The average age was 30.41 ± 9.4. Turner et al. found that the rate of admission to the clinic decreased as the patients aged (13). Bencsik et al. determined the average onset age of the disease was 28 (14). McDonnel and Hawkins found that the average onset age for MS was 31.6 (15). A study by Birgili showed that the average age of onset was 30.41 (16). The literature shows that the most common age of onset is the young-adult period (13-16).

Among all patients, the proportion of female patients who live in Malatya was 69.6%; this proportion was 70% in patients who lived upstate. Although this finding was not statistically significant, it is similar to those of studies. In a study conducted by Totaro et al. in Italy, the female/male ratio was 2/1 in patients with MS (17). In a study by Benito-Leon et al. in Spain, the rate was 1.6/1 (18). Houzen et al. found a ratio of 2.85/1 in Japan (19). Modrego and Pina studied 44 MS patients and found a ratio of 1.93/1 (20). When the literature is analyzed, it is seen that MS disease is more common in female than male.

The percentage of urban versus rural residence for patients who lived in Malatya was 88.4% versus 11.6%. The urban versus rural residence ratio of patients who lived upstate was 52.5% versus 47.5%. In other words, the percentage of patients in rural areas for upstate patients was higher than for patients who live in Malatya. This result was also statistically significant (p≤0.001). A study conducted by Turner et al. in 2013, including 14723 patients, showed that the rates of rural patients' access to health services were lower than those living in urban areas (13). In the current study, there were more presentations from urban areas than rural areas. This finding suggests that the current study population provides good correlational results even if the values are lower than those of other studies.

In the present study, final EDSS scores were recorded. The average EDSS value of patients from Malatya was 2.53 ± 1.41, and scores of those from upstate were 1.73 ± 1.19 (p:0.003). It may be that group-2 patients with high EDSS scores could not present because of distance. While the minimum EDSS score was 0, the maximum was 7.5. Bufill et al. found the mean EDSS score was 4 in Spain in 1995 (21). Benito-Leon et al. reported a mean EDSS score of 2.5 (18). The literature suggests that mean EDSS scores can vary due to differences in sample populations.

The results were examined in terms of lower, upper, and both extremities. The patients from upstate had more motor complaints in the upper, lower, and both extremities (p:0.010, 0.049, and 0.027, respectively). Houzen et al. studied 27 patients in Japan, and 40.7% had motor complaints (19). Tola et al. studied 54 patients in Spain, and 49% had motor complaints (22). Bufill et al. stated that the most common symptom in patients was motor complaints (21). Literature researches conducted in different geographical locations showed that motor complaints are common. When the experimental results of the current study are examined, it is evident that our findings parallel those of the literature.

In the present study, brainstem complaints were not statistically significant between the groups; only vertigo was more common in patients from upstate. A study by Kantarcı et al. in 1998 (23) found that 21% of MS patients had brainstem and cerebellar symptoms. Various investigators from other countries also studied brainstem complaints. Totaro et al. found that 13.3% of patients in Italy had brainstem complaints (17). When the literature is examined from this perspective, it can be seen that the frequency of brainstem complaints varies. Because this city was the first to be studied, comparison data could not be obtained. This topic should be studied in the future.

The ratio of cognitive and psychiatric complaints was higher in patients from upstate. These differences were statistically significant (p:0.004, p≤0.001, respectively). It is known from the literature that there is less participation in intra-community activities in parallel with cognitive impairment in MS patients (24). This situation causes MS patients to have more difficulty performing routine household chores and to have difficulty in recruitment (24). For this reason, the risk of developing a psychiatric

disorder tends to increase (24). Rao et al. measured the frequency of cognitive impairment in MS patients and found that the frequency of cognitive impairment ranged from 43 to 70% (24). In the present study, patients from upstate had lower EDSS scores. Despite this situation, cognitive complaints were more common in patients who lived upstate. Patti et al. measured the frequency of cognitive impairment in patients with low EDSS scores (25).They found at least one of the neuropsychological tests showed deterioration in more than half of the patients (25). On the other hand, it was found that the EDSS score was <2 in 65.6% of the patients. This result also parallels those of previous studies (11,26,27). These findings suggest that cognitive impairment is a severe problem for MS patients, and neuropsychological tests should be included in routine clinical practice. Cognitive monitoring should be performed before the detectable physical disability. Early cognitive screening can prevent severe cognitive impairments in the future (25). Another conclusion drawn from our study is that clinicians should increase the examined patient population and follow patients for the long term. This would lead to more extensive results.

Other clinical complaints were also more common in group 2: fatigue, nausea, vomiting, hair loss, and visits for blood tests (p:0.029 / p:0.046, respectively).

The rate of admission with sexual dysfunction was low. Statistically significant results were not obtained for this complaint. In a study conducted in Cardiff, UK, in 2015, it was found that patients diagnosed with MS did not express complaints or were not adequately questioned by the neurologist regarding fatigue or sexual dysfunction (28). The low rate of complaints of sexual dysfunction may be explained by failure to ask about it.

LIMITATIONS

The number of patients and the short duration of follow-up are limitations of this study. Cognitive complaints were evaluated according to the patients' anamnesises. Tests for cognitive assessment were not used.

CONCLUSION

Patients who come from long distances should be questioned more carefully in terms of attacks because they have more clinical complaints. With increased numbers of patients and more extended periods will be more suitable for generalization purposes.

Competing Interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical Approval: The Ethics Committee approved clinical trials of Inonu University (with the decision number of 2017/13-14 in June 2017).

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