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Exploring the experience of multiple sclerosis patients in Turkey: Insights from a national survey

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Abstract

Objective: To evaluate sociodemographic profile, clinical characteristics, disability and treatment status of multiple sclerosis (MS) patients in Turkey with respect to patient perspectives and expectations. *Methods:* A total of 2,176 MS patients participated in this cross-sectional questionnaire survey including items on sociodemographic, disease and treatment characteristics, daily life and perspectives and expectations. *Results:* Mean (SD) patient age was 36.4(9.4) years and 76.3% of patients were females. The numbness/weakness in the extremities (57.3%) was the most common presenting symptom. Overall, 56.8% reported treatment switch (due to attacks in 47.3%), while 22.2% reported physical disability and 39.7% reported work-related problems. Males had higher rate of MS-related physical disability (33.0% vs. 19.0%, p<0.001) than females. Use of an assistive device was a more common in patients with longer disease duration (≥15 years; 39.0%) and in those under IV treatment (64.0%). Nearly half of patients reported significant concerns related to uncertainty of the future and impaired quality of life as well as lack of hope for future improvement. The majority of patients reported that they would prefer less frequent SC injection dosing and 43.3% reported preference for monthly high-efficacy SC injection.
Conclusion: This nationwide questionnaire-based study in Turkish MS patients revealed the altered disability status with respect to sociodemographic profile, and altered treatment expectations specific to the route of administration, in addition to significant concerns regarding the uncertainty of the future, impaired quality of life and lack of hope for future improvement in nearly half of patients.

Keywords: Multiple sclerosis, patient profile, disease background, treatment, disability status, patient's perspectives, preferences and expectations

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune inflammatory and demyelinating disease particularly common in the young working-class population, leading to significant economic and social burden.[1-3]

Relapsing-remitting MS (RRMS) is the most common MS type characterized by neurological dysfunction episodes followed by disease remission and stability, which may evolve into . secondary progressive MS (SPMS) with increasing worsening of the disease and permanent

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disability.[3-5]

Given the clinical heterogeneity among MS patients and the variability in disease progression and accumulation of disability, early identification of disease trajectories and appropriate therapeutic targets in each individual is of critical importance for the success of management.[6-8]

The introduction of newer disease-modifying therapies (DMT) is important in this regard, given they facilitate implementation of a treatment strategy focusing on the prevention of disability progression and the use of personalized medicine aimed at tailoring the therapeutic strategy not only to patients' characteristics and disease activity but also to patients' needs and preferences.[1,3,7,9-13]

The MS studies addressing the patient´s perspective on disease progression and treatment preferences are considered important to improve treatment adherence and satisfaction, by increasing the likelihood of provision of a treatment complying with the preferences and expectations of the patients.[12-18]

Therefore, this questionnaire-based nationwide survey across Turkey aimed to evaluate sociodemographic profile, clinical characteristics, disability and treatment status of MS patients in relation to the patient perspectives and expectations.

METHODS

Study population

A total of 2,176 adult MS patients participated on a voluntary basis in this cross-sectional questionnaire survey conducted in 78 provinces across Turkey and Turkish Republic of Northern Cyprus, in collaboration with Turkish Society of Multiple Sclerosis, between November 2022 and December 2022.

The study was conducted by the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee.

Questionnaire from

The questionnaire form elicited items on sociodemographic characteristics (age, gender, educational status, marital status), disease background (type of MS, family history, age at diagnosis, disease duration), MS diagnosis and follow-up characteristics (symptoms on admission, first-admission specialty, time from presentation to diagnosis, diagnostic tests, follow up physician, frequency of control visits, MS nurse support), current treatment status, treatment preferences, disability (EDSS awareness), daily life (work-related problems, most significant concern related to MS), and current/future MS treatment expectations. The questionnaire was applied online through the Facebook platform of the Turkish Society of Multiple Sclerosis.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY). Chi-square ($\chi 2$) test was used for the comparison of categorical data. Data were expressed as "mean (standard deviation; SD)", median (minimum-maximum) and percent (%) where appropriate. $p<0.05$ was considered statistically significant.

RESULTS

Sociodemographic characteristics and disease background

Mean (SD) patient age was 36.4(9.4) years (25-45 years in 74.7%) and 76.3% of patients were females. Most of the patients were college graduates (66.2%), and married (61.3%) and employed (52.8%) patients (Table 1).

The patient distribution according to seven geographical regions, representative of the Turkish MS population in Turkey, indicated that most of patients were from Marmara region (56.0%), followed by Central Anatolia (12.0%), Aegean (10.0%), Mediterranean +Cyprus (9.0%), Eastern Anatolia (7.0%), Black Sea (4.0%) and Southeastern Anatolia (2.0%) regions (Table 1).

RRMS (44.1%) was the most prevalent MS type reported by the patients, while the MS type was unknown by the patient in 36.5% of cases. Median (min-max) age at diagnosis was 35(8-73) years (25-44 years in 72.9%) and duration of MS was >5 years in 52.6% of patients. Family history of MS was reported by 18.7% of patients (Table 1).

MS diagnosis and follow-up characteristics

The most common presenting symptoms were numbness and/or weakness in the lower and upper extremities (57.3%), vision problems/ double vision (51.7%) and fatigue (41.9%). Neurology (40.5%) and ophthalmology (26.7%) were the most common first-admission specialties (Table 2).

The average time from neurology consultation to diagnosis was 1.2 months and MRI (88.4%) was the most commonly used diagnostic test (Table 2).

Table 1: Sociodemographic characteristics and disease background

SOCIODEMOGRAPHIC CHARACTERISTICS		
Patient age (year)	mean(SD)	36.4(9.4)
	median(min-max)	36(18-73)
Age category, n(%)	<25 y	211(9.7)
	25-45 y	1626(74.7)
	>45 y	339(15.6)
Gender, n(%)	Female	1660(76.3)
	Male	516(23.7)
Educational status, n(%)	Primary education	179(8.2)
	Secondary education	557(25.6)
	University	1440(66.2)
Marital status, n(%)	Married	1333 (61.3)
	Single	649 (29.8)
	Divorced	194 (8.9)
Occupational status, n(%)	Employed	1149(52.8)
	Unemployed + Housewife + Student	863(39.7)
	Retired	164(7.5)
Geographical region, n(%)	Marmara	1211(56.0)
	Central Anatolia	267(12.0)
	Aegean	214(10.0)
	Mediterranean +Cyprus	203(9.0)
	Eastern Anatolia	146(7.0)
	Black Sea	84(4.0)
	Southeastern Anatolia	51(2.0)
DISEASE BACKGROUND		
Type of MS, n(%) (n=2176)	PPMS	177 (8.1)
	RRMS	960 (44.1)
	SPMS	244 (11.2)
	Unknown by the patient	795(36.5)
Family history for MS, n(%)	Yes	407(18.7)
	First-second degree relatives	320(14.7)
	Distant relative	134(6.2)
Age at diagnosis (year), n(%)	Median(min-max)	35(8-73)
	<25	270(12.4)
	25-45	1586(72.9)
	>45	296(13.6)
Disease duration, n(%)	<1 year	183(8.4)
	1-5 year	849(39.0)
	6-10 year	522(24.0)
	11-15 year	343(15.8)
	>15 years	279(12.8)

MS: Multiple sclerosis; PPMS: Primary progressive MS; RRMS: Relapsing remitting MS; SPMS: Secondary progressive MS

Follow-up visits were performed every 3 to 6 months in most patients (60.4%), and by the same physician who had initially diagnosed the disease in 55.6% of patients. Overall, 33.9% of patients received MS nurse support and 23.3% had telemedicine visits during the pandemic (Table 2).

Table 2: MS diagnosis and follow-up characteristics

MS DIAGNOSIS		
Symptoms on admission, n(%)		
Numbness-weakness in lower and upper extremities		1247(57.3)
Vision problems/double vision		1147(52.7)
Fatigue		911(41.9)
Loss of balance		732(33.6)
Impaired walking		374(17.2)
Urinary continence/incontinence		242(11.1)
Memory problems		205(9.4)
Other		413(19.0)
First-admission specialty, n(%)		
Neurology		882(40.5)
Ophthalmology		582(26.7)
Neurosurgery		158(7.3)
Internal Medicine		160(7.4)
Orthopedics		115(5.3)
Physical therapy and rehabilitation		82(3.8)
Other		197(9.1)
Diagnostic work-up before MS diagnosis, n(%)		
MRI		1923(88.4)
Blood tests		1501(69.0)
CSF analysis		1130(51.9)
Other (VEP, SEP, OCT, BAEP)		559(25.7)
Unknown		84(3.9)
FOLLOW UP		
Follow up physician for treatment, n(%)		2097(96.4)
Same with the diagnosing physician		1165(55.6)
Different physician		932(44.4)
Frequency of control visits during MS treatment, n(%)		2097(96.4)
Once in a month		159(7.6)
Every 3 months		574(27.4)
Once in 6 months		692(33.0)
Once in a year		518(24.7)
Once in 2 years		59(2.8)
On demand (during attack)		95(4.5)
MS nurse support for treatment or follow up, n(%)	Yes	737(33.9)
	Useful for treatment monitoring	684(31.4)
	Not useful for treatment monitoring	53(2.4)
Use of telemedicine visits during pandemic, n(%)		506(23.3)

MS: Multiple sclerosis; CSF: Cerebrospinal fluid; MRI: Magnetic resonance imaging

Treatment history, current treatment status and treatment preferences

The average time from diagnosis to treatment was 10.2 months (0-3 months in 74.7%). Overall, 56.8% of patients reported to have treatment switch by the physician, while 36.9% were still on the first prescribed drug. The main reasons for treatment switches were attacks (47.3%), progression on MRI (25.0%) and poor compliance (22.9%) (Table 3).

Patient on oral, IV and SC therapies comprised the 56.8%, 24.4% and 18.8% of the study population, respectively. The majority (91.2%) of patients reported that they would prefer less frequent SC injection dosing over more frequent dosing, mostly due to injection site problems (37.5%), pain (33.5%) and dislike of injection (31.7%). Monthly high-efficacy SC injection was preferred by 43.3% of patients due to high-efficiency (28.7%), prolonged injection intervals

Table 3: Treatment characteristics and preferences

TREATMENT CHARACTERISTICS		
Onset of treatment after diagnosis (yes), n(%)		2097(96.4)
Time from diagnosis to treatment (month) (n=2097), n(%)	0-3 months	1567(74.7)
	3-12 months	284(13.5)
	1-5 year	145(6.9)
	>5 year	101(4.8)
Treatment status, n(%)	Treatment switch (by the physician)	1192(56.8)
	Still on the first prescribed drug	773(36.9)
	Treatment discontinuation (by the patient)	82(3.9)
	Treatment discontinuation (by the physician)	78(3.7)
	Temporary withdrawal (by the physician)	67(3.2)
Reason for treatment switch, n(%)	Attacks	564(47.3)
	Progression on MRI	298(25.0)
	Poor compliance	273(22.9)
	Other	335(28.1)
Route of MS treatment , n(%)	Oral	1191(56.8)
	Intravenous therapy	512(24.4)
	SC injection	394(18.8)
TREATMENT PREFERENCES		
SC injection preferences, n(%)	Less frequent dosing	1985(91.2)
	More frequent dosing	191(8.8)
Reasons for not preferring more frequent dosing, n(%)	Injection site problems	744(37.5)
	Pain	665(33.5)
	Dislike of injection	630(31.7)
	Dislike of SC injection	461(23.2)
	Difficulty in self-administration	437(22.0)
	Dislike of at-home injections	202(10.2)
	Less effective therapy	187(9.4)
	Other	536(27.0)
Monthly high-efficacy SC injection preference, n(%)	Not preferred	402(18.5)
	Preferred	942(43.3)
	Due to high-efficacy	*625(28.7)*
	Due to prolonged injection intervals	*487(22.4)*
	Due to self-administration at home	*175(8.0)*
	Other	*89(4.1)*
	Not sure	832(38.2)

MS: Multiple sclerosis; SC: Subcutaneous; MRI: Magnetic resonance imaging

(22.4%), and the possibility of self-administration at home (8.0%) (Table 3).

Disability, daily life and treatment expectations

Overall, 22.2% of patients reported that they have MS-related physical disability, while considerable walking impairment (not using assistive devices, 11.7%) was the most common type of disability. EDSS awareness was noted in 22.5% of patients (Table 4). Work-related problems were reported by 39.7% of patients, including difficulty keeping pace (23.2%) and loss of job (16.5%) (Table 4).

Fatigue (29.6%), uncertainty of the future (19.2%), and impaired quality of life (12.8%) were reported to be the most significant concerns related to be diagnosed with the MS disease (Table 4).

Overall, 45.5% of patients reported that they have hope for improvement in their current situation or disease in the future. Longer dosing

Table 4: Disability, daily life and treatment expectations

DISABILITY AND DAILY LIFE		
MS-related physical disability, n(%)		483(22.2)
Course of disability, n(%)	Progressive	154(7.1)
	Non-progressive	395(18.2)
Description of disability, n(%)	Considerable walking impairment	254(11.7)
	Considerable loss of dexterity	169(7.8)
	Using assistive devices (cane, walker or wheelchair)	170(7.8)
	Other	114(5.2)
Work-related problems (yes), n(%)	Total	864(39.7)
	Difficulty keeping pace	504(23.2)
	Loss of job	360(16.5)
Knowledge on EDSS(yes), n(%)		490(22.5)
Most significant concern, n(%)		
Fatigue		645(29.6)
Uncertainty of the future		417(19.2)
Impaired quality of life		279(12.8)
Risk of new attacks		154(7.1)
Disease progression		158(7.3)
Loss of independence/disability		139(6.4)
Other		237(10.9)
None		147(6.8)
EXPECTATIONS		
Hope for improvement (current situation/ disease) in the future, n(%)	Yes	990(45.5)
	No	423(19.4)
	No idea	763(35.1)
Current expectations related to MS treatment, n(%)	Longer dosing intervals	646(29.7)
	Less hospital visits	473(21.7)
	Self-administration of HEDs at home	341(15.7)
	Other	716(32.9)
Future expectations/hopes related to MS treatment, n(%)	Eradication of MS	1508(69.3)
	Reversal of disability	293(13.5)
	No more attacks or MRI progression	219(10.1)
	No expectations in the near future	132(6.1)
	Other	24(1.1)

MS: Multiple sclerosis; EDSS: Expanded Disability Status Scale; HED: high-efficacy drugs; MRI: Magnetic resonance imaging

intervals (29.7%), fewer hospital visits (21.7%) and self-administration of high-efficacy drugs at home (15.7%) were the current expectations related to MS treatment. Future expectations/hopes related to MS treatment included eradication of MS (69.3%), reversal of disability (13.5%) and experiencing no more attacks or MRI progression (10.1%) (Table 4).

Gender-based comparisons

Males vs. females had a lower rate of fatigue on admission (34.0% vs. 44.0%, p<0.001), and a higher rate of MS-related physical disability (33.0% vs. 19.0%, p<0.001). Treatment switch and EDSS awareness rates were similar between male and female groups (Table 5).

Age-based comparisons

Symptoms on admission significantly differed with respect to age groups, such as lower rate of vision problems (p=0.016 and p=0.001, respectively) and higher rate of impaired walking (p=0.037 and p=0.009, respectively) in the >45 years age group vs. in the younger age (<25 years and 25-45 years) groups (Table 5).

Also, fatigue and loss of balance were more common, but MS-related physical disability and work-related problems were less common in the <25 years age group compared to older age (25-45 years and >45 years) groups (p<0.001 for each) (Table 5).

Comparisons based on route of MS drug application

IV vs. SC treatment was significantly less common in females (p=0.002) and more common in males (p=0.002). IV treatment was more common compared to both SC and oral treatments in SPMS patients (p=0.033 and p=0.003, respectively) and in patients with ≥15 years of disease duration (p<0.001 for each) (Table 6).

Still being on the first prescribed drug was more commonly reported by patients on SC treatment than those on oral and IV treatments (p<0.001 for each), and also by patients on oral treatment than those on IV treatment (p<0.001) (Table 6).

Patients receiving IV treatment reported a higher rate of MS-related disability than those receiving oral treatment (p<0.001) (Table 6).

The less-frequent hospital visits (p=0.008 and p<0.001, respectively) and the self-administration of HEDs at home (p<0.001 for each) were the expectations reported by higher percentage of patients on IV treatment, while longer dosing intervals (p<0.001 for each) were reported by higher percentage of patients on SC treatment, compared to the other routes (Table 6).

Comparisons based on MS disability

The disability status of "no assistive device" was more common than "using assistive device" in married patients (66.0% vs. 55.0%, p=0.021). In divorced patients, "using assistive device" was significantly more common than "loss of

Table 5: Symptoms on admission, treatment switch and disability by patient demographics

	Gender		Age (years)		
	Female (n=1660)	**Male (n=516)**	**<25 (n=211)**	**25-45 (n=1626)**	**>45 (n=339)**
Symptoms on admission, n(%)					
Vision problems/double vision	736(44.0)	221(43.0)	98(46.0)[b]	737(45.0)[c]	122(36.0)
Numbness-weakness in extremities	970(58.0)	277(54.0)	125(59.0)	939(58.0)	183(54.0)
Impaired walking	281(17.0)	93(18.0)	33(16.0)[b]	264(16.0)[c]	77(23.0)
Loss of balance	560(34.0)	172(33.0)	88(42.0)[e]	528(32.0)	116(34.0)
Fatigue	737(44.0)	174(34.0)[a]	117(55.0)[e]	670(41.0)	124(37.0)
Treatment switch (yes), n(%)	900(56.0)	292(59.0)	84(41.0)[e]	893(57.0)[c]	215(66.0)
EDSS awareness (yes), n(%)	370(22.0)	120(23.0)	40(19.0)	370(23.0)	80(24.0)
MS-related physical disability (yes), n(%)	315(19.0)	168(33.0)[a]	12(6.0)[e]	328(20.0)[d]	143(42.0)
Work-related problems (yes)[*], n(%)	617(78.2)	247(68.6)	66(31.0)[e]	637(39.0)[c]	161(47.0)

MS: Multiple sclerosis; EDSS: Expanded Disability Status Scale

[*]Based on the number of employed responders (total: 1149, male: 360 and female: 789)

[a]p<0.001 compared to females; [b]p<0.05, [c]p<0.01 and [d]p<0.001 compared to >45 years; [e]p<0.001 compared to older age groups

Table 6: Comparisons based on route of MS drug application

	Route of MS drug		
	Subcutaneous (n=394)	**Oral (n=1191)**	**Intravenous (n=512)**
Gender, n(%)			
Female	319(81.0)[a]	910(76.0)	369(72.0)
Male	75(19.0)[a]	281(24.0)	143(28.0)
MS type, n(%)			
PPMS	35(9 f.0)	63(5.0)	60(12.0)
RRMS	144(37.0)	553(46.0)	245(48.0)
SPMS	34(9.0)[a]	112(9.0)[b]	91(18.0)
Disease duration, n(%)			
≤ 5 years	216(55.0)[c]	634(53.0)[c]	149(29.0)
≥15 years	45(11.0)[c]	118(10.0)[c]	102(20.0)
Current treatment status, n(%)			
Still on the first prescribed drug	253(64.0)	432(36.0)[c,d]	88(17.0)[b]
Treatment switch (by the physician)	82(21.0)	713(60.0)[c,d]	397(78.0)[b]
MS-related physical disability, n(%)	5(19.0)	48(24.0)[c]	95(40.0)
Work-related problems, n(%)	117(30.0)	441(37.0)	285(56.0)
Current treatment expectations, n(%)			
Less hospital visits	40(10.0)	274(23.0)[b,d]	150(29.0)[b]
Self-administration of HEDs at home	53(13.0)[c]	148(12.0)[c]	127(25.0)
Longer dosing intervals	193(49.0)	373(31.0)[d]	69(13.0)[b]

MS: Multiple sclerosis; PPMS: Primary progressive MS; RRMS: Relapsing remitting MS; SPMS: Secondary progressive MS; HED: high-efficacy drugs

[a]p<0.05, [b] p<0.01 and [c]p<0.001 compared to IV treatment; [d]p<0.001 compared to SC route

dexterity" and "no assistive device" (23.0% vs. 14% and 10%, p=0.036 and p=0.001, respectively) (Table 7).

Longer disease duration (≥15 years) was associated with higher likelihood of using an assistive device than not using an assistive device or loss of dexterity (39.0% vs. 26.0% and 23.0%, p=0.007 and p=0.002, respectively) (Table 7).

For the IV treatment, higher percentage of patients were using assistive devices than those with no assistive device or with loss of dexterity (p=0.003 and p=0.007, respectively). For the oral treatment, a lower percentage of patients were using assistive devices than those with no assistive device or with loss of dexterity (p=0.011 and p=0.010, respectively) (Table 7).

No difference was noted between disability types concerning difficulty keeping pace, while loss of job was more common in those using assistive devices compared to those not using assistive devices (51.0% vs. 30.0%, p<0.001) (Table 7).

DISCUSSION

In this nationwide survey of 2176 MS patients across Turkey, at least 50% of MS patients reported having treatment switches (mostly due to attacks) and more than 20% described MS-related physical disability, while work-related problems were reported by ~ 40% of patients along with significant concerns related to uncertainty of the future and impaired quality of life.

According to the National Institute of Clinical Excellence (NICE), a timeline to diagnose MS is recommended to be no longer than three months, including <6 weeks between onset symptoms and the first neurological consultation and <6 weeks between the neurological consultation and MS diagnosis.[19] The average 1.2 months from neurological observation to diagnosis in our cohort seems in accordance with the recommended timeline. However, the median time from the onset of symptoms to MS diagnosis varies considerably between countries with reported ranges of 0-9 months as well as those extend from 25 months up to 3 years, possibly due to differences in the referral process, diagnostic criteria and healthcare

Table 7: Comparisons based on MS disability

	Type of disability		
	Using assistive device (cane, walker or wheelchair) (n=170)	**No assistive device (n=254)**	**Loss of dexterity (n=169)**
Gender, n(%)			
Female	91(59.0)	167(66.0)	110(65.0)
Male	63(41.0)	87(34.0)	59(35.0)
Marital status, n(%)			
Married	84(55.0)	168(66.0)[a]	104(62.0)
Single	34(22.0)	61(24.0)	41(24.0)
Divorced/widow(er)	36(23.0)	25(10.0)[b]	24(14.0)[a]
Disease duration, n(%)			
≤ 5 years	20(13.0)	68(27.0)[c]	39(23.0)[a]
≥15 years	60(39.0)	66(26.0)[b]	39(23.0)[b]
Route of MS drug, n(%)			
Oral	48(32.0)	111(45.0)[a]	77(47.0)[a]
SC injection	5(3.0)	14(6.0)	7(4.0)
IV injection	95(64.0)	120(49.0)[b]	81(49.0)[b]
EDSS awareness, n(%)	66(43.0)	80(31.0)	64(38.0)
Work-related problems, n(%)			
Difficulty keeping pace	55(36.0)	94(37.0)	70(41.0)
Lost his/her job	78(51.0)	76(30.0)[c]	68(40.0)

MS: Multiple sclerosis; EDSS: Expanded Disability Status Scale; SC: Subcutaneous; IV: intravenous
[a]p<0.05, [b] p<0.01 and [c]p<0.001 compared to using assistive device

access.[20-24] Hence, diagnostic delay is considered to remain a significant challenge,[18,20,21,25] particularly for cases presenting with vague symptoms, instead of symptoms typical for MS, mandating various differential diagnoses.[18,20,21,25,26]

MS patients are considered more likely to have prompt diagnosis and to receive appropriate treatment, when equal access to highly specialized MS centers with experienced clinicians is allowed.[7] The diagnostic delay reduces the available therapeutic options and the opportunity for early intervention which may result in increased relapse rate as well as irreversible sequelae.[21,23,25] Notably, the first admission specialty was neurology in nearly half of our patients, and more than half of the patients reported that they were followed by the same physician who initially diagnosed their disease. Also, the onset of treatment was within 1 year of diagnosis (early) in the majority of our patients.

In a population-based Danish cohort study among RRMS patients, treatment was reported to be initiated in 1922 patients within 1 year (early), in 2126 patients between 1 and 4 years (intermediate) and in 1160 patients from 4 to 8 years (late).[27] The authors also reported that the hazard of receiving a disability pension increased with a prolonged delay of treatment initiation.[27]

Previous studies indicated no differences between male and female MS patients in terms of the first specialty sought, previous misdiagnosis, frequency of relapses or the current EDSS scores.[21,22,24,25] Similarly, in our study, other than the higher rate of fatigue in females, no gender difference was noted on admission symptoms or first-admission specialties, current treatment status or relapse rates. However, a higher rate of disability was reported by males, despite the similar rate of relapse between females and males. While relapses significantly increase the hazard of all-cause disability worsening events, pre-existing disability and older age were considered the principal risk factors for incomplete relapse recovery.[6,28] The likelihood of DMTs to mask the presence of disease activity is also considered for the patients having increased disability levels without showing disease activity.[6,29]

While the marital status of MS patients has not been specifically addressed in terms of the diagnostic delay in most studies, some studies

reported that married patients experienced shorter diagnostic delays than single patients.[21,22] In the present cohort, divorced/widow(er) status was associated with an increased likelihood of disability necessitating the use of assistive devices (cane, walker or wheelchair), while married patients were more likely to have a disability with no need for assistive devices. Indeed, the presence of a spouse is suggested to be a positive factor even in the earlier course of the disease, by shortening the time needed to diagnose via the earlier discerning of symptoms and encouraging early medical consultation.[21,22]

In our cohort, patients with a disability necessitating the use of a cane, walker or wheelchair reported higher divorce rates, a longer (>15 years) disease duration and a more frequent loss of job than those with a disability but not using an assistive device and those with a considerable loss of dexterity. In a retrospective analysis of the Danish MS patient registry, the median time from onset of MS to retirement (receipt of an early pension) was reported to be 10 years, compared with 24 years among matched control individuals.[30] Also, in a study across nine European countries, authors reported an unemployment rate of 50% among patients of working age with an EDSS score of 3.0 along with a steady decline in utility score with increasing EDSS score.[31]

Even moderate levels of disability in MS patients are likely to be highly disruptive to normal living due to the unpredictable and debilitating nature of relapses experienced by many patients early in the disease course.[32] The EDSS awareness was similar across our disability groups, regardless of the use of assistive devices or having only loss of dexterity.

In our cohort, receiving IV treatment, which was more common in males, in patients with ≥15 years of disease duration and in SPMS patients, was associated with a higher rate of treatment switch, disability and use of assistive devices. Treatment switch was also more commonly reported by patients older than 45 years of age. In a previous nationwide study conducted with 1379 MS patients in Turkey in 2018, longer diagnostic process and younger age at diagnosis were associated with a higher likelihood of treatment discontinuation for any reason and/or treatment switching.[18] The association of longer duration of disease (10–14 years vs. <5 years) with increased likelihood of poor treatment adherence was also reported in a French national web-based survey among MS patients.[33] Also, in a study with 3205 newly diagnosed RRMS patients from 24 Italian centers, younger age, diagnosis delay, higher baseline EDSS and use of interferons (vs. other treatments) were independently associated with higher inefficacy switch rates but comorbidities and interferons were associated with higher switches for intolerance/safety.[34]

In our cohort, nearly half of the patients reported significant concerns related to the uncertainty of the future, the impaired quality of life and a lack of hope for future improvement. These findings support that concerns about disability and fear for their future are common in the MS population given that they are often diagnosed in the peak productive years and of the age to possibly start a career and/or a family.[35] Hence, inspiring hope for the future and patient education on a variety of topics (plan of care, treatment side effects, injection anxiety, social isolation, and realistic treatment expectations) are considered key factors in enabling informed treatment decisions and maintaining self-care and healthy coping in the setting of MS.[35-37]

Nearly half of our patients reported that they have hope for improvement in their current situation or disease in the future, and eradication of MS, reversal of disability and prevention of MRI progression were the main future expectations/hopes. Considering the current treatment expectations, less frequent SC injection dosing was the main expectation in our patients receiving SC therapy who were also more likely to have MS for <5 years, while fewer hospital visits and self-administration of HEDs at home were the leading expectations in patients receiving IV therapy who were also more likely to have MS for ≥15 years. In a study among 125 MS patients, the most important attribute for MS patients was reported to be side effects of DMTs, followed by delay in disability progression, and route and frequency of administration.[15] Also, more recently diagnosed (<5 years) patients were worried more about side effects of treatment and were less concerned about treatment efficacy in the delay of MS progression than those with a longer disease duration.[15] Patient preferences are considered to be strongly correlated with the disease duration and DMT experience.[12] Several studies reported that MS patients strongly preferred preventing long-term disability progression over preventing relapses and are willing to accept an increase in the severity of side effects to delay disease progression.[15,38-40]

Developing and maintaining realistic treatment expectations in addition to tolerability/safety issues

and treatment burden are considered essential in treatment adherence among MS patients.[41,42] In this regard, our findings emphasize that eliciting and incorporating patient´s perspective and preferences regarding many aspects of treatment (route of administration, posology, concerns regarding specific side effects and safety issues, use of high efficacy drugs) in treatment decision making may positively influence adherence and satisfaction.[7,14,15,43]

The major strength of the current study is the inclusion of a representative sample of overall MS population in our country (database on 2176 MS patients). However, there are certain limitations of the study. First, the use of self-reported data without objective verification (such as medical records) is an important limitation which leads to a concern of reporting bias especially for the clinical parameters such as MS type, age at diagnosis, disease duration and time from presentation to diagnosis and the reasons for treatment switch. Second, the lack of data on neurocognitive disability status and psychometric qualitative measurements is another limitation. Third, given that approximately 70,000 people are affected by MS in Turkey and there are 10,000 followers of our social media account, our study population comprises 20% of those following our account on the social media platform. This is another limitation given that not all patients may have been on the Facebook platform due to fear of stigmatization, have access to computers or be comfortable with online survey or interview.

In conclusion, this nationwide questionnaire-based study in Turkish MS patients revealed the altered disability status with respect to sociodemographic profile and altered treatment expectations specific to the route of ongoing MS drug, in addition to significant concerns regarding the uncertainty of the future, impaired quality of life and lack of hope for future improvement in nearly half of patients. An improved disease-awareness among patients and clinicians and an improved access of MS patients to highly specialized MS centers with experienced clinicians seems important for timely diagnosis and implementation of a personalized treatment tailored to the individual disease trajectories, clinical worsening and disability attainment as well as to the patient´s perspective and preferences.

DISCLOSURE

Ethics: The study was conducted by the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee.

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