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Original Article

Association of neuropathic pain with bladder and bowel dysfunction, functional disability, and quality of life of patients with multiple sclerosis

Alper Mengi[1], Bengi Gül Türk[2], Melih Tütüncü[2], Sabahattin Saip[2], Aksel Siva[2], Uğur Uygunoğlu[2]

[1]Department of Pain Management, Edirne Sultan 1. Murat State Hospital, Edirne, Türkiye
[2]Department of Neurology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye

ABSTRACT

Objectives: To investigate the association between neuropathic pain (NP) and bladder/bowel dysfunction in multiple sclerosis (MS) and evaluate the association of NP with functional disability, quality of life, anxiety, depression, and sleep quality.

Patients and Methods: Patients diagnosed with MS based on the 2017 Revised McDonald criteria between who were between 18 and 65 years of age were included in our study. We analyzed data of 175 patients (56 male, 119 female). The patients were assessed for demographic and clinical characteristics, NP, bladder/bowel dysfunction, disability, health perception and quality of life, anxiety and depression, and sleep quality.

Results: MS patients with NP had significantly higher Expanded Disability Status Scale (EDSS) scores, Hospital Anxiety and Depression Scale (HADS) for the subscales anxiety and depression, and Pittsburgh Sleep Quality Index (PSQI) scores ($p<0.05$). The patients with NP had a higher proportion of female patients and musculoskeletal pain ($p<0.05$). The patients with NP had significantly lower scores for Functional Independence Measure bladder and bowel scores; Monitoring My Multiple Sclerosis scale physical status, relationships, energy, and cognitive/mental and total scores. Sex, EDSS scores, HADS scores for anxiety subscale, and PSQI scores for subjective sleep quality subscale were independent predictors of NP ($p=0.008$, 0.002, 0.029, and 0.024, respectively; adjusted $R^2=0.438$).

Conclusion: Female sex, greater disability, higher anxiety levels, and poorer subjective sleep quality increase the likelihood of NP in MS. We found that bladder and bowel dysfunctions are more common among patients with NP; however, bladder or bowel dysfunction was not a predictor of NP.

Keywords: Anxiety, bladder, intestine, multiple sclerosis, neuropathic pain, sleep quality

Multiple sclerosis (MS) has a heterogeneous clinical presentation, with common symptoms including visual impairment, sensory impairment, muscular weakness, gait impairment, cognitive impairment, and fatigue.[1] Notably, pain is one of the common and disturbing symptoms in patients with MS.[2,3] Pain in such patients can be classified into three types: nociceptive, neuropathic, or mixed. Neuropathic pain (NP) is the most common pain in patients with MS, and it can present as dysesthetic extremity pain, different types of neuralgia, or Lhermitte's sign. In particular, dysesthetic extremity pain is the most common NP in MS.[4,5]

Poor bladder and bowel control is a common problem in MS, with bladder and bowel dysfunction affecting 19%-80% and approximately 50% of patients, respectively. Bladder and bowel dysfunctions lead to social isolation, low self-esteem, and activity limitations, significantly affecting the quality of life of such patients.[6] Bladder and bowel dysfunctions have been found to be associated with disease duration and disability.[6,7]

Pain in patients with MS significantly impairs quality of life, participation in social activities, and activities of daily living.[3] This indicates the importance of routine pain assessment and identification of factors associated with pain. Pain in MS has been found to be associated with factors such as long disease duration, progressive type, higher disability, older age, female sex, depression, fatigue, and anxiety.[8-10] However, compared with general pain, MS-associated NP has received less attention from researchers. Some previous studies have suggested that NP can be associated with higher disability, fatigue, or depression.[11,12]

Corresponding author: Alper Mengi, MD. Department of Pain Management, Edirne Sultan 1. Murat State Hospital, Edirne, Türkiye.
E-mail: a_mengi22@hotmail.com
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To date, our clinical daily practice has revealed that patients with MS who exhibit NP also have a high prevalence of incontinence and related dysfunctions, affecting their quality of life. However, we could not find any study investigating this association, except for one study that reported higher Expanded Disability Status Scale (EDSS) bladder/bowel functional system scores in MS patients with NP.[11] Therefore, we primarily aimed to investigate the association between NP and bladder/bowel dysfunctions in MS patients, and our secondary aim was to evaluate the association of NP with functional disability, quality of life, anxiety, depression, and sleep quality.

PATIENTS AND METHODS

This cross-sectional study was approved by the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Clinical Research Ethics Committee (decision no: 99, date: 26.04.2022). The study included patients who presented to the outpatient neurology MS clinic of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine between May and November 2022 and met the inclusion and exclusion criteria. All patients who accepted the study protocol provided consent to participate in the study after reading the informed consent form. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria for the study were as follows: patients diagnosed with MS based on the 2017 Revised McDonald criteria,[13] between 18 and 65 years, and were literate.

Exclusion criteria were as follows: patients who experienced an MS attack and presented with changes in disability or existing complaints (e.g., pain and bladder/bowel dysfunctions) over the past 3 months; those with pain syndrome caused by a neurological disease other than MS (radiculopathy, nerve injuries, etc.); those presenting with a history of psychiatric diseases such as depression, anxiety, and bipolar disorder and/or severe cognitive dysfunction (patients who did not report a history of psychiatric disease were assessed using Hospital Anxiety and Depression Scale (HADS) and those presenting with exceeding cut-off values[14] were excluded to avoid interference of psychological symptoms and focus on specific aspects of pain); and those presenting with a history of infectious, chronic inflammatory disease and cancer, diabetes, cardiac pathologies (e.g., coronary artery disease and heart failure), chronic kidney failure, chronic liver failure, drug and alcohol addiction, permanent urinary catheterization, and pregnancy.

Assessment of patients and assessment criteria

Patients enrolled in the study underwent detailed neurological examination and structured face-to-face interviews for collecting demographic data (age, sex, education status, occupation, marital status, income level), household members, body mass index, duration of MS-associated clinical symptoms, time since MS diagnosis, MS type, NP, musculoskeletal pain, trigeminal neuralgia, headache, spasm associated with pain, Lhermitte's sign, regular use of drugs for analgesia within the past 3 months, urinary and fecal incontinence, disability, health perception and quality of life, anxiety and depression, and sleep quality. In order to determine the presence and type of pain in MS patients, patients were questioned by researcher A.M., a pain specialist and physiatrist, about whether they had pain, if any, its location, character, onset, severity, radiation, associated symptoms, and factors that exacerbate and relieve pain. Nociceptive and NP were distinguished using clinical examination and the Douleur Neuropathique-4 (DN4) questionnaire. For the diagnosis of NP, the participants were assessed using the DN4 questionnaire. This questionnaire comprises 10 items, of which the first 7 items are related to pain sensation and characteristics, and other items are related to the findings of the physical examination. A total score of ≥4 indicates the presence of NP, whereas a score of <4 indicates the absence of NP.[15] Musculoskeletal pain was evaluated as pain originating from bones, joints, muscles, vertebral column, tendons or related soft tissues with nociceptive characteristics, such as low back pain, neck pain, and joint pain. Regular pain-management drugs used in the past 3 months—analgesics (including paracetamol, nonsteroidal anti-inflammatory drugs, opioids), antiepileptics (including pregabalin, gabapentin and carbamazepine), and antidepressants—were recorded.

Sphincter dysfunction was assessed using the sphincter control section of Functional Independence Measure (FIM) instrument, which includes subscales for bladder and bowel management. FIM subscales are scored using a 7-point Likert scale, ranging from 1 to 7.[16] FIM has been found to be valid and reliable in evaluating the effect of disability in MS patients.[17]

Patients were assessed for disability using the EDSS. This scale is the most widely accepted tool for measuring clinical disability in MS patients. The scores on this scale range from 0 (normal neurological exam) to 10 (death due to MS).[1,18]

Participants' self-perceptions of health and quality of life were assessed using the Monitoring My Multiple Sclerosis (MMMS) scale. This scale comprises 26 items, divided into 4 subscales (physical, relationships, energy, and cognitive/mental), and uses a 4-point Likert scale for scoring. The scale scores range from 26 to 104, with higher scores indicating greater patient satisfaction with their health status and functioning. In a previous study, this scale was adapted to Turkish and proved to be a valid and reliable tool.[19]

The participants were evaluated for anxiety and depression using the HADS. It is scored using a 4-point Likert scale, for each item ranging from 0 to 3. Higher scores indicate higher anxiety and depression. The cut-off score is 10 and 7 for the anxiety and depression subscales, respectively.[14]

Participants' sleep quality was assessed using the validated Turkish version of the Pittsburgh Sleep Quality Index (PSQI), which is a widely used measure of sleep quality, with scores ranging from 0 to 3. The scores for each item are summed to obtain a total score of 0-21, with higher scores indicating greater sleep disturbance. This index comprises 19 self-reported items that generate 7 component scores.[20]

Statistical analysis

Statistical analyses were performed with SPSS version 19.0 (Armonk, NY: IBM Corp). The data were evaluated for the normality of distribution using Kolmogorov-Smirnov test and histograms. Descriptive data were expressed as mean ± standard deviation, minimum and maximum, median and interquartile range or number and frequency, where applicable. For continuous variables, the study groups were evaluated using independent samples t-test or Mann-Whitney U test. Conversely, categorical variables were compared using Pearson's chi-square test and Fisher-Freeman-Halton exact test. The Pearson correlation coefficients were used to assess the association between continuous variables. The binary logistic regression analysis was used to identify factors associated with the presence of NP. The confidence interval was set at 95% and p value <0.05 was considered statistically significant.

RESULTS

In the present study, we analyzed data of 175 patients, of whom 56 were male (32%) and 119 were female (68%). The patients' demographic and clinical characteristics are presented in Table 1. Seventy-seven (44%) patients included in the study had NP. In the patients with NP (16 male, 61 female, mean: 37.6±9.9 years), 58 patients were relapsing-remitting and 19 were progressive MS. There was no significant difference in MS type between patients with and without NP (p=0.081). The patients with NP were found to have significantly higher scores on EDSS; HADS for the subscales anxiety and depression; and PSQI for the components subjective sleep quality, sleep latency, sleep efficiency, sleep disturbance, and daytime dysfunction as well as higher total PSQI scores (p<0.001, <0.001, 0.019, <0.001, 0.002, 0.011, <0.001, 0.001, and <0.001, respectively). The group with NP had a higher proportion of female patients and patients with musculoskeletal pain (p=0.005 and 0.002, respectively).

There was no difference between the groups in terms of regular medication (analgesics, antiepileptics, or antidepressants) use over the past 3 months (p=0.075, 0.057, and 0.192, respectively). The patients with NP had significantly lower scores for FIM bladder and bowel dysfunction, MMMS physical status, relationships, energy, cognitive/mental subscales, and total scores compared to the patients without NP (p<0.001, 0.008, <0.001, 0.042, 0.001, <0.001, and <0.001, respectively). There were no significant differences between the study groups in terms of other demographic and clinical characteristics (Table 2).

There was a significant positive correlation between the DN4 and EDSS scores; HADS anxiety and depression scores; PSQI total scores; and PSQI scores for the subscales subjective sleep quality, sleep latency, sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction (p<0.001, <0.001, 0.004, <0.001, <0.001, 0.001, 0.008, <0.001, 0.008, and <0.001, respectively). Conversely, there was a significant negative correlation between the DN4 and FIM scores for bladder and bowel dysfunction; MMMS scores for the subscales physical status, relationships, energy, and cognitive/mental; and total MMMS scores (<0.001, <0.001, <0.001, 0.001, <0.001, <0.001, and <0.001) (Table 3).

The parameters that were found to be significantly different between the two groups were evaluated for their effect on the presence of NP using a binary logistic regression analysis. Sex, EDSS scores, HADS scores for anxiety subscale, and PSQI scores for subjective sleep quality subscale were found to be independent predictors of NP (p=0.008, 0.002, 0.029, and 0.024, respectively; adjusted R^2=0.438) (Table 4).

DISCUSSION

The present study found that MS patients with NP had poor bladder and bowel control, quality of life, sleep quality, and disability, as well as high anxiety and depression scores. We found that among patients with NP, the proportion of female patients and patients with musculoskeletal pain was high. In patients with MS, female sex, greater disability, higher anxiety levels, and poorer subjective sleep quality increase the likelihood of NP.

According to Truini et al.,[5] 31% of patients with MS present with one or more types of NP. In addition, Truini et al.[5] reported a prevalence of 12%-28%, 2%-5%, and 15% for neuropathic extremity pain, trigeminal neuralgia, and Lhermitte's sign in patients with MS. Conversely, Drulovic et al.,[9] reported a prevalence of approximately 52%-56%, 52.9%, 19.2%, and 5.7% for NP, neuropathic extremity pain, Lhermitte's sign, and trigeminal neuralgia in patients with MS. Notably, the results of the current

TABLE 1
Demographic and clinical characteristics of MS patients

Patients (n=175)				
	(Mean ± SD) (min-max)		n	%
Age (years)	37.2±10.5 (18.0-65.0)	**Sex**		
		Male	56	32.0
		Female	119	68.0
BMI (kg/m²)	24.3±4.8 (16.4-40.4)	**MS type**		
		Relapsing-remitting	142	81.1
		Progressive	33	18.9
Duration of MS-associated clinical symptoms (years)	9.7±7.6 (1.0-36.0)	**Neuropathic extremity pain**		
		Yes	64	36.6
		No	111	63.4
Time since MS diagnosis (years)	7.6±7.1 (1.0-36.0)	**Lhermitte's sign**		
		Yes	29	16.6
		No	146	83.4
EDSS	2.4±1.8 (0.0-8.0)	**Trigeminal neuralgia**		
		Yes	7	4
		No	168	96
DN4 score	3.1±2.6 (0.0-9.0)	**Musculoskeletal pain**		
		Yes	25	14.3
		No	150	85.7
FIM Bladder score	5.8±1.9 (1.0-7.0)	**Headache**		
		Yes	12	6.9
		No	163	93.1
FIM Bowel score	6.6±0.6 (4.0-7.0)	**Tonic spasm associated pain**		
		Yes	5	2.9
		No	170	97.1
MMMS scale		**Living with**		
Physical	27.3±5.6 (12.0-40.0)	Family	109	62.3
Relationships	23.9±3.9 (11.0-32.0)	Parents	58	33.1
Energy	7.8±1.9 (3.0-12.0)	Sibling	2	1.1
Cognitive/mental	13.9±2.6 (7.0-20.0)	Alone	6	3.4
Total	72.8±12.5 (39.0-99.0)			
HADS		**Education level**		
Anxiety	5.9±3.6 (0.0-11.0)	Primary school	26	14.9
Depression	4.5±2.9 (0.0-8.0)	Secondary school	14	8.0
PSQI score		High school	50	28.6
Subjective sleep quality	1.1±0.7 (0.0-3.0)	University	85	48.6
Sleep latency	1.1±1.0 (0.0-3.0)	**Occupation**		
Sleep duration	0.5±0.7 (0.0-3.0)	Housewife	41	23.4
Sleep efficiency	0.5±0.7 (0.0-2.0)	Office worker	75	42.9
Sleep disturbance	1.3±0.7 (0.0-3.0)	Heavy duty worker	19	10.9
Use of sleep medication	0.2±0.7 (0.0-3.0)	Not working	40	22.9
Daytime dysfunction	0.7±0.8 (0.0-3.0)	**Marital status**		
Global	5.4±3.3 (0.0-15.0)	Married	106	60.6
		Single	66	37.7
		Divorced	3	1.7
		Income level		
		Income more than expense	4	2.3
		Income less than expense	34	19.4
		Income equal to expense	137	78.3

SD: Standard deviation; min: Minimum; max: Maximum; BMI: Body mass index; EDSS: Expanded Disability Status Scale; DN4: Douleur Neuropathique-4; FIM: Functional Independence Measure; MMMS: Monitoring My Multiple Sclerosis; HADS: Hospital Anxiety and Depression Scale; PSQI: Pittsburgh Sleep Quality Index; MS: Multiple sclerosis.

TABLE 2
Comparison of groups with and without neuropathic pain

	Patients with neuropathic pain n=77					Patients without neuropathic pain n=98					
	n	%	Mean ± SD	Median	IQR	n	%	Mean ± SD	Median	IQR	p
Age (years)			37.6±9.9					36.8±11.0			0.617[a]
BMI (kg/m²)			24.7±5.2					24.1±4.4			0.400[a]
Duration of MS-associated clinical symptoms (years)			10.2±7.7					9.3±7.5			0.435[a]
Time since MS diagnosis (years)			7.7±7.0					7.6±7.3			0.953[a]
FIM bladder score				6.0	2.0				7.0	1.0	<0.001[b]
FIM bowel score			6.5±0.6					6.7±0.6			0.008[a]
EDSS			3.0±1.6					1.8±1.9			<0.001[a]
MMMS scale											
Physical			25.6±5.4					28.7±5.3			<0.001[a]
Relationships			23.1±4.1					24.4±3.7			0.042[a]
Energy			7.3±1.9					8.2±1.7			0.001[a]
Cognitive/mental				13.0	4.0				15.0	1.0	<0.001[b]
Total			69.1±12.7					75.7±11.5			<0.001[a]
HADS											
Anxiety			8.1±5.0					4.9±3.4			<0.001[a]
Depression			6.1±4.6					4.6±3.7			0.019[a]
PSQI score											
Subjective sleep quality			1.3±0.7					0.9±0.6			<0.001[a]
Sleep latency			1.4±1.1					0.9±1.0			0.002[a]
Sleep duration			0.6±0.8					0.5±0.6			0.198[a]
Sleep efficiency			0.7±0.8					0.4±0.6			0.011a
Sleep disturbance			1.6±0.8					1.1±0.6			<0.001[a]
Use of sleep medication				0.0	0.0				0.0	0.0	0.104[b]
Daytime dysfunction			0.9±0.8					0.5±0.7			0.001[a]
Global			6.7±3.6					4.4±2.7			<0.001[a]
Sex											
Male	16	20.8				40	40.8				0.005[c]
Female	61	79.2				58	59.2				
MS type											
Relapsing-remitting	58	75.3				84	85.7				0.081[c]
Progressive	19	24.7				14	14.3				
Musculoskeletal pain											
Yes	18	23.4				7	7.1				0.002[c]
No	59	76.6				91	92.9				
Headache											
Yes	6	7.8				6	6.1				0.664[c]
No	71	92.2				92	93.9				
Tonic spasm associated pain											
Yes	4	5.2				1	1				0.100[c]
No	73	94.8				97	99				
Living with											
Family	55	71.4				54	55.1				0.255[c]
Parents	17	22.1				41	41.8				
Sibling	1	1.3				1	1.0				
Alone	4	5.2				2	2.0				

TABLE 2
Continued

	Patients with neuropathic pain n=77					Patients without neuropathic pain n=98					
	n	%	Mean ± SD	Median	IQR	n	%	Mean ± SD	Median	IQR	p
Education level											
Primary school	11	14.3				15	15.3				0.300[c]
Secondary school	8	10.4				6	6.1				
High school	24	31.2				26	26.5				
University	34	44.2				51	52.0				
Occupation											
Housewife	26	33.8				15	15.3				0.471[c]
Office worker	29	37.7				46	46.9				
Heavy duty worker	10	13.0				9	9.2				
Not working	12	15.6				28	28.6				
Marital status											
Married	53	68.8				53	54.1				0.061[d]
Single	21	27.3				45	45.9				
Divorced	3	3.9				0	0.0				
Income level											
Income more than expense	2	2.6				2	2.0				0.712[c]
Income less than expense	14	18.2				20	20.4				
Income equal to expense	61	79.2				76	77.6				
Regular use of drugs											
Analgesics	12	15.6				7	7.1				0.075[c]
Antiepileptics	9	11.7				4	4.1				0.057[c]
Antidepressants	9	11.7				6	6.1				0.192[c]

[a]Independent samples t-test; [b]Mann-Whitney U test; [c]Yates' chi-square test; [d]Fisher's exact test; BMI: Body mass index; EDSS: Expanded Disability Status Scale; DN4: Douleur Neuropathique-4; FIM: Functional Independence Measure; MMMS: Monitoring My Multiple Sclerosis; HADS: Hospital Anxiety and Depression Scale; PSQI: Pittsburgh Sleep Quality Index; MS: Multiple sclerosis; IQR: Interquartile range.

study are similar to those of previous studies in terms of the prevalence of trigeminal neuralgia and Lhermitte's sign; however, they differ from the previous studies in terms of NP and neuropathic extremity pain prevalence. This difference may be attributed to the use of different assessment tools for diagnosing NP or neuropathic extremity pain or to differences in age distribution, disease stage, and time since diagnosis in our study cohort.[12,21]

According to Ferraro et al.,[11] NP was associated with involvement of sensory functional system in patients with MS. In particular, MS patients with NP had higher EDSS scores than all other patients with or without pain included in the study and MS patients with non-NP. Further, EDSS scores for sensory, pyramidal, and bowel/bladder functions were found to be higher in patients with NP. Moreover, Ferraro et al.[11] reported clinical disability as a potential key factor for the development of pain. Solaro et al.[21] found that EDSS scores were higher in MS patients with NP than in patients without pain and those with nociceptive pain. In addition, they reported that compared with nociceptive pain, EDSS scores were independently associated with NP. The present study evaluated the total EDSS score and not subscale scores, and we found that disability assessed with EDSS was a predictor of NP. Solaro et al.[21] also reported that patients with longer disease duration and higher EDSS scores had a higher central nervous system lesion burden, possibly increasing the likelihood of having a lesion affecting the somatosensory system, further leading to NP. Although we demonstrated a relationship between NP and EDSS scores, we did not find an association between disease duration and pain. Moreover, although it has been demonstrated that disability evaluated with EDSS is associated with NP and that the prevalence of disability increases over time, we could not report any data to explain why we did not detect an association between NP and disease duration. This may be attributed to a slower course of the disease in the study participants.

Although we found a higher prevalence of bladder or bowel dysfunction in patients with NP than in patients without NP, these two dysfunctions had no effect on NP. Lin et al.[22] reported that bladder and bowel problems are associated with fatigue and level of disability measured by EDSS. Carotenuto et al.[23] found that bowel or bladder dysfunction is associated with advanced age, progressive MS, and high levels of physical disability. Furthermore, the aforementioned study indicated that

TABLE 3
Correlations with DN4 scores in MS patients

	n=175	
	p	r
FIM bladder score	<0.001	-0.361
FIM bowel score	<0.001	-0.280
EDSS	<0.001	0.439
MMMS scale		
Physical	<0.001	-0.386
Relationships	0.001	-0.256
Energy	<0.001	-0.371
Cognitive/mental	<0.001	-0.393
Total	<0.001	-0.393
HADS		
Anxiety	<0.001	0.352
Depression	0.004	0.217
PSQI score		
Subjective sleep quality	<0.001	0.330
Sleep latency	0.001	0.244
Sleep duration	0.463	0.056
Sleep efficiency	0.008	0.199
Sleep disturbance	<0.001	0.357
Use of sleep medication	0.008	0.201
Daytime dysfunction	<0.001	0.291
Global	<0.001	0.377

r: Pearson correlation coefficient; EDSS : Expanded Disability Status Scale; DN4: Douleur Neuropathique-4; FIM: Functional Independence Measure; MMMS: Monitoring My Multiple Sclerosis; HADS: Hospital Anxiety and Depression Scale; PSQI: Pittsburgh Sleep Quality Index; MS: Multiple sclerosis.

TABLE 4
The binary logistic regression analysis of the factors affecting the presence of neuropathic pain

	B	OR	95% CI lower-upper	p
Sex	1.363	3.908	1.417-10.776	0.008
EDSS	0.544	1.723	1.229-2.415	0.002
HADS anxiety	0.152	1.164	1.016-1.334	0.029
PSQI, subjective sleep quality	1.128	3.089	1.159-8.235	0.024

Nagelkerke Adjusted R^2: 0.438. Reference categories: for the presence of neuropathic pain: no neuropathic pain, for sex: male, musculoskeletal pain: no musculoskeletal pain.
OR: Odds ratio; CI: Confidence interval; EDSS: Expanded Disability Status Scale; HADS: Hospital Anxiety and Depression Scale; PSQI: Pittsburgh Sleep Quality Index.

bowel or bladder dysfunction is associated with impaired cognitive function, regardless of physical disability and disease course. Alvino et al.[24] found that moderate or severe bowel dysfunction is more common among MS patients with progressive disease, severe disability, advanced age, and long disease duration; moreover, they found that female sex, ambulation disorder, and bladder symptoms are predictors of the level of bowel dysfunction. However, only the association between bladder or bowel dysfunction and NP was examined in the present study, preventing us from reporting an association of bladder or bowel dysfunction with parameters other than NP. To our knowledge, no study has investigated the association between NP and bladder or bowel dysfunction to date, except for the study by Ferraro et al.,[11] which reported that patients with NP have higher scores on EDSS bowel/bladder functional system. However, EDSS does not score the bladder and bowel functions separately. EDSS scores are evaluated based on prominent dysfunctions; hence, systems with less dysfunction may be neglected.

Kahraman et al.[25] reported that MS patients with NP have higher EDSS and depression scores than MS patients without pain or patients with musculoskeletal pain. Heitmann et al.[12] found that disability along with depression and fatigue are predictors of NP in MS patients in early phases of the disease. Another study reported that higher levels of pain in such patients are associated with more fatigue, anxiety, and sleep quality after statistically controlling for age, sex, EDSS score, and social support status.[26] The present study found that anxiety and poor subjective sleep quality are independent predictors of NP,

but there was no such relationship between depression scores and NP. Patients with a clinical diagnosis of psychiatric illness and anxiety and depression scores above cut-off values were excluded from the present study. Although this may help eliminate the possible effects of mood-associated problems on the relationship between pain and other evaluated parameters, it may have affected our analysis of relationship between depression and NP.

Solaro et al.[21] reported that compared to the group without pain, the group with both NP and nociceptive pain included a higher proportion of women. However, they found no differences in sex distribution among patients with NP and nociceptive pain. This may be attributed to a higher sensitization to pain among women and to hormonal and/or specific psychosocial factors. Hadjimichael et al.[27] reported that increased pain intensity in patients with MS is positively associated with female sex. In contrast, another study found that pain scores were similar among female and male patients and that female sex may not be a key factor for developing pain in MS.[11] However, the present study found that female sex was a predictor of NP. To our knowledge, this is the first study to report that female sex may be predictive of NP.

Study limitations

This study has some limitations. This was a single-center study, which made it difficult to generalize the results. Our study was cross-sectional and this design prevented us from establishing a causal relationship between NP and other variables. There is no consensus on the pain classification in MS, and the majority of patients in our study had relapsing-remitting MS and relatively low EDSS scores. Therefore, the results cannot be generalized to patients with more disabilities. Data on the severity of NP, electromyography, and urodynamic testing in MS patients were not available in this study. NP in MS patients can be assessed using different tools. The current study used DN4, which includes both self-assessment and physical examination sections, making it more sensitive than generic screening instruments.[3] However, the DN4 score is not effective in detecting NP patterns such as trigeminal neuralgia or Lhermitte's sign. Therefore, the assessment of NP in MS patients requires clinical examination and a face-to-face interview.[21] The use of an assessment tool other than DN4 may produce different results. Finally, factors previously reported to have a potential impact on NP in MS, such as fatigue and cognitive function, were not evaluated in the present study.

In conclusion, we found that bladder and bowel dysfunctions were more common among patients with NP. Additionally, female sex, higher disability, greater anxiety, and poorer sleep quality were associated with a higher likelihood of NP. Therefore, the simultaneous presence of these findings may serve as a practical indicator for clinicians: the emergence of one finding could heighten suspicion for the development of the other, thus supporting earlier detection of complications and improving prognostic assessment. Their monitoring may be valuable for long-term patient follow-up, aiding in the identification of disease progression and the tailoring of symptom-focused therapeutic strategies. Further studies that use objective assessment techniques such as urodynamic testing or electromyography instead of subjective reporting are warranted for the evaluation of the association between bladder or bowel dysfunction and NP.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Filippi M, Bar-Or A, Piehl F, Preziosa P, Solari A, Vukusic S, et al. Multiple sclerosis. Nat Rev Dis Primers. 2018;4:43. Erratum in: Nat Rev Dis Primers. 2018;4(1):49.
2. Kratz AL, Whibley D, Alschuler KN, Ehde DM, Williams DA, Clauw DJ, et al. Characterizing chronic pain phenotypes in multiple sclerosis: a nationwide survey study. Pain. 2021;162:1426-33.
3. Yilmazer C, Lamers I, Solaro C, Feys P. Clinical perspective on pain in multiple sclerosis. Mult Scler. 2022;28:502-11.
4. Brola W, Mitosek-Szewczyk K, Opara J. Symptomatology and pathogenesis of different types of pain in multiple sclerosis. Neurol Neurochir Pol. 2014;48:272-9.
5. Truini A, Barbanti P, Pozzilli C, Cruccu G. A mechanism-based classification of pain in multiple sclerosis. J Neurol. 2013;260:351-67.
6. Dawson S, Smith C, Norton C, Kilonzo M, Drake MJ, Cotterill N. Conservative interventions for urinary or faecal incontinence, or both, in adults with multiple sclerosis. Cochrane Database Syst Rev. 2018;2018:CD013150.
7. Lakin L, Davis BE, Binns CC, Currie KM, Rensel MR. Comprehensive approach to management of multiple sclerosis: addressing invisible symptoms-a narrative review. Neurol Ther. 2021;10:75-98.

8. Marck CH, De Livera AM, Weiland TJ, Jelinek PL, Neate SL, Brown CR, et al. Pain in people with multiple sclerosis: associations with modifiable lifestyle factors, fatigue, depression, anxiety, and mental health quality of life. Front Neurol. 2017;8:461.
9. Drulovic J, Basic-Kes V, Grgic S, Vojinovic S, Dincic E, Toncev G, et al. The prevalence of pain in adults with multiple sclerosis: a multicenter cross-sectional survey. Pain Med. 2015;16:1597-602.
10. Solaro C, Brichetto G, Amato MP, Cocco E, Colombo B, D'Aleo G, et al.; PaIMS Study Group. The prevalence of pain in multiple sclerosis: a multicenter cross-sectional study. Neurology. 2004;63:919-21.
11. Ferraro D, Plantone D, Morselli F, Dallari G, Simone AM, Vitetta F, et al. Systematic assessment and characterization of chronic pain in multiple sclerosis patients. Neurol Sci. 2018;39:445-53.
12. Heitmann H, Biberacher V, Tiemann L, Buck D, Loleit V, Selter RC, et al. Prevalence of neuropathic pain in early multiple sclerosis. Mult Scler. 2016;22:1224-30.
13. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17:162-73.
14. Aydemir Ö, Güvenir T, Küey L, Kultur S. Hospital Anxiety and Depression Scale Turkish form: validation and reliability study. Türk Psikiyatri Der. 1997;8:280-7.
15. Unal-Cevik I, Sarioglu-Ay S, Evcik D. A comparison of the DN4 and LANSS questionnaires in the assessment of neuropathic pain: validity and reliability of the Turkish version of DN4. J Pain. 2010;11:1129-35.
16. Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. Adv Clin Rehabil. 1987;1:6-18.
17. Granger CV, Cotter AC, Hamilton BB, Fiedler RC, Hens MM. Functional assessment scales: a study of persons with multiple sclerosis. Arch Phys Med Rehabil. 1990;71:870-5.
18. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 1983;33:1444-52.
19. Polat C, Tülek Z, Kürtüncü M, Eraksoy M. Validity and reliability of the Turkish Version of the Monitoring My Multiple Sclerosis Scale. Noro Psikiyatr Ars. 2017;54:131-6.
20. Agargun M. Pittsburgh uyku kalitesi indeksinin gecerligi ve guvenirligi. Turk Psikiyatri Dergisi 1996;7:107-15.
21. Solaro C, Cella M, Signori A, Martinelli V, Radaelli M, Centonze D, et al.; Neuropathic Pain Special Interest Group of the Italian Neurological Society. Identifying neuropathic pain in patients with multiple sclerosis: a cross-sectional multicenter study using highly specific criteria. J Neurol. 2018;265:828-35.
22. Lin SD, Butler JE, Boswell-Ruys CL, Hoang P, Jarvis T, Gandevia SC, et al. The frequency of bowel and bladder problems in multiple sclerosis and its relation to fatigue: a single centre experience. PLoS One. 2019;14:e0222731.
23. Carotenuto A, Costabile T, Moccia M, Falco F, Petracca M, Satelliti B, et al. Interplay between cognitive and bowel/bladder function in multiple sclerosis. Int Neurourol J. 2021;25:310-8.
24. Alvino B, Arianna F, Assunta B, Antonio C, Emanuele D, Giorgia M, et al. Prevalence and predictors of bowel dysfunction in a large multiple sclerosis outpatient population: an Italian multicenter study. J Neurol. 2022;269:1610-7. Erratum in: J Neurol. 2022;269:2824-5.
25. Kahraman T, Özdoğar AT, Ertekin Ö, Özakbaş S. Frequency, type, distribution of pain and related factors in persons with multiple sclerosis. Mult Scler Relat Disord. 2019;28:221-5.
26. Amtmann D, Askew RL, Kim J, Chung H, Ehde DM, Bombardier CH, et al. Pain affects depression through anxiety, fatigue, and sleep in multiple sclerosis. Rehabil Psychol. 2015;60:81-90.
27. Hadjimichael O, Kerns RD, Rizzo MA, Cutter G, Vollmer T. Persistent pain and uncomfortable sensations in persons with multiple sclerosis. Pain. 2007;127:35-41.