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**RESEARCH**

# Impact of sexual and neurogenic lower urinary tract dysfunction on multiple sclerosis patients' quality of life and health perceptions

## Cinsel ve nörojenik alt üriner sistem disfonksiyonunun multipl skleroz hastalarının yaşam kalitesi ve sağlık algıları üzerindeki etkisi

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**Abstract**

**Purpose:** To investigate the impact of neurogenic lower urinary tract dysfunction (NLUTD) and sexual dysfunction (SD) on multiple sclerosis (MS) patients' quality of life and health perceptions and evaluate the possible relationship with disease parameters.

**Materials and Methods:** A total of 192 patients with MS were included in the study. Along with the King's Health (KHQ) and COOP/WONCA questionnaires, Arizona Sexual Experience Scale (ASEX), Beck Depression Scale (BDI), Monitoring My Multiple Sclerosis Scale (MMMS) were used to evaluate the patients' quality of life and self-perception of health.

**Results:** The median age of the patients was 39.5 years (18–66 years). In contrast, SD was present in 34.4%, 51.6% of the patients presented with NLUTD. Patients with NLUTD had significant differences in terms of age, education level, duration of disease, EDSS, BDI, ASEX, and MMMS scores. The majority of the study group had minor disability (82.8% had an EDSS score less than 3). Patients with SD showed higher disability, depression, and disrupted self-perception of their health status. In addition, quality of life measures correlated with the presence of NLUTD, SD and depression along with higher disability and altered self perception of their health status.

**Conclusion:** NLUTD and SD significantly effect quality of life and well being. Increasing awareness about the impact of NLUTD and SD symptoms in patients with MS will provide a comprehensive approach in clinical practice.

**Keywords:**. Multiple sclerosis; neurogenic lower urinary tract dysfunction; sexual dysfunction; self perceptions of health; quality of life

**Öz**

**Amaç:** Nörojenik alt üriner sistem disfonksiyonu (NLUTD) ve cinsel disfonksiyonun (CD) multipl skleroz hastalarının yaşam kalitesi ve sağlık algıları üzerindeki etkisini araştırmak ve hastalık parametreleri ile olası ilişkisini değerlendirmek.

**Gereç ve Yöntem:** Çalışmaya toplam 192 MS hastası dahil edildi. Hastaların yaşam kalitelerini ve sağlık algılarını değerlendirmek için King's Yaşam anketi (KHQ) ve COOP/WONCA anketleri yanı sıra Arizona cinsel deneyim ölçeği (ASEX), Beck depresyon ölçeği (BDÖ), Multipl skleroz izlem ölçeği (MMMS) kullanıldı.

**Bulgular:** Hastaların yaş ortancası 39,5 (18-66) idi. Hastaların % 34,4'ünde CD mevcutken, % 51,6'sında NLUTD mevcuttu. NLUTD olan hastaların yaş, eğitim düzeyi, hastalık süresi, EDSS, BDÖ, ASEX ve MMMS skorları açısından anlamlı fark vardı. Çalışma grubunun büyük çoğunluğunun hafif özürlüğü vardı (% 82,8'inin EDSS puanı üçten azdı). CD olan hastalarda daha fazla özürlülük, depresyon ve sağlık durumlarına ilişkin algılarında bozulma görüldü. Ek olarak, yaşam kalitesi ölçümleri, NLUTD, CD ve depresyon varlığıyle birlikte daha fazla özürlülük ve sağlık durumlarıyla ilişkili değişen algıları ile korele olarak bulundu.

**Sonuç:** NLUTD ve CD yaşam kalitesini ve iyilik halini önemli ölçüde etkiler. MS'li hastalarda NLUTD ve CD semptomlarının etkisi konusunda farkındalığın artması, klinik pratikte kapsamlı bir yaklaşım sağlayacaktır.

**Anahtar kelimeler**: Multip skleroz; nörojenik alt üriner sistem disfonksiyonu; cinsel disfonksiyon; sağlık algısı; yaşam kalitesi

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## INTRODUCTION

Relapsing remitting type of multiple sclerosis (RRMS) presents with demyelinating episodes and neurological signs determined by the location of the lesion within the central nervous system. Clinical manifestations often include impaired sensation, muscle weakness, and ataxia[1]. Also, patients with multiple sclerosis (PwMS) suffer from invisible, externally imperceptible complaints, such as fatigue, cognitive deficits, sexual dysfunction, and urinary tract dysfunction[2].

The approach of health-related quality of life (HRQoL) has considered the unique perspective of patients[3]. Considering the quality of life helps clinicians evaluate treatment outcomes, make treatment decisions, and assess the patient's perspective. In addition, HRQoL assessment puts patient priorities forwards and strengthens clinician-patient communication[4]. In clinical practice, neurologists follow up the PwMS with varied outcome measures, relapses, disability, and magnetic resonance imaging activity. However, HRQoL should also be considered during the management of these patients[5].

It is well known that HRQoL and health perception are related to the degree of disability and various psychosocial factors[5]. However, neurogenic lower urinary tract dysfunction (NLUTD) occur in 50-80% of PwMS, affecting social life[6]. Furthermore, the prevalence of sexual dysfunction (SD) is reported approximately 40-80% in females and 50-90% in male patients[7]. Besides, SD can significantly impact HRQoL[8]. NLUTD is also reported to harm sexual life[9]. Despite the impact of NLUTD and SD symptoms on patients' lives; they refrain from informing their physicians. Furthermore, clinicians may not be aware of the significance of these complaints. Several patients do not seek medical assistance as they are ashamed to share symptoms with their physicians[9].

In this study, we aimed to evaluate the impact of NLUTD and SD on the quality of life and health perception of pwMS. Furthermore, we investigated the relationship of NLUTD and SD with disease parameters. We hypothesized that NLUTD and SD have an impact on health perception and quality of life in PwMS. The COOP/WONCA test is a valid tool which obtains a valuable information in MS. Our study is the first to use COOP/WONCA test in evaluating HRQoL in Turkish people with MS.

## MATERIALS AND METHODS

### Study design and participants

The cross-sectional study was carried out at the University of Health Sciences, Izmir Bozyaka Education and Research Hospital, MS Unit which is one of the important MS centers of Aegean Region. We evaluated the patients consequtively between January 2021 and August 2021. We enrolled the participants according to the inclucion and exclucion criteria. Experienced neurologists (NE, AK) carried out all study procedures.

The following inclusion criteria were applied for participation in the study: Patients ≥18 years old, diagnosed according to McDonald 2017 diagnostic criteria, free from relapse in the past three months, with a disease duration of at least one year, and an Expanded Disability Status Scale (EDSS) score ≤6. Except for RRMS, the patients with a history of concomitant neurologic or psychiatric disorders, concomitant NLUTD, and bowel symptoms, and urinary tract infections in the last month, and urinary tract disorders irrelevant to MS were excluded from the study. Patients who could not answer the questionnaire questions due to language or cognitive limitations were also excluded.

We enrolled 215 patients with a definite diagnosis of RRMS. Of them, 10 patients had concomitant bowel symptoms, three had a history of early relapse, four had EDSS scores higher than six, one patient had bipolar disorder, and five had urinary tract infections or other urinary tract diseases. Thus, 192 patients with MS were enrolled in the study. Detailed information on demographic data, disease duration, relapse, annual relapse rate (ARR), and EDSS score were recorded. In addition, patients were asked and recorded whether they had symptoms including urinary urgency, increased frequency during the day, nocturia, hesitancy, urge incontinence, incomplete emptying, weak, and interrupted stream, feeling of incomplete bladder emptying after voiding. NLUTD was clinically diagnosed and categorized according to the EDSS functional system score[10].

The current study was organized following the ethical roles recommended in the Declaration of Helsinki. The University of Health Sciences, Izmir Bozyaka Education and Research Hospital's ethical committe approved this study on 30 December 2020 (Approval number: 8). All participants were included in the study after giving written informed consent.

### Measures

### King's Health Questionnaire (KHQ)

We used KHQ to evaluate the impact of symptoms associated with NLUTD symptoms on QoL. It consists of 21 questions and eight domains (general health perception, impact of incontinence, role limitations, physical limitations, social limitations, personal relationships, emotions, sleep/energy). It also has two separate scales for incontinence and symptom severity. There is no total score for the KHQ; each domain is scored separately. The scores for the domains are calculated according a standardized formula. Each domain's score range from 0 to 100. A higher score represents the worst QoL.[11] Incontinence severity and symptom severity scores range from 0-100 and 1-30, respectively. Akkoc et al. reported that the Turkish KHQ is validated and reliable in PwMS. The Cronbach's alpha score was determined to be between 0.59 and 0.91[12]

### Arizona Sexual Experience Scale (ASEX)

We assessed sexual dysfunction using the Turkish version of the ASEX questionnaire. The reliability and validity of ASEX questionnaire in Turkish was performed by Soykan A.[13]. Soyan et al reported the Cronbach's alpha score in the ASEX questionnare between 0.89 and 0.90[13]. There are two types questionnaires for men and women. Each item on the questionnaire has a 6-point Likert scale. The total score aligns from 5 to 30. If the total score is ≥19, any items scores 5 or 6, or any three items score 4, a relationship with SD was suspected[14].

### Beck Depression Inventory (BDI)

We used the Beck Depression Scale (BDI) to examine depressive symptoms. It is recommended as a screening test to identify depression in PwMS. The total score was scaled from 0-63. Total scores 11-17, 18-29, and 30-63 are associated with mild, moderate, and severe depression[15,16]. Hisli performed the reliability and validity of ASEX in Turkish [17]

### COOP/WONCA questionnaire

We used the Dartmouth version of the COOP/WONCA charts to measure HRQoL. The COOP/WONCA charts are simple, easy to understand, used in patients with low education levels, and self-reported. The charts were developed to evaluate patients' general health status with chronic diseases for primary care physicians. The reliability and validity of the COOP/WONCA charts were conducted by Calıskan et al.[18] Eight simple questions about physical fitness, mood and feelings, daily activities, social activities, changes in health status, general health, pain, and quality of life were included. Higher scores indicate the worse health status (1 point represents no limitation; 5 points representseverely limited).[19] Pappalardo et al reported a inter-rater agreement of 0.8, ranging from 0.64 to 0.91, as expressed by the alpha coefficient. They showed intra-rater agreement 0.82, ranging from 0.78 to 0.96.[4] The COOP/WONCA charts are valuable tools with good psychometric properties for determining HRQoL in PwMS. Moreover, patients complete it in less than 5 minutes[4,20].

### Monitoring My Multiple Sclerosis Scale (MMMS)

We used the MMMS to determine the health status of PwMS from their perspective. The MMMS was produced by Gulick et al. in 2011, and the Turkish reliability and validity of the instrument were conducted by Polat et al. in 2017. A higher score indicates that patients are more satisfied with their health status and functioning (Score ranges:26-104)[21,22]. In the study of Polat et al., Cronbach's alpha coefficients calculated to evaluate internal consistency were between 0.643 and 0.89[22]

### Statistical analysis

Statistical Analysis was performed by using the SPSS version 21 software (Armonk, NY: IBM Corp). The Conformity of the continuous variables to assess normal distribution was evaluated using histograms, Q-Q plot and Kolmogorov-Smirnov test. Because only the variables "age" and "total score of COOP-WONCA" revealed normal distribution, all the continuous variables were presented as median (minimum – maximum) values. Categorical variables were reported as frequency and percentage. In the analytic analyses, the relationship of categorical variables was assessed with a chi-square test. A comparison of median values between two groups was achieved using Mann-Whitney U test. The Spearman correlation coefficient was applied to evaluate the relationships among the continuous variables. The statistical significance level was considered as a p value less than 0.05.

## RESULTS

The median age of the study population was 39.5

years (18 – 66 years). While 125 (65.1%) patients were female, 67 (34.9%) patients were males. The demographic and clinical characteristics of the study ppoulation are presented in Table 1. The answers to the lower urinary tract symptoms questions determined the presence of NLUTD. 51.56% of patients had NLUTD-related symptoms. The frequency of NLUTD-related symptoms in patients was as follows: Urinary urgency (80.80%), increased daytime frequency (76.76%), urge incontinence (60.6%), nocturia (64.6%), incomplete emptying (65.6%), weak stream (23.23%), interrupted stream (39.39%), the feeling of incomplete bladder emptying after voiding (65.6%). 3.03% of patients with NLUTD were using intermittent self-catheterization.

According to the BDI, depression in 122 (63.54%) of 192 patients. 54.91% had mild, 30.32% moderate, and 14.75% severe depressive symptoms. According to the ASEX tool, SD was detected in 66 (34.38%) of 185 patients. Seven (3.65%) participants did not complete the ASEX tool. Except for the data of these seven patients, all data were included in the study.

We divided the study population into two groups according to the presence of NLUTD. A statistical difference was found in age (p=0.026), and level of education (p=0.043), duration of disease (p<0.001), EDSS (p<0.001), scores of BDI (p<0.001), ASEX (p<0.001), and MMMS (p<0.001). No statistically significant difference was found in ARR between groups (p= 0.763) (Table 1). In addition, we divided the study population into two groups according to SD. There was a significant difference between patients regarding the presence of SD in terms of age (p= 0.033), gender (p<0.001), EDSS scores (p= 0.015), and EDSS neurogenic bladder (p= 0.001), BDI (p<0.001), ASEX (p<0.001) and MMMS (p< 0.001) (Table 1).

**Table 1. Demographical and clinical characteristics of the study population.**

| | | NLUTD Status | | | SD Status | | |
|---|---|---|---|---|---|---|---|
| | All patients (n= 192) | Yes (n= 99) | No (n= 93) | p value | Yes (n= 66) | No (n= 119) | p value |
| Age, years | 39.5 (18 – 66) | 41 (19 – 58) | 37 (18 – 66) | 0.026 | 41 (21 – 66) | 38 (18 – 58) | 0.033 |
| Female n (%) | 125 (65.1) | 66 (66.7) | 59 (63.4) | 0.639* | 58 (87.6) | 60 (50.4) | <0.001* |
| Education, years | 12 (1 – 18) | 11 (1 – 18) | 12 (5 – 18) | 0.043 | 11 (5 – 18) | 12 (1 – 18) | 0.126 |
| Disease Duration, years | 7.5 (1 – 34) | 9 (1 – 33) | 5 (1 – 34) | <0.001 | 8 (1 – 34) | 7 (1 – 29) | 0.123 |
| ARR | 0.44 (0.06 – 3.5) | 0.47 (0.06 – 3.5) | 0.38 (0.06 – 3.3) | 0.763 | 0.34 (0.06 – 3.5) | 0.5 (0.06 – 3.3) | 0,217 |
| EDSS | 1.25 (0 – 6) | 2 (1 – 6) | 1 (0 – 6) | <0.001 | 2 (0 – 6) | 1 (0 – 6) | 0.015 |
| EDSS neurogenic bladder | 1 (0 – 3) | 1 (1 – 3) | 0 (0 – 0) | <0.001 | 1 (0 – 3) | 0 (0 – 3) | 0.001 |
| BDI | 13 (0 – 46) | 16 (0 – 41) | 9 (0 – 46) | <0.001 | 17 (3 – 41) | 11 (0 – 46) | <0.001 |
| ASEX | 15 (5 – 30) | 17 (5 – 30) | 13 (5 – 30) | <0.001 | 21 (15 – 30) | 13 (5 – 30) | <0.001 |
| MMMS | 71 (15 – 104) | 64 (15 – 94) | 77 (46 – 104) | <0.001 | 62 (26 – 97) | 75 (15 – 104) | <0.001 |

ARR: Annualized relapse rate, ASEX: The Arizona Sexual Experiences Scale, BDI: Beck Depression Inventory, EDSS: Expanded Disability Status Scale, MMMS: Monitoring My Multiple Sclerosis Scale, NLUTD: Neurogenic lower urinary tract dysfunction, SD: Sexual dysfunction.
Note that the analyses were performed using Mann Whitney U Test and *Pearson chi-square test.

Correlation analysis was investigated between the COOP/WONCA domains and the clinical and demographic parameters. A correlation was found between all domains of COOP/WONCA and the duration of the presence of NLUTD, EDSS, BDI, ASEX, and MMMS scores. A significant correlation was found between the related domain of physical fitness and age, education level, and disease duration. We observed a strong correlation between daily activities, age, and disease duration. Similarly, a strong correlation was found between overall health status and age, duration of education, and duration of illness. We did not detect any correlation between any of the domains of COOP/WONCA, and ARR. The detailed correlation coefficients and p-values are shown in Table 2.

**Table 2. Correlation coefficient analysis of COOP/WONCA domains and clinical parameters**

| COOP/WONCA domains | | Age | Education duration | Disease duration | ARR | EDSS | EDSS NLUTD | NLUTD duration | BDI | ASEX | MMMS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Physical Fitness | R | 0.243 | -0.235 | 0.176 | 0.054 | 0.280 | 0.229 | 0.192 | 0.278 | 0.181 | -0.379 |
| | p value | 0.001 | 0.001 | 0.014 | 0.459 | <0.001 | 0.001 | 0.008 | <0.001 | 0.014 | <0.001 |
| Feeling | r | 0.043 | -0.099 | 0.106 | 0.060 | 0.252 | 0.282 | 0.200 | 0.528 | 0.387 | -0.476 |
| | p value | 0.554 | 0.171 | 0.145 | 0.412 | <0.001 | <0.001 | 0.005 | <0.001 | <0.001 | <0.001 |
| Daily Activities | r | 0.215 | -0.124 | 0.179 | 0.007 | 0.362 | 0.374 | 0.328 | 0.623 | 0.491 | -0.603 |
| | p value | 0.003 | 0.087 | 0.013 | 0.921 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Social Activities | r | 0.080 | -0.139 | 0.093 | 0.109 | 0.261 | 0.324 | 0.308 | 0.607 | 0.384 | -0.516 |
| | p value | 0.267 | 0.055 | 0.200 | 0.131 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Change in Health | r | -0.009 | -0.014 | 0.079 | 0.052 | 0.169 | 0.221 | 0.220 | 0.308 | 0.180 | -0.323 |
| | p value | 0.906 | 0.850 | 0.274 | 0.478 | 0.019 | 0.002 | 0.002 | <0.001 | 0.015 | <0.001 |
| Overall Health | r | 0.224 | -0.165 | 0.209 | 0.015 | 0.413 | 0.438 | 0.381 | 0.632 | 0.446 | -0.624 |
| | p value | 0.002 | 0.022 | 0.004 | 0.834 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Quality of Life | r | 0.029 | -0.023 | 0.042 | 0.097 | 0.235 | 0.241 | 0.247 | 0.551 | 0.309 | -0.510 |
| | p value | 0.692 | 0.756 | 0.562 | 0.181 | 0.001 | 0.001 | 0.001 | <0.001 | <0.001 | <0.001 |
| Pain | r | 0.099 | -0.173 | 0.104 | 0.139 | 0.280 | 0.301 | 0.290 | 0.556 | 0.392 | -0.465 |
| | p value | 0.174 | 0.016 | 0.151 | 0.054 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

ARR: Annualized relapse rate, ASEX: The Arizona Sexual Experiences Scale, BDI: Beck Depression Inventory, EDSS: Expanded Disability Status Scale, MMMS: Monitoring My Multiple Sclerosis Scale**,** NLUTD: Neurogenic lower urinary tract dysfunction. Note that the analyses were performed using Spearman's correlation coefficient.

We compared the scores of COOP/WONCA domains concerning the presence of a NLUTD. We showed that patients with NLUTD had significantly worse scores in all domains, which was compatible with worse quality of life (p<0.005) (Table 3). When we compared scores in the COOP/WONCA domains according to the presence of NLUTD, patients with SD had significantly worse scores in all domains (p <0.005) except physical fitness (p= 0.083) (Table 3).

**Table 3. Relationship between the COOP-WONCA and the presence of Neurogenic bladder and Sexual Dysfunction.**

| | | NLUTD Status | | | SD Status | | |
|---|---|---|---|---|---|---|---|
| COOP/WONCA domains | All patients (n= 192) | Yes (n= 99) | No (n= 93) | p value[a] | Yes (n= 66) | No (n= 119) | p value[a] |
| Physical Fitness | 4 (1 – 5) | 4 (1 – 5) | 3 (1 – 5) | 0.001 | 4 (1 – 5) | 3 (1 – 5) | 0.083 |
| Feeling | 3 (1 – 5) | 4 (1 – 5) | 3 (1 – 5) | 0.001 | 4 (1 – 5) | 3 (1 – 5) | <0.001 |
| Daily Activities | 2 (1 – 5) | 3 (1 – 5) | 2 (1 – 4) | <0.001 | 3 (1 – 5) | 2 (1 – 5) | <0.001 |
| Social Activities | 2 (1 – 5) | 3 (1 – 5) | 2 (1 – 5) | <0.001 | 3 (1 – 5) | 2 (1 – 5) | 0.001 |
| Change in Health | 3 (0 – 5) | 3 (1 – 5) | 3 (0 – 5) | 0.012 | 3 (1 – 5) | 3 (0 – 4) | 0.001 |
| Overall Health | 3 (0 – 5) | 4 (1 – 5) | 3 (0 – 5) | <0.001 | 4 (1 – 5) | 3 (0 – 5) | <0.001 |
| Quality of Life | 3 (1 – 5) | 3 (1 – 5) | 2 (1 – 5) | 0.003 | 3 (1 – 5) | 3 (1 – 5) | 0.001 |
| Pain | 3 (1 – 5) | 3 (1 – 5) | 2 (1 – 5) | <0.001 | 4 (1 – 5) | 3 (1 – 5) | <0.001 |

NLUTD: Neurogenic lower urinary tract dysfunction, SD: Sexual dysfunction.
Note that the analyses were performed usingMann Whitney U Test.

Correlation analysis was examined between COOP/WONCA and KHQ. A strong correlation was found between all domains of the COOP/WONCA, which assessed HRQoL, and all domains of the KHQ, which assessed the impact of symptoms associated with neurogenic bladder on quality of life. Detailed correlation coefficients and p-values are provided in Table 4.

**Table 4. Corelation coefficient analysis between COOP-WONCA and Kings' Health Questionaire domains.**

| COOP/WONCA domains | | General health perceptions | Incontinence impact | Role limitations | Physical limitations | Social limitations | Limitations in personal relationships | Emotional problems | Sleep and energy disturbances | Incontinnce severity measures | Symptom Severity |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Physical Fitness | r | 0.281 | 0.269 | 0.339 | 0.297 | 0.295 | 0.181 | 0.232 | 0.222 | 0.293 | 0.286 |
| | p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.012 | 0.001 | 0.002 | <0.001 | <0.001 |
| Feeling | r | 0.415 | 0.318 | 0.327 | 0.350 | 0.312 | 0.184 | 0.278 | 0.254 | 0.339 | 0.354 |
| | p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Daily Activities | r | 0.603 | 0.429 | 0.441 | 0.444 | 0.442 | 0.324 | 0.369 | 0.378 | 0.400 | 0.439 |
| | p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Social Activities | r | 0.457 | 0.344 | 0.354 | 0.419 | 0.372 | 0.226 | 0.346 | 0.329 | 0.286 | 0.392 |
| | p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.002 | <0.001 | <0.001 | <0.001 | <0.001 |
| Change in Health | r | 0.399 | 0.255 | 0.236 | 0.232 | 0.258 | 0.209 | 0.264 | 0.244 | 0.255 | 0.290 |
| | p value | <0.001 | <0.001 | 0.001 | 0.001 | <0.001 | 0.004 | <0.001 | 0.001 | <0.001 | <0.001 |
| Overall Health | r | 0.735 | 0.441 | 0.428 | 0.457 | 0.476 | 0.358 | 0.433 | 0.458 | 0.336 | 0.474 |
| | p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Quality of Life | r | 0.520 | 0.287 | 0.363 | 0.385 | 0.344 | 0.242 | 0.308 | 0.401 | 0.316 | 0.368 |
| | p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| Pain | r | 0.576 | 0.316 | 0.344 | 0.297 | 0.305 | 0.307 | 0.279 | 0.375 | 0.310 | 0.377 |
| | p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

Note that the analyses were performed using Spearman's correlation coefficient.

In addition, correlation analysis was performed between MMMS score and age, duration of education, duration of disease, duration of the presence of NLUTD, scores of ARR, EDSS, EDSS-neurogenic bladder, BDI, ASEX. A strong correlation was found between the MMMS score and all parameters except ARR. The detailed correlation coefficients and p-values are shown in Table 5.

**Table 5. Corelation coefficient analysis between Monitoring My Multiple Sclerosis Scale and demographical and clinical characteristics.**

| | Monitoring My Multiple Sclerosis Scale | |
|---|---|---|
| **Demographical and clinical characteristics** | **r** | **p value** |
| Age | -0.227 | **0.002** |
| Duration of Education | 0.221 | **0.002** |
| Duration of disease | -0.223 | **0.002** |
| ARR | 0.010 | 0.888 |
| EDSS | -0.438 | **<0.001** |
| EDSS neurogenic bladder | -0.406 | **<0.001** |
| NLUTD Duration | -0.395 | **<0.001** |
| BDI | -0.655 | **<0.001** |
| ASEX (n=185) | -0.507 | **<0.001** |

ARR: Annualized relapse rate, ASEX: The Arizona Sexual Experiences Scale, BDI: Beck Depression Inventory, EDSS: Expanded Disability Status Scale, NLUTD: Neurogenic lower urinary tract dysfunction. Note that the analyses were performed using Spearman's correlation coefficient.

## DISCUSSION

Invisible symptoms are common in PwMS and can significantly affect mental health, social roles, work-life, daily life, and quality of life[8,23,24]. Assessing individual perceptions of health provides an opportunity to understand the problems from the patient's perspective. Our study focused on the impact of NLUTD and SD on the well-being and health-related quality of life of MS patients. From the perspective of PwMS, our study showed that the presence of the symptoms of NLUTD and SD have a significant impact on patient's daily life and HRQOL. Parker et al. reported that invisible symptoms have a more significant impact than visible symptoms on patients' self-perception of health status and may lead to a further reduction in quality of life[23]. The study by Altmann et al. focused on describing the views of both PwMS and MS specialists on the relationship between sexuality and MS and also presenting their perspectives[8]. It is reported that although 84% of PwMS would like their MS specialists to ask about sexuality, only 19% have been asked. In addition, 95% of PwMS reported that SD would impact their quality of life[8].

The majority of our study population consisted of nondisabled patients or patients with a mild degree of disability, according to EDSS scores (Table 1). Di Filippo et al. reported that 44% of patients with mild EDSS had NLUTD, increasing this rate in patients with moderate disability[24]. Similarly, we found that 51.56% of our study population had NLUTD. A positive association between EDSS and neurogenic bladder symptoms has been previously reported, which is consistent with our study; a higher EDSS score was found in patients with NLUTD. In patients with NLUTD, we found higher age, lower education level, longer disease duration, higher EDSS, higher BDI, ASEX, and lower MMMS score. There was no significant correlation between gender and the overall frequency of NLUTD, which is consistent with the study by Aharony et al[25]. Moreover, in the present study, we found higher age, longer duration of disease, lower educational level, higher EDSS, higher BDI, ASEX, and MMMS scores in patients with SD. Duration of disease and depression have been suggested as important factors associated with SD[26,27]. Koseoglu et al. suggested that increasing age was an independent factor for SD, and higher EDSS scores might be related to SD because of concomitant depression[26]. In agreement with recent studies, we showed that female MS patients had more frequent sexual problems than males[9]. Furthermore, in line with recent studies, we found that the sexual performance of PwMS was negatively affected in the context of co-existing NLUTD[27,28].

One study reported that MS patients with bladder symptoms had a lower HRQL score, which was related to the duration of the disease[29]. The COOP/WONCA charts have been recommended in recent studies as a valuable tool with good psychometric properties for measuring HRQoL in PwMS[4,20]. Taghipour et al. showed a robust linear relationship between COOP/WONCA charts and Short-Form 36 Health Survey (SF -36) in PwMS[20]. Pappalardo et al. reported a highly significant relationship between the scores of each domain of COOP/WONCA and the MSQoL-54 composite (physical health and mental health)[4]. Our study was the first to use COOP/WONCA charts to assess HRQoL in PwMS in Turkey. Patients with NLUTD or SD symptoms in our study reported worse HRQoL than participants without these symptoms, according to the COOP /WONCA assessments. Statistically, patients with NLUTD were found to have significantly worse scores for each questionnaire item. Similarly, there were statistically significant worse scores in all COOP/WONCA domains in patients with SD symptoms, except physical fitness (Table 3).

Akkoc et al. demonstrated that the KHQ could be used to study the effect of incontinence on the quality of life of PwMS in Turkey. A significant correlation was reported between most KHQ, MSQoL-54, and EDSS scores. On the other hand, role limitation, physical limitation, and personal relationships showed low correlation with MSQoL-54[12]. Reese et al. indicated a consistent correlation between KHQ and SF -36 domains in patients with overactive bladder[30]. Our study revealed a correlation between all KHQ and COOP/WONCA domains, indicating that COOP/WONCA is an excellent tool to performing HRQoL in disease-specific aspects.

Assessing and monitoring patients' subjective perceptions of health status and functioning provides a perspective. Patients can evaluate their health status regarding physical health, relationships, energy, and cognitive/mental abilities in the MMMS tool[21]. In recent studies, a strong negative correlation was found between the EDSS and the MMMS, suggesting that the score of physical subscale correlates with patients' functional status[21,22]. In addition, anxiety and depression were correlated with the MMMS[22]. Here,

we demonstrated strong negative correlations between age, disease duration, scores of EDSS, EDSS-neurogenic bladder, duration of the presence of neurogenic bladder, BDI, and ASEX scores.

The strengths of our study were the inclusion of a large group of PwMS and having an appropriate female-to-male ratio based on the proportion of MS prevalence rate. Moreover, this is the first study in Turkey to use COOP/WONCA charts to assess HRQoL in PwMS. However, some limitations of the study should be noted. All instruments used in this study were based on self-report. Compared with observational or laboratory-based studies, responses may be biased.

On the other hand, self-report questionnaires may have also contributed to more sincere and accurate responses. However, observational or laboratory studies are challenging in sex research for various reasons, including ethical, financial, and time constraints. Another challenge is finding a patient population that would voluntarily participate in such a study. For these reasons, we could not confirm the diagnosis of SD in the laboratory.

In conclusion, presense of NLUTD and SD impacts quality of life and well being. The MMMS, COOP/WONCA, and Kings' Health questionnaires provide valuable information about well-being from the patient's perspective. These questionares can be used in MS outpatient clinic practices and for follow-up. The growing awareness of the impact of NLUTD and SD symptoms in PwMS will contribute to a comprehensive approach in the clinical setting. We concluded that the COOP/WONCA test is an easy and essential test for evaluating HRQoL in PwMS.

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