



## Relation between Voiding Dysfunction and Quality of Life in Multiple Sclerosis Patients

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### ABSTRACT

**Background:** Multiple sclerosis (MS) is a chronic neurological disease characterized by inflammation, demyelinating and eventual neurodegeneration in the central nervous system. This can result in a variety of symptoms that markedly affect the patient's quality of life (QoL). One common manifestation of MS is voiding dysfunction. Therefore, this study was carried out to study the impact of voiding dysfunction on the QoL among MS patients.

**Methods:** This cross-sectional study included 60 patients recruited from MS Outpatient Clinic of Neurology department at Zagazig University Hospitals and El Sheikh Zayed Al Nahyan Hospital, they were diagnosed as MS as per the 2017 Revised McDonald Diagnostic Criteria. We studied the relation between QoL and voiding dysfunction in MS patients using International Prostate Symptom Score (IPSS) as well as Multiple Sclerosis International Quality of Life (MusiQoL) scores.

**Results:** Statistically significant differences were revealed between IPSS severity and all of activities of daily living ( $p=0.035$ ), psychological wellbeing ( $p=0.007$ ), symptoms ( $p=0.01$ ), relation with friends ( $p=0.005$ ), relation with family ( $p=0.037$ ), coping ( $p=0.045$ ) and MusiQoL index ( $p=0.004$ ) (all were significantly lower in patients with moderate/severe IPSS score). Statistically significant negative correlations also were found between IPSS severity and all of psychological wellbeing ( $p=0.006$ ), symptoms ( $p=0.011$ ), relation with friends ( $p=0.025$ ), relation with family ( $p=0.007$ ), coping ( $p=0.014$ ) and rejection ( $p=0.006$ ), also highly significant negative correlations were revealed between IPSS severity with activities of daily living dimension score ( $p<0.001$ ) and MusiQoL index ( $p=0.001$ ).

**Conclusion:** Various levels of severity of lower urinary tract symptoms (LUTS) (mild, moderate and severe) were observed among MS patients, with mild LUTS being predominantly observed. Findings indicated that the severity of LUTS is closely linked with reductions in various QoL dimensions. Particularly, patients with moderate to severe LUTS reported significantly lower QoL scores, underscoring the profound impact of urinary dysfunction on their daily lives and overall well-being.

**Keywords:** Multiple Sclerosis, Voiding Dysfunction, Quality of Life.

### INTRODUCTION

Multiple sclerosis (MS) is a chronic neurological disease characterized by

inflammation, demyelinating and eventual neurodegeneration in the central nervous system. Multiple sclerosis can manifest at any age, although

it typically occurs in individuals between the ages of 20 and 50. The disease affects women at a rate three times greater than males [1]. Globally, there are 8 million individuals currently living with MS. [2].

Lower urinary tract symptoms (LUTS) are common manifestations in MS, affecting 50-80% of patients over the course of the disease. These symptoms have a significant negative effect on patients' quality of life (QoL) and their capacity to fulfill social roles [3].

Symptoms of neurogenic LUTS in MS might range from urine retention to incontinence or a combination of both. It was shown that LUTS limited the everyday activities in MS patients with bladder dysfunction. The physical and clinical load of both conditions had a detrimental impact on their QoL, leading to feelings of humiliation, sadness, skin fragility, and social isolation [4].

In addition, LUTS restrict their freedom of movement, necessitates special equipment to help them urinate in the restroom, and makes them reliant on caregivers. Moreover, this issue hinders their engagement in health development programs, leading to an increase in the disease's secondary consequences and a further decline in their QoL. The presence of LUTS in MS can increase the monetary costs of nursing care, incontinence therapies, and associated urinary tract infections [5]. Thus, this research aimed to study the impact of voiding dysfunction on the QoL among MS patients.

## METHODS

Between September 2022 to March 2023, this cross-sectional study included 60 patients recruited from MS Outpatient Clinic of Neurology department at Zagazig University Hospitals and El Sheikh Zayed Al Nahyan Hospital.

The study was authorized by the research ethical council of Zagazig University's Faculty of Medicine, and all participants provided written informed permission. The research followed the guidelines laid out in the Declaration of Helsinki, which is part of the World Medical Association's Code of Ethics for Research Involving Humans. This study was performed after the Institutional Review Board consent (IRB#9725/2-9-2022).

Cases with the following criteria were included: Patients aged  $\geq 18$  years old classified as young adults (18 – 39 years) and older adults ( $\geq 40$  years) [6], who had MS definitively diagnosed by a neurologist based on the 2017 Revised McDonald

Diagnostic Criteria [7], were physically and mentally able to answer questions included in the study and were willing to participate.

Exclusion criteria: cases who had MS relapse within the previous month of the study, patients who were on treatment with corticosteroids, cases who had bladder dysfunction for a different cause (prior to the onset of MS), as well as pregnant females were excluded from the study.

Each patient underwent a thorough medical history and a detailed history of MS including: date of first attack, date of diagnosis, duration of disease, total number of relapses, date of last attack, date of last steroid therapy, MS phenotype, previous disease modifying therapies and current disease modifying therapy. Additionally, each patient underwent a full clinical examination according to MS sheet in Neurology department, Zagazig University Hospitals.

Expanded Disability Status Scale (EDSS) score was calculated for all patients. Higher levels of disability are represented by increments of half a unit, and the scale goes from 0 (no disability) to 10 (MS-related mortality). Deficits in Functional Systems (FS) in individuals without any ambulatory disability determine scores ranging from 1 to 3.5. Both FS deficits and ambulatory ability contribute to the range of possible scores (4.0–9.5) [8]. Scores between 0 and 3.5 on the EDSS indicate mild MS, while scores between 4 and 9.5 indicate moderate to severe MS [9].

## *Study Questionnaire:*

**The International Prostate Symptom Score (IPSS):** It has been suggested for a preliminary evaluation of symptoms affecting the lower urinary tract [10]. Scoring on a scale from 0 to 5, the IPSS comprises seven questions pertaining to irritative and obstructive symptoms, as well as an extra question concerning general satisfaction with the urine situation. This assessment measures the irritative or storage symptoms by asking questions regarding the frequency, urgency, and nocturnal polyuria on a daily basis (maximum score of 15), obstructive or voiding symptoms (maximum score of 20) include incomplete bladder emptying, urine flow interruption, poor urine flow, and the need to exert force while starting to urinate. According to the total scores on all seven questions, three levels of severity were established: mild (0–7), moderate (8–19), and severe (20–35). Many studies reported the validity of using the IPSS in women [11].

**The Arabic version of Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL) (5.4):** This self-administered questionnaire assesses various aspects of patients' lives and provides insight into how MS affects their everyday life. The original creator of the survey also handled the language validation and Arabic translation (Mapi Research Trust, Lyon, France)[12].

The MusiQoL questionnaire include a total of 31 questions across 9 dimensions (subscales): activities of daily living (8 items), psychological wellbeing (4 items), symptoms (4 items), relationships with friends (3 items), relationships with family (3 items), sentimental and sexual life (2 items), coping (2 items), rejection (2 items), and relationships with healthcare system (3 items). The mean of these subscale scores was used to calculate the index score.

#### **Laboratory Investigations**

All patients were subjected to the following: Complete Blood Count, C-reactive protein, Erythrocyte Sedimentation Rate, Urine analysis, Urine culture and sensitivity, Liver and kidney functions tests, Cerebrospinal fluid oligoclonal bands and Immunoglobulin G index.

#### **Radiological Investigations**

**Magnetic Resonance Imaging (MRI) of the brain and cervico-dorsal spine (MS protocol):** MRI was conducted using either a 1.5 Tesla MRI scanner or a 3 Tesla MRI scanner when required. MRI sequences included T1, T2, Fluid attenuated inversion recovery, Diffusion weighted imaging, Apparent diffusion coefficient and contrast-enhanced T1 images (in both the axial and sagittal planes). MRI data included site of MS lesions, T2 lesion count and presence or absence of black holes and active lesions.

**Pelviabdominal ultrasonography:** It was done in all cases to exclude local causes of bladder dysfunction.

#### **Statistical analysis**

All data were collected, tabulated and statistically analyzed using IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Descriptive statistics were calculated for all variables, including mean, standard deviation, median, and interquartile range. Additionally, the count (number) and percentage of each category for categorical variables were determined. The Mann-Whitney test was conducted to compare the distributions of two independent

groups when the assumptions of normality and homogeneity of variance were not met. Our statistical tools of choice included chi-square, Fischer exact, and Monte Carlo tests for comparing qualitative data across categories as needed. In order to find the direction and intensity of the link between two ordinal or non-normally distributed continuous variables, Spearman's rank correlation coefficient was computed. In order to establish statistical significance, the p-value (meaningfulness threshold) was established at  $\alpha = 0.05$ . Results were deemed statistically significant when the p-values were less than 0.05.

#### **RESULTS**

About 75% of studied patients were young adults (18-39 years), with the rest being older adults (40 years and above). Females comprised 75% of the participants, while males made up 25%. Among the patients, 63.3% had relapsing-remitting multiple sclerosis (RRMS), 26.7% had secondary progressive multiple sclerosis (SPMS) and 10% had primary progressive multiple sclerosis (PPMS). The mean of the EDSS was 3.67 with 56.7% of patients classified as having moderate to severe disability (EDSS 4 - 9.5). The median total number of relapses was 3, The median disease duration was 7 years (Table 1).

We assessed urinary symptoms severity in studied patients by utilizing the IPSS score. The severity of IPSS varied, with the majority experiencing mild symptoms (66.7%), followed by moderate (28.3%) and severe (5%) with a median total score of 5 and a median quality of life score of 3 (Table 2). Regarding the relation between LUTS with age, sex and MS-specific data, we found non-significant relation between them (Table 3).

In studying the relation between IPSS severity and MusiQoL scores, we found statistically significant differences between IPSS severity and all of activities of daily living ( $p=0.035$ ), psychological wellbeing ( $p=0.007$ ), symptoms ( $p=0.01$ ), relation with friends( $p=0.005$ ), relation with family ( $p=0.037$ ), coping ( $p=0.045$ ) and MusiQoL index ( $p=0.004$ ) (all were significantly lower in patients with moderate/severe IPSS score) (Table 4).

Statistically significant negative correlations also were found between IPSS severity and all of psychological wellbeing ( $p=0.006$ ), symptoms ( $p=0.011$ ), relation with friends ( $p=0.025$ ), relation with family ( $p=0.007$ ), coping ( $p=0.014$ ) and rejection ( $p=0.006$ ), also highly significant negative correlations were revealed between IPSS severity

with activities of daily living dimension score (p<0.001) and MusiQoL index (p=0.001) (Table 5).

**Table (1):** Demographic data and multiple sclerosis characteristics of studied patients:

|                              | <b>N=60</b>         | <b>%</b>           |
|------------------------------|---------------------|--------------------|
| <b>Age:</b>                  |                     |                    |
| Young adult (18 – 39 years)  | 45                  | 75%                |
| Older adult (≥ 40 years)     | 15                  | 25%                |
| <b>Sex:</b>                  |                     |                    |
| Female                       | 45                  | 75%                |
| Male                         | 15                  | 25%                |
| <b>MS Phenotype:</b>         |                     |                    |
| PPMS                         | 6                   | 10%                |
| RRMS                         | 38                  | 63.3%              |
| SPMS                         | 16                  | 26.7%              |
| <b>EDSS</b>                  |                     |                    |
| Mild (1 - 3.5)               | 26                  | 43.3%              |
| Moderate to severe (4 - 9.5) | 34                  | 56.7%              |
|                              | <b>Mean ± SD</b>    | <b>Range</b>       |
| EDSS                         | 3.67 ± 1.81         | 1 – 7.5            |
|                              | <b>Median (IQR)</b> | <b>Range</b>       |
| Total number of relapses     | 3(2 – 5)            | 1 – 25             |
| Duration of disease (years)  | 7(4 – 12)           | 4 months – 24 year |

IQR interquartile range, SD Standard Deviation, EDSS Expanded Disability Status Scale, PPMS Primary Progressive Multiple Sclerosis, RRMS Relapsing Remitting Multiple Sclerosis, SPMS Secondary Progressive Multiple Sclerosis

**Table (2):** International Prostate Symptom Score results among studied patients:

|   | <b>N=60</b>         | <b>%</b>     |
|---|---------------------|--------------|
| <b>Severity</b>                         |                     |              |
| Mild                                    | 40                  | 66.7%        |
| Moderate                                | 17                  | 28.3%        |
| Severe                                  | 3                   | 5%           |
|   | <b>Median (IQR)</b> | <b>Range</b> |
| Total score                             | 5(2 – 9)            | 0 – 30       |
| Quality of life due to urinary symptoms | 3(0 – 4)            | 0 – 6        |

IQR interquartile range

**Table (3):** Relation between IPSS severity, demographic data and MS characteristics of studied patients:

|                              | <b>Mild</b>     | <b>Moderate/severe</b> | $\chi^2$ | <b>P</b> |
|------------------------------|-----------------|------------------------|----------|----------|
|                              | <b>N=40 (%)</b> | <b>N=20 (%)</b>        |          |          |
| <b>Age:</b>                  |                 |                        |          |          |
| Young adult (18 – 39 years)  | 33 (82.5%)      | 12 (60%)               | 3.6      | 0.058    |
| Older adult (≥ 40 years)     | 7 (17.5%)       | 8 (40%)                |          |          |
| <b>Gender:</b>               |                 |                        | Fisher   | 0.753    |
| Female                       | 29 (72.5%)      | 16 (80%)               |          |          |
| Male                         | 11 (27.5%)      | 4 (20%)                |          |          |
| <b>EDSS:</b>                 |                 |                        | 2.172    | 0.141    |
| Mild (1 - 3.5)               | 20 (50%)        | 6 (30%)                |          |          |
| Moderate to severe (4 - 9.5) | 20 (50%)        | 14 (70%)               |          |          |

|                                 |                     |                     |          |          |
|---------------------------------|---------------------|---------------------|----------|----------|
| <b>MS phenotype:</b>            |                     |                     |          |          |
| <b>PPMS</b>                     | 4 (10%)             | 2 (10%)             | MC       | 0.867    |
| <b>RRMS</b>                     | 26 (65%)            | 12 (60%)            |          |          |
| <b>SPMS</b>                     | 10 (25%)            | 6 (30%)             |          |          |
|                                 | <b>Median (IQR)</b> | <b>Median (IQR)</b> | <b>Z</b> | <b>P</b> |
| <b>Total number of relapses</b> | 3(2 – 4)            | 4.5(1.25 – 8.5)     | -1.483   | 0.138    |
| <b>Disease duration (years)</b> | 7.5(3.25 – 12)      | 6.5(4 – 11.25)      | -0.047   | 0.962    |

χ<sup>2</sup>Chi square test, MC Monte Carlo test, IQR interquartile range, Z Mann Whitney test, \*p<0.05 is statistically significant.

EDSS Expanded Disability Status Scale, PPMS Primary Progressive Multiple Sclerosis, RRMS Relapsing Remitting Multiple Sclerosis, SPMS Secondary Progressive Multiple Sclerosis

**Table (4):** Relation between IPSS severity and MusiQoL scores of studied patients:

|   | <b>Mild (n=40)</b>  | <b>Moderate/severe (n=20)</b> | <b>Z</b> | <b>P</b> |
|---|---------------------|-------------------------------|----------|----------|
|   | <b>Median(IQR)</b>  | <b>Median(IQR)</b>            |          |          |
| <b>Activities of daily living</b>       | 62.5(40.6 – 81.92)  | 46.9(22.7 – 58.6)             | -2.111   | 0.035*   |
| <b>Psychological wellbeing</b>          | 43.8(31.25-73.43)   | 20.84(1.56 – 48.44)           | -2.714   | 0.007*   |
| <b>Symptoms</b>                         | 67.71(39.06-86.46)  | 46.88(32.81- 57.81)           | -2.594   | 0.01*    |
| <b>Relation with friends</b>            | 75(50 – 89.59)      | 31.25(10.42 – 72.92)          | -2.8     | 0.005*   |
| <b>Relation with family</b>             | 100(63.54 – 100)    | 75(50 – 91.67)                | -2.089   | 0.037*   |
| <b>Sentimental and sexual life</b>      | 75(50 – 100)        | 87.5(50 – 100)                | -0.722   | 0.47     |
| <b>Coping</b>                           | 93.75(75 – 100)     | 75(50 – 100)                  | -2.006   | 0.045*   |
| <b>Rejection</b>                        | 81.25(53.13 – 100)  | 75(28.13 – 100)               | -1.398   | 0.162    |
| <b>Relation with health care system</b> | 83.3(66.7 – 100)    | 83.3(58.3 – 100)              | -0.241   | 0.809    |
| <b>MusiQoL index</b>                    | 69.79(62.99 – 82.7) | 59.08(44.27 – 68.84)          | -2.917   | 0.004*   |

IQR interquartile range, Z Mann Whitney test \*p<0.05 is statistically significant

**Table (5):** Correlation between MusiQoL scores and IPSS severity among studied patients:

|   | <b>r</b> | <b>P</b> |
|---|----------|----------|
| <b>Activities of daily living</b>       | -0.481   | <0.001** |
| <b>Psychological wellbeing</b>          | -0.489   | 0.006*   |
| <b>Symptoms</b>                         | -0.451   | 0.011*   |
| <b>Relation with friends</b>            | -0.29    | 0.025*   |
| <b>Relation with family</b>             | -0.347   | 0.007*   |
| <b>Sentimental and sexual life</b>      | -0.084   | 0.525    |
| <b>Coping</b>                           | -0.316   | 0.014*   |
| <b>Rejection</b>                        | -0.351   | 0.006*   |
| <b>Relation with health care system</b> | -0.151   | 0.251    |
| <b>MusiQoL index</b>                    | -0.51    | 0.001**  |

r Spearman rank correlation coefficient \*p<0.05 is statistically significant \*\*p≤0.001 is statistically highly significant

### DISCUSSION

Urinary dysfunction is a prevalent and distressing symptom among individuals with MS, affecting approximately 80% of patients during the course of their disease. It encompasses a spectrum of LUTS, including urgency, frequency, nocturia, urinary incontinence, and urinary retention [13].

In the current study, we studied the relation between the QoL and voiding dysfunction in MS

patients using IPSS and MusiQoL scores. 75% of participants were young adults (18-39 years), with the rest being older adults (40 years and above). Females comprised 75% of the participants, while males made up 25%.

The current study findings echo common trends seen in MS researches. More females are affected than males, and the disease often strikes young adults. The studies by AlJumah et al. [14] and Barin



et al. [15] reinforce these trends, showing a female predominance and a younger age of onset.

In the current study, we observed various clinical characteristics related MS phenotype and disability status. Among the patients, 63.3% had RRMS, 26.7% had SPMS, and 10% had PPMS. The mean of the EDSS was 3.67 with 56.7% of patients classified as having moderate to severe disability (EDSS 4 - 9.5). The median total number of relapses was 3, The median disease duration was 7 years.

The predominance of RRMS aligns with global trends. The findings from Torad et al. [16] and Barin et al. [15] corroborate our observations, demonstrating a similar distribution of MS phenotypes and highlighting the variability in disability levels. While there may be variations in disease duration and specific clinical characteristics, the overall patterns remain consistent.

We evaluated the IPSS score to assess urinary symptoms. Most patients reported mild symptom severity (66.7%), followed by moderate (28.3%) and severe (5%), with a median total score of 5 and a median quality of life score of 3.

Similar patterns were reported by Gündoğdu et al. [17] and Gustavsen et al. [18], where most patients suffered mild LUTS (45.2% and 35.9% respectively), followed by moderate LUTS, with severe symptoms reported in just 11.9% and 5.7% respectively. Our study and their studies exhibit similarities with minor discrepancies due to the utilization of different scales.

In the current study, there was a statistically non-significant relation between IPSS severity and both age and gender, which is in line with the study performed by Gündoğdu et al. [17]

However, Nazari et al. [19] reported significant associations between IPSS severity and both age and gender. They found that as age increased, the frequency of moderate to severe LUTS also notably raised. Additionally, they observed a significant difference in IPSS scores between male and female patients, finding that males are more likely than females to report severe LUTS. Variations in findings between the two studies could be attributed to differences in sample size.

The current study didn't reveal a statistically significant relation between IPSS severity and clinical characteristics of MS patients comprising EDSS, MS phenotype, total number of relapses and disease duration. Similarly, Gündoğdu et al. [17] found no significant differences in IPSS severity

based on disease duration, EDSS scores, or MS subtypes.

On contrary to our findings, Nazari et al. [19] found significant associations between the prevalence of LUTS and various clinical characteristics of MS patients; where longer disease duration, higher scores of the EDSS and progressive courses were linked to higher prevalence rates of moderate to severe LUTS.

The current study revealed a significant relationship between IPSS severity and various MusiQoL domains among MS patients. We found a statistically significant decrease in QoL scores across several domains, including activities of daily living, psychological well-being, symptoms, relations with friends and family, coping, and the overall MusiQoL index, among patients with moderate to severe IPSS scores compared to those with mild scores.

The findings of the present study are consistent with those reported by Nazari et al. [20], who also observed a significant impact of IPSS severity on various aspects of QoL among MS patients. This consistency strengthens the validity of our results and underscores the widespread negative consequences of LUTS on the QoL of individuals with MS.

On studying the correlation between MusiQoL scores and IPSS severity among studied patients, we found that all QoL domains show statistically significant negative correlations except "Sentimental and sexual life" and "Relation with health care system" domains. Additionally, "Activities of daily living" and "MusiQoL index" have statistically highly significant negative correlations ( $p \leq 0.001$ ).

The current study findings and those by Gustavsen et al. [18] and Philippova et al. [21] revealed statistically significant correlations between LUTS severity and QoL dimensions, indicating that higher levels of LUTS are linked to poorer QoL outcomes in MS patients. Despite variations in assessment tools, there is overlap in some dimensions.

The current study strength points include that it was conducted at 2 different centers providing more variability of patient's characteristics.

#### ***Limitations:***

Since this study is a small-scale, cross-sectional study involving only 60 cases, there is bound to be some selection bias in the results. Future research

should focus on longitudinal studies to track the progression of LUTS in MS patients and evaluate the efficacy of various treatment modalities. Additionally, employing larger sample sizes will enhance the generalizability of the findings.

### CONCLUSIONS

Our study concluded that various degrees of LUTS severity (mild, moderate and severe) were observed among MS patients, with mild LUTS being predominantly observed. Findings indicated that the severity of LUTS is closely linked with reductions in various QoL dimensions. Particularly, patients with moderate to severe LUTS reported significantly lower QoL scores, underscoring the profound impact of urinary dysfunction on their daily lives and overall well-being.

Based on our study findings, we recommend integrating regular LUTS screening into MS management protocols for early detection and intervention. An interdisciplinary approach involving neurologists, urologists, and rehabilitation specialists is essential. Additionally, conducting awareness workshops for MS patients on symptoms, potential LUTS and management strategies, as well as using mobile applications for information dissemination, is advised.

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