Is There a Relationship Between Overactive Bladder and Sexual Dysfunction in Women With Multiple Sclerosis?

Frédérique Le Breton, Camille Chesnel, Philippe Lagnau, Rebecca Haddad, Pascal Lacroix, Gabriel Miget, Gerard Amarenco, Claire Hentzen

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Key words: Sexual dysfunction, Multiple Sclerosis, Women, Female, Sexual disorders, Sexual activity, Overactive bladder, Detrusor overactivity.

Authors: Frédérique LE BRETON (MD) [(1)], Camille CHESNEL (MD) [(1)], Philippe LAGNAU (MD) [(1)], Rebecca HADDAD (MD) [(1)], Pascal LACROIX (MD) [(1)], Gabriel MIGET (MD) [(1)], Gerard AMARENCO (PhD) [(1)] , Claire HENTZEN (MD) [(1)]

Institution

1 : Clinical Research Group in Neurourology (GREEN), GRC 01, APHP, Sorbonne Universities. Service of Neurourology. Tenon Hospital. Paris. France.

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Corresponding Author: Frédérique LE BRETON
Department of Neurourology. Tenon Hospital. Paris. France
4 rue de la Chine 75790 Paris cedex 20
EMail : frederique.lebreton@aphp.fr

Abréviations
SD : Sexual Dysfunction
MS : Multiple Sclerosis
EDSS: Expanded Disability Status Scale
LUTD: Lower Urinary Tract Symptoms
FSFI: Female Sexual Function Index
USP: Urinary Symptom Profile

Abstract

background: Lower urinary tract Symptoms (LUTS) and Sexual dysfunction (SD) are common in women with MS and affect quality of life.

Aim: The aim of this study was to determine the relationship between sexual dysfunction (SD) and overactive bladder in women with Multiple Sclerosis (MS).

Methods: From January 2019 to January 2021, we evaluated 89 female MS patients admitted for LUTS in a Neuro-Urology Department. SD was investigated using the Female Sexual Function Index (FSFI). All subjects completed the Urinary Symptom Profile scale (USP) and Hospital Anxiety and Depression Scale (HAD A/HAD D). Neurological impairment was assessed using the Expanded Disability Status Scale (EDSS). All patients underwent neurological examination and urodynamic studies. Univariate analysis and Multivariate logistic regression analysis were performed to identify predictors of SD in women with MS (FSFI<26.55).

Outcomes: Primary outcome was to determine the association between sexual dysfunction in women with MS and LUTS (overactive bladder, stress incontinence or voiding dysfunction).

Results: Sexual dysfunction (FSFI<26,55) affected 74% of women with MS, even with low physical disabilities (EDSS<5). Univariate analysis showed that overactive bladder was more frequent in SD group, but no statistical difference was found (p<0.12). No relationship was found between sexual dysfunction and stress incontinence (p=0,47), voiding dysfunction (p= 0,79) or urinary retention (p=0,96). Multivariate logistic regression analysis identified overactive bladder to be an independent predictor of sexual dysfunction [aOR 0.03 (CI 0,0.98)]. Sexual dysfunction was not associated with detrusor overactivity on urodynamic studies or with impairment mobility but was strongly associated with the presence of depression (p<0.01)

Clinical implications: sexual disorders in women with MS should be assessed as much as urinary disorders

Strengths and limitations: this study included the largest cohort of women with MS. But the sample was obtained in an outpatient setting with low neurological impairment.

Conclusion: In our study, SD was frequent affecting young women with no anticholinergic treatment and low physical impairment. Overactive bladder seemed to be independent predictor of sexual dysfunction. Conversely, SD was not associated with detrusor overactivity, neurological impairment, or duration of disease but was strongly associated with depression.

Title: Is there a relationship between overactive bladder and sexual dysfunction in women with Multiple Sclerosis?

Introduction

Multiple Sclerosis is a chronic disease which frequently affects young women with a 3/1 female to male ratio. In MS a general demyelination process interrupts the continuity of the neural pathways and alters the neural function that is essential for normal sexual activity. The onset of symptoms starts at a time when women are generally sexually active and often desire a family life. Sexual satisfaction is a determining factor of life quality, self-esteem, and social relationships. MS has a negative impact on sexual activity and adversely affects patient's quality of life (1–3).

SD is one of the most widespread symptoms of the disease affecting 50 to 83% of women with MS (4–6). However, SD is often underdiagnosed. Furthermore, at any time during the course of MS, SD seems to affect women more frequently than men (7,8) and is more frequent than in other populations presenting chronic diseases (e.g. Rheumatoid arthritis) (4). Despite the high prevalence and even though sexual dysfunction can appear with mild handicap, 63% of patients never express their symptoms to their physician (9). The main sexual problems encountered by women with MS include the loss of libido, impaired orgasm, reduced vaginal lubrication and the loss of genital sensation (2,10)

Although meta-analysis have linked MS to SD, no clear-cut pathophysiological mechanisms have been identified to explain this potential association. The etiology of SD in patients with MS may be multifactorial and include physical, organic, hormonal, and psychogenic factors. A direct contributor of SD in MS may be the neurological damage along the brain and spinal cord pathways. Such demyelinating lesions might cause the primary SD, which manifests as a disorder of the sexual response. A multidimensional model has been described by Foley and Iverson (11) : Primary Sexual Dysfunction refers to physiologic impairments directly due to demyelinating lesions in the spinal cord or brain in MS. Neurological lesions can affect sexual response, resulting in decreased libido, difficulties with sexual arousal, decreased or lack of vaginal lubrication, loss of genital sensation, and the inability to reach orgasm. Secondary SD is caused by MS symptoms that do not directly relate to nervous system

and include increased fatigue, impaired motility, bladder and bowel dysfunction, spasticity and pain resulting from inadequate lubrication. Finally, tertiary SD is related to psychological, emotional, social and cultural aspects of MS that may interfere with sexual functioning such as altered self-image, lowered self-esteem, depression and anger.

Lower urinary tract dysfunction (LUTD) is very common in patients with MS. Approximately 80% of all MS patients will develop voiding dysfunction or urinary incontinence during the course of their disease (6,10). According to the International Continence Society (ICS), overactive bladder is a clinical syndrome (OAB) defined, as urinary urgency, with urinary frequency and nocturia, with or without urge incontinence. It affects 73,45% of patients with MS (12) resulting in patient frustration. The mechanism underlying overactive syndrome in women is complex and can be multifactorial (obesity, birth, prolapse, age, metabolic syndrome…) and not always associated with detrusor overactivity on urodynamic studies. The presence of detrusor overactivity (DO), detrusor underactivity (DU) and/or detrusor- sphincter dyssynergia (DSD) is the result of a complex alteration of the brain and spinal cord control in neurological disease.

Many factors such as physical disability, urinary incontinence or bowel disorders have been suggested to contribute to sexual dysfunction (SD) in patients with MS. In women with spinal cord injuries, urinary incontinence may affect sexual activity and detrusor overactivity seems to be an independent factor of sexual dysfunction (13). Orgasm has been shown to be associated with bladder contraction amid the overall perineal muscle contraction. Women with sphincter deficiency may experience incontinence with certain movements or positions during intercourse that place pressure on the bladder (14). In comparison, in women with MS the relationship remains unclear.

The primary outcomes of this cross-sectional study was to analyze the association between SD in women with MS as measured by the Female Sexual Function Index (FSFI) and the presence of overactive bladder. The secondary outcomes were to determine the relationship between SD and detrusor overactivity on urodynamic studies, duration of disease, neurological impairment, and depression.

Materials and methods:

Participants and data collection: This cross-sectional study was conducted from January 2019 to January 2021. We consecutively included 89 female patients with MS admitted for a first neuro urological evaluation in an Outpatient Neuro-Urology department of a University Hospital.

Inclusion criteria were diagnosis of MS according to the McDonald revised criteria, age over 18, and lower urinary tract symptoms (LUTS). This population had no specific bladder treatment meaning no Anticholinergic drug medication, no detrusor Botulinum Toxin injections and no clean intermittent catheterization. Exclusion criteria were pre-existing major chronic disease, and mental inability to respond to the questions.

LUTS were assessed by the Urinary Symptom Profile questionary (USP) assessing stress incontinence, overactive bladder and voiding dysfunction. All patients with LUTS underwent urodynamic studies. The assessment included urine analysis, post-void ultrasonography and a urodynamic study following the International Continence Society (ICS) standards (measure of residual urine by catheterization, cystomanometry in a half-seated position and filling of the bladder at a 50 ml/min filling rate with physiological saline solution). According to ICS criteria, detrusor overactivity is defined by the presence of involuntary detrusor contractions during the filling phase (15).

We divided patients into groups with SD (FSFI< 26.55) and without SD (FSFI> 26.55), and with or without detrusor overactivity (DO). Between groups, we analyzed association of SD with overactive bladder, stress incontinence, voiding dysfunction, post void volume, detrusor overactivity, depression, anxiety, MS duration, EDSS, and urinary tract infection (significance: $p < 0.05$).

The primary outcome was the relationship between sexual dysfunction and LUTS (overactive bladder, stress incontinence or voiding dysfunction) in women with MS.

Secondary outcomes were the relationship between sexual dysfunction and and/or detrusor overactivity on urodynamic studies, neurological impairment (EDSS), duration of disease, and depression.

Data collected and tools used

The data collected included age, duration of disease, clinical pattern, anticholinergic drug scale, Urinary Symptom Profile (USP), and urinary tract infection. Depression and anxiety were evaluated using the Hospital Anxiety and Depression scale (HAD-A/HAD-D) whilst neurological impairment was assessed using the Expanded Disability Status Scale (EDSS).

Sexual function was assessed with the Female Sexual Function Index (FSFI)(16,17). The FSFI is a short 19-item, multidimensional, self-rating questionnaire developed to assess different dimensions of female sexual function including desire, arousal, lubrication, orgasm, satisfaction and pain over the last 4 weeks. It consists in the addition of the score of six subscales (sexual desire, arousal, lubrication, orgasm, satisfaction and dyspareunia), mounting to a total maximum score of 36. In this index, the score of each item ranges from 1 to 6 points in the dimension of desire, and from 0 to 5 points in all other dimensions. The total index score is the sum of the scores of all 6 dimensions. The score of each dimension is equal to the sum of the scores of all the items in that dimension, multiplied by a specific coefficient, as follows: Desire = 0.6, arousal = 0.3, lubrication = 0.3, orgasm = 0.3, satisfaction = 0.4 and pain = 0.4. The scores range from 1.2 to 6 points for the dimension of desire and from 0 to 5 points for all other dimensions. The total score of sexual dysfunction ranges from 1.2 to 36 points, and a higher score indicates better sexual function. In the present study, sexual dysfunction was defined by a cut off score of 26.55 (only if all questions had been answered) as reported by Wiegel (17).

The Hospital Anxiety and Depression Scale (HAD Scale) is a validated scale for screening significant anxiety and depression in patients attending a general medical clinic (18). The HAD scale is a self- rating questionnaire of 14-items with each item scored from 0 to 3. 7 items assess anxiety, and 7 assess depression with a total score of 21 for each.

The Urinary Symptom Profile (USP) has been developed to assess urinary symptoms in men and women with stress incontinence (0 to 9), overactive bladder (0 to 21) and voiding dysfunction (0 to 9) (19).

Sexual dysfunction may be altered by medication (ie antidepressants). These treatments were not listed but anticholinergic effect was evaluated using the Anticholinergic Drug Scale (ADS).

Statistical analysis

Statistical analysis was carried out using R 3.2.3 software (R Foundation for Statistical Computing, Vienna, Austria, http:// www.R-project.org) and R studio version 1.0.136. Means, percentages and standard deviations were used to describe the population and the responses to the questionnaire. Comparisons between sexual dysfunction groups and the presence of overactive bladder, EDSS scale and duration of disease were assessed using Student test for quantitative variables and chi-square or Fischer exact tests for categorial variables. A *p* value of less than 0.05 was considered statistically significant. A multivariate logistic regression analysis was used to identify variables associated with female sexual dysfunction (FSFI <26.55), including, EDSS, detrusor overactivity, overactive bladder on USP scale, duration of MS, depression and anxiety.

Ethics, consent and permissions

This study was approved by a local ethics committee (CPP IdF00001072). All participants provided written informed consent before enrolment.

Results

A total of 89 patients were included in the study and mean age was 46,11 (SD 11,49). 71 women (80%) had a Relapsing Remitting Form of MS (80%) and 65 (73%) had low physical impairment (EDSS<5). No women were treated using clean intermittent self-catheterization, anticholinergic drugs or botulinum toxin injections. The anticholinergic burden as measured by the Anticholinergic Drug Scale (ADS = 0,58) was low and had no impact on sexual dysfunction.

Demographic and clinical variables are described in Table 1. Table 1 presents participant s' demographic and clinical details (age, disease duration, clinical pattern of MS, EDSS, anticholinergic drug scale, urinary score profile and FSFI scale, marital status, HAD scale).

Using the established FSFI cut-off point, 66 (74 %) women with MS scored less than 26.55 and were categorized as having SD. In this group, women with MS mainly reported orgasm disorders (FSFI orgasm=1,57, sd 1,69), issues with arousal (FSFI-arousal=2,01, sd 1,88), dyspareunia (FSFI-Pain= 2,07, sd 2,37), lubrication disorders(FSFI- lubrication = 2,22, sd 2,26), desire disorders (FSFI-Desire = 2,58, sd 1,66) and no satisfaction (FSFI-satisfaction = 3,24, sd 1,32).

All women completed the USP scale and underwent Urodynamic studies. On univariate analysis, overactive bladder was more frequent in the group with FSFI<26,55, but no statistical difference was found (p<0.12). No relationship was found between sexual dysfunction and stress incontinence (p=0,47), voiding dysfunction (p= 0,79), urinary retention > 100ml (p=0,96) or the presence of urinary tract infection (p=0,36). The multivariate linear regression analysis adjusted for overactive bladder, detrusor overactivity, depression, anxiety and EDSS revealed that the presence of overactive bladder (Adjusted Odds ratio (aOR) 2.35, 95% confidence interval (CI)1.1,5) was an independent predictor of sexual dysfunction (FSFI<26,55) (Table 3).

Urodynamic studies revealed that 38 women (43%) had detrusor overactivity whilst 51 women (57%) had no detrusor overactivity. SD (FSFI <26.55) was present in 23 (60.52%) women with detrusor overactivity and in 43 women (85%) with no detrusor overactivity. The presence of detrusor overactivity was not associated with sexual dysfunction (FSFI<26,55) (Table 2). The multivariate linear regression analysis adjusted for overactive bladder, detrusor overactivity, depression, anxiety and EDSS revealed an inverse relationship between detrusor overactivity and sexual dysfunction (Adjusted Odds ratio (aOR) 0.03, 95% confidence interval (CI) 0,0.98) (Table 3)

Sexual dysfunction was not associated with age, neurological impairment (EDSS) or duration of disease. Regarding patients with an EDSS scale <5 (65 patients), 74% of patients had a sexual dysfunction. Regarding patients with an EDSS scale >5 (24 patients), 75% of patients had sexual disorders (p=0,57). Sexual dysfunction (FSFI<26,55) was present at the onset of the disease and was not associated with duration of disease (p = 0,63). On univariate analysis, we found a negative correlation between duration of disease and orgasm disorders (p = 0,01), lubrication disorders (p = 0,02) and pain (p= 0,02). Sexual dysfunction (FSFI<26,55) was not associated with age (p=0,73), but we found a negative correlation between age and FSFI desire (p-value = 0.01), FSFI arousal (p=0,002), FSFI lubrication (p=0,002), FSFI orgasm (p=0,03)

Symptoms of depression and anxiety were higher in the sexual dysfunction group (30 patients) versus the no-sexual dysfunction group (8 patients). A negative correlation was found between SD and HAD depression (p=0,001) as well as between SD and HAD Anxiety scale (p=0,06).

The multivariate linear regression analysis adjusted for overactive bladder, detrusor overactivity, depression, anxiety and EDSS revealed an inverse relationship between detrusor overactivity and sexual dysfunction (Adjusted Odds ratio (aOR) 0.03, 95% confidence interval (CI) 0,0.98). The presence of overactive bladder (Adjusted Odds ratio (aOR) 2.35, 95% confidence interval (CI)1.1,5) was an independent predictor of sexual dysfunction (FSFI<26,55) after adjustment for EDSS, detrusor overactivity, duration of disease, depression and anxiety. (Table 3)

Discussion:

This study included the largest female population evaluating sexual and urinary disorders. 74% of women with MS reported sexual dysfunction (FSFI<26.55). SD mainly consisted of orgasm disorders and difficulties becoming aroused. This study confirms that SD in women with MS is a widespread problem. However, there is a wide variation in the reported prevalence of SD in women with MS due to the difference between MS patient cohorts in terms of disability, duration of disease, as well as the different methods chosen to evaluate sexual dysfunction (mail, phone, self-report, in-person interview) (1). In a 2019 systemic review including 24 cross sectional studies, Polat reported that the prevalence of SD in women with MS ranged from 16.9% to 85%, and was higher than in healthy controls (20–25), and than in young women with other chronic diseases (rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, and ankylosing spondylitis) (26). The most common sexual difficulties reported were problems with low desire (20.5-88%) (n = 15 studies), having difficulties becoming aroused (7.9-89%) (n = 15 studies), inability to experience orgasm (4.5-77%) (n = 21 studies), lack of lubrication (5.6-60.6%) (n = 16 studies), pain (5.7-72%) (n = 5 studies) and lack of sensation in the genital area (17.6-61.7%) (n = 8 studies) (1,5,7,26,27). Although the prevalence is high, SD in women receives relatively little attention when compared to male sexual dysfunction (1,28,29). In a recent systematic review, Azimi and al. reported a meta-analysis of 9 cross sectional studies using the FSFI and the 26.55 cut off point value to determine SD. It showed that in women with MS, SD had a widely varying prevalence, ranging from 27% to 95%, and a pooled estimate of 55% (95% CI 41%-69%)(30). Analyzing studies using FSFI scores, Zhao found a 1.87-fold increased risk of SD in women who were affected by MS in comparison with controls (2). He found that women with MS had significantly lower values in total FSFI scores as compared with healthy controls (SMD - 2.41, 95% CI ;P= .001) (21–24). Lew Starowicz indicated that up to 85% of women with MS report one or more sexual dysfunctions, up to 35% report 5 or more sexual dysfunctions, and up to 13% describe 10 or more SD (31). SD has a significantly negative impact on the quality of life of patients with MS, and can be associated with the underlying neurological disease as well as mental dimensions of the quality of life (3,21,32).

The type of questionnaire can influence the assessment of sexual dysfunction. The most commonly used questionnaire is the FSFI which is a standardized tool assessing sexual function in women. It has been validated in the French language but not

specifically for assessment of sexual function in case of neurological disease. The MSISQ-19 seems to be more specific in patients with MS as Celik and al. reported a greater prevalence of SD (n= 44 women) using the MSISQ 19 compared with generic questionnaires (ASEX)(7). Conversely, Fragala an al. found a statistically significant association between detrusor overactivity and SD using the FSFI in men , which was not found using the MSISQ (33).

The population in this study were not using any medical treatments that could potentially interfere with sexual function such as anticholinergic medication, botulinum toxin injection or intermittent catheterization. However, anticholinergic medication does not seems to interfere with sexual dysfunction as Di Marco and al. reported in a series of 18 women with MS that the initiation of an anticholinergic treatment did not affect sexual function (34). Meanwhile the treatment of a neurogenic bladder has shown to be effective in improving sexual dysfunction as Giannantoni and al. demonstrated that Botulinum A toxin induced positive effect on sexual dysfunction in 31 women with MS (35).

Neurogenic bladder and sexual dysfunction

Several studies have shown that LUTS in women with MS can be the source of a significant reduction in health-related quality of life. Using self-report measures, Dandan and al. found that the most prevalent urinary symptom was urinary frequency, with a pooled prevalence estimate of 73.45%, followed by urgency at 63.87%.(12) .In the present study, overactive bladder was higher in the SD group (8,46 vs 7,48) however, no statistical difference was found ($p<0,12$) on univariate analysis. No relationship was found between SD and stress incontinence or voiding dysfunction. Multivariate analysis showed that overactive bladder was an independent predictor of sexual dysfunction. The fear of incontinence in social or sexual situations, especially if occurring during orgasm (climaturia) may have an impact on arousal because of the similar sensations upcoming for orgasm and incontinence. Zivadinov et al. (n= 70)(27) and Fraser et al (n=219)(36) observed negative associations between urinary problems and sexuality. Zidavinov and al. suggested an association between bowel and bladder and sexual dysfunction (n=70) and that this might be attributed to the impairment of autonomic control.

Although the epidemiology of DO may consistently differ based on the definitions used in the literature, the presence of detrusor overactivity reflects the neurological damage of the spinal cord or the brain. A recent meta-analysis showed a prevalence of DO in women with MS ranging from 27% to 91%(33). In our study, 38 women (42%) had detrusor overactivity whilst 51 women (57%) had no detrusor overactivity. SD was present in both women with and without detrusor overactivity (SD in women with MS with DO =60.42% vs SD in women with MS without DO = 85%). However, univariate analysis did not find any association between sexual dysfunction and detrusor overactivity. Multivariate analysis revealed that detrusor overactivity did not seem to be an independent factor of sexual dysfunction. Borello-France and al. (n=133) reported that patients bothered by their urge incontinence had higher levels of orgasms when compared to women which weren't bothered by their urge incontinence and concluded that urge incontinence does not seems to be a risk factor for anorgasmia (38). It has been shown that women with complete spinal cord injury (SCI) at the midthoracic level show perceptual responses to vaginal and/or cervical self-stimulation (including sexual response, and orgasm). It has been suggested that the vagus nerves could convey genital sensory input directly to the brain in women, completely bypassing SCI at any level. This hypothesis could also be extended to women with MS (13).

Fragala and al. suggested that in men with MS, the presence of PdetmaxIDC ≥20 cmH_2O, MCC <135 ml and compliance ≤3 ml/cmH_2O may significantly predict the presence of moderate and severe erectile dysfunction. However, no such relationship was found in a model including the previous variables and female sexual dysfunction (33). Other recent studies have not found any association between SD and bladder disorders. Although Lew-Starowicz and al. (n=137 women) analyzed bowel and bladder dysfunctions together, they observed a significant association with sexuality (39), but the types of LUTS was not described. Bartnik and al. (n=218) did not find such a relationship in terms of bladder problems and SD in remittent forms of MS. (8).

Influence of depression

Depression is admitted to be one of the most common comorbidities in MS and is known to be a strong risk factor for SD in the general population (not affected by MS) (40). Women with MS may have a negative self-image and less confidence about their sexuality. Only 38/89 women were screened with HAD because the questionary has

been introduced later in the study. However, we found a strong association between SD and depression, even though the sample was small (38/89 patients). Independently of age, duration of disease, impairment mobility and urinary dysfunction, FSFI negatively affected women with MS who had depression and anxiety. Antidepressant treatments that can interfere with sexual function were not specifically analyzed in this study but the anticholinergic burden assessed using the anticholinergic drug scale was low (ADS=0,58)

These results are consistent with the literature which widely confirms the relationship between sexual dysfunction and depression regarding all types of MS (21,23,27,31,41–43). Mood disorders such as depression and anxiety were found to be associated with developing SD. Bartnik's study (n=218=) indicated that the PHQ-9 score is correlated negatively with the FSFI general score. Hols and al. suggested that SD can even trigger depression (25). In a large sample prospective study (n=1663), Mark and al. found that morbid depression is an important risk factor for SD in patients with MS(43). In 2018, Solmaz and al. reported that in women with MS, SD was strongly associated with depression and anxiety. He reported that patients with MS (n= 42) had statistically significant lower FSFI and SF-36 scores and higher BDI (Beck Depression Inventory) and BAI (Beck Anxiety Inventory) scores when compared with healthy subjects (24).

Duration of disease and neurological impairment

The analyzed group mainly consisted of women without active relapse (Relapsing Remitting form 80%) and low neurological impairment as the average EDSS score was 3.56. No relationship was found between SD and the duration of disease or between SD and EDSS. Nevertheless, SD was present even in case of low neurological impairment, whether or not patients had any specific treatments for their neurogenic bladder (anticholinergic drug, intermittent catheterization). Several studies confirm such findings (23,44). Merghati-Khoei et al. (n= 132) demonstrated a weak correlation (r = .22) between length of the disease and general sexual performance (44). Bartnik (n= 218 women) reported no association between the duration of the disease and the occurrence of SD in the relapsing remitting form of MS (8). Nortvedt and al. (n=194) suggested that bladder and sexual problems were associated with a marked reduction in the quality of life, also in patients with low physical disability (EDSS<4.0) (3).

Conversely, Zhao observed that patients with a long duration (>10 years) of MS had lower total FSFI scores than those with shorter MS duration (< 10 years)(2,20–24). Mohammadi et al. (*n* = 226), indicated that duration of the disease longer than 9 years was one of the strongest predictors of SD (OR = 3.13)(41), but the study included patients with all forms of the disease. Ashtari and al. (n=237) reported that SD could occur at any time during the disease and with any level of disability (45). In the Narcom project (n= 6739), Orasanu and al. found that severe symptoms of SD were positively correlated with long duration of MS and high symptom scores of MS(46).

Several studies have confirmed that SD can be present even without severe physical or neurological impairment (45). Demirkiran and al. (n=35) and Mohammadi and al. (n=226) reported that female SD might occur in MS patients even if there was no severe disability (41,47) . Bartnik and al. (n=218) reported the lack of association between motor deficit and the occurrence of SD. Furthermore, Fragala and al reported that the EDSS scale was a predictive factor of desire disorders in men with no difference found in women(33). In contrast, Merghati-Khoei et al, Gumus and al. and Nazari and al found that Sexual dysfunction evaluated by the FSFI was associated with the level of disability (21,44,48). These results suggest that there may be a potential connection between MS duration, disability and SD in women with MS, although this remains controversial

This study has some limitations as it is a cross-sectional study and our population sample was obtained in an outpatient setting. The population mainly consisted of women with a remitting relapsing form (80%) and with low disabilities since 65 women (74%) had an EDSS scale <5. Furthermore, we didn’t take into account antidepressant medication although it can affect sexual dysfunction. Finally, bowel function, which several reports have related to sexual and bladder dysfunction was not assessed.

Conclusion:

In Women with MS and no medical intervention for their neurogenic bladder, the diagnosis of overactive bladder seems to be an independent predictor of sexual dysfunction. In contrast, detrusor overactivity does not seem to be a predictor of sexual

dysfunction. Interestingly, SD is present even in patients with low physical impairment and is strongly associated with depression. Further research is necessary to understand the potential underlying mechanisms and different pathways of sexual disorders in MS patients with urinary disorders.

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593 Tables

594

595 Table 1 Demographic, neurological, sexual and urodynamics characteristics of patients

596

	Mean (sd) or Nb (%)	**Number**
Nb of subjects n		89
Age, years, mean (sd)	46,11 (11,49)	89
Duration of disease, years, mean (sd)	12,75 (8,79)	88
Multiple sclerosis variants, n (%)		
Relapsing-remitting	71 (80%)	89
Primary progressive	7 (8%)	89
Secondary progressive	11 (12%)	89
EDSS	3,56 (1,68)	89
FSFI total mean (sd)	17,63 (10,79)	89
FSFI-desir, mean (sd)	3,06 (1,7)	89
FSFI-arousal, mean (sd)	2,82 (2,14)	89
FSFI-Lubrification, mean (sd)	2,93 (2,42)	89
FSFI-Orgasm, mean (sd)	2,51 (2,2)	89
FSFI-satisfaction, mean (sd)	3,84 (1,55)	89
FSFI-pain, mean (sd)	2,97 (2,59)	89
FSFI<26,55	66 (74%)*	89
FSFI>=26,55	23 (26%)	89
HAD anxiety, mean (sd)	8,11 (4,35)	38
HAD depression, mean (sd)	5 (3,15)	38
Detrusor overactivity n (%)	38 (43%)*	89
No Detrusor overactivity n (%)	51 (57%)*	89
ADS	0,56 (1,12)	89

USP stress incontinence	1,84 (2,43)	89
USP overactive bladder	8,51 (3,58) *	89
USP voiding dysfunction	2,25 (2,33)	89
Urinary infection Yes	18 (20%)	89
Urinary infection No	71 (80%)	89
Post void volume (ml)	68,63 (102,42)	89

597 Values are presented as mean±standard deviation or number (%). EDSS, Expanded
598 Disability Status Scale; MS, Multiple Sclerosis; USP, Urinary Symptoms Profile; ADS,
599 anticholinergic drug scale ; FSFI, Female Sexual Function Index; HAD= Hospital
600 Anxiety and Depression Scale

601 Table 2. Comparison of clinical and urodynamic characteristics according to the
602 presence of sexual dysfunction
603

	FSFI < 26,55		FSFI >26,55		**P-VALUE**
	Mean (sd) or Nb (%)	**Number**	**Mean (sd) or Nb (%)**	**Number**	
Nb of subjects n		66		23	
Age, years, mean (sd)	46,35 (11,69)	66	45,43 (11,12)	23	0,73
Duration of disease, years, mean (sd)	12,48 (8,69)	65	13,52 (9,23)	23	0,63
FSFI total mean (sd)	**13,02 (8,44)**	**66**	**30,86 (2,87)**	**23**	
FSFI-desir, mean (sd)	2,58 (1,66)	66	4,43 (0,82)	23	
FSFI-arousal, mean (sd)	2,01 (1,88)	66	5,14 (0,65)	23	
FSFI-Lubrification, mean (sd)	2,22 (2,26)	66	4,96 (1,6)	23	
FSFI-Orgasm, mean (sd)	1,57 (1,69)	66	5,2 (0,83)	23	
FSFI-satisfaction, mean (sd)	3,24 (1,32)	66	5,58 (0,52)	23	
FSFI-pain, mean (sd)	2,07 (2,37)	66	5,55 (0,9)	23	
HAD					
HAD Anxiety, mean (sd)	8,7 (4,45)	30	5,88 (3,27)	8	0,06*
HAD Depression, mean (sd)	5,6 (3,21)	30	2,75 (1,58)	8	<0,001*
USP					
USP stress	1,95 (2,42)	66	1,52 (2,48)	23	0,47

incontinent. mean (sd)					
USP overactive bladder. mean (sd)	8,86 (3,49)	66	7,48 (3,72)	23	0,12*
USP dysuria. mean (sd)	2,29 (2,25)	66	2,13 (2,6)	23	0,79
Urodynamic studies					
Detrusor overactivity n (%)	23 (35%)*	66	15 (65%)	23	0,01
No Detrusor overactivity n (%)	43 (65%)*	66	8 (35%)	23	
ADS mean (sd)	0,58 (1,11) *	66	0,52 (1,16)	23	0,84
Urinary infection Yes n (%)	11 (12%)	66	7 (08%)	23	0,36
Urinary infection No n (%)	55 (62%)	66	16 (18%)	23	0,40
Post void volume mean (sd)	69,02 (85,9)	66	67,52 (141,97)	23	0,96

Values are presented as mean±standard deviation or number. P.value <0,05 was considered statistically significant. FSFI, Female Sexual Function Index ; ADS, Anticholinergic Drug Scale ; EDSS, Expanded diability Status Scale ; HAD, Hospital Anxiety and Depression Scale; USP, Urinary Symptom Profile.

Table 3. Multivariate analysis according to the presence of sexual dysfunction (FSFI<26.55)

	aOR (CI 95%)	p
EDSS> 5: Yes vs No	1.16 (0.05,28.01)	0.929
Detrusor overactivity: Yes vs No	0.03 (0,0.98)	0.049
HAD anxiety	1.21 (0.84,1.74)	0.299
HAD depression	2.16 (0.96,4.84)	0.062
Duration of disease	0.92 (0.77,1.1)	0.37
Overactive bladder (USP)	2.35 (1.1,5) *	0.027

Multivariate logistic regression analysis adjusted for EDSS, presence of detrusor overactivity, overactive bladder, HAD Depression and Anxiety, duration of disease. Values are presented as aOR : adjusted Odd Ratio, CI confidence Interval and P value. EDSS, Expanded disability Status Scale; HAD, Hospital Anxiety and Depression Scale; USP, Urinary Symptom Profile