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

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

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

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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

33 **Abstract**

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

36

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

39

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

48

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

52

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

62

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

65

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

68

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

74

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

77

78 Introduction

79

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

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

96

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

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

114

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

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

135

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

141

142

143 Materials and methods:

144

145 Participants and data collection: This cross-sectional study was conducted from January
146 2019 to January 2021. We consecutively included 89 female patients with MS admitted
147 for a first neuro urological evaluation in an Outpatient Neuro-Urology department of a
148 University Hospital.

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

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

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

167

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

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

173

174

175 Data collected and tools used

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

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

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

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

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

208

209 Statistical analysis

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

220

221 Ethics, consent and permissions

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

224

225 Results

226 A total of 89 patients were included in the study and mean age was 46,11 (SD 11,49).
227 71 women (80%) had a Relapsing Remitting Form of MS (80%) and 65 (73%) had low
228 physical impairment (EDSS<5). No women were treated using clean intermittent self-
229 catheterization, anticholinergic drugs or botulinum toxin injections. The anticholinergic
230 burden as measured by the Anticholinergic Drug Scale (ADS = 0,58) was low and had
231 no impact on sexual dysfunction.

232

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

237

238 Using the established FSFI cut-off point, 66 (74 %) women with MS scored less than
239 26.55 and were categorized as having SD. In this group, women with MS mainly
240 reported orgasm disorders (FSFI orgasm=1,57, sd 1,69), issues with arousal (FSFI-
241 arousal=2,01, sd 1,88), dyspareunia (FSFI-Pain= 2,07, sd 2,37), lubrication
242 disorders(FSFI- lubrication = 2,22, sd 2,26), desire disorders (FSFI-Desire = 2,58, sd
243 1,66) and no satisfaction (FSFI-satisfaction = 3,24, sd 1,32).

244

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

254 Urodynamic studies revealed that 38 women (43%) had detrusor overactivity whilst 51
255 women (57%) had no detrusor overactivity. SD (FSFI <26.55) was present in 23
256 (60.52%) women with detrusor overactivity and in 43 women (85%) with no detrusor
257 overactivity. The presence of detrusor overactivity was not associated with sexual
258 dysfunction (FSFI<26,55) (Table 2). The multivariate linear regression analysis adjusted
259 for overactive bladder, detrusor overactivity, depression, anxiety and EDSS revealed an
260 inverse relationship between detrusor overactivity and sexual dysfunction (Adjusted
261 Odds ratio (aOR) 0.03, 95% confidence interval (CI) 0,0.98) (Table 3)

262

263 Sexual dysfunction was not associated with age, neurological impairment (EDSS) or
264 duration of disease. Regarding patients with an EDSS scale <5 (65 patients), 74% of
265 patients had a sexual dysfunction. Regarding patients with an EDSS scale >5 (24
266 patients), 75% of patients had sexual disorders ($p=0,57$). Sexual dysfunction
267 (FSFI<26,55) was present at the onset of the disease and was not associated with
268 duration of disease ($p = 0,63$). On univariate analysis, we found a negative correlation
269 between duration of disease and orgasm disorders ($p = 0,01$), lubrication disorders ($p =$
270 $0,02$) and pain ($p= 0,02$). Sexual dysfunction (FSFI<26,55) was not associated with age
271 ($p=0,73$), but we found a negative correlation between age and FSFI desire (p -value =
272 0.01), FSFI arousal ($p=0,002$), FSFI lubrication ($p=0,002$), FSFI orgasm ($p=0,03$)

273

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

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

285 Discussion:

286 This study included the largest female population evaluating sexual and urinary
287 disorders. 74% of women with MS reported sexual dysfunction (FSFI<26.55). SD mainly
288 consisted of orgasm disorders and difficulties becoming aroused. This study confirms
289 that SD in women with MS is a widespread problem. However, there is a wide variation
290 in the reported prevalence of SD in women with MS due to the difference between MS
291 patient cohorts in terms of disability, duration of disease, as well as the different
292 methods chosen to evaluate sexual dysfunction (mail, phone, self-report, in-person
293 interview) (1). In a 2019 systemic review including 24 cross sectional studies, Polat
294 reported that the prevalence of SD in women with MS ranged from 16.9% to 85%, and
295 was higher than in healthy controls (20–25), and than in young women with other
296 chronic diseases (rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis,
297 and ankylosing spondylitis) (26). The most common sexual difficulties reported were
298 problems with low desire (20.5-88%) (n = 15 studies), having difficulties becoming
299 aroused (7.9-89%) (n = 15 studies), inability to experience orgasm (4.5-77%) (n = 21
300 studies), lack of lubrication (5.6-60.6%) (n = 16 studies), pain (5.7-72%) (n = 5 studies)
301 and lack of sensation in the genital area (17.6-61.7%) (n = 8 studies) (1,5,7,26,27).
302 Although the prevalence is high, SD in women receives relatively little attention when
303 compared to male sexual dysfunction (1,28,29). In a recent systematic review, Azimi
304 and al. reported a meta-analysis of 9 cross sectional studies using the FSFI and the
305 26.55 cut off point value to determine SD. It showed that in women with MS, SD had a
306 widely varying prevalence, ranging from 27% to 95%, and a pooled estimate of 55%
307 (95% CI 41%-69%)(30). Analyzing studies using FSFI scores, Zhao found a 1.87-fold
308 increased risk of SD in women who were affected by MS in comparison with controls
309 (2). He found that women with MS had significantly lower values in total FSFI scores as
310 compared with healthy controls (SMD - 2.41, 95% CI ;P= .001) (21–24). Lew Starowicz
311 indicated that up to 85% of women with MS report one or more sexual dysfunctions, up
312 to 35% report 5 or more sexual dysfunctions, and up to 13% describe 10 or more SD
313 (31). SD has a significantly negative impact on the quality of life of patients with MS,
314 and can be associated with the underlying neurological disease as well as mental
315 dimensions of the quality of life (3,21,32).

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

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

325

326 The population in this study were not using any medical treatments that could potentially
327 interfere with sexual function such as anticholinergic medication, botulinum toxin
328 injection or intermittent catheterization. However, anticholinergic medication does not
329 seem to interfere with sexual dysfunction as Di Marco and al. reported in a series of
330 18 women with MS that the initiation of an anticholinergic treatment did not affect
331 sexual function (34). Meanwhile the treatment of a neurogenic bladder has shown to be
332 effective in improving sexual dysfunction as Giannantoni and al. demonstrated that
333 Botulinum A toxin induced positive effect on sexual dysfunction in 31 women with MS
334 (35).

335

336 Neurogenic bladder and sexual dysfunction

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

352 Although the epidemiology of DO may consistently differ based on the definitions used
353 in the literature, the presence of detrusor overactivity reflects the neurological damage
354 of the spinal cord or the brain. A recent meta-analysis showed a prevalence of DO in
355 women with MS ranging from 27% to 91%(33). In our study, 38 women (42%) had
356 detrusor overactivity whilst 51 women (57%) had no detrusor overactivity. SD was
357 present in both women with and without detrusor overactivity (SD in women with MS
358 with DO =60.42% vs SD in women with MS without DO = 85%). However, univariate
359 analysis did not find any association between sexual dysfunction and detrusor
360 overactivity. Multivariate analysis revealed that detrusor overactivity did not seem to be
361 an independent factor of sexual dysfunction. Borello-France and al. (n=133) reported
362 that patients bothered by their urge incontinence had higher levels of orgasms when
363 compared to women which weren't bothered by their urge incontinence and concluded
364 that urge incontinence does not seem to be a risk factor for anorgasmia (38). It has
365 been shown that women with complete spinal cord injury (SCI) at the midthoracic level
366 show perceptual responses to vaginal and/or cervical self-stimulation (including sexual
367 response, and orgasm). It has been suggested that the vagus nerves could convey
368 genital sensory input directly to the brain in women, completely bypassing SCI at any
369 level. This hypothesis could also be extended to women with MS (13).
370 Fragala and al. suggested that in men with MS, the presence of PdetmaxIDC \geq 20
371 cmH₂O, MCC <135 ml and compliance \leq 3 ml/cmH₂O may significantly predict the
372 presence of moderate and severe erectile dysfunction. However, no such relationship
373 was found in a model including the previous variables and female sexual dysfunction
374 (33). Other recent studies have not found any association between SD and bladder
375 disorders. Although Lew-Starowicz and al. (n=137 women) analyzed bowel and bladder
376 dysfunctions together, they observed a significant association with sexuality (39), but
377 the types of LUTS was not described. Bartnik and al. (n=218) did not find such a
378 relationship in terms of bladder problems and SD in remittent forms of MS. (8).

379

380 Influence of depression

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

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

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

403

404 Duration of disease and neurological impairment

405 The analyzed group mainly consisted of women without active relapse (Relapsing
406 Remitting form 80%) and low neurological impairment as the average EDSS score was
407 3.56. No relationship was found between SD and the duration of disease or between SD
408 and EDSS. Nevertheless, SD was present even in case of low neurological impairment,
409 whether or not patients had any specific treatments for their neurogenic bladder
410 (anticholinergic drug, intermittent catheterization). Several studies confirm such findings
411 (23,44). Merghati-Khoei et al. (n= 132) demonstrated a weak correlation ($r = .22$)
412 between length of the disease and general sexual performance (44). Bartnik (n= 218
413 women) reported no association between the duration of the disease and the
414 occurrence of SD in the relapsing remitting form of MS (8). Nortvedt and al. (n=194)
415 suggested that bladder and sexual problems were associated with a marked reduction
416 in the quality of life, also in patients with low physical disability (EDSS<4.0) (3).

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

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

436

437 This study has some limitations as it is a cross-sectional study and our population
438 sample was obtained in an outpatient setting. The population mainly consisted of
439 women with a remitting relapsing form (80%) and with low disabilities since 65 women
440 (74%) had an EDSS scale <5. Furthermore, we didn't take into account antidepressant
441 medication although it can affect sexual dysfunction. Finally, bowel function, which
442 several reports have related to sexual and bladder dysfunction was not assessed.

443

444 Conclusion:

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

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

604

605

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

610

611

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

614

	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

615

616 Multivariate logistic regression analysis adjusted for EDSS, presence of detrusor
617 overactivity, overactive bladder, HAD Depression and Anxiety, duration of disease.

618 Values are presented as aOR : adjusted Odd Ratio, CI confidence Interval and P value.

619 EDSS, Expanded disability Status Scale; HAD, Hospital Anxiety and Depression Scale;

620 USP, Urinary Symptom Profile

621