Overactive bladder syndrome and sexual dysfunction in women with fibromyalgia and their relationship with disease severity

F. Salaffi[1], M. Di Carlo[1], S. Farah[1], V. Giorgi[2], N. Mosca[3], P. Sarzi-Puttini[2]

[1]Rheumatology Clinic, Ospedale "Carlo Urbani", Università Politecnica delle Marche, Jesi, Ancona; [2]Rheumatology Unit, Internal Medicine Department, ASST Fatebenefratelli-Sacco, Milan; University School of Medicine, Milan; [3]Azienda Sanitaria Unica Regionale (ASUR) Marche, Area Vasta 2, Dipartimento Integrazione Ospedale-Territorio, Regione Marche, Italy.

Abstract

Objective

The aim of this study was to evaluate the prevalence and severity of overactive bladder syndrome (OAB) and sexual dysfunction in fibromyalgia (FM) patients, as well as their relationship with disease severity.

Methods

Consecutive adult female patients with FM were enrolled. Patients filled in a comprehensive questionnaire package including demographic variables, disease severity assessment (revised Fibromyalgia Impact Questionnaire [FIQR]), neuropathic pain features (PainDetect Questionnaire [PDQ]), severity of OAB symptoms (Overactive Bladder Symptom Score [OABSS]), and determining sexual functioning (Female Sexual Function Index [FSFI]).

Results

The study included 481 patients, 116 (24.11%) had mild OAB, 82 patients (17.04%) had moderate OAB, and 34 patients had serious OAB (7.06%). In 14.17% of patients the bladder condition was causing them major issues in terms of discomfort. In 7.87% of patients the bladder condition was causing them significant problems. Sexual dysfunctions were found in 91 patients (18.91%). Using the FSFI as dependent variable, multivariate analysis revealed a positive relationship between sexual dysfunction and variables of disease burden (FIQR, $p<0.0001$; PDQ, $p<0.0001$, widespread pain index [WPI], $p=0.0037$). Using OABSS as the dependent variable, multivariate regression revealed a substantial contribution from FIQR ($p<0.0001$), PDQ ($p=0.0037$), and WPI ($p=0.0030$).

Conclusion

FM has the potential to affect both psychological and physiological processes in women with OAB and sexual dysfunction. These results emphasise the importance of a multidisciplinary approach to treat patients with overactive bladder syndrome and sexual dysfunction in FM.

Key words

fibromyalgia, overactive bladder syndrome, sexual dysfunction, neuropathic pain, health-related quality of life

Fausto Salaffi, MD, PhD
Marco Di Carlo, MD
Sonia Farah, Eng
Valeria Giorgi, MD
Nadia Mosca, MD
Piercarlo Sarzi-Puttini, MD

Please address correspondence to:
Marco Di Carlo,
Clinica Reumatologia,
Università Politecnica delle Marche,
Ospedale Carlo Urbani,
via Aldo Moro 25,
60035 Jesi (AN), Italy.
E-mail: dica.marco@yahoo.it

Received on June 17, 2021; accepted in revised form on September 20, 2021.

Funding: this research was supported by Azienda Sanitaria Unica Regionale (ASUR) Marche, Area Vasta 2, Italy.
Competing interests: none declared.

Introduction

Fibromyalgia (FM) is characterised by a wide range of symptoms, including widespread chronic pain, exhaustion, non-restorative sleep, sleep disturbance, fatigue, depression, anxiety, cognitive impairment such as memory and attention issues, headache, numbness/tingling, and genitourinary symptoms such as overactive bladder (OAB) (1, 2) and sexual dysfunction (3-7). These symptoms characterise FM in accordance with different sets of classification criteria introduced in recent years and the disease severity level (8, 9), and all these symptoms have a negative impact on quality of life (QoL) (10).

OAB is characterised by urgency, with or without urinary incontinence, typically with frequency and nocturia, according to the International Continence Society's concept from 2002 (11-13). This disorder has a significant negative impact on an individual's physical and social functioning, including sleep habits, health-related QoL (HRQoL), work life, and social relationships (14, 15). Previous research has found a higher prevalence of OAB in European patients (11.8%) (16). It has been discovered that as an individual's age increases, the prevalence of OAB rises from 12 to 20% (17). FM patients have substantially more OAB symptoms, and the connection between FM and OAB severity is statistically significant (18). The pathophysiology of OAB may include pathways involving feedback from the bladder as well as peripheral and central nervous system mechanisms of sensitisation (19). Several studies indicate that OAB and some of the more well-known central sensitisation syndromes, such as irritable bowel syndrome (20), idiopathic back pain and FM overlap (21, 22).

A recently published meta-analysis found a strong connection between FM and female sexuality alterations (10). Sexual dysfunction affects 86.9% of women with FM, while 76.5% of men with FM can experience it. This is a high prevalence as compared to the healthy population, which has a prevalence of 23.6% for women and 6.7% for men (22). According to Collado-Mateo *et al*., 76% of women with FM have sexual issues, compared to 15% of healthy controls (23). Sexual dysfunction was related to depression, anxiety, tenderness, and memory issues in FM patients. Sexual dysfunction refers to a wide range of conditions marked by a clinically relevant impairment in a person's ability to respond sexually or feel sexual pleasure (24). Women with FM had lower sexual arousal and excitement, less orgasms, less self-pleasing/masturbation, more vaginal tightness during penetration, and more discomfort during intercourse, compared to healthy women (25). Sexual dysfunction's aetiology in FM is not completely understood and is assumed to be multifactorial. Tikiz *et al*. proposed that FM is directly linked to sexual dysfunction, rather than through a psychological mechanism, and that depression coexists with FM but has no impact on sexual function (30). FM's allodynia may be a key element: FM patients have lower pain thresholds (28), so pain during intercourse is likely. Gordon *et al*. found vulvar pain problems in around 20.6% of women with FM (26), and Aydin and colleagues discovered that up to 50% of FM patients complain of pain during sexual intercourse (dyspareunia) (6). This pain may be related in particular to vaginal tightness during intercourse, a hypothesis sustained by Shaver *et al*. (25).

Despite the well-known impact of genitourinary symptoms and sexual function on HRQoL, few randomised controlled trials used these variables as outcome measures. The revised Fibromyalgia Impact Questionnaire (FIQR) is frequently used in FM research to determine the disease's effects (9), but since it omits any questions regarding OAB and sexual function, the relationship between OAB and other variables in this population is unknown.

The aim of this study was to investigate the prevalence of female OAB and sexual dysfunction in FM patients, as well as their possible relationship with disease severity and neuropathic pain features.

Material and methods

Study design and sample

This cross-sectional research was carried out at the Rheumatology Clinic of

the Università Politecnica delle Marche, Italy, a regional referral centre for the diagnosis and treatment of FM.

This study included adult female patients diagnosed with FM according to the American College of Rheumatology's (ACR) 2010/2011 criteria (31, 32). The widespread pain index (WPI), symptom severity scale (SSS), and the occurrence of symptoms over more than three months were used to identify patients. Laboratory tests were used to rule out other conditions that could explain the symptoms. FM patients were included if they i) were at least 18 years old and in heterosexual relationships, ii) were diagnosed with FM, and iii) were eager to participate in the study and capable of understanding the procedure and questions. Patients with diseases of the central or peripheral nervous systems (Alzheimer's disease or other dementias, Parkinson's disease, motor neuron disease, polyneuropathy, multiple sclerosis, spinal lesions, patients with signs of large nervous fibre involvement, *e.g.* wasting and weakness, deep-seated pain, impaired vibration perception, loss of reflexes, ataxia) were excluded. Just the interviewer and the subject were present during the interviews, which took place in a private room behind closed doors. The confidentiality of the participants was respected. The information gathered was only available to the investigators. All patients who took part in the study signed an informed consent document to undergo the study's evaluation. The study procedures were approved by the local ethics committee (Comitato Unico Regionale - ASUR Marche, no. 1970/AV2).

Self-reported measures

The patients filled in a detailed questionnaire package including demographic information, disease duration, disease-related and QoL variables. Age, sex, marital status (single, married, divorced/separated), and level of education (primary, secondary, high school/university) were the demographic variables. In addition, the patients were given four separate sets of questionnaires to measure FM severity, identify neuropathic pain features, quantify the severity of OAB symptoms, and determine sexual functioning.

FM disease severity - FIQR

The FIQR is a more recent variant of the FIQ (33). It is made up of 21 items with 11-point numerical rating scales (0-10) that look at three major domains (function, overall health status, symptoms) in relation to the previous week. The total score (range 0–100, with higher values suggesting greater severity) is the number of the three domains' ratings: the algebraic sum of the 9-items function domain (range 0–90) is divided by three, the algebraic sum of the 2-items overall health status domain (range 0–20) is left alone, and the algebraic sum of the 10-items symptoms domain (range 0–100) is split in half. The severity states for FIQR were determined by combining the mean 75th and 25th percentiles of adjacent categories: 0–23 for remission, 24–40 for mild disease, 41–63 for moderate disease, 64–82 for severe disease, and >82 for very severe disease (9).

Screening tool for neuropathic pain features - PainDetect Questionnaire (PDQ)

The PDQ is a self-administered questionnaire that does not require an objective assessment. The PDQ consists of four items in which the patient describe the temporal pattern of pain (score -1 or +1 depending on the indicated temporal pattern), a mannequin in which pain irradiation may be represented (irradiated pain +2 points), and seven 5-point scales in which the patient can report characteristic neuro-pattern symptoms (sudden pain, allodynia, hyperalgesia, dysesthesia) (34, 35). The final score (which ranges from -1 to 38) can be viewed in terms of the likelihood of neuropathic pain: under 12 is low, above 19 is high, and between 13 and 18 is uncertain (36).

OAB symptom severity - Overactive Bladder Symptom Score (OABSS)

The OABSS was used to calculate the severity of OAB symptoms. Homma and coworkers realised the questionnaire, which was later validated by the Italian community (37, 38). The OABSS had a reasonable to excellent test-retest reliability (39). Daytime frequency (score 0–2), nighttime frequency (score 0–3), urgency (score 0–5), and urgency incontinence (score 0–5) are the four symptom ratings that make up the overall OABSS (37). The overall score varies from 0 to 15, with a higher score suggesting more severe OAB symptoms. To be included in this study, all the participants had at least a total score of 3 and an urgency score of 2 (40-42). Patients were categorised into four groups according to symptoms: none (OABSS score less than 2), mild (OABSS score between 2 and 5), moderate (OABSS score between 6 and 11), and severe (OABSS score greater than 11) (12 or more).

Sexual functioning - The Female Sexual Function Index (FSFI)

Despite the recent development of many new measures for female sexual dysfunction, the FSFI remains the gold standard for screening and one of the most widely used questionnaires. The FSFI is a multidimensional, brief scale for evaluating sexual function in women (43). The scale has undergone preliminary psychometric testing, which included reliability, convergent validity, and discriminant validity tests (44). The 19-item scale assesses sexual function over the previous four weeks and produces domain scores in six areas: sexual desire, arousal, lubrication, orgasm, pleasure, and pain. On a scale of 0 (or 1) to 5, each domain is rated. The ideal cut-off for distinguishing women with and without sexual dysfunction was found to be a total FSFI score of 26.55 (43). Filocamo *et al*. developed an Italian version of the FSFI questionnaire that is validated and accurate (45). Since the Cronbach's alpha values were at least 0.92 in the entire study, the findings show that FSFI is sufficiently suitable in terms of internal consistency and reliability. Using the Pearson product-moment correlation coefficient, it also showed very good test–retest reliability (>0.92 in the entire sample).

Statistical analysis

MedCalc statistical programme, v. 19.0 (Ostend, Belgium), for Windows XP

was used to analyse the results. For categorical variables, numbers and percentages were used, while for continuous variables, mean values, standard deviation (SD), or median values were used, depending on the distribution of the data as determined by the Shapiro-Wilk test. The chi-squared or Fisher's exact tests were used to compare proportional differences between groups. The Pearson's correlation coefficient (r) and a corresponding significance test were used to compare continuous variables using the Student's t-test or 1-way analysis of variance (ANOVA) with multiple comparisons and the Pearson's correlation coefficient (r). The strength of the correlation was interpreted for r values as: very mild (0.00–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (0.80–1.00). Multiple regression analysis was used to examine the relationship between one dependent variable, OABSS and FSFI respectively, and one or more independent variables such as age, disease duration, body mass index (BMI), FIQR total score, PDQ, and WPI (variable you expect to influence or predict the value of the dependent variable) (46). Multiple regression analysis was performed using the enter method (enter all variables in the model in one single step, without checking). Subsequently, since the FIQR was found to be an independent predictor of both OABSS and FSFI, a second multiple regression analysis was conducted, still considering OABSS and FSFI as dependent variables and the individual items of the FIQR as independent variables. Statistical significance was considered for p value <0.05.

Results

The study involved 511 patients; 30 (5.9%) were not included in the final analysis due to incompletion of data collection.

The clinical and descriptive characteristics of the 481 patients are summarised in Table I. All data have a normal distribution. The mean age was 48.13 years (SD 9.19), the mean BMI was 26.06 (SD 2.64), FM lasted a mean of 4.83 (SD 4.59) years, and a pharmacological treatment was taken by 81.91% of patients.

Table I. Distribution of demographics and clinical characteristics of women with fibromyalgia.

	Mean	Median	SD	25 - 75 P	normal distribution*
Age (years)	48.13	48.00	9.19	43.00 - 55.00	0.0006
Disease duration (years)	4.83	3.00	4.59	2.00 - 6.00	<0.0001
BMI (kg/m^2)	26.06	25.90	2.64	24.40 - 27.70	<0.0001
WPI score	7.87	7.00	4.63	5.00 - 11.00	<0.0001
PDQ score	14.69	12.00	7.91	9.00 - 18.00	<0.0001
FIQR physical function	8.54	7.00	5.58	4.33 - 12.00	<0.0001
FIQR overall impact	5.77	4.00	4.76	2.00 - 9.00	<0.0001
FIQR symptoms	19.01	17.00	10.10	10.00 - 26.50	<0.0001
FIQR total score	33.33	28.83	18.59	18.16 - 45.20	<0.0001
FSFI score	14.01	11.00	9.10	7.00 - 21.00	<0.0001
OABSS score	3.84	2.00	3.62	1.00 - 5.00	<0.0001

SD: standard deviation; P: percentile; BMI: Body Mass Index; WPI: Widespread Pain Index; PDQ: Pain Detect Questionnaire; FIQR: Revised Fibromyalgia Impact Questionnaire; FSFI: Female Sexual Function Index; OABSS: Overactive Bladder Symptom Score.
*Shapiro-Wilk test for the normal distribution hypothesis.

Table II. ANOVA test among the groups of the overactive bladder syndrome severity and sexual dysfunction levels.

OABSS Source of variation	Sum of squares	Degrees of freedom	Mean square		
Between groups (influence factor)	5989.1339	3	1996.3780		
Within groups (other fluctuations)	333.5397	477	0.6992		
Total	6322.6736	480			
F-ratio			2855.05		
Significance level			p <0.001		
Factor	n	Percentage	Mean	SD	Difference (p<0.05)* from factor (nr)
(1) no OAB	249	51.76%	1.20	0.58	(1)(2)(4)
(2) mild OAB	116	24.11%	3.77	0.59	(2)(3)(4)
(3) moderate OAB	82	17.04%	8.30	1.49	(1)(3)(4)
(4) severe OAB	34	7.06%	12.61	0.88	(1)(2)(3)
FSFI Source of variation	Sum of squares	Degrees of freedom	Mean square		
Between groups (influence factor)	25866.1838	1	25866.1838		
Within groups (other fluctuations)	13941.6832	479	29.1058		
Total		39807.8669	480		
F-ratio			888.69		
Significance level			p <0.001		
Factor	n	Percentage	Mean	SD	Difference (p<0.05)* from factor (nr)
(1) no sexual dysfunction	390	81.09%	10.47	5.70	(2)
(2) sexual dysfunction	91	18.91%	29.19	3.80	(1)

OABSS: Overactive Bladder Symptom Score; SD: standard deviation; OAB: overactive bladder syndrome; FSFI: Female Sexual Function Index. *Scheffé test for all pairwise comparisons.

The mean cumulative FIQR score was 33.33 (SD 18.59), the mean PDQ score was 14.69 (SD 7.91), and the WPI score was 7.87 (SD 4.63). The OABBS mean score was 3.84 (SD 3.62) (range 0–15), while the FSFI score was 14.01 (SD 9.10).

Mild OAB affected 116 patients (24.11%), moderate OAB affected 82 patients (17.04%), and extreme OAB

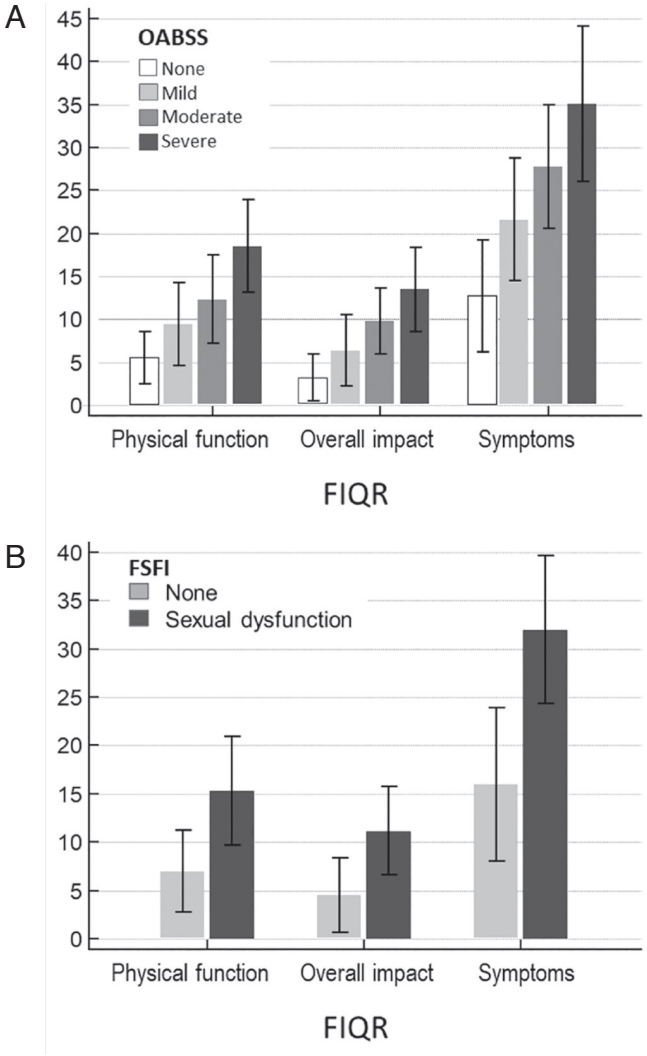

Fig. 1. Distribution of OABSS (**A**) and FSFI (**B**) subgroup scores according to the FIQR.

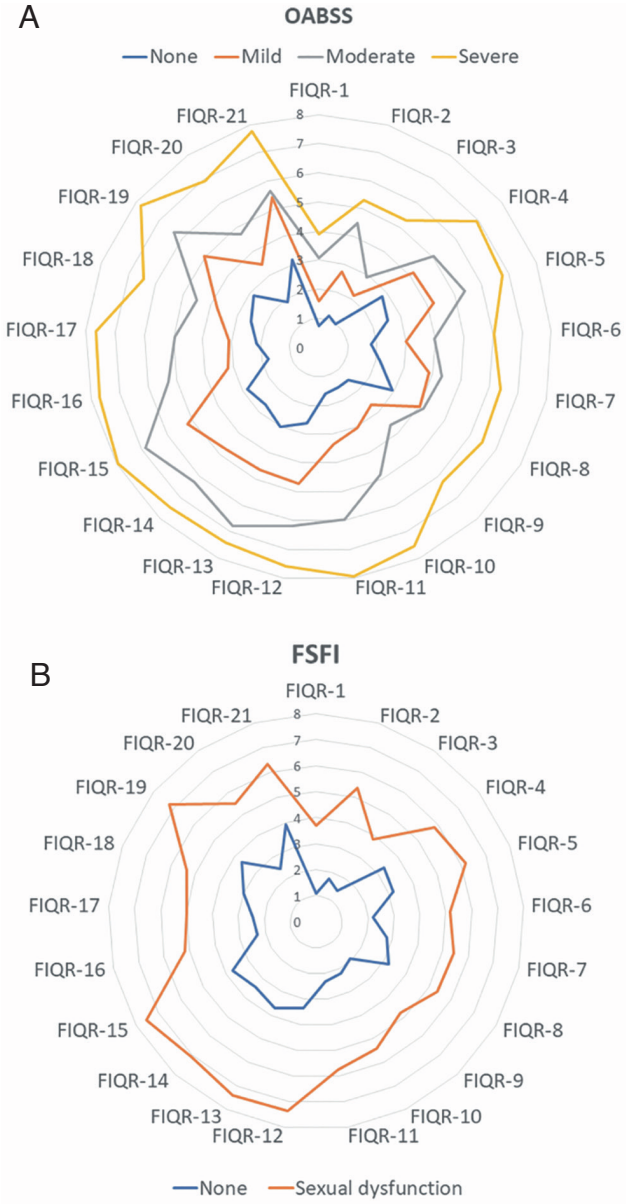

Fig. 2. (right) Spidergram of individual values for the different severity levels of OABSS (**A**) and FSFI (**B**).

affected 34 patients (7.06%). 14.17% of patients described that their bladder condition was causing them serious problems. 7.87% of patients reported that their bladder disease was causing them many problems. According to the FSFI cut-off of 26.55, ninety-one women with FM (18.91%) had sexual dysfunctions (Table II).

For each patient category, the ANOVA revealed major differences between the OABSS (F ratio = 2855.05; $p<0.05$) and FSFI (F ratio = 888.69; $p<0.05$) subgroups (Table II).

The OABSS, FSFI, and FIQR had a r of 0.703 and 0.712 ($p<0.0001$), respectively. The OABSS, FSFI, and PDQ values ($r=0.676$; $p<0.0001$ and $r=0.717$; $p<0.0001$, respectively) and the OABSS, FSFI, and WPI values ($r=0.627$; $p<0.0001$ and $r=0.629$; $p<0.0001$, respectively) both had statistically significant correlations.

The severity of OAB symptoms showed a direct association with FIQR, suggesting that the more extreme the OAB symptom, the higher the FIQR subdomains (physical activity, overall impact and symptoms) (Fig. 1a). A similar direct association with the FIQR was seen in the distinction of patients with sexual dysfunction and no sexual dysfunction (Fig. 1B).

The 21 FIQR items were found to have a significant effect on the components of disease severity symptoms (feeling overwhelmed, sleep quality, depression level, memory problems, tenderness level, environmental sensitivity). Individual values for the different severity levels of OABSS are shown in Figure 2A. The correlation of the 21-items and the FSFI showed a prevalent impact on the components of disease severity symptoms (pain, fatigue, sleep quality, tenderness level, environmental sensitivity). Figure 2B shows the individual values for the different severity levels of FSFI.

The multivariate regression analysis using OABSS as dependent variable showed a significant contribution of disease severity ($p<0.0001$), neuropathic pain features ($p=0.0037$) and extent of pain ($p=0.0030$) (coefficient

of determination R2-adjusted = 0.602) (Table III). Age, disease duration, and BMI were not significantly associated with these scores. At the same time, a multivariate analysis, using FSFI as dependent variable, found a positive association between disease severity (FIQR) (p<0.0001), neuropathic pain features (PDQ) (p<0.0001) and extent of pain (WPI) (p=0.0037) (coefficient of determination R2-adjusted = 0.578) (Table III).

Further multivariate regression analyses were conducted to see which of the 21 individual items of the FIQR were linked to the severity of genitourinary symptoms and sexual dysfunction (OABSS and FSFI, dependent variables). The items FIQR-10 (cannot achieve goals), FIQR-11 (feel overwhelmed), FIQR-15 (sleep quality), FIQR-16 (depression level), FIQR-17 (memory problems), and FIQR-21 (environmental sensitivity) all had a significant contribution to OABSS (coefficient of determination R2-adjusted = 0. 611); the items FIQR-15 (sleep quality), FIQR-16 (depression level), FIQR-19 (tenderness level), and FIQR-21 (environmental sensitivity) had a significant contribution to FSFI score (Table IV). Interestingly, the item related to the sexual dysfunction regards tenderness to touch.

Table III. Multiple regression analyses using OABSS and FSFI as dependent variables.

OABSS - Dependent variable	Coefficient	Standard error	t	p	r partial
(Constant)	-2.1785				
Age	0.0005753	0.01149	0.0501	0.9601	0.002300
Disease duration	0.003425	0.02313	0.148	0.8823	0.006801
BMI	0.02100	0.03982	0.527	0.5981	0.02422
FIQR total score	0.1088	0.009419	11.554	<0.0001	0.4688
PDQ	0.06731	0.02305	2.920	0.0037	0.1329
WPI	0.1028	0.03446	2.984	0.0030	0.1358
FSFI – dependent variable					
(Constant)	0.2974				
Age	-0.02658	0.02967	-0.896	0.3708	-0.04111
Disease duration	0.07392	0.05971	1.238	0.2163	0.05677
BMI	0.03540	0.1028	0.344	0.7307	0.01581
FIQR total score	0.1695	0.02432	6.971	<0.0001	0.3050
PDQ	0.4100	0.05952	6.888	<0.0001	0.3016
WPI	0.2594	0.08898	2.915	0.0037	0.1327

OABSS: Overactive Bladder Symptom Score; FSFI: Female Sexual Function Index; BMI: Body Mass Index; FIQR: Revised Fibromyalgia Impact Questionnaire; PDQ: PainDetect Questionnaire; WPI: Widespread Pain Index.

Discussion

FM is a chronic heterogeneous syndrome that affects 2–3% of the general population worldwide, with females in their forties and fifties being particularly vulnerable (47). The symptomatology comprises chronic, widespread pain with generalised tenderness on light palpation, exhaustion, stiffness, dyscognition, and also sexual dysfunction and genitourinary symptoms (3-6, 48-54), up to a full-blown OAB syndrome (48, 49).

Several findings support the hypothesis that FM and OAB are related (55-59). Chung and colleagues discovered that 21 out of 53 subjects diagnosed with FM had OAB, a prevalence (40.6%) which was higher than in adults aged 30 or older in the general population (22.9%) (18). After adjusting for gender, age group, and location of residence, people with FM had significantly more OAB symptoms, with a statistically significant connection between FM and the severity of OAB. FM could be diagnosed in 30% of OAB subjects and 5% of normal controls. Urge incontinence was found to be more frequent in the OAB community than in the OAB+FM group (60, 61).

Dysfunction of sensory receptors and sensitisation in central and peripheral nervous systems, resulting in bladder hypersensitivity, are probably the pathophysiological mechanisms underlying OAB. Central sensitisation is a concept used to characterise an induced state of spinal hypersensitivity that is related to several chronic pain conditions, many of which are similar to OAB, which anyway does not include pain, although many OAB patients classify their symptoms as unpleasant or even painful (19, 62).

Accordingly, central sensitisation can play a key role in the abnormal and widespread pain sensitivity seen in FM patients, characterised clinically by spontaneous pain, pain elicited by usually benign stimuli (allodynia), exaggerated and prolonged painful sensation in response to noxious stimuli (hyperalgesia), and pain which extends beyond the site of injury in these circumstances (secondary hyperalgesia) (63). In the present study, a substantial contribution from disease severity as measured by the FIQR (p<0.0001) and widespread pain intensity (p=0.0030) has been found, by means of multivariate analysis using OABSS as the dependent variable. A connection between the severity of OAB symptoms and FIQR was also revealed, suggesting that the higher the FIQR, the more extreme the OAB symptoms (physical function, overall impact and symptoms).

There is also evidence that a peripheral neuropathic factor, primarily neurogenic inflammation, plays a role in FM central sensitisation (64, 65). Microneurography studies in FM patients have shown the presence of spontaneous activity, multiple spikes, irregular sensitisation, anomalies in nociceptive fibre activity, as well as recurrent systemic symptoms related to dysesthetic, evoked, paroxysmal, and thermal domains, all of which are characteristic of neuropathic pain (66). This is coherent with the conclusion that OABSS (dependent variable) correlates with the neuropathic pain features (p=0.0037).

Sexual function is an important aspect of women's life, complicated by biological, sociocultural, and psychological influences. Sexual dysfunction is a general term that refers to a group of disorders marked by a clinically relevant impairment in a person's ability to respond sexually or feel sexual pleasure. Female sexual dysfunction is classified as a sexual interest/arousal condition, orgasmic disorder, or genito-pelvic pain/penetration disorder in

Table IV. Multiple regression analyses using OABSS and FSFI as dependent variables for each item of the FIQR.

OABSS	Coefficient	Standard error	t	*p*	r partial
(Constant)	-0.9957				
FIQR-1	-0.01105	0.05888	-0.188	0.8512	-0.008759
FIQR-2	0.1246	0.05747	2.168	0.0507	0.1007
FIQR-3	0.2314	0.06325	3.658	0.0903	0.1683
FIQR-4	0.02259	0.06294	0.359	0.7199	0.01675
FIQR-5	0.09742	0.06447	1.511	0.1314	0.07036
FIQR-6	0.1014	0.06341	1.599	0.1105	0.07444
FIQR-7	0.02824	0.06015	0.469	0.6389	0.02191
FIQR-8	0.03023	0.04517	0.669	0.5036	0.03122
FIQR-9	0.008154	0.06777	0.120	0.9043	0.005616
FIQR-10 (cannot achieve goals)	0.2596	0.07798	3.329	0.0009	0.1535
FIQR-11 (feel overwhelmed)	0.1391	0.07022	1.980	0.0483	0.09205
FIQR-12	-0.05886	0.07373	-0.798	0.4251	-0.03723
FIQR-13	-0.02163	0.06792	-0.319	0.7502	-0.01486
FIQR-14	0.05650	0.07319	0.772	0.4405	0.03601
FIQR-15 (sleep quality)	0.1824	0.06125	2.978	0.0031	0.1377
FIQR-16 (depression level)	0.1947	0.06639	2.933	0.0035	0.1356
FIQR-17 (memory problems)	-0.1465	0.06514	-2.248	0.0250	-0.1044
FIQR-18	-0.02086	0.05920	-0.352	0.7248	-0.01644
FIQR-19	0.08170	0.05866	1.393	0.1643	0.06488
FIQR-20	0.1127	0.06165	1.829	0.0681	0.08505
FIQR-21 (environmental sensitivity)	0.1265	0.04189	3.020	0.0027	0.1396
FSFI					
(Constant)	1.5668				
FIQR-1	-0.1440	0.1656	-0.870	0.3850	-0.04056
FIQR-2	0.2340	0.1616	1.448	0.1484	0.06742
FIQR-4	0.1068	0.1770	0.603	0.5465	0.02815
FIQR-5	0.2049	0.1813	1.130	0.2589	0.05268
FIQR-6	0.1537	0.1783	0.862	0.3892	0.04020
FIQR-7	0.01193	0.1691	0.0706	0.9438	0.003293
FIQR-8	0.1832	0.1270	1.442	0.1500	0.06716
FIQR-9	-0.01683	0.1906	-0.083	0.9297	-0.004123
FIQR-10	0.1195	0.2193	0.545	0.5860	0.02543
FIQR-11	0.07760	0.1975	0.393	0.6945	0.01834
FIQR-12	0.3814	0.2458	1.959	0.0578	0.07720
FIQR-13	0.1233	0.2073	0.595	0.5524	0.02775
FIQR-14	0.07101	0.1910	0.372	0.7102	0.01735
FIQR-15 (sleep quality)	0.4313	0.1722	2.504	0.0126	0.1161
FIQR-16 (depression level)	0.4739	0.1867	2.538	0.0115	0.1177
FIQR-17	-0.1690	0.1832	-0.923	0.3567	-0.04302
FIQR-18	0.05081	0.1665	0.305	0.7603	0.01424
FIQR-19 (tenderness level)	0.3630	0.1650	2.200	0.0283	0.1022
FIQR-20	0.1867	0.1734	1.077	0.2820	0.05021
FIQR-21 (environmental sensitivity)	0.2429	0.1178	2.062	0.0398	0.09580

OABSS: Overactive Bladder Symptom Score; FSFI: Female Sexual Function Index; FIQR: Revised Fibromyalgia Impact Questionnaire.

the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (67). In female patients with FM, Burri *et al*. reported trouble with lubrication, sexual discomfort, and increased sexual tension (68). Pressure, weakness, stiffness, functional disabilities, negative body image, sexual assault, and drug therapy are all linked to the development of sexual dysfunction in FM patients (54, 69). Kayhan *et al*. discovered a prevalence of any sexual condition of 47.9% in patients with FM, and this value was substantially higher than in the control group (12.8%) (54). However, 18.91% women with FM had sexual dysfunctions, according to our results. This may be related to the method of evaluation: our study used a systematic assessment, through a validated questionnaire, rather than an interview.

There may be multiple mechanisms by which chronic widespread pain causes sexual dysfunction in FM patients (4-7, 50, 51). In the above cited study by Kayhan *et al*., patients with FM who had poor sexual functioning had a higher VAS score, implying that pain is a major factor in the development of female sexual dysfunction in FM patients (54). Ablin *et al*. discovered a connection between sexual dysfunction and the number of tender points measured using manual palpation (70). Another study revealed that women with FM who presented with dyspareunia had a lower pain tolerance and a higher number of tender points than those who did not (71). According to these results, a recent meta-analysis found that the pain score difference between patients with FM and healthy controls was important in the domains of sexual functioning (10). We discovered a connection between sexual dysfunction and pain intensity on the FIQR domain, PDQ, and WPI in FM patients, with these scores being higher in patients with FM and sexual dysfunction than in patients with FM who did not have sexual dysfunction. Interestingly, the FIQR item "tenderness level" (FIQR-19) correlated with the FSFI but not with the OABSS score, suggesting that tenderness to touch is a key element in sexual dysfunction in these patients. In addition, we showed that sexual dysfunction is not only related to pain, tenderness and severity of FM, but also to the neuropathic features of this pain, implying that a key role is played by central and peripheral sensitisation. This is coherent with the fact that studies in vulvodynia patients found many characteristics of sensitisation, such as, structural changes in vulvar innervation, including epithelial cell sprouting, rise in intraepithelial nerve endings and papillary TRPV1 afferent fibres. Mechanical and thermal low threshold stimuli evoke vulvar allodynia, which is likely linked to local peripheral sensitisation of both polymodal C-mechano-heat nociceptors and normally mechano-sensitive C-nociceptors. Since these peripheral mechanisms are linked to irregular temporal summation in response to pressure stimuli, and since allodynia is not limited to the vulvar vestibule, the role of both peripheral and central sensitisa-

tion mechanisms in the pathogenesis of vulvodynia has been proposed (73).

Mood disturbances are one of the many causes that can influence sexual function in women with FM, although some researchers have found no link (51). Tikiz *et al*., for example, found no substantial difference in the FSFI score between patients with FM only and FM plus major depression and concluded that co-existing major depression had no additional negative impact on sexual function (30). However, it has been found a strong negative association between the FSFI score and the Beck depression inventory among the studies pooled in a meta-analysis, indicating that depression is one of the mental conditions frequently observed in women with FM, possibly contributing to sexual dysfunction (53). In a similar study it has been found that patients with a higher Beck Depression Inventory score had lower FSFI ratings, implying that depression exacerbated FM-related female sexual dysfunction (74). The connection between sexual dysfunction and depression was also found in other chronic diseases, such as rheumatoid arthritis (RA) and multiple sclerosis; for example, a study showed that FM and RA patients had a substantially higher incidence of sexual dysfunction than balanced controls, and sexual dysfunction was found to be more common in FM patients (97%) than in RA patients (84%) but there were no statistical differences (51). Age, marital and job status, pain severity, level of anxiety, and level of depression were all found to be significantly correlated with sexual dysfunction in FM in a univariate study. In the multivariate analysis, only the severity of depression was correlated with sexual dysfunction in patients with FM. Our study confirms the finding that depression is a factor both positively and independently correlated with sexual dysfunction in women with FM.

In a variety of clinical settings, self-report questionnaires can play a significant role in frequently monitoring psychological problems (75). When compared to the gold standard clinical interview, these instruments typically have moderate to high sensitivity and specificity, and range in length from 5 to 14 items. However, due to a lack of time to administer the tools in a busy clinic setting and a lack of staff training in tool administration, scoring, and interpretation, these tools may still be inadequately used in clinical practice. Previous research has found that the single-item measures may be useful to rule out individuals who do not require further psychological assessment or intervention for depression (76).

Antidepressant treatment can also impact sexual functioning, so differences in the likelihood of sexual side effects are an important consideration for patients taking antidepressants (77). Montejo *et al*. showed that sexual dysfunction is very common in patients receiving long-term treatment with antipsychotics, and it is associated with a great impact in a substantial proportion of patients (78). Clayton *et al*. demonstrated a higher incidence of treatment-emergent sexual dysfunction with escitalopram compared with duloxetine and placebo (79). The incidence of treatment-emergent dysfunction for duloxetine seems significantly lower than that observed for paroxetine (80, 81).

People with FM have increased sensitivity to a range of environmental stimuli and are more vulnerable to environmental stress in every group than rheumatic disease monitors (82). This backs up the hypothesis that FM patients have heightened vigilance and are more susceptible to environmental stresses. In fact, environmental sensitivity (item FIQR-21) was discovered to be one of the FIQR items that was significantly associated both with the OABSS and with the FSFI in our study.

Reports of violence against children, adolescents, and women have progressively increased over the last several decades (83-85). Increased rates of melancholy, suicide, alcoholism, anxiety, and somatic illnesses (*i.e*. abdominal pain, headaches) are frequently connected with a history of physical and/or sexual abuse (86, 87). It was hypothesised that FM patients with a history of sexual or physical abuse would report higher levels of somatic complaints and more frequent use of the health-care system than healthy community controls, and that FM patients with a history of sexual or physical abuse would report higher levels of somatic complaints and more frequent use of the health-care system (88).

Sleep disorders and cognitive dysfunction are also two of the most common symptoms in FM patients (89). Sleep recordings show decreased sleep quality, increased waking, decreased slow-wave sleep, and the presence of irregular alpha waves (alpha-delta) in non-rapid eye movement sleep. Patients with FM can also experience sleep problems such as apnoea or periodic limb movements (90). As compared to the others, patients with objective sleep disorders had higher pain, tender point index, and FIQ ratings, as well as more depressive symptoms. Sleep deprivation was also linked to the severity of disease, pain, and sexual dysfunction (91). A strong association was found between patients with a Pittsburgh Sleep Quality Index (PSQI) score of >5 (poor sleep quality) and sexual dysfunction in a study conducted in 54 patients (92). We discovered a statistically significant link between item FIQR-15 (sleep quality) and not only the FSFI, but also with the OABSS, in line with previous research showing that sensitisation and pain are exacerbated by disturbed sleep. Cognitive dysfunction in FM consists of memory issues, inattention, learning difficulties, slow processing speed, and executive functioning problems, and is documented by around 70% of people with fibromyalgia (FM). These cognitive issues, dubbed "fibrofog," have a detrimental impact on perceptions of disease seriousness and general mental health (93), as well as the ability to maintain a social network or function, and conduct a wide variety of everyday activities. In our study, item FIQR-17 concerning cognitive dysfunction, correlated just with the OABSS and not with the FSFI.

The results of the current study should be viewed in light of many limitations. To begin with, our patients' ages ranged from young to elderly (17 years up to 67 years old), which included both premenopausal and postmenopausal women. Both age and menopausal status influence quality of sleep and sexual life,

but we did not use any questionnaires to assess our patients' menopausal status. Additionally, our research was conducted by rheumatologists rather than urologists or sex therapists. As a result of this bias, our results could be distorted. A further limitation of the study is that certain conditions (*e.g.* depression) associated with FM were assessed only with the FIQR items, without being subjected to a more comprehensive assessment. Finally, this is a cross-sectional investigation. As a result, this study could have a drawback in terms of generalisation, and a causal relationship could not be established. Moreover, no information was available if patients were exposed to previous traumatic events (such as sexual abuse) and no information was available regarding treatment.

In conclusion, FM has the potential to induce overactive bladder syndrome and sexual dysfunction in women through both psychological (depression, anxiety, exhaustion, sleep, etc.) and physiological (low pain tolerance, vulvodynia, body pain before, during, or after sex, etc.) pathways. These physiological (pain) and psychological (depression) factors are also interconnected. Another pathway is that sexual dysfunction can cause psychological (and even physiological) stress in women, as well as a major negative impact on HRQoL, facilitating the production of FM. The importance of a multidisciplinary approach to treating patients with these conditions is highlighted by our findings. However, no longitudinal studies have looked at this series of events. To establish the causal relationship and mechanism of association between FM and genitourinary and sexual dysfunction, further longitudinal studies are required.

References

1. SARZI-PUTTINI P, GIORGI V, ATZENI F *et al*.: Fibromyalgia position paper. *Clin Exp Rheumatol* 2021; 39 (Suppl. 130): S186-93.
2. ALCIATI A, NUCERA V, MASALA IF *et al*.: One year in review 2021: fibromyalgia. *Clin Exp Rheumatol* 2021; 39 (Suppl. 130): S3-12.
3. AMASYALI AS, TAŞTABAN E, AMASYALI SY *et al*.: Effects of low sleep quality on sexual function, in women with fibromyalgia. *Int J Impot Res* 2016; 28: 46-9.
4. MUTTI GW, DE QUADROS M, CREMONEZ LP, SPRICIGO D, SKARE T, NISIHARA R: Fibromyalgia and sexual performance: a cross-sectional study in 726 Brazilian patients. *Rheumatol Int* 2021; 41: 1471-7.
5. CLIMENT-SANZ C, MARCO-MITJAVILA A, PASTELLS-PEIRÓ R, VALENZUELA-PASCUAL F, BLANCO-BLANCO J, GEA-SÁNCHEZ M: Patient reported outcome measures of sleep quality in fibromyalgia: A COSMIN systematic review. *Int J Environ Res Public Health* 2020; 17: 2992.
6. BERMAN JR: Physiology of female sexual function and dysfunction. *Int J Impot Res* 2005; 17 (Suppl. 1): S44-51.
7. PAZMANY E, LY HG, AERTS L *et al*.: Brain responses to vestibular pain and its anticipation in women with Genito-Pelvic Pain/Penetration Disorder. *Neuroimage Clin* 2017; 16: 477-90.
8. SALAFFI F, DI CARLO M, FARAH S *et al*.: Diagnosis of fibromyalgia: comparison of the 2011/2016 ACR and AAPT criteria and validation of the modified Fibromyalgia Assessment Status. *Rheumatology* (Oxford) 2020; 59: 3042-9.
9. SALAFFI F, DI CARLO M, BAZZICHI L *et al*.: Definition of fibromyalgia severity: findings from a cross-sectional survey of 2339 Italian patients. *Rheumatology* (Oxford) 2021; 60: 728-36.
10. BESIROGLU MDH, DURSUN MDM: The association between fibromyalgia and female sexual dysfunction: a systematic review and meta-analysis of observational studies. *Int J Impot Res* 2019; 31: 288-97.
11. ABRAMS P, CARDOZO L, FALL M *et al*.: The standardisation of terminology in lower urinary tract function: Report from the standardization sub-committee of the International Continence Society. *Urology* 2003; 61: 37-49.
12. OONNELL KA, SINGER J, RAJAN S: Stimulus-associated urinary urges in overactive bladder syndrome. *Neurourol Urodyn* 2018; 37: 284-90.
13. CHUN JY, SONG M, HAN JY, NA S, HONG B, CHOO MS: Clinical factors associated with dose escalation of solifenacin for the treatment of overactive bladder in real-life practice. *Int Neurourol J* 2014; 18: 23-30.
14. BARTOLI S, AGUZZI G, TARRICONE R: Impact on quality of life of urinary incontinence and overactive bladder: a systematic literature review. *Urology* 2010; 75: 491-500.
15. MELOTTI IG, JULIATO CR, DE ALBUQUERQUE COELHO SC, LIMA M, RICCETTO CL: Is there any difference between depression and anxiety in overactive bladder according to sex? A systematic review and meta-analysis. *Int Neurourol J* 2017; 21: 204-11.
16. LOZANO-ORTEGA G, WALKER D, ROGULA B *et al*.: The relative efficacy and safety of mirabegron and onabotulinumtoxin a in patients with overactive bladder who have previously been managed with an antimuscarinic: a network meta-analysis. *Urology* 2019; 127: 1-8.
17. SCHNEIDER T, MARSCHALL-KEHREL D, HANISCH JU, MICHEL MC: Do gender, age or lifestyle factors affect responses to antimuscarinic treatment in overactive bladder patients? *Int J Clin Pract* 2010; 64: 1287-93.
18. CHUNG JH, KIM SA, CHOI BY *et al*.: The association between overactive bladder and fibromyalgia syndrome: a community survey. *Neurourol Urodyn* 2013; 32: 66-9.
19. REYNOLDS WS, DMOCHOWSKI R, WEIN A, BRUEHL S: Does central sensitization help explain idiopathic overactive bladder? *Nat Rev Urol* 2016; 13: 481-91.
20. KAPLAN SA, DMOCHOWSKI R, CASH BD, KOPP ZS, BERRIMAN SJ, KHULLAR V: Systematic review of the relationship between bladder and bowel function: implications for patient management. *Int J Clin Pract* 2013; 67: 205-16.
21. ELIASSON K, ELFVING B, NORDGREN B, MATTSSON E: Urinary incontinence in women with low back pain. *Man Ther* 2008; 13: 206-12.
22. RICO-VILLADEMOROS F, CALANDRE EP, RODRIGUEZ-LOPEZ CM *et al*.: Sexual functioning in women and men with fibromyalgia. *J Sex Med* 2012; 9: 542-9.
23. COLLADO-MATEO D, OLIVARES PR, ADSUAR JC, GUSI N: Impact of fibromyalgia on sexual function in women. *J Back Musculoskelet Rehabil* 2020; 33: 355-61.
24. KATZ H, NEWTON-JOHN TRO, SHIRES A: Sexual difficulties in the population with musculoskeletal chronic pain: a systematic review. *Pain Med* 2021; 22: 1982-92
25. SHAVER JL, WILBUR J, ROBINSON FP, WANG E, BUNTIN MS: Women's health issues with fibromyalgia syndrome. *J Womens Health* (Larchmt) 2006; 15: 1035-45.
26. GORDON AS, PANAHIAN-JAND M, MCCOMB F, MELEGARI C, SHARP S: Characteristics of women with vulvar pain disorders: responses to a Web-based survey. *J Sex Marital Ther* 2003; 29(Suppl. 1): 45-58.
27. BORNSTEIN J, PRETI M, SIMON JA *et al*.: Descriptors of vulvodynia: a multisocietal definition consensus (International Society for the Study of Vulvovaginal Disease, the International Society for the Study of Women Sexual Health, and the International Pelvic Pain Society). *J Low Genit Tract Dis* 2019; 23: 161-3.
28. BENDTSEN L, NORREGAARD J, JENSEN R, OLESEN J: Evidence of qualitatively altered nociception in patients with fibromyalgia. *Arthritis Rheum* 1997; 40: 98-102.
29. NAPPI PR, CUCINELLA L, MARTELLA S, ROSSI M, TIRANINI L, MARTINI E: Female sexual dysfunction (FSD): Prevalence and impact on quality of life (QoL). *Maturitas* 2016; 94: 87-91.
30. TIKIZ C, MUEZZINOGLU T, PIRILDAR T, TASKN EO, FRAT A, TUZUN C: Sexual dysfunction in female subjects with fibromyalgia. *J Urol* 2005; 174: 620-3.
31. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al*.: The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res* (Hoboken) 2010; 62: 600-10.
32. WOLFE F, CLAUW DJ, FITZCHARLES MA *et al*.: Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR preliminary diagnostic criteria for fibromyalgia. *J Rheumatol* 2011; 38: 1113-22.

33. BENNETT RM, FRIEND R, JONES KD, WARD R, HAN BK, ROSS RL: The Revised Fibromyalgia Impact Questionnaire (FIQR): validation and psychometric properties. *Arthritis Res Ther* 2009; 11: R120.
34. DI CARLO M, MUTO P, BENFAREMO D, LUCHETTI MM, ATZENI F, SALAFFI F: The neuropathic pain features in psoriatic arthritis: a cross-sectional evaluation of prevalence and associated factors. *J Rheumatol* 2020; 47: 1198-203.
35. DI CARLO M, VENTURA C, CESARONI P, CAROTTI M, GIOVAGNONI A, SALAFFI F: Sural nerve size in fibromyalgia syndrome: study on variables associated with cross-sectional area. *Front Med* (Lausanne) 2020; 7: 360.
36. FREYNHAGEN R, BARON R, GOCKEL U, TÖLLE TR: painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006; 22: 1911-20.
37. HOMMA Y, YOSHIDA M, SEKI N *et al*.: Symptom assessment tool for overactive bladder syndrome – overactive bladder symptom score. *Urology* 2006; 68: 318-23.
38. ACQUADRO C, KOPP Z, COYNE KS *et al*.: Translating overactive bladder questionnaires in 14 languages. *Urology* 2006; 67: 536-40.
39. HUNG MJ, CHOU CL, YEN TW *et al*.: Development and validation of the Chinese overactive bladder symptom score for assessing overactive bladder syndrome in a RESORT study. *J Formos Med Assoc* 2013; 112: 276-82.
40. XU D, ZHAO M, HUANG L, WANG K: Overactive bladder symptom severity, bother, help-seeking behavior, and quality of life in patients with type 2 diabetes: a path analysis. *Health Qual Life Outcomes* 2018; 16: 1.
41. CHUANG FC, HSIAO SM, KUO HC: The Overactive Bladder Symptom Score, International Prostate Symptom Score-Storage Subscore, and Urgency Severity Score in Patients with Overactive Bladder and Hypersensitive Bladder: which scoring system is best? *Int Neurourol J* 2018; 22: 99-106.
42. YAMAGUCHI O, NISHIZAWA O, TAKEDA M *et al*.: Clinical guidelines for overactive bladder. *Int J Urol* 2009; 16: 126-42.
43. WIEGEL M, MESTON C, ROSEN R: The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. *J Sex Marital Ther* 2005; 31: 1-20.
44. MESTON CM: Validation of the Female Sexual Function Index (FSFI) in women with female orgasmic disorder and in women with hypoactive sexual desire disorder. *J Sex Marital Ther* 2003; 29: 39-46.
45. FILOCAMO MT, SERATI M, LI MARZI V *et al*.: The Female Sexual Function Index (FSFI): linguistic validation of the Italian version. *J Sex Med* 2014; 11: 447-53.
46. ARMITAGE P, BERRY G, MATTHEWS JNS: Statistical methods in medical research. 4th ed. Blackwell Science, 2002.
47. SALAFFI F, DE ANGELIS R, GRASSI W: MArche Pain Prevalence; INvestigation Group (MAPPING) study: Prevalence of musculoskeletal conditions in an Italian population sample: results of a regional community-based study. I. The MAPPING study. *Clin Exp Rheumatol* 2005; 23: 819-28.
48. CLAUW DJ, SCHMIDT M, RADULOVIC D, SINGER A, KATZ P, BRESETTE J: The relationship between fibromyalgia and interstitial cystitis. *J Psychiatr Res* 1997; 31: 125-31.
49. CHELIMSKY G, HELLER E, BUFFINGTON CA, RACKLEY R, ZHANG D, CHELIMSKY T: Co-morbidities of interstitial cystitis. *Front Neurosci* 2012; 6: 114.
50. KALICHMAN L: Association between fibromyalgia and sexual dysfunction in women. *Clin Rheumatol* 2009; 28: 365-9.
51. ORELLANA C, CASADO E, MASIP M, GALISTEO C, GRATACÓS J, LARROSA M: Sexual dysfunction in fibromyalgia patients. *Clin Exp Rheumatol* 2008; 26: 663-6.
52. TUTOGLU A, BOYACI A, KOCA I, CELEN E, KORKMAZ N: Quality of life, depression, and sexual dysfunction in spouses of female patients with fibromyalgia. *Rheumatol Int* 2014; 34: 1079-84.
53. AYDIN G, BAŞAR MM, KELEŞ I, ERGÜN G, ORKUN S, BATISLAM E: Relationship between sexual dysfunction and psychiatric status in premenopausal women with fibromyalgia. *Urology* 2006; 67: 156-61.
54. KAYHAN F, KÜÇÜK A, SATAN Y, İLGÜN E, ARSLAN Ş, İLIK F: Sexual dysfunction, mood, anxiety, and personality disorders in female patients with fibromyalgia. *Neuropsychiatr Dis Treat* 2016; 12: 349-55.
55. WEIN AJ: Overactive bladder: defining the disease. *Am J Manag Care* 2000; 6: S559-564.
56. HAYLEN BT, DE RIDDER D, FREEMAN RM *et al*.: An international Urogynecological association (IUGA)/international continence society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn* 2010; 29: 4-20.
57. IRWIN DE, KOPP ZS, AGATEP B, MILSOM I, ABRAMS P: Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. *BJU Int* 2011; 108: 1132-8.
58. CHUANG YC, LIU SP, LEE KS *et al*.: Prevalence of overactive bladder in China, Taiwan and South Korea: results from a cross-sectional, population-based study. *Low Urin Tract Symptoms* 2019; 11: 48-55.
59. GANZ ML, SMALARZ AM, KRUPSKI TL *et al*.: Economic costs of overactive bladder in the United States. *Urology* 2010; 75: 526-32.
60. VAUGHAN CP, JOHNSON TM, ALA-LIPASTI MA *et al*.: The prevalence of clinically meaningful overactive bladder: bother and quality of life results from the population-based FINNO study. *Eur Urol* 2011; 59: 629-36.
61. SOYUPEK F, SOYUPECK S, AKKUS S, OZORAK A: The coexistence of the fibromyalgia syndrome and the overactive bladder syndrome. *J Musculoskeletal Pain* 2007; 15: 31-7.
62. LATREMOLIERE A, WOOLF CJ: Central sensitization: a generator of pain hypersensitivity by central neural plasticity. *J Pain* 2009; 10: 895-926.
63. SARZI-PUTTINI P, ATZENI F, MEASE PJ: Chronic widespread pain: from peripheral to central evolution. *Best Pract Res Clin Rheumatol* 2011; 25: 133-9.
64. KIM SH: Skin biopsy findings: implications for the pathophysiology of fibromyalgia. *Med Hypotheses* 2007; 69: 141-4.
65. MARTINEZ-LAVIN M: Fibromyalgia is a neuropathic pain syndrome. *J Rheumatol* 2006; 33: 827-8.
66. LAI HH, VETTER J, JAIN S, GEREAU RW 4TH, ANDRIOLE GL: The overlap and distinction of self-reported symptoms between interstitial cystitis/bladder pain syndrome and overactive bladder: a questionnaire-based analysis. *J Urol* 2014; 192: 1679-85.
67. MCCABE MP, SHARLIP ID, ATALLA E *et al*.: Definitions of sexual dysfunctions in women and men: A Consensus Statement From the Fourth International Consultation on Sexual Medicine 2015. *J Sex Med* 2016; 13: 135-43.
68. BURRI A, LACHANCE G, WILLIAMS FM: Prevalence and risk factors of sexual problems and sexual distress in a sample of women suffering from chronic widespread pain. *J Sex Med* 2014; 11: 2772-84.
69. OSTENSEN M: New insights into sexual functioning and fertility in rheumatic diseases. *Best Pract Res Clin Rheumatol* 2004; 18: 219-32.
70. ABLIN JN, GUREVITZ I, COHEN H, BUSKILA D: Sexual dysfunction is correlated with tenderness in female fibromyalgia patients. *Clin Exp Rheumatol* 2011; 29 (Suppl. 69): S44-48.
71. TERZI H, TERZI R, KALE A: The relationship between fibromyalgia and pressure pain threshold in patients with dyspareunia. *Pain Res Manag* 2015; 20: 137-40.
72. TYMPANIDIS P, CASULA MA, YIANGOU Y, TERENGHI G, DOWD P, ANAND P: Increased vanilloid receptor VR1 innervation in vulvodynia. *Eur J Pain* 2004; 8: 129-33.
73. PUKALL CF, BINIK YM, KHALIFÉ S, AMSEL R, ABBOTT FV: Vestibular tactile and pain thresholds in women with vulvar vestibulitis syndrome. *Pain* 2002; 96: 163-75.
74. YILMAZ H, YILMAZ SD, POLAT HA, SALLI A, ERKIN G, UGURLU H: The effects of fibromyalgia syndrome on female sexuality: a controlled study. *J Sex Med* 2012; 9: 779-85.
75. SALAFFI F, SARZI-PUTTINI P, CIAPETTI A, ATZENI F: Clinimetric evaluations of patients with chronic widespread pain. *Best Pract Res Clin Rheumatol* 2011; 25: 249-70.
76. TURON H, CAREY M, BOYES A, HOBDEN B, DILWORTH S, SANSON-FISHER R: Agreement between a single-item measure of anxiety and depression and the Hospital Anxiety and Depression Scale: A cross-sectional study. *PLoS One* 2019; 14: e0210111.
77. CLAYTON AH, PRADKO JF, CROFT HA *et al*.: Prevalence of sexual dysfunction among newer antidepressants. *J Clin Psychiatry* 2002; 63: 357-66.
78. MONTEJO AL, MAJADAS S, RICO-VILLADEMOROS F *et al*.: Frequency of sexual dysfunction in patients with a psychotic disorder receiving antipsychotics. *J Sex Med* 2010; 7: 3404-13.
79. CLAYTON A, KORNSTEIN S, PRAKASH A, MALLINCKRODT C, WOHLREICH M: Changes in sexual functioning associated with duloxetine, escitalopram, and placebo in the treatment of patients with major depressive disorder. *J Sex Med* 2007; 4 (4 Pt 1): 917-29.
80. DELGADO PL, BRANNAN SK, MALLINCKRODT CH *et al*.: Sexual functioning assessed

in 4 double-blind placebo- and paroxetine-controlled trials of duloxetine for major depressive disorder. *J Clin Psychiatry* 2005; 66: 686-92.
81. MONTEJO AL, PERAHIA DG, SPANN ME *et al*.: Sexual function during long-term duloxetine treatment in patients with recurrent major depressive disorder. *J Sex Med* 2011; 8: 773-82.
82. PRINS MA, WOERTMAN L, KOOL MB, GEENEN R: Sexual functioning of women with fibromyalgia. *Clin Exp Rheumatol* 2006; 24: 555-61.
83. LESERMAN J: Sexual abuse history: prevalence, health effects, mediators, and psychological treatment. *Psychosom Med* 2005; 67: 906-15.
84. CHOU KL: Childhood sexual abuse and psychiatric disorders in middle-aged and older adults: evidence from the 2007 Adult Psychiatric Morbidity Survey. *J Clin Psychiatry* 2012; 73: e1365-71.
85. OU W, LI Z, ZHENG Q, CHEN W, LIU J, LIU B, ZHANG Y: Association between childhood maltreatment and symptoms of obsessive-compulsive disorder: a meta-analysis. *Front Psychiatry 2021;* 11: 612586.
86. ARNOLD RP, ROGERS D, COOK DAG: Medical problems of adults who were sexually abused in childhood. *Br Med J* 1990; 300: 705-8.
87. WALKER EA, KATON WJ, HANSOM J *et al*.: Medical and psychiatric symptoms in women with childhood sexual abuse. *Psychosom Med* 1992; 54: 658-63.
88. ALEXANDER RW, BRADLEY LA, ALARCÓN GS *et al*.: Sexual and physical abuse in women with fibromyalgia: association with outpatient health care utilization and pain medication usage. *Arthritis Care Res* 1998; 11: 102-15.
89. DIAZ-PIEDRA C, CATENA A, SANCHEZ AI, MIRO E, MARTINEZ MP, BUELA-CASAL G: Sleep disturbances in fibromyalgia syndrome: the role of clinical and polysomnographic variables explaining poor sleep quality in patients. *Sleep Med* 2015 ;16: 917-25.
90. SPAETH M, RIZZI M, SARZI-PUTTINI P: Fibromyalgia and sleep. *Best Pract Res Clin Rheumatol* 2011; 25: 227-39.
91. KOCA TT, KARACA ACET G, TANRIKUT E, TALU B: Evaluation of sleep disorder and its effect on sexual dysfunction in patients with fibromyalgia syndrome. *Turk J Obstet Gynecol* 2016; 13: 167-71.
92. AMASYALI AS, TASTABAN E, AMASYALI SY *et al*.: Effects of low sleep quality on sexual function, in women with fibromyalgia. *Int J Impot Res* 2016; 28: 46-9.
93. KRAVITZ HM, KATZ RS: Fibrofog and fibromyalgia: a narrative review and implications for clinical practice. *Rheumatol Int* 2015; 35: 1115-25.