Regarding the pain of men: characteristics of fibromyalgia in male patients

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Abstract

Objective

Fibromyalgia (FM) is a chronic pain disorder with a female predominance. The impact of gender on the epidemiologic and clinical characteristics, as well as therapeutic strategies for FM patients, remains incompletely understood. This study aims to outline the clinical and epidemiologic profiles of male FM patients in comparison to female patients.

Methods

A retrospective cross-sectional observational study was conducted, encompassing all patients diagnosed with FM in the electronic medical record database of a tertiary hospital from 2010-2021. Each patient file was individually reviewed, and data was collected.

Results

A total of 3044 patients were diagnosed with FM, of which 401 were male (13.2%). A random cohort of 438 female patients was created for comparison with the male cohort. The average age of male patients at the time of their FM diagnosis was notably higher than that of females (52.7 years vs. 44.9 years, p<0.001). Obesity was more prevalent among female patients (16% vs. 9.2% for males, p=0.003), while obstructive sleep apnoea was more common in males (6.7% vs. 1.8%, p<0.001). Male patients exhibited a significantly higher prevalence of post-traumatic stress disorder (PTSD) than females (14% vs. 5.7%, p<0.001). Among male patients, 48% were treated with medical cannabis compared to 34.6% of females (p<0.001).

Conclusion

Distinct clinical gender-specific characteristics were identified in our real-world cohort of FM patients. PTSD and the use of medical cannabis were more prevalent among male patients, whereas obesity was more common in females. Further studies exploring the clinical and pathogenic mechanisms underlying these differences are recommended.

Key words

fibromyalgia, post-traumatic stress disorder, gender, cannabis, male

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Received on January 22, 2025; accepted in revised form on March 26, 2025.

Competing interests: none declared.

Introduction

Fibromyalgia (FM) is a chronic pain disorder marked by widespread pain, fatigue, sleep disturbances, cognitive dysfunction, and frequent psychiatric comorbidities (1). In the United States, FM prevalence is estimated to be between 2% and 8%, affecting 5–10 million adults (2). The disorder predominantly affects middle-aged women, accounting for 75–90% of diagnosed cases.

The precise prevalence of FM in men remains uncertain, with the female-to-male diagnosis ratio estimated at around 7:1. Men with FM are often underdiagnosed, partly due to the prevailing stereotype that FM is predominantly a 'woman's disease' and a general lack of awareness among healthcare professionals (3). Moreover, some men are reluctant to seek care in specialised clinics, often driven by feelings of embarrassment, leading them to confront the condition independently (4). This female predominance is evident in pharmaceutical advertising, which predominantly features women with FM, in the membership demographics of patient support groups, and in testimonies from FM patients who are almost exclusively women (5).

Notably, the proportion of male FM patients may be influenced by the criteria used to make the diagnosis. The change in diagnostic criteria which occurred in 2010-2011, which replaced the original tender point-based criteria with symptom-based criteria, appears to have increased the proportion of males among patients (6).

The specific epidemiologic and clinical characteristics of men with FM are not well-defined, and available data often present conflicting results (7). Men and women may experience FM differently. Men tend to report more severe symptoms and a more significant impact on their quality of life (8). In a survey involving 1163 men with FM, half reported adverse effects on their careers (9). Many believed that societal expectations for men to be resilient and the primary family providers exacerbated these impacts. These men expressed greater dissatisfaction with the healthcare system, perceived disparities in treatment, and felt they had less access to disease information compared to women (10). They also reported a more profound impact on their quality of life, relationships, and careers than women did.

Furthermore, they were found to exhibit more neuropsychiatric symptoms than women, particularly depression and anxiety (11). There is also a notable association between FM and post-traumatic stress disorder (PTSD) in male patients (12).

The primary objective of the current study was to delineate the clinical profiles of male FM patients in comparison to their female counterparts within a substantial cohort.

Methods

We conducted a retrospective cross-sectional observational study at the Tel Aviv Sourasky Medical Centre. Using the MDClone system, the hospital's electronic medical record database, we retrieved the records of 3044 patients diagnosed with FM who received treatment in outpatient clinics from 2010 to 2021.

Eligibility criteria included patients of both genders aged 18 years and older who were diagnosed with FM by a rheumatologist or pain specialist during their visit. Due to the retrospective nature of the study, ACR diagnostic criteria were not implemented but rather the diagnosis relied on the clinical evaluation at the time of encounter. This was also the case regarding the clinical diagnosis of psychiatric comorbidities including PTSD, depression and anxiety. Each patient file was individually reviewed, and data were collected on sociodemographic characteristics, medical and psychiatric diagnoses, and treatment regimens, including the use of medical cannabis.

Statistical power evaluation

A statistical power analysis was performed prior to data analysis to determine the sample size required to detect clinically meaningful differences between male and female FM patients. Considering previous studies reporting gender differences in key variables such as PTSD prevalence and cannabis use, a medium effect size (Cohen's d

≈ 0.5) was anticipated. With an alpha (type I error) level set at 0.05 and power (1-β) targeted at 0.8 (80%), calculations indicated that a minimum of approximately 64 subjects per group were required to detect significant differences. Given that our final analysis included cohorts of 401 males and 438 females, our study possessed sufficient power (>95%) to identify statistically significant differences between groups for key variables of interest.

Ethics approval

The study received approval from the local institutional ethics committee, the Helsinki Committee of the Tel Aviv Medical Centre, Tel Aviv, Israel (IRB number: TLV-0111-21).

Statistical analyses

Categorical variables were presented as numbers and percentages and were compared using either Pearson's Chi-squared test or Fisher's exact test. Continuous variables were expressed as mean ± standard deviation (SD) or median ± interquartile range (IQR). They were compared using the t-test or Mann-Whitney test depending on the data distribution. The normality of data distribution was assessed using the Shapiro-Wilk test, histograms, and Q-Q plots.

For the primary study outcome measures, odds ratios (OR) and their 95% confidence intervals (CI) were reported. A two-tailed *p*-value of less than 0.05 was deemed statistically significant. All statistical analyses were conducted using SPSS (IBM SPSS Statistics for Windows, v. 25.0, released in 2013).

Results

Out of the 3044 patients with FM included in this study, the majority were females, accounting for 2643 (86.8%), while 401 (13.2%) were males. This resulted in a female-to-male ratio of 6.59:1. For comparison purposes, we created a random cohort of 438 female patients and juxtaposed it with the male cohort. The average age of male patients was notably higher than that of their female counterparts, with mean ages of 52.7 years and 44.9 years, respectively (p<0.001) (Table I).

A significant majority of patients (2557; 84%) received care at the Rheumatology Institute, while 487 (16%) were treated at the Pain Clinic. Obesity, defined as body mass index over 29, was more prevalent among female patients, with 16% of females being obese compared to 9.2% of males (p=0.003). Conversely, obstructive sleep apnoea syndrome was more common among male patients, with a prevalence of 6.7% in males compared to 1.8% in females (p<0.001).

In terms of psychiatric comorbidities, male patients exhibited a significantly higher prevalence of PTSD, at 14% compared to 5.7% in females (p<0.001). However, there were no significant differences between the two genders concerning other psychiatric conditions, such as depression and anxiety. Notably, only three male patients had a documented diagnosis of erectile dysfunction.

Medical therapy

Female patients were more commonly prescribed amitriptyline and tramadol. There were no discernible differences in the prescription of pregabalin or duloxetine between the two genders. Interestingly, almost half of the male patients (48%) were treated with medical cannabis, a figure significantly higher than the 34.6% of female patients (p<0.001). In males, smokers were more prone to use medical cannabis (57% *vs*. 45% of non-smokers), whereas such correlation was not seen in women.

A significant correlation was identified between a PTSD diagnosis and the use of medical cannabis across both genders. Only 3% of male patients versus 8.7% of women underwent psychotherapy (p=0.01).

Table I. Cohort of female and male patients with fibromyalgia.

	Female (n=438)	Male (n=401)	*p*-value
Age (mean, SD)	44.9 ± 2.1	52.7 ± 3.5	<0.001
Smokers (n)	18.3	22	0.15
Medical condition			
Obesity n (%)	70 (16)	36 (9.2)	0.003
OSA n (%)	7 (1.8)	26 (6.7)	<0.001
PTSD n (%)	25 (5.7)	56 (14)	<0.001
Depression n (%)	76 (17.4)	77 (19.2)	0.48
Anxiety n (%)	39 (8.9)	26 (6.5)	0.19
Medical therapy			
Amitriptyline n (%)	120 (27.3)	79 (19.7)	0.34
Tramadol n (%)	29 (6.6)	20 (4.9)	0.15
Pregabalin n (%)	127 (27.1)	105 (26)	0.34
Duloxetine n (%)	82 (18.7)	75 (19)	0.21
Medical cannabis n (%)	151 (34.6)	192 (48)	<0.001
Psychotherapy n (%)	38 (8.7)	12 (3)	<0.001

Discussion

In the current study, our objective was to delineate a distinct clinical profile for males with FM, drawing from a real-world cohort of patients monitored at a tertiary care centre. As anticipated, we observed a female predominance with a ratio of 6.6 to 1. Earlier studies have reported a female-to-male ratio ranging from 9:1 to as low as 4:1 in an unbiased study (13). This variance is influenced by diagnostic methods, criteria employed, and the setting of the diagnosis (*i.e*. primary care versus specialised clinics) (4).

Within our cohort, male patients were notably older than their female counterparts. This might suggest a prolonged symptomatic period before being referred to a specialised clinic and a potential delay in diagnosis. While this delay may be attributed to women experiencing more intense pain symptoms, it may also reflect a more limited awareness on the part of primary care physicians regarding the occurrence of FM in male patients (14, 15).

In terms of clinical profiles, male patients exhibited lower rates of obesity but higher rates of obstructive sleep apnoea and PTSD. No significant gender differences were observed for other psychiatric comorbidities such as depression and anxiety. Additionally, men were more likely to be treated with medical cannabis than women.

Obesity has a strong bidirectional link with FM. While obesity elevates the risk of developing FM, it also adversely impacts the disorder's clinical course. Obese FM patients tend to experience heightened pain, increased depressive symptoms, reduced mobility, diminished function, and rely more on medications (16, 17). In a study involving 224 FM patients, 30% were overweight and over 40% were obese, with no observed gender differences (18). However, a study by Segura-Jiménez *et al*. revealed a higher prevalence of obesity among female patients compared to healthy controls (19). In contrast, male patients and healthy controls showed no significant differences in body composition or weight status. The lower obesity rates in our study might be attributed to cultural differences or potential underreporting in medical records.

Previous research indicates that male patients often exhibit altered sleep respiratory patterns and non-refreshing sleep, with over 60% experiencing apnoea-hypopnea syndrome (4). This aligns with our findings of a higher prevalence of OSA among male fibromyalgia patients (13). Moreover, FM might serve as an indicator for undetected sleep apnoea in males (4).

FM is frequently associated with psychiatric disorders, including depression, anxiety, bipolar disorder, personality disorders, obsessive-compulsive disorders, and PTSD (20, 21). The clinical and epidemiological overlap between FM and PTSD is particularly intriguing, and in some patients, both syndromes may be triggered by a single traumatic event (22). Genetic predisposition may play a role in both conditions, thus interacting with the external (environmental) component which must inherently play a role (23). One of our most interesting findings in the current study relates to the significantly higher rates of PTSD among male patients compared to female patients. We can only speculate regarding the explanations for this finding. In the Israeli population, PTSD among males is often related to traumatic experiences encountered during military service in combat or as a result of similar security-related events (*e.g*. acts of terrorism). In this context, PTSD is a relatively well-accepted diagnosis on a societal level and one which a male patient may be relatively more willing to acknowledge. In the female population, on the other hand, combat-related PTSD is expected to be less common, while the disorder may be more frequently related to a history of sexual trauma, including although not limited to cases of child abuse (24, 25). While such a history has frequently been reported in association with FM, some female patients may be more reluctant to report this kind of traumatic event, particularly in the setting of a rheumatology clinic, thus contributing to the finding described above. On the other hand, significant differences are known to exist between males and females in many aspects of pain processing, ranging from the genetic, molecular, cellular, and systems-level mechanisms of acute and chronic pain (26), most recently even to the gender-based difference in the analgesic effects of caffeine (27). Thus, it is reasonable to assume that the difference in prevalence of PTSD may represent a true finding, reflecting inter-gender variability in the pathogenetic processes underlying FM.

Interestingly, despite the higher rate of PTSD in male patients, the use of psychotherapy was significantly lower in men than in women. CBT is highly recommended in the management of FM with beneficial effects on pain, sleep, and disability (28-30). Psychotherapy is also crucial in the treatment of PTSD (31). Low accessibility and financial issues may explain the low rates of psychotherapy in both groups, possibly aggravated by feelings of shame in men (32).

Erectile dysfunction was documented in only three males in our cohort. A study by Batmaz *et al*. highlighted significant sexual dysfunction in male FM patients compared to healthy controls, correlating with older age, widespread pain, and diminished quality of life (14).

The scant mentions of erectile dysfunction in our cohort might underscore rheumatologists' or pain specialists' limited awareness of this facet of male FM or a reluctance to discuss it despite its profound impact on patients' well-being. Concerning medical treatment, men, especially those diagnosed with PTSD, were more inclined to use medical cannabis than women. This aligns with a previous study indicating that one-third of male patients used cannabinoids, with unstable mental health, opioid-seeking behaviour, and male gender being associated with herbal cannabis use (33).

The strength of this study lies in its representation of an unbiased cohort of FM patients from a tertiary care hospital. However, it does have limitations: being retrospective and based on medical charts, some associated medical conditions might have been underreported.

Conclusion

Our real-world cohort of FM patients revealed significant gender-specific clinical characteristics. PTSD and medical cannabis use were notably more prevalent among male patients, while obesity was more common in females. Further investigations into the clinical and pathogenic mechanisms underlying these disparities are warranted.

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