Patients With Fibromyalgia, Depression, and/or Anxiety and Sex Differences

Marcela Henao-Pérez1, Diana Carolina López-Medina1, Alejandra Arboleda2, Sara Bedoya Monsalve1, and Julián Andrés Zea1

Abstract
Fibromyalgia is a syndrome characterized by chronic widespread pain, with a multifactorial etiopathogenesis and high incidence of neuropsychiatric comorbidity. It has been inaccurately considered a pathological condition affecting only middle-aged women. The study aimed to explore the association of sociodemographic and clinical factors in patients with fibromyalgia with depression and/or anxiety. The present study is an analysis of a cross-sectional study of a secondary source. The prevalence ratio (PR) between the demographic and clinical variables of patients with fibromyalgia and concomitant depression and/or anxiety was calculated. Overall, 1,106 medical records were obtained with a confirmed diagnosis of fibromyalgia between 2010 and 2016; of these, 318 (28.75%) patients had an associated diagnosis of depression and/or anxiety. Approximately 28% women (295 of 1,052) and 42.6% men (23 of 54) suffered from depression and/or anxiety. In the adjusted explanatory model of depression and/or anxiety in patients with fibromyalgia, the relationship between sex (female PR = 0.5 [0.28–0.86]) and low socioeconomic strata (PR = 0.53 [0.33–0.70]) remained constant. In the study population, patients with fibromyalgia belonging to lower social strata were less likely to present with depression and anxiety. The male sex may pose as a risk factor for depression and/or anxiety in patients with fibromyalgia. Fibromyalgia has a huge impact on men’s physical as well as mental health.

Keywords
fibromyalgia, depression, anxiety, men, women

Received March 24, 2022; revised June 10, 2022; accepted June 13, 2022

Introduction
Fibromyalgia (FM) is a syndrome characterized by chronic widespread pain, with a multifactorial etiopathogenesis and high incidence of neuropsychiatric comorbidity (Knaster et al., 2012; Marques et al., 2017). The perception of FM has evolved over the past few decades and has incorporated a series of symptoms beyond pain, which contribute to the global spectrum of this pathological condition (Fitzcharles & Yunus, 2012). Psychological symptoms are prevalent in patients with FM, which could influence the pain severity and contribute to poor overall health (Yunus et al., 1991). Patients with FM are more likely to experience depression (20%–80%) and anxiety (13%–63.8%) compared with healthy controls (Fietta et al., 2007).

FM has been inaccurately considered a pathological condition that only affects the middle-aged women (Häuser & Fitzcharles, 2018). The prevalence of FM may vary based on the different classification criteria, in particular, when applying the 1990 criteria, which tends to underdiagnose the condition in male populations (Kleykamp et al., 2021). In addition, men are less likely
to identify symptoms and to be diagnosed with FM compared with women (Vincent et al., 2013).

The difference in the presentation of this pathology by sex can be explained by the hypothesis that women have a lower pain threshold than men (Schiltenwolf & Pogatzki-Zahn, 2015). Besides, in Western countries, women consult the health care services more frequently when they experience somatic and psychological symptoms (Aggarwal et al., 2006).

As FM is considered a disease that mainly affects women, doctors may overlook this diagnosis in male patients with chronic widespread pain; besides, the stigma of suffering from a pathology that mainly affects women could have a great influence on underdiagnosis (Häuser et al., 2011; Muraleetharan et al., 2018).

A limited number of studies have examined the sociodemographic and clinical differences in patients with FM and neuropsychiatric comorbidity (Henao-Pérez et al., 2020; Kleykamp et al., 2021; Thieme et al., 2004). This led to establish the aim of the present study to explore the association of these factors in a patient population with FM and concomitant depression and/or anxiety treated in a specialized center from 2010 to 2016.

Method

This study involves the analysis of cross-sectional study of a secondary source, with secondary analysis of the “Neuropsychiatric comorbidity in patients with fibromyalgia” study data (Henao-Pérez et al., 2019, 2020), based on the medical records from 2010 to 2016. Overall, 1,106 patients above the age of 18 years with a confirmed diagnosis of FM (in accordance with the American Association of Rheumatology criteria) who were treated at a medical institution specialized in neurology were included in this study. To avoid any information bias, researchers performed a thorough check of the database. The study incorporates all variables in the medical records, including comorbidities of depression and anxiety, which had to be documented as a personal history or as a diagnosis at the time of consultation, according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV; American Psychiatric Association, 1994).

SPSS 23 program was used for the analyses. The determination of frequencies by groups, normality distribution analysis using the Kolmogorov–Smirnov test, measurement of central tendency and dispersion of quantitative variables, and binary logistic regression were performed.

The Program for Epidemiological Analysis of Tabulated Data version 3.1 (EPIDAT 3.1) was used to estimate the epidemiological association measures (disease prevalence ratio [PR]) between the demographic and clinical variables of patients with FM and concomitant depression and/or anxiety. According to the literature, a history of hypothyroidism was considered a confounding variable (Samuels, 2014), which was controlled using multivariable binary logistic regression.

The present study received the approval of the Research Ethics Committee of the Neurological Institute of Colombia, registered in Act No. 67.

Results

Between 2010 and 2016, 1,106 patients diagnosed with FM were treated at the medical institution. Most of the patients were residents of the department of Antioquia, Colombia, and only 1% resided in other departments of the country. The sociodemographic characteristics of the study population are presented in Table 1.

Of the 1,106 patients with FM, 318 (28.75%) were diagnosed with depression and/or anxiety and 788 (71.24%) did not present these psychopathologies. Accordingly, two groups of patients were constituted.

The median (Mdn) age among patients with depression and/or anxiety was 54.5 years (interquartile range [IQR] = 15 years). Approximately 28% women (295 of 1,052) and 42.6% men (23 of 54) suffered from depression and/or anxiety.

The personal history most frequently observed in both the groups was migraine, whereas the most frequent symptoms identified in both the groups were myalgia, sleep disorders, chronic fatigue, and headache (Table 2).

Table 3 presents the types of therapies and drugs used in the study population. As a single agent or in combination, these drugs failed to prove a relationship with the reduction of the prevalence of depression and/or anxiety in patients with FM.

Variables with a significant relationship in the bivariate analysis (sex, socioeconomic strata, educational level, history of premenstrual syndrome, and the presence of chronic fatigue) and those recognized in the literature (myalgia, sleep disorders, and cognitive disorders) were included in the multivariate analysis, and control was made for history of hypothyroidism. Chronic fatigue and premenstrual syndrome increased the association with depression and/or anxiety in patients with FM in this population. The significant relationship between sex (women are less likely to experience depression and/or anxiety than men with FM) and socioeconomic strata was constant in the adjusted model (Table 4).

Discussion

The purpose of this study was to explore the association between the sociodemographic and clinical factors in patients with FM and the presence of depression and/or anxiety.
In the present study, most patients were women. This is consistent with the other studies reported in the literature in which FM is more prevalent in females (Neumeister & Neumeister, 2020; Queiroz, 2013). However, the authors of few studies have questioned these epidemiological data due to the lack of standardized diagnostic procedures for detecting FM, which could influence the precision and variability of the results (Conversano et al., 2020).

When patients with FM are compared with healthy controls, a significantly higher prevalence of mood disorders has been reported (Fietta et al., 2007; Wan et al., 2019). In the present study population, the presence of depression/anxiety was identified in 28.75% of patients. This value is consistent with that reported in the literature, where patients with FM are more likely to experience depression (20%–80%) and anxiety (13%–63.8%) (Fietta et al., 2007). Distinctive personality traits have been described in patients with FM, where low levels of conscientiousness and extroversion along with high levels of neuroticism predominate, in addition to the presentation of pain catastrophizing. All these traits together could act as risk factors for the development of these two psychopathologies (Conversano et al., 2020).

When analyzing by sex, the percentage of men with depression and/or anxiety was reported to be higher than that of women. The low rate of diagnosis of FM in men has made the study of gender differences difficult. However, few reports described that these psychological symptoms were significantly more prevalent in men with FM compared with healthy male controls (Yunus et al., 2000). A study conducted in Israel reported significantly higher levels of depression and worse health outcomes in men than in women (Buskila et al., 2000). In the study by Ruiz Pérez et al. (2007), men with FM had a worse self-perceived health status, a higher percentage of psychiatric history and current mental pathology, and a greater impact of the disease when compared with women. Moreover, men were identified to avail more sick leaves compared with women. The presence of an elevated frequency of psychiatric disorders was reported in men with FM, which is contrary to what happens in the general population, where women present with depression and anxiety disorder more frequently than men (Shimamoto & Rappeneau, 2017; Steel et al., 2014).

According to this finding, the adjusted model revealed that the male sex in patients with FM can be a risk factor for depression and/or anxiety, unlike the results obtained in other studies, such as that by Jiang et al. (2020), where no differences related to sex could be identified, or that by De Heer et al. (2017), where sex did not have any association but the study confirmed

| Table 1. Sociodemographic Characteristics of Patients With Fibromyalgia With or Without Depression and/or Anxiety. |
|---------------------------------------------------------------|---------------------------------------------------------------|
| Sociodemographic Characteristics | Depression/anxiety (318) | No depression/anxiety (788) |
| Age (Me, IQR) | 54.5 (15) | 54 (15) |
| Sex (female) | 295 (92.8) | 757 (96.1) |
| Socioeconomic strata | | |
| Missing data | 205 (64.5) | 596 (75.6) |
| Low | 35 (11) | 84 (10.6) |
| Middle | 78 (24.5) | 108 (13.7) |
| Educational level | | |
| Missing data | 170 (56.5) | 474 (58.9) |
| None | 9 (2.8) | 12 (1.5) |
| Basic (primary and secondary) | 76 (23.9) | 159 (20.2) |
| Technical/Technological | 34 (10.7) | 87 (11) |
| Professional (undergraduate/postgraduate) | 22 (6.9) | 7 (8) |
| Employment (yes) | 128 (42.5) | 330 (41) |
| Marital status | | |
| Missing data | 36 (12) | 98 (12.1) |
| Married | 115 (38.2) | 318 (39.5) |
| Single | 75 (24.9) | 178 (22.1) |
| Civil union | 35 (11.6) | 97 (12) |
| Widower | 25 (8.3) | 54 (6.7) |
| Separated | 15 (5) | 60 (7.5) |

Note. IQR = interquartile range.
that poor self-perception of the disease was a risk factor for depression and anxiety symptoms. Contrary to the findings reported in the two aforementioned studies and the present study, a study on 77,087 veterans diagnosed with FM reported that comparison of sexes revealed that women with FM were more likely to be diagnosed with psychiatric disorders than men (Arout et al., 2018).

Miró et al. (2012) postulated that the stigma of suffering from a “women’s” disease could contribute to men presenting more affective distress. In addition, other factors, such as the environmental and sociocultural pressure, could have influenced the ability to modulate pain in both the sexes throughout the evolution. Moreover, creating cultural stereotypes may have favored the presence of more psychological disorders (Conversano et al., 2020).

Another aspect that has been analyzed in the literature is the unemployment rate in male patients with FM, which is considerably higher than that in the general male population (Buskila et al., 2000). This finding may be associated with the significantly higher levels of depression reported in men than that in women. In a traditional society where men are expected to be the main providers, such unemployment rate in men with FM could lead to a lower self-esteem and may negatively affect the mood. In the present study, such relationship was not identified.

Finally, men have a lower ability to accept the limitations and deficiencies that are caused by FM than women (Segura-Jiménez et al., 2016). Moreover, they tend to provide a greater dimension to bodily symptoms and disregard the expression of feelings concerning the disease and its consequences (Conversano et al., 2020). All these

| Table 2. Symptoms and Comorbidities in Patients With Fibromyalgia With or Without Depression and/or Anxiety. |
|---------------------------------------------------------------|
| Clinical presentation | Depression/anxiety (318) n (%) | No depression/anxiety (788) n (%) |
| **Symptoms** | | |
| Myalgia | 211 (66.4) | 565 (71.7) |
| Sleep disorders | 205 (64.5) | 458 (58.1) |
| Chronic fatigue | 175 (55) | 361 (45.8) |
| Headache | 158 (49.7) | 365 (46.3) |
| Myasthenia | 137 (43.1) | 311 (39.5) |
| Paresthesia | 89 (28) | 211 (26.8) |
| Cognitive disorder | 60 (18.9) | 126 (16) |
| Dizziness | 59 (18.6) | 130 (16.5) |
| Gastrointestinal symptoms | 46 (14.5) | 93 (11.8) |
| Auditory symptoms | 31 (9.7) | 58 (7.4) |
| Dry eye/mouth | 16 (5) | 43 (5.5) |
| Respiratory symptoms | 9 (2.8) | 20 (2.5) |
| Skin symptoms | 6 (1.9) | 18 (2.3) |
| Urinary symptoms | 1 (0.3) | 12 (1.5) |
| **Comorbidities** | | |
| Migraine | 211 (66.4) | 565 (71.7) |
| Hypertension | 91 (28.6) | 218 (27.7) |
| Bone diseases | 57 (17.9) | 130 (16.5) |
| Hypothyroidism | 51 (16) | 138 (17.5) |
| Dyslipidemia | 29 (9.1) | 82 (10.4) |
| Autoimmune diseases | 21 (6.6) | 52 (6.6) |
| Irritable bowel syndrome | 21 (6.6) | 45 (5.7) |
| Diabetes mellitus | 20 (6.3) | 53 (6.7) |
| Neurological sequelae | 12 (3.8) | 31 (3.9) |
| Obesity | 10 (3.1) | 36 (4.6) |
| COPD | 6 (1.9) | 10 (1.3) |
| Cancer | 6 (1.9) | 22 (2.8) |
| Premenstrual syndrome | 5 (1.6) | 3 (0.4) |
| Cognitive disorder | 5 (1.6) | 22 (2.8) |
| Sleep disorder | 3 (0.9) | 12 (1.5) |
| TMJ disorder | 2 (0.6) | 7 (0.9) |
| BPAD | 1 (0.3) | 15 (1.9) |

Note. COPD = chronic obstructive pulmonary disease; TMJ = temporomandibular joint; BPAD = bipolar affective disorder;
data support the concept that sex-specific psychological factors exist in chronic pain, similar to that described in FM (Mogil, 2012).

This study reports a predominance of the middle socioeconomic level and basic education (primary and secondary) in both the groups. The low economic level proved to be an associated protective factor against depression/anxiety in patients with FM who were adjusted for the variables of sex, educational level, and clinical factors of the entity. This finding should be carefully applied as it does not reliably represent the entire population because of the large proportion of missing data and the absence of patients from high strata or high educational level in this study sample.

It has been reported in the literature that FM and mental illness affect all socioeconomic strata. However, the behaviors among different populations differ. According to Fitzcharles et al. (2014), based on the evaluation of the educational level in patients with FM, a lower economic strata was associated with greater severity of symptoms and functional impairment, regardless of the level of pain, depression, and anxiety. According to Kang et al.

### Table 3. Pharmacological and Nonpharmacological Therapies in Patients With Fibromyalgia With or Without Depression and/or Anxiety.

| Treatment                          | Depression/anxiety n (%) | No depression/anxiety n (%) |
|-----------------------------------|--------------------------|-----------------------------|
| Undergoing pharmacological treatment | 296 (93.1)              | 722 (91.6)                  |
| Complementary therapies*          | 12 (3.8)                 | 51 (6.5)                    |
| Psychological therapy             | 6 (1.9)                  | 22 (2.8)                    |
| Medication type                   |                          |                             |
| Serotonin or dual-action reuptake inhibitors | 174 (54.7)              | 408 (51.8)                  |
| Acetaminophen                     | 143 (45)                 | 313 (39.7)                  |
| Pregabalin                        | 132 (41.5)               | 299 (37.9)                  |
| Combination therapyb              | 75 (23.6)                | 146 (18.5)                  |
| Tricombination treatmentc         | 46 (14.5)                | 84 (10.7)                   |
| Opiates                           | 102 (32.1)               | 226 (28.7)                  |
| NSAIDs                            | 28 (8.8)                 | 98 (12.4)                   |
| Steroids                          | 4 (1.3)                  | 21 (2.7)                    |
| Biological                        | 4 (1.3)                  | 6 (0.8)                     |
| Tricyclic antidepressants         | 9 (2.8)                  | 40 (5.1)                    |

*Supplementary treatment according to the WHO: acupuncture, meditation, yoga, Tai-chi, among others. **Combination therapy: Single or dual serotonin reuptake inhibitors and GABAergic. ***Tricombination treatment: serotonin or dual-action reuptake inhibitors, GABAergic, and acetaminophen.

### Table 4. Associated Sociodemographic and Clinical Characteristics in Patients With Fibromyalgia With or Without Depression and/or Anxiety.

| Variable                              | PR (95% CI)       | Adjusted PR (95% CI) |
|---------------------------------------|-------------------|----------------------|
| Sex (female)                          | 0.65 [0.47, 0.91]*| 0.5 [0.28, 0.86]*    |
| Socioeconomic strata (low)            | 0.70 [0.50, 0.97]*| 0.53 [0.33, 0.70]**  |
| Educational levela                    |                  |                      |
| None                                  | 1                 | 0.70 [0.40, 1.17]     |
| Bachelor’s degree                     | 0.56 [0.33, 0.96]*| 0.99 [0.26, 1.68]     |
| Technical/technological               | 0.42 [0.32, 0.56]*| 0.99 [0.57, 1.54]     |
| Professional                          | 0.37 [0.26, 0.52]*| 0.83 [0.51, 1.39]     |
| History of premenstrual syndrome      | 2.17 [1.25, 3.74]*| 4.09 [0.95, 18.32]    |
| History of hypothyroidism             | 0.92 [0.71, 1.19]  | 0.97 [0.61, 1.5]      |
| Myalgias                              | 0.83 [0.69, 1.01]  | 0.87 [0.62, 1.1]      |
| Chronic fatigue                       | 1.30 [1.07, 1.56]**| 1.11 [0.99, 1.73]     |
| Sleep disorders                       | 1.21 [0.99, 1.47]  | 1.11 [1, 1]           |
| Cognitive disorder                    | 1.15 [0.91, 1.45]  | 0.97 [0.66, 1.39]     |

*PR = prevalence ratio; CI = confidence interval. Each category was analyzed separately.

Note. NSAIDs = nonsteroidal anti-inflammatory drugs; WHO = World Health Organization.

**p < .05. ***p ≤ .001.
(2016), belonging to a low socioeconomic strata was associated with a higher dysfunction, disease severity, and lower quality of life.

The differences in the behavior of the socioeconomic and educational factors of the Colombian population compared with that in other populations with FM should be carefully interpreted, and the indirect relationship between psychosocial and behavioral factors and the self-perceived health status should be considered (Moor et al., 2017; Pathirana & Jackson, 2018).

We would like to highlight the pharmacological and nonpharmacological therapy provided to the present study population. The statistical analyses did not present any significant association; however, the low percentage of psychological management is striking, considering that it is a multicausal pathology in which the mental component plays a primary role in the quality of life and prognosis of the population. FM is a complex disorder, which requires a multidisciplinary management. Currently, besides providing the pharmacological therapy, emphasis is placed on educating patients regarding self-care, cognitive-behavioral therapy, and exercise (Duque & Fricchione, 2019).

Despite the contributions made by neurologists and mental health specialists regarding an interdisciplinary management of FM, myths and questions related to the etiology of this pathology remain, which hinders the provision of a comprehensive approach for the treatment of patients with FM. A trend toward a biopsychosocial model of FM highlights the neurological underpinnings of this condition and attributes the importance of psychosocial factors in the predisposition, triggering, and chronication of FM symptoms. Currently, emphasis is placed on the accurate detection of psychopathologies associated with FM, timely referral to a mental health specialist, and the promotion of nonpharmacological therapies, which provide these patients with better clinical results and quality of life (Häuser & Fitzcharles, 2018).

One of the limitations of this research is the cross-sectional design of the study, which does not allow the establishment of causal relationships from the data collected. Other limitations are the low number of men in the study population and the missing data in sociodemographic variables. For these reasons, the inclusion of more men with FM and a prospective cohort design is recommended for future studies to evaluate whether the sex-based differences persist over time, thus providing substantial evidence to the results described in this study.

In conclusion, FM is more frequent in women, although depression and anxiety were more prevalent among men with this disease in a Colombian population during the period of 2010–2016. The authors of this research consider that the study of FM in men has been neglected, particularly in relation to the deleterious effects that can impact the mental health of this population. In addition, men with FM should be considered a risk population for concomitant psychiatric pathologies. This kind of studies provides guidance to clinicians for developing individualized therapies based on sex-related differences.

Acknowledgments

We would like to thank the entire staff of the facilitating institution and the three students who assisted in data collection and could not continue until the end of the study due to work commitments in the Mandatory Social Service.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The Universidad Cooperativa de Colombia financially supported this study through the Research Fund under project code INV3038.

ORCID iD

Marcela Henao-Pérez https://orcid.org/0000-0002-7337-2871

References

Aggarwal, V., MeBeth, J., Zakrzeswka, J., Lunt, M., & Macfarlane, G. (2006). The epidemiology of chronic syndromes that are frequently unexplained: Do they have common associated factors? International Journal of Epidemiology, 35(2), 468–476. https://doi.org/10.1093/ije/dyi265

American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: Author.

Arout, C., Sofuoglu, M., Bastian, L., & Rosenheck, R. (2018). Gender differences in the prevalence of fibromyalgia and in concomitant medical and psychiatric disorders: A National Veterans Health Administration Study. Journal of Women’s Health, 27(8), 1035–1044. https://doi.org/10.1089/jwh.2017.6622

Buskila, D., Neumann, L., Alhoashele, A., & Abu-Shakra, M. (2000). Fibromyalgia syndrome in men. Seminars in Arthritis and Rheumatism, 29(1), 47–51. https://doi.org/10.1053/sarh.2000.8363

Conversano, C., Ciaccchini, R., Orru, G., Bazzichhi, M., Gemignani, A., & Miniati, M. (2020). Gender differences on psychological factors in fibromyalgia: A systematic review on male’s experience. Clinical and Experimental Rheumatology, 39(3), 174–185. https://doi.org/10.5556/clinexpheumatol/73g6np
Al-Andalus project. *Pain Research and Management*, 2016, Article 5135176. https://doi.org/http://dx.doi.org/10.1155/2016/5135176

Shimamoto, A., & Rappeneau, V. (2017). Sex-dependent mental illnesses and mitochondria. *Schizophrenia Research*, 187, 38–46. https://doi.org/10.1016/j.schres.2017.02.025

Steel, Z., Marnane, C., Iranpour, C., Chey, T., Jackson, J., Patel, V., & Silove, D. (2014). The global prevalence of common mental disorders: A systematic review and meta-analysis 1980-2013. *International Journal of Epidemiology*, 43(2), 476–493. https://doi.org/10.1093/ije/dyu038

Thieme, K., Turk, D. C., & Flor, H. (2004). Comorbid depression and anxiety in fibromyalgia syndrome: Relationship to somatic and psychosocial variables. *Psychosomatic Medicine*, 66(6), 837–844. https://doi.org/10.1097/01.psy.0000146329.63158.40

Vincent, A., Lahr, B., Wolfe, F., Clauw, D., Whipple, M., Oh, T., . . . St Sauver, J. (2013). Prevalence of fibromyalgia: A population-based study in Olmsted County, Minnesota, utilizing the Rochester Epidemiology Project. *Arthritis Care & Research*, 65(5), 786–792. https://doi.org/10.1002/acr.21896

Wan, B., Gebauer, S., Salas, J., Jacobs, C., Breeden, M., & Scherrer, J. (2019). Gender-stratified prevalence of psychiatric and pain diagnoses in a primary care patient sample with fibromyalgia. *Pain Medicine*, 20(11), 2129–2133. https://doi.org/10.1093/pm/pnz084

Yunus, M., Ahles, T., Aldag, J., & Masi, A. (1991). Relationship of clinical features with psychological status in primary fibromyalgia. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, 34(1), 15–21. https://doi.org/10.1002/art.1780340104

Yunus, M., Inanici, F., Aldag, J., & Mangold, R. (2000). Fibromyalgia in men: Comparison of clinical features with women. *The Journal of Rheumatology*, 27(2), 485–490.