Fibromyalgia: gender differences and sleep-disordered breathing

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Running title: Gender differences in fibromyalgia

Abstract

Objective. The prevalence of fibromyalgia (FM) is much lower in men than in women. Therefore, current knowledge about this chronic pain syndrome emerged mainly from research on women. The aim of the present study was to compare clinical symptoms and sleep parameters between women and men FM patients.

Methods. Forty FM patients (18 men and 22 women) aged 48.00±8.45 years were evaluated with questionnaires on pain, sleep, fatigue, depression, anxiety and functional impact, and polysomnography (PSG).

Results. 61% of men FM patients had an apnea-hypopnea index (AHI) greater than 15, compared to 31.8% of women, and desaturation index (DI) above five was twice more prevalent in men than in women. In addition, men patients had lower sleep quality (16.05±2.92*% vs.* 13.08±3.88*%*; p= 0.01) and slow wave sleep (SWS) (stage 3 duration: 9.02±7.84*% vs.* 14.44±7.32*%*; p= 0.03) than women. No differences were found between the two groups in level of pain, emotional distress, or daily functioning. However, pain in men, fatigue in women, and functional impact in both sexes seemed to be related to worse sleep quality. Also in women, alterations in total sleep time (TST) and rapid eye movement (REM) sleep features appeared to be related to emotional status.

Conclusions. Alterations in sleep respiratory patterns were more highly prevalent in men than in women FM patients. More so in men FM patients, the alterations in sleep patterns, non-refreshing sleep, and other FM-related symptoms observed in this population might be part of a primary sleep-disordered breathing.

Keywords: fibromyalgia, gender differences, polysomnography, sleep-disordered breathing, psychological measures

Introduction

The progress made in the research on fibromyalgia (FM) and the use of biopsychosocial explanatory models have shown important interrelations between pain severity, fatigue, sleep disorders, genetic, immunologic and psychosocial factors in FM syndrome (1,2). Nonetheless, greater knowledge is required to establish a unified hypothesis regarding the pathogenesis of FM.

Several studies have found an increased prevalence of FM among women compared to men in community samples from different countries (3-5). With regard to the Spanish population, a national survey showed that 2.4% of the general population over 20 years of age had a diagnosis of FM. Prevalence rates by gender were 4.2% and 0.2% for men and women respectively (6).

Since there is a lower prevalence of FM in men than in women among the general population, research in this domain has been basically developed on FM women samples; studies of this syndrome in men are scarce. Consequently, few studies have analyzed gender differences in the clinical picture of FM patients. Regarding pain assessment, a majority of studies have revealed that women show a lower sensibility threshold to pain than men (4,7), and some studies have found significant gender differences regarding tender point count (8-10). On the other hand, contradictory results have been reported regarding other somatic symptoms, overall FM impact, and physical impairment. In a North American population (469 FM women and 67 FM men), Yunus *et al.* concluded that men had less fatigue and generalized pain perception than women (8), and no significant gender differences were found in functional impact between the two groups. Nevertheless, in an Israeli sample of 40 FM men and 40 FM women, Buskila *et al*. (11) found that men reported more severe symptoms and decreased physical function than women. Similarly, Hooten, Townsend, and Decker (12) reported lower scores in physical and social functioning for 33 FM men compared to 33 FM women, before and after undergoing multidisciplinary pain rehabilitation. In keeping with these findings, two Spanish studies have reported a worse perception of health, and a higher overall impact of FM in men compared to FM women (13, 14). While some studies on gender differences in psychological status in FM have reported no difference in psychopathology and emotional distress (7, 9, 10), four studies have informed of a linkage between depression, gender and FM (11, 13, 15, 16). However, in the latter studies, divergent findings were obtained. Vishne *et al*. (15) have informed of higher rates of FM among women with major depression, as compared to men. In another study among a German population, Lange *et al*. (16) reported that women with FM showed a worse depression status than men. Conversely, Buskila *et al*. (11) found higher levels of depression in FM men, and Ruiz Pérez and colleagues (13) reported that, in a Spanish FM population, men had a higher percentage of psychiatric history and current mental illness.

Although the majority of FM patients have poor sleep quality, and insomnia is a common problem among this population (17, 18), very few studies have analyzed these alterations and their associations with other clinical symptoms. Accumulating evidence supports the notion that sleep disturbances have an important influence on musculoskeletal pain (19, 20), fatigue (21), daily functioning, and psychological status (22, 23). The use of objective measures such as polysomnography (PSG) in FM have revealed significant sleep physiology alterations in continuity, sleep architecture, and sleep microarchitecture associated with self-reported sleep problems and its clinical picture in this population. Moreover, a considerable prevalence of associated sleep disorders in FM patients has been detected, such as sleep-disordered breathing (SDB), restless leg syndrome (RLS), and periodic leg movements (PLM) (for review, see (24)).

Gender differences in FM sleep features remain practically unknown. With respect to self-reported sleep quality, in a sample of 80 FM patients, Buskila *et al*. (11) found that sleep problems (assessed by a visual analogue scale (VAS)) had stronger relationships with quality of life in FM men than women. Nevertheless, no significant differences were found in two studies that used validated instruments for measuring self-reported sleep quality (7, 15). Similarly, to date, gender differences in objective measures obtained by electrophysiological techniques such as PSG have not been thoroughly examined in FM patients. Only one study has examined gender differences in the prevalence of SDB in FM patients, reporting a high prevalence of sleep apnea syndrome (SAS) in men comparing with women, which suggests that SAS could be a frequent cause of FM in men (25).

As stated above, clinical and psychosocial gender differences in FM remain controversial, with divergent findings. Practically no in-depth analysis of sleep features, comparing both genders, has been conducted. The aim of this cross-sectional study was to analyse whether FM manifestations (pain, fatigue, functional impact, emotional status, perceived sleep quality, and main objective sleep parameters) differed as a function of sex.

Patients and methods

Subjects

Eighteen men, mean age 48.89 ± 8.54, and twenty-two women, 47.27 ± 8.48, with FM participated in the study. The patients, recruited from the Rheumatology Service and Pain Unit of the Hospital Universitario Virgen de las Nieves, and from AGRAFIM —an FM association in Granada (Spain)— were diagnosed with FM using widely accepted and published criteria (17). Participants were asked to complete a 1–1.5 h semi-structured interview. The interview focused on sociodemographic characteristics, onset and time course of symptoms, history of present illness, past medical history, medications, work, and personal and psychological status. Body mass index

(BMI) was calculated for each participant. Exclusion criteria were as follows: (1) pregnancy; (2) having a medical history of significant head injury or neurological disorder; (3) having major concomitant medical conditions (e.g., inflammatory rheumatic diseases, uncontrolled endocrine disorders, etc.); (4) having major depressive disorder with suicide ideation or other major Axis I diagnoses (APA, 2000) (26); (5) having a severe hypnotic dependence; (6) tobacco use in excess of 10 cigarettes per day and unwillingness to discontinue this consumption the previous day to the PSG.

After the interview, participants were given a set of questionnaires to be completed at home, with detailed explanations about how to complete them. A psychologist was available by telephone to answer any doubts about the instruments. FM participants who fulfilled inclusion criteria and had completed the aforementioned assessment were enrolled into a domiciliary PSG.

This study was reviewed and approved by the Ethics Committee of the University of Granada (Spain), and all participants gave their written informed consent.

Subjective measures

McGill Pain Questionnaire (MPQ) (27)

This questionnaire assesses several dimensions of pain experience using 15 (sensory and affective) verbal pain descriptors, a current pain index, and a VAS to evaluate pain intensity during the previous week (ranging from 1 = no pain to 10 = extreme pain). Several studies have reported the validity of the Spanish version of the MPQ .The internal consistency of the MPQ, as reported by Masedo and Esteve, was 0.74 (28).

Multidimensional Fatigue Inventory (MFI) (29, 30)

This inventory explores aspects such as physical and mental fatigue, motivation, and reduced activity, using 20 items. In this study, a general score for fatigue was used. The internal consistency of the adapted version of this instrument in a Spanish FM population has shown an alpha coefficient of 0.83 (7).

Fibromyalgia Impact Questionnaire (FIQ) (31)

The FIQ is composed of 10 items. The first item assesses functional capacity for daily living (ranging from 0 to 3). Items 2 and 3 ask patients to mark the number of days they felt well/unable to work. Items 4 through 10 are scales marked on 10 levels, which rate work difficulty, pain, fatigue, morning tiredness, stiffness, anxiety, and depression. The internal consistency of the FIQ showed an alpha coefficient of 0.82 in the Spanish version of Rivera and González (32).

Hospital Anxiety and Depression Scale (HADS) (33)

This scale assesses anxiety and depression symptoms in non-psychiatric hospital contexts. The HADS includes 14 items (grouped into anxiety and depression dimensions) that are assessed on a scale from 0 to 3. This instrument has shown good internal consistency (0.84 for the Depression subscale, and 0.85 for the Anxiety scale) and external validity, with adequate sensitivity and specificity in a Spanish population (34).

Pittsburgh Sleep Quality Index (PSQI) (35)

This instrument includes 19 items that explore seven dimensions of sleep quality: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The PSQI has acceptable internal consistency (ranging between 0.67 and 0.81), sensitivity, and specificity (36).

Nocturnal polysomnography study

All participants underwent a full-night polysomnography study at home, which was recorded and digitized by SomnoScreen PSG-Tele System (SomnoMedics). Gold electrodes were placed according to the International 10-20 System for recording the electroencephalogram (EEG). Polysomnographic signals included the following EEG channels: F3-A2, F4-A1, C3-A2, C4-A1, O1-A2, O2-A1 that were sampled at 128 *Hz* and online filtered analogically (0.2-35 *Hz)*; 2 electrooculogram channels; chin and bilateral anterior tibialis surface electromyography; 2 electrocardiographic leads; nasal and oral airflow (nasal pressure and thermistor); respiratory effort of thorax and abdomen (inductance plethysmography), body position; and finger oximetry. Two trained researchers applied the portable device, and sensors used for PSG recording.
Sleep stages were visually scored off-line with the DOMINO-Software (DOMINO 2.2.0. supplied with the SomnoScreen PSG-Tele) in a blind manner, and according to Rechtschaffen and Kales (37) criteria based on 30 s epoch for hypnograms. Following the ASDA 92 criteria (38), cortical arousals were defined as bursts of waking cortical activity lasting more than 3 s. Scoring of respiratory and movement events was based on the American Academy of Sleep Medicine (AASM) manual for scoring sleep (2007) (39). The VIII.4.B scoring rule was used for the definition of hypopnea in this study.

Statistical analysis

The SPSS-20.0 statistical package (SPSS, Inc., Chicago, IL, USA) was used to perform analyses. The main explanatory variable was group (FM men *vs.* women). Data were summarized as mean (standard deviation), and percentages. Differences in sociodemographic or clinical characteristics were compared between men and women with t tests or Chi-square statistics. Likewise, paired t-tests were used to compare pain, fatigue, daily functioning, emotional status, perceived sleep quality, sleep architecture variables, total sleep time (TST), sleep efficiency (SE), respiratory parameters, and movement events in PSG. To determine the homogeneity of variance, the Levene's test was applied. Relations between variables were examined using Pearson's correlations.

Results

Gender differences in sociodemographic and clinical characteristics

Table I summarizes the sociodemographic and clinical characteristics of patients included in the study. The results of the Pearson Chi-square test showed that there were only two significant differences between men and women: marital status, and drug intake. 95 *%* of the women, and 55.6 *%* of the men were married (x^2 = 7.08; p<0.05). Although men had a higher percentage of overall drug intake than women, there were no significant differences in anti-depressants, anti-inflammatory, or hypnotic drug therapy; conversely, we found a significant lower percentage of analgesic intake (x^2 = 12.48; p<0.05) in FM men compared to women. Regarding tobacco consumption, only two men and three women were occasional smokers (3-4 cigarettes per week usually at the weekend). The remaining parameters (age, body mass index (BMI), duration symptoms, duration since diagnosis, educational level, and employment status) were similar in both groups (all p>0.05).

-Please, insert Table I about here-

Gender differences in sleep, pain, fatigue, psychological status, and daily functioning

Table II lists measures of pain, fatigue, sleep quality, anxiety, depression, and daily functioning. Except for a worse sleep quality in men, measured by PSQI (t= 2.68; p<0.05), none of these variables were found to be significantly different between FM men and women (all p>0.05).

-Please, insert Table II about here-

Gender differences in sleep variables

There was no difference between groups in TST, SE, percentage of stage 2, 3-4 and rapid eye movement (REM) sleep, slow wave sleep latency (SWSL), and REM sleep latency (REML) (see Table III). Regarding slow wave sleep (SWS), a separate analysis of stage 3 and stage 4 showed that men had a lower percentage in stage 3 compared to women (mean ± SD, 9.02 ± 7.84 *vs.* 14.44 ± 7.32; p= 0.03).

-Please, insert Table III about here-

Men patients had significantly greater alterations in respiratory and oxymetry variables than women (see Figure 1). FM men had higher AHI (27.25 ± 24.77 *vs.* 12.80 ± 9.75; p<0.05) and oxygen desaturation (20.11 ± 23.00 *vs.* 7.25 ± 8.62; p<0.05). Thus, 61% of men FM patients had an apnea-hypopnea index (AHI) greater than 15, compared to 31.8% of women; a desaturation index (DI) above five was twice more prevalent in men. Men also showed more transient arousals associated with respiratory events compared to women (t= 2.33; p<0.05).

-Please, insert Figure 1 about here-

In keeping with previous studies in a general population, and in patients diagnosed with obstructive sleep apnea (OSA) (40), we found significant correlations between age, BMI, and respiratory variables in the women's group. AHI and DI seemed to be positively associated with

BMI (r= 0.649 and r= 0.638; p<0.05, respectively) and age (r= 0.457 and r= 0.501; p<0.05, respectively). Despite the fact that men presented higher prevalence and levels of severity in respiratory parameters than women (see Figure 1), the aforementioned correlations were not significant in men (p>0.05).

Independent bivariate analyses were performed to evaluate the associations between respiratory and sleep parameters in each group (women *vs.* men), as shown in Table IV. As expected, significant associations were found between sleep stage index (SSI) and general arousability in men (r= 0.517; p<0.05), and women (r= 0.548; p<0.01). However, desaturation and respiratory arousal indexes showed positive and significant correlations with SSI (r= 0.595 and r= 0.590; p<0.01, respectively), only in men. In the same way, alterations of sleep architecture could be affected by SDB in men, a higher AHI was associated with less duration (r= -0.514; p<0.05), and longer onset (r= 0.520; p<0.05) of REM sleep. Furthermore, this last parameter was associated with a higher number of desaturations during sleep in FM men (r= 0.661; p<0.01). As shown in Table IV, the respiratory arousal index (RAI) correlated positively with sleep stage 2 (r= 0.487; p<0.05), and negatively with SWS and REM duration in men (r= -0.476; p<0.05 and r= -0.609; p<0.01, respectively). In contrast, REM sleep onset showed a significant and positive relationship with regard to this parameter in men and women (r= 0.511; p<0.05 and r= 0.631; p<0.01, respectively). In women, leg movement index (LMI) correlated positively with stage 2 duration (r= 0.458; p<0.05), REML (r= 0.465; p<0.05) and SWSL (r= 0.640; p<0.01), and negatively with duration of SWS (r= -0.424; p<0.05). Also in women, higher scores on the periodic leg movement index (PLMI) was associated with longer stage 2 duration (r= 0.460; p<0.05), and delayed REM sleep onset (r= 0.498; p<0.05). In FM men, leg movement events were significantly correlated with greater REML (*r*= 0.478; *p*<0.05) such as FM women. In addition, sleep continuity measured by SSI was significantly and positively correlated with LMI (*r*= 0.482; *p*<0.05).

-Please, insert Table IV about here-

In order to assess how sleep patterns might be related to pain, fatigue, psychological status, and daily functioning, we performed Pearson's bivariate correlations in each gender group, as shown in Table V. In the women's group, fatigue and anxiety were negatively associated with the duration of REM stage (*r*= -0.466 and *r*= -0.424; *p*<0.05, respectively), and duration of stage 2 correlated positively with FIQ scores (*r*= 0.439; *p*<0.05). Furthermore, emotional distress was higher when women presented a lower duration in TST (anxiety: *r*= -0.517; *p*< 0.05, and depression: *r*= -0.556; *p*<0.01). In contrast, men had higher pain perception when the duration of stage 2 was greater (*r*= 0.487; *p*<0.05), and SWS was shorter (*r*= 0.494; p<0.05); worse daily functioning was associated with shortened stage 3 (*r*= -0.567; *p*<0.05).

-Please, insert Table V about here-

Discussion

In the present study, self-reported measures of pain, fatigue, daily functioning, psychological status, sleep quality, daily functioning, and objective sleep recordings with PSG, were used in to explore gender differences in clinical and psychosocial features of subjects with FM.

Regarding sociodemographic aspects, only marital status was significantly different between men, and women. A higher percentage of women were married, whereas a significant percentage of men were single. Nonetheless, there are studies that have reported no significant gender differences in the marital status of FM samples (10-13); one study conducted in a Spanish FM population obtained the same findings regarding this sociodemographic variable, which is congruent with our results (7). Further research should explore the impact of FM syndrome on marital status, given that it is a critical factor of health-related quality of life in any population (41).

Although we did not find gender differences in self-reported measures of pain in our sample, the majority of comparative studies on pain in FM men and women, assessing tenderness and pain threshold using objective measures such dolorimeter or algometer devices, showed that women reported greater tenderness than men, and presented lower thresholds to pain (4, 7, 11). The findings from previous studies, and the higher level of analgesic intake in women compared to men in our study sample, suggest the relevance of pain assessment by algometer or dolorimeter.

Similarly, we did not observe gender differences between FM males and females regarding fatigue in our sample. These results were in line with studies conducted in North American (9) and in a Spanish (7, 13) FM population.

FM patients in the present study showed no significant gender differences regarding psychological status, which concurs with other recent studies (7, 9, 10). However, contradictory results have been reported concerning psychological status in FM women and men. Thus, two studies carried out in Israeli (11) and Spanish (13) populations reported greater psychopathology in men. However, it should be mentioned that the aforementioned studies used Likert scales, and telephone interviews, respectively, to assess affective distress, rather than the standardized instruments used in the present study. A further two studies reported worse emotional status in FM women than in FM men (15, 16), and the same trend was reported for other chronic pain problems such as cancer, or osteoarthritis (for review, see Filligim *et al*. (42)). It may be that FM men —unlike men suffering from other chronic conditions— experience greater affective distress because of the stigma attached to their having a “woman's disease”, and accordingly, the psychological status of men is more similar to that of women; accordingly, further research is necessary in order to clarify this aspect.

Similarly, regarding functional impact, no significant gender differences were found in FM impact measured by FIQ. Buskila was unable to find gender differences in functional impact using this instrument (11) in Israeli FM patients. In contrast, in a study carried out in a Spanish FM population (14), overall FM impact was significantly higher in men when measured using an FIQ-total score.

In light of these controversial findings in respect of psychological status and functional impact, future research should perhaps contemplate studies on larger samples, and examine the influence of sociocultural factors in FM clinical and psychological manifestations.

In reference to gender differences in sleep quality, our data analysis revealed that men showed higher levels of sleep complaints, which is in keeping with the results reported by Buskila *et al*. (11), *i.e.* a higher percentage of sleep complaints among forty FM men, age-matched with 40 FM women. The high prevalence of SDB in the FM men in the present study could be contributing to this level of poor subjective quality of sleep in men. Several studies have reported worse perceived sleep quality in women than men, in the case of a general population (43), although objective measures of sleep patterns have shown that women sleep objectively better across age, and that, in the case of younger women, sleep is more resistant to external stressors (44, 45). In line with these last results, we found a longer duration of stage 3 in the FM women group, although sleep variables such as TST, and sleep efficiency, seemed to be similarly altered in both groups.

The association between general arousability in sleep parameters indicated that women's sleep was similarly fragmented, and affected by disruptive arousability during REM and SWS. It is noteworthy that despite the fact that women participants in this study did not meet the diagnosis criteria for PLM or RLS, the occurrence of these disorders in FM (46, 47) might partly explain their deteriorated sleep architecture and continuity due to leg movement events during sleep. Additionally, bearing in mind that a considerable number of the women in our sample had altered respiratory parameters during sleep, the significant correlations in related leg movement indexes might be explained by previous findings in clinical populations with suspected SDB, according to which, women complained significantly more of restless legs, and scored higher on the PLM (48). Although we found no gender differences in pain, fatigue, emotional distress, or daily functioning, these variables presented different associations with sleep parameters, depending on gender. Thus, while superficial sleep seemed to increase pain in men, sleep architecture changes were not related with pain perception in women; in the case of the latter, these findings are divergent from previous studies on FM, the majority of which have reported higher levels of pain associated with non-restorative sleep (24). The use of an algometer, or dolorimeter for pain assessment might have elucidated this aspect of our study more clearly. On the other hand, fatigue seemed to be affected by decreased REM sleep solely in the case of women, as has been previously observed in FM patients (mainly women) compared to healthy controls (49). We found that, in our FM women sample, emotional status seemed to be influenced by sleep alterations; thus, a shorter TST was associated with higher scores in depression, and shorter REM sleep duration was associated with more anxiety. These latter associations also coincide with previous findings, e.g. Anch *et al*. (49) described an association between psychological distress and altered sleep physiology. Moreover, self-reported measures in FM patients indicate a strong link between perceived sleep quality and mood, in studies basically conducted on FM women samples (21-23, 50).

Given that the mean age of women in this study was 47.27, it should also be taken into consideration that a significant number of the women in our study were in a perimenopausal stage; accordingly, gender differences in our sample could have been influenced by the hormonal status of FM women (51). Furthermore, results obtained from bivariate analyses seemed to be in line with results reported by Divakaran *et al*. (52), who linked mood symptoms with poor sleep in women among the general population, and with gonadal steroid levels during the perimenopausal period.

With regard to functional impact, both FM men and women showed similarly significant associations between sleep architecture and social functioning, thus indicating that longer durations of stage 2 in women, and shorter durations of stage 3 in men, seemed to be related with worse functional impact. In line with these findings, in a sample of 94 women and 7 men suffering from FM, Theadom *et al*. (23) reported that perceived poor sleep quality was predictive of pain, fatigue, and impaired social functioning. Furthermore, Miró *et al*. (20) suggested that sleep quality, measured by PSQI, could be a mediator in the relationship between pain and social functioning in FM women patients.

One of the main findings of this study was the presence of extremely high levels in parameters relating to SDB in men. An AHI greater than 15 was found in over 50*%* of men, compared to 32*%* of women. Similarly, desaturation and respiratory arousal indexes were also very high in FM men. Taking into account that the occurrence of SDB in a general population, regardless of symptoms, is between 6–24% (53), the prevalence of this clinical parameter in our study seemed to be extremely high in FM men. Although FM women showed lower levels on respiratory parameters than men, their scoring in variables such as AHI and DI was also higher as compared to women in the general population. By way of example, Duran *et al*. (2001) (54) reported a prevalence of 7 % of AHI above 15 in women in a large sample comprised of Spanish adults.

Although very few studies have analysed respiratory parameters during sleep in FM patients, some studies have reported significant alterations of SDB in this clinical population *e.g.* in 1999, Sergi *et al*. (55), in a sample of 16 FM women and one man, found that 15 of the 17 FM patients presented a typical periodic breathing pattern, associated with relative hypocapnia, that could explain short apneas/hypopneas and slight sleep in these patients. These findings concurred with subsequent studies that showed how sleepiness was associated with this typical breathing pattern (56) and upper-airway resistance syndrome (UARS) (57) in an FM population. All of the aforementioned studies relating to SDB were conducted mainly on FM women. However, in 1996, May *et al*. (25) found a high prevalence of OSA in FM men patients, and concluded that this respiratory illness did not seem to be associated with FM women.

As has been observed in populations affected by SDB (58), we expected significant associations between respiratory events, and sleep quality measured by different PSG parameters. Thus, we found a significant negative association between the percentage of REM and AHI in FM men. Sleep continuity, measured by SSI, was higher when men had a higher number of oxygen desaturations. Moreover, a bivariate analysis revealed that men had fragmented sleep, and worse sleep architecture due to respiratory events. In contrast, we found practically no significant associations between respiratory and sleep variables in the women analyzed in our study. Only sleep REM latency was found to be greater when they had more respiratory arousals. Despite 10 of the 22 women in our study presenting an AHI higher than 10, and nine of them showing a DI above five, compared to the men, their quality of sleep measured by PSG seemed not to be affected by respiratory alterations. This lack of association between conventional sleep respiratory parameters, and sleep patterns in FM women in our study, could be explained by the fact that, in general, women scored lower on sleep parameters such us AHI, and DI. In addition, previous studies have reported that, in general population and in FM, women with SDB are more likely to have partial obstructions, and the duration of apneic events is longer in men (59).

Bivariate analyses showed positive and significant associations between respiratory parameters, age, and BMI in women. In contrast, although men presented higher prevalence and severity in respiratory abnormalities in the present study than women, and despite overweight being considered a risk factor for SDB in general population (40), we did not find significant relationships between BMI and respiratory parameters in FM men.

These findings on SDB in our study suggest that a considerable number of FM patients could have been misdiagnosed as suffering from SDB. It should be noted that FM patients had not been diagnosed of this type of medical respiratory problems by a physician before to participate in the present study. It is noteworthy that the latest instrument for diagnosing FM developed by the American College of Rheumatology, for example, assesses a myriad of functional and physical symptoms that, in some cases, could be the epiphenomenon aspect (60) of primary sleep disorders such as OSA or UARS (59). Unfortunately, respiratory screening based on clinical history, physical examination, polygraphy, or PSG is not yet routinely performed in FM patients.

Our study has several limitations. First, due to the cross-sectional nature of the study, it is impossible to determine whether the relationships explored in bivariate analyses are causal. Second, the sample size was low in terms of generalizing our findings. Furthermore, this latter did not allow us to stratify subjects by age, a variable that shows sex differences in its interaction with sleep and associated SDB. In addition, the lack of control of hormonal status in women could be a confounding factor in our conclusions due to its influence on sleep and women's higher risk of having SDB in the menopausal transition. (51-53). Third, pain symptoms were only evaluated using a self-report questionnaire; assessing pain with a pressure algometer would have provided an objective measure, in order to validate pain self-reports and compare with previous studies in FM population that have observed gender differences using algometer or dolorimeter devices. Fourth, although we excluded participants with a severe dependence on psychotropic medications, the use of multiple drugs was an added complication in the study of polysomnography variables due to changes in sleep quality, and worsening of sleep disorders such as SDB and related leg movement disorders (61). However, although this might be considered a methodological limitation, it makes our study more representative of the general clinical population with FM.

In conclusion, abnormalities in sleep respiratory patterns were significantly more frequent in men FM patients than in women FM patients. Regarding gender-related differences in the rest of the variables studied, only sleep quality, explored by self-reported and objective sleep measures, was better in women. Nevertheless, significant and different associations with sleep parameters were found depending by gender. Thus, pain in men, fatigue in women, and daily functioning in both groups, seemed to be affected by a worse sleep quality assessed by PSG. Emotional status also appeared to be affected by reduced TST and REM sleep in women.

The high prevalence of SDB, and its significant association with the clinical picture of FM, suggest that maybe there is an important link between these disorders and the physiopathological mechanisms of FM.

Respiratory screening based on clinical history, physical examination, and polygraphy or PSG should be performed in FM patients in order to adequately target patients' sleep problems and their clinical consequences.

Further research is necessary in the future to explore how treatment of SDB could improve the clinical picture, psychological status, and quality of life in FM patients.

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Table I. Sociodemographic and clinical features in FM patients.

Variable	Total (n=40)	Men (n=18)	Women (n=22)	*p*-value
	M±SD	M±SD	M±SD	
Age	48.00±8.45	48.89±8.54	47.27±8.48	0.554
Body mass index (kg/m²)	26.46±4.17	26.63±2.96	26.34±5.02	0.836
Duration since diagnosis (years)	3.81±3.05	4.18±2.58	3.46±3.46	0.256
Educational level (%)				0.159
No studies	5.0	5.6	4.5	
Basic education	30.0	11.1	45.5	
Compulsory Secondary	5.0	11.1	0	
Higher Secondary	10.0	11.1	9.1	
Vocational Training	22.5	22.2	22.7	
University	27.5	38.9	18.2	
Employment status (%)				0.330
Active	48.7	44.4	52.4	
Retired	15.4	22.2	9.5	
Unemployed	15.4	5.6	23.8	
Temporary disability	10.3	16.7	4.8	
Permanent disability	10.3	11.1	9.5	
Marital status (%)				0.011
Single	20.0	38.9	4.5	
Married	77.5	55.6	95.5	
Widowed	2.5	5.6	0	
Drug therapy (%)				
Anti-depressants	57.5	61.1	54.5	0.676
Anti-inflammatory drugs	57.5	66.7	50.0	0.289
Analgesics	47.5	16.7	72.7	0.000
Hypnotics	40.0	44.4	36.4	0.604

p-value: t-Student and Chi-square comparisons (FM men group *vs.* FM women group).

Table II. Gender comparison of pain, fatigue, sleep, psychological status and daily functioning in FM patients.

	Total (n=40)	Men (n=18)	Women (n=22)	
	M±SD	M±SD	M±SD	*p*- value
MPQ-Current pain	2.88±1.17	2.78±0.88	3.00±1.40	0.570
MPQ-pain in past week	7.45±1.52	7.67±1.49	7.27±1.58	0.438
MPQ-Sensorial	14.49±5.85	14.67±6.52	14.32±5.34	0.862
MPQ-Affective	5.59±3.86	6.50±4.72	4.81±2.84	0.196
MFI20-Global	4.90±2.09	5.28±2.98	4.59±0.54	0.317
PSQI	14.42±3.75	16.05±2.92	13.08±3.88	0.011
HADS-Anxiety	10.12±4.92	10.21±5.19	10.04±4.82	0.912
HADS-Depression	9.80±4.37	9.50±4.20	10.04±4.60	0.701
FIQ	58.17±15.63	58.04±19.63	58.27±11.93	0.964

FIQ: Fibromyalgia Impact Questionnaire; HADS: Hospital Anxiety and Depression Scale; MFI: Multidimensional Fatigue Inventory; MPQ: McGill Pain Questionnaire; PSQI: Pittsburgh Sleep Quality Index; *p*-value: FM men *vs.* FM women t-Student comparison.

Table III. Gender comparison of polysomnographic variables in FM patients.

	Total (n=40)	Men (n=18)	Women (n=22)	
Sleep variables	M±SD	M±SD	M±SD	*p*-value
Total sleep (min)	397.22±56.17	392.31±51.65	401.22±60.50	0.624
Sleep efficiency (%)	80.97±6.77	79.70 ±7.34	82.02±6.27	0.285
Stage shift index (n/h)	11.21±6.45	13.03±8.16	9.73±4.28	0.132
% Stage 1	5.83±3.11	5.56±3.36	6.07±2.96	0.624
% Stage 2	46.07±11.40	47.52±13.53	44.86±9.49	0.472
% Stage 3	12.00±7.93	9.02±7.84	14.44±7.32	0.030
% Stage 4	2.71±4.25	3.83±5.32	1.80±2.95	0.137
% Stages 3 and 4	14.71±8.75	12.85±9.00	16.25±8.42	0.227
% REM	14.35±4.83	13.74±4.67	14.83±5.01	0.483
REM latency (min)	143.20±67.98	150.60±84.66	137.15±51.91	0.541
Deep sleep latency (min)	93.82±96.59	99.10 ±109.68	89.50±86.88	0.759

%: percentage of the different sleep stages as a fraction of total time in bed; p-value: FM men *vs.* FM women t-Student comparison.

Table IV. Bivariate correlations among sleep variables and polysomnographic events in both groups.

PSG events	Sex	SSI	TST	SE	S1	S2	S3	S4	S3/4	REM	REML	SWSL
AHI	M	0.463	0.069	0.026	-0.022	0.449	-0.253	-0.269	-0.379	-0.514*	0.520*	0.259
	W	0.258	0.369	0.129	0.128	0.166	-0.226	0.189	-0.130	-0.009	0.265	0.204
DI	M	0.595**	0.122	-0.101	0.122	0.231	-0.184	-0.178	-0.265	-0.404	0.661**	0.145
	W	0.386	0.347	0.141	0.188	0.167	-0.375	0.327	-0.211	0.104	0.127	0.162
AI	M	0.517*	0.063	0.047	0.142	0.589*	-0.522*	-0.264	-0.610**	-0.559*	0.388	0.432
	W	0.548**	0.242	0.074	0.433*	0.561**	-0.440*	-0.053	-0.401	-0.551**	0.750**	0.148
RAI	M	0.590**	0.009	-0.037	0.080	0.487*	-0.420	-0.187	-0.476*	-0.609**	0.511*	0.310
	W	0.266	0.256	0.059	0.216	0.241	-0.084	0.019	-0.067	-0.398	0.631**	0.182
LMI	M	0.482*	0.177	-0.108	-0.028	0.335	-0.198	-0.325	-0.364	-0.419	0.478*	0.165
	W	0.051	0.009	-0.059	0.224	0.458*	-0.364	-0.307	-0.424*	-0.362	0.465*	0.640**
PLMI	M	-0.052	0.009	-0.065	0.028	0.089	-0.097	-0.292	-0.257	0.115	-0.058	0.180
	W	-0.099	-0.097	-0.043	-0.094	0.460*	-0.207	-0.246	-0.266	-0.422	0.498*	0.223

AHI: apnea-hypopnea index; AI: arousal index; DI: desaturation index; LMI: leg movement index; M: men; PLMI: periodic leg movement index; RAI: respiratory arousal index; REM: duration rapid eye movement sleep; REML: REM sleep latency; SE: sleep efficiency; SSI: stage shift index; SWSL: slow wave sleep latency; S1: duration stage 1; S2: duration stage 2, S3: duration stage 3; S3/4: duration stage 3 and 4; S4: duration stage 4; TST: total sleep time; W: women.; * p <0.05; ** p <0.01.

Table V. Bivariate correlations between objective sleep parameters, pain, fatigue, psychological status and daily functioning in FM patients.

	Sex	TST	SE	S1	S2	S3	S4	S3/4	REM	SWSL	REML
Current pain	M	0.076	0.021	0.155	0.052	0.116	-0.131	0.024	-0.276	0.029	0.084
(MPQ)	W	-0.079	0.169	-0.025	0.390	0.048	-0.219	-0.044	-0.405	-0.255	0.214
Pain in past week	M	0.301	0.179	0.092	0.455	-0.258	-0.287	-0.394	-0.343	0.066	0.190
(MPQ)	W	-0.230	-0.340	-0.093	-0.134	-0.045	0.000	-0.039	-0.039	-0.101	-0.058
Sensorial scale	M	0.212	0.185	0.181	0.487*	-0.343	-0.331	-0.494*	-0.299	0.351	0.203
(MPQ)	W	-0.052	-0.130	0.019	-0.005	-0.286	0.028	-0.240	0.246	-0.139	-0.173
Affective scale	M	-0.094	-0.062	0.279	0.028	0.034	-0.118	-0.040	-0.304	0.070	0.151
(MPQ)	W	0.139	0.076	0.073	-0.139	-0.029	0.142	0.024	0.272	-0.129	-0.298
General fatigue	M	0.198	0.140	-0.102	0.396	-0.314	-0.242	-0.416	-0.051	0.383	0.087
(MFI)	W	-0.219	-0.308	0.031	0.330	-0.304	-0.232	-0.351	-0.466*	0.172	0.305
Anxiety	M	0.083	0.057	0.201	0.031	0.068	-0.116	-0.010	-0.127	-0.117	0.194
(HADS)	W	-0.517*	-0.309	-0.169	0.404	-0.395	-0.087	-0.374	-0.424*	0.106	0.291
Depression	M	-0.049	-0.226	0.280	-0.027	-0.216	0.153	-0.098	-0.290	-0.125	0.462
(HADS)	W	-0.556**	-0.398	-0.140	0.268	-0.343	-0.067	-0.321	-0.384	0.181	0.144
Daily functioning	M	0.450	0.392	0.304	0.442	-0.567*	0.142	-0.410	-0.093	-0.004	0.185
(FIQ)	W	-0.287	-0.124	0.072	0.439*	-0.357	-0.234	-0.392	-0.371	-0.031	0.294

FIQ: Fibromyalgia Impact Questionnaire; HADS: Hospital Anxiety and Depression Scale; M: men; MFI: Multidimensional Fatigue Inventory; MPQ: McGill Pain Questionnaire; PSQI: Pittsburgh Sleep Quality Index; REM: duration REM sleep; REML: REM sleep latency; SE: sleep efficiency; SWSL: slow wave sleep latency; S1: duration stage 1; S2: duration stage 2; S3: duration stage 3; S3/4: Duration stage 3 and 4; S4: duration stage 4; TST: total sleep time; W: women; ** p <0.01; * p <0.05.

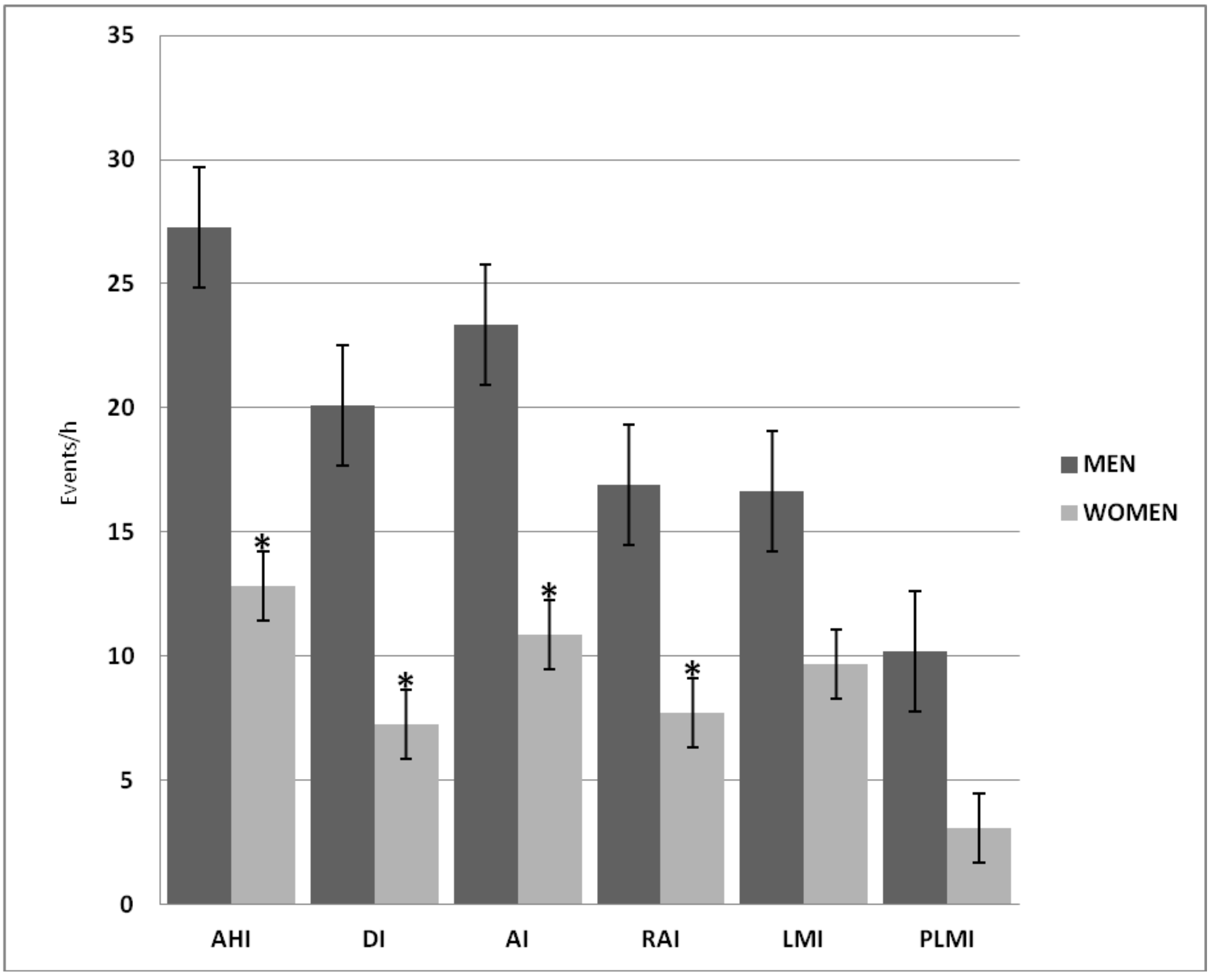

Figure 1. Gender differences in polysomnographic events.

AHI: apnea-hypopnea index; AI: arousal index; DI: desaturation index; LMI: leg movement index; PLMI: periodic leg movement index; RAI: respiratory arousal index; * p <0.05: FM men vs. FM women t-Student comparison.