



Prevalence of migraine in patients with fibromyalgia

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Abstract

Objective

To evaluate the prevalence of migraine in patients with fibromyalgia and the impacts of these comorbidities on the daily life of patients.

Methods

Questionnaires were applied to fibromyalgia patients. The questionnaires were applied through a Google forms application link and in person, printed. We used FIQ, PHQ-9, and ID migraine. And for patients with a positive ID migraine, we applied the Midas subsequently.

Results

Seventy fibromyalgia patients were recruited, age of 47.31 ± 14.5 years. Sixty-five (92.86%) were female and 5 (7.14%) were male. We obtained a prevalence of 60% ($n = 42$) of migraine associated with fibromyalgia. Among the analyzed variables, severity of depression ($p = 0.007$), aggregate severity of depression ($p = 0.004$), and impact of fibromyalgia ($p = 0.008$) were significantly associated. Among the migraine patients, the vast majority, 34/42 (80.95%), were classified as having severe disability.

Conclusion

There is a high prevalence of migraine in patients with fibromyalgia that has an associated impact on patients' lives, which makes clinical and psychosocial management of these patients necessary.

Keywords:

Migraine
Fibromyalgia
Depression
Midas
ID migraine



Introduction

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue injury, or described in terms of such injury, always subjective in its experiences".¹ It can be subdivided into 2 main types, the acute and the chronic, in the present study we will mainly address the so-called chronic. Chronic pain (CP) (non-oncologic), according to the International Association for the Study of Pain (IASP), is a disease with no apparent biological value that persists beyond the normal time of tissue healing, lasting more than 6 months. It is estimated that CP affects between 30 and 40% of the Brazilian population, and is the main cause of absenteeism, sick leave, early retirement, workers' compensation, and low productivity.²

The persistence of CP prolongs the existence of these harmful symptoms and may even exacerbate them, besides having consequences on the quality of life, leading to depression, anxiety, physical and functional disability, and others.³

Among the most frequent and harmful pains to its bearers are fibromyalgia and migraine. Fibromyalgia is defined as a chronic pain syndrome, without etiological knowledge, that presents itself through the musculoskeletal system, non-autoimmune and non-inflammatory, with sleep and mood alterations and lasting more than 3 months.^{4,5} It is a common disease in Brazil, present in up to 2.5% of the general population, predominantly in females, mainly between 35 and 44 years of age, and is second only to osteoarthritis among the diseases with the highest incidence that affect the locomotor system. It is difficult to diagnose because it does not present alterations in imaging exams and there is no laboratory marker.⁶

Fibromyalgia presents as main symptom the diffuse and chronic pain, affecting the axial and peripheral skeleton, besides being associated with decreased REM sleep, periodic limb movements, restless legs syndrome, morning fatigue, and pain on awakening.

The physiopathology as well as the etiology is also uncertain, and, until now there are only hypotheses, such as social, emotional, and family factors, added to a factor of greater response to painful stimuli, the low level of cardiovascular conditioning, and muscular performance. It is also associated with other comorbidities, which contribute to the suffering and worsening of the quality of life of these patients.^{5,7}

Headaches are among the most common complaints in doctor's offices and emergency rooms, and they can be divided into primary and secondary ones.⁸ Most patients present with one of the primary types of pain, but the diagnosis needs to be made accurately. In 1988, a new international classification of headaches was published, obtaining parameters to complete the clinical diagnosis in most primary headaches. Complementary tests are rarely needed. Among the most common headache disorders are tension-type headache, migraine, chronic daily headache from transformed migraine, and cluster headache. The current classification was an update of the first version and is in its third edition.⁹ Migraine is surely one of the most frequent headaches mentioned above, with a varied clinical symptomatology, for which more therapeutic proposals are available. Moreover, its characteristics are prevalent and disabling.¹⁰

Despite differences in pain distribution, fibromyalgia and migraine are commonly found associated in the same patient. Fibromyalgia was found in 30% of patients with migraine.¹¹ In addition, of both clinical and statistical relevance, patients with migraine and fibromyalgia report a greater number of medical and psychiatric comorbidities than those with fibromyalgia alone¹¹, such as suicide risk, anxiety, depression, sleep disturbances, and headache severity.¹² Furthermore, the high concomitance of the diseases suggests that these disorders may share some degree of common pathophysiology.¹¹ Notably, there are several controversies of the impact of fibromyalgia on migraine, or vice versa. Therefore, the present study aims to assess the prevalence of migraine in patients with fibromyalgia and the impacts of these associated comorbidities on the patients' daily lives.

Methods

This research was a cross-sectional study, on the presence of migraine and its impact on the lives of patients diagnosed with fibromyalgia (FM).

The study included patients of both genders over the age of eighteen (18) years, previously diagnosed as having fibromyalgia and diagnosed by a rheumatologist, according to the New Guidelines for the diagnosis of the disease, of the Brazilian Society of Rheumatology.⁶ The volunteers were recruited both by convenience sampling at the Rheumatology Outpatient Clinic of the Barbacena



Medical School, between January 2022 to November 2, 2022. Furthermore, patients with cognitive deficits, which would have made it impossible to answer the questionnaires, and those who did not agree to participate in the study were excluded.

For those who agreed to participate in the research, after signing the Free and Informed Consent Form, the division of patients with migraine was performed by the research team members and was done according to the Migraine ID criteria.¹³ All patients motivated by the complaint of fibromyalgia, previously diagnosed with the disease were presented with the questions proposed by the FIQ (Fibromyalgia Impact Questionnaire)¹⁶, the PHQ-9¹⁵ and the ID-Migraine.¹³ The participants, suffering from fibromyalgia, were then divided into two groups: one group of migraine patients; and another group of non-migraine patients.

Initially, we applied the Fibromyalgia Impact Questionnaire (FIQ)¹⁴ which involves questions related to functional capacity, work status, psychological disorders, and physical symptoms. It is composed of 19 questions, organized into 10 items. The higher the score, the greater the impact of fibromyalgia on quality of life. The FIQ is valid for use in clinical and research situations. Several subsequent studies of patients with FM have used this instrument and verified the negative impact of FM.

The Migraine ID Questionnaire¹³ was devised to establish the validity and reliability of a brief, self-administered migraine screening tool for patients with headache complaints, seen in the primary care setting. The authors analyzed nine diagnostic screening questions, resulting in a subset of three items comprising disability, nausea, and light sensitivity. These three questions together provided optimal performance, with a sensitivity of 81% (95% CI, 77% to 85%), a specificity of 75% (95% CI, 64% to 84%) and positive predictive value (PPV) of 93% (95% CI, 89% to 95%). Test-retest reliability was good, with a kappa of 0.68 (95% CI, 54% to 82%) and Cronbach's alpha for the total scale was 0.70. It is concluded that ID-MigraineTM is a valid and reliable screening tool for migraine, improving the recognition of migraine in primary care.

For patients who were ID-Migraine positive, migraine was characterized according to the International Classification (ICHD-3)⁹ and applied the MIDAS (Migraine Disability Assessment).¹⁵

The MIDAS¹⁵ was developed as a useful tool in identifying

migraineurs with different degrees of headache-related disability. In addition, this questionnaire is brief, simple to use, consistent, highly reliable, and consistently correlates with clinicians' clinical judgment. The higher the MIDAS score, the greater the impact of migraine on the patient's daily activities.¹⁵

Among the instruments used to identify individuals at risk of depression is the Patient Health Questionnaire-9 (PHQ-9).¹⁰ The PHQ-9 was applied to all research participants. The PHQ-9 was originally developed to identify five common mental disorders in primary health care: depression, anxiety, alcohol abuse, somatoform disorders and eating disorders. The PHQ-9 is characterized by its relatively quick application, which would be an advantage in epidemiological studies compared to others validated for Brazil.¹⁶

The PHQ9 is subdivided into nine questions, the respondent marks one of the four options regarding symptoms experienced in the last 15 days: none of the days, several days, more than half the number of days, almost every day.¹⁷ At least 5 results marked as "more than half the number of days" are required to be regarded to consider the presence of major depressive disorder. Between 2 and 4 results marked "more than half the number of days" should be regarded as some other depressive disorder. The options mentioned above are given a value of 0 to 3 points. The total sum of the 9 questions provides a score between 0 and 27 points in which the severity of the depression is evaluated. Values of 1-4 - minimal depression; 5-9 mild depression; 10-14 moderate depression; 15-19 moderate severe depression; 20-27 severe depression. Diagnoses of depression also require some social, occupational, or other important functional impairment, which is remedied by question 10 of the questionnaire.

Ethical aspects

The present study was approved by the ethics committee of the Faculdade de Medicina de Barbacena under opinion number 5.019.750.

Statistical Analysis

The data from the questionnaires were transcribed into a spreadsheet and processed in STATA v. 9.2 statistical software, row by column tables with absolute and relative frequencies were produced, the existence of association among the study variables was measured by the Chi-square, Fisher's Exact, and Kruskal-Wallis tests. Values were considered significant when $p \leq 0,05$.



Results

A total of 70 fibromyalgia patients were recruited, the mean age was 47.31 ± 14.5 . Of these, 65 (92.86%) were female and 5(7.14%) were male. Of the total patients 42 (60%) were classified as migranous and 28 (40%) as non-migranous by migraine ID.

Among the total 70 patients, 8(11.43%) were classified with minimal depression on PHQ-9, 20 (28.57%) with mild depression, 13 (18.57%) with moderate depression, 14(20%) with moderately severe depression and 15(21.43%) with severe depression. Among the non-migrant patients, most 12 (42.86%) had mild depression symptoms, followed by minimal symptoms 5 (17.86%). Whereas among migrants, most 12(28.57%) had severe depression, followed by moderately severe depression 9(23.81%). The distribution of depression symptoms was quite similar between migrants and non-migrants for the minimal, moderate, and moderately severe categories (Table 1).

Table 1. (PHQ-9) Association between the frequencies of depression severity among the fibromyalgia group and the migraine + fibromyalgia group.

Depression Severity	Non-Migraine Frequency/percentage	Migraine Frequency/percentage	Total
Non – Minimal	5(17,86%)	3 (7,14%)	8(11,43%)
Mild	12(42,68%)	8(19,5%)	20(28,57%)
Moderate	3(10,71%)	10(23,81%)	13(18,57%)
Moderately Severe	5(17,86%)	9(21,43%)	14(20%)
Severe	3(10,71%)	12(28,57%)	15(21,43%)
Total	28(40%)	42(60%)	70
P Value	P=0,062 (Fisher's exact)		
	P=0,0065 (Kruskal-Wallis)		

When we aggregate the cases of minimal depression and mild depression in one group and the cases of moderate depression, moderately severe depression and severe depression in another group we observe that of the 28 non-migrant patients, 17 (60.71%) were classified as having "minimal depression" or "mild depression" on the PHQ-9, while 11 (39.29%) were classified as having "moderate depression", "moderately severe depression " or "severe depression". On the other hand, of the 42 migrant patients, 11 (26.19%) were classified as having "minimal depression" or "mild depression", while 31 (73.81%) were classified as having "moderate depression", "moderately severe depression", or "severe depression". In this aggregate analysis the P value by Fisher's exact test was 0.008 and 0.004 by Pearson's chi square test (Table 2).

Table 2. (PHQ-9) Association between the frequencies of depression severity among the fibromyalgia group and the migraine + fibromyalgia group. (aggregated groups)

Depression Severity	Non-Migraine Frequency/percentage	Migraine Frequency/percentage	Total
Non-Minimal / Mild	17(60,71%)	11 (26,19%)	28(40%)
Moderate/ModSevere*/ Severe	12(39,29%)	31(73,81%)	42(60%)
Total	28(40%)	42(60%)	70
Valor de P	P=0,004 (Pearson's chi-squared)		

*ModSevere: ModeratelySevere Depression

Among the total 70 patients 2 (2.86%) were classified with mild impact in the fibromyalgia impact questionnaire FIQ, while 18 (25.71%), had moderate impact and 50 (71.43%) had severe impact (Table 3).

Table 3. (FIQ) Correlation between fibromyalgia impact frequencies among the fibromyalgia group and the migraine + fibromyalgia group.

Fibromyalgia Severity	Non-Migraine Frequency/percentage	Migraine Frequency/percentage	Total
Mild	2 (7,14%)	0 (0%)	2 (2,86%)
Moderate	11 (39,29%)	7 (16,67%)	18 (25,71%)
Severe	15 (53,57%)	35 (83,83%)	50 (71,43%)
Total	28 (40%)	42 (60%)	70
P value	P=0,008 (Fisher's Exact)		

Among the total 28 non-migrant patients 2 (7.14%) had mild impact, 11 (39.29%) had moderate impact and 15 (53.57%) had severe impact. In the group of 42 migrants the vast majority were cases of severe impact 35 (83.33%) followed by moderate impact 7 (16.67%) and no cases of mild impact.

The MIDAS was applied to all 42 patients classified as migranous. The vast majority 34 (80.95%) were classified as having severe disability, followed by 7 (16.67%) patients with moderate disability, 1(2.38%) case of mild disability and no case with no disability.

Table 4. (MIDAS) Assessment of the impact of migraine on migraine patients

Impact of migraine	Frequency(%)
Severe disability	34 (80,95%)
Moderate disability	7 (16,67%)
Mild disability	1 (2,38%)
No disability	0
Total	42

Discussion

In the present study, 70 fibromyalgia patients were recruited, the majority being female (65) (92.86%), corroborating



the fact that fibromyalgia is a predominant disorder in women, as already exposed in other studies.^{11, 18, 19} Of these patients, 60% were classified as migraine by the ID migraine, a result similar to that of a previous epidemiological study in which a 55.8% prevalence of migraine was observed among patients with fibromyalgia.¹¹

Although the pathophysiology and pathogenesis of Fibromyalgia are poorly understood, it is believed that central sensitization mechanisms occur in the syndrome, as in migraine, due to an imbalance of neuromediators involved in transmission and nociceptive control in the Central Nervous System (CNS), in genetically predisposed subjects^{20, 21}, that is, in fibromyalgia patients there is evidence of a generalized reduction of the pain threshold to different types of stimuli at the somatic level, not only in spontaneous painful areas, but also in non-painful control sites.²²⁻²⁴

In relation to the results obtained by the PHQ-9, it appears that depression significantly affects migrants and non-migrants, which agrees with other studies²⁵⁻²⁷ that show a high prevalence of depressive symptoms in chronic pain patients.

The subgroup analysis showed that patients with only fibromyalgia (39.29%) had moderate to moderately severe and severe depression, while in the group with both conditions (fibromyalgia and migraine) 73.8% had moderate to moderately severe and severe depression, suggesting that patients with migraine associated with fibromyalgia are affected more severely. To date, no studies were found in the databases searched that evaluated the association of fibromyalgia and migraine with the severity of depressive symptoms, however, it is reported the relationship of migraine with depressive disorder.²⁸

In addition to the evaluation by the PHQ-9 instrument, the FIQ questionnaire was used to evaluate the impact of fibromyalgia on the patients' activities of daily living.

In the group of migraine patients, a higher prevalence of severe impact 83.83% was observed, it is important to emphasize that no score was obtained among the patients that classified them with "mild" impact of fibromyalgia. These results suggest that the rheumatologic disease influences the onset of pain originating from the nervous system.²⁹

Therefore, it is understood that there is a very relevant impact exerted on the lives of patients with fibromyalgia syndrome, in several spheres. It is important to point out that the frequency of headache crises is positively associated with fibromyalgia. Both processes have in common the central sensitization process. Moreover, migraine, a type

of primary headache, can trigger a fibromyalgia picture in predisposed individuals. This pathology of the nervous structures can course with allodynia (pain perception in front of a non-harmful stimulus) outside the cephalic segment during the migraine crisis due to thalamic involvement.³⁰ Furthermore, dysregulation of the serotonergic system and diffuse hyperalgesia associated with an abnormal pattern of nitric oxide synthesis possibly link the two previously mentioned conditions.

In addition to the FIQ and PHQ9 instruments, the MIDAS was applied to the group of migraine patients. In the evaluation of the impact of migraine on the patients in the present study, 80.95% were classified with severe disability and 16.67% with moderate disability. A study conducted by other researchers where 50 patients with migraine were evaluated, of these, 42% had severe disability, 20% had moderate disability, 8% had mild disability, and 30% had minimal disability. With this, it is observed that the association of the two pathologies presented a higher prevalence of patients classified with severe disability by the MIDAS.

The strength of the study was the statistical significance found for both the severity of depression and the impact of fibromyalgia and the high percentage of individuals with severe disability migraine, indicating that when the two clinical conditions are associated, they cause great psychological harm and to the patients' activities and their daily living.

The main limitation of the study was the sample size, suggesting the need for more representative samples of patients with fibromyalgia.

Conclusion

The high prevalence of migraine in patients with fibromyalgia found (60%) added to the impact on the lives of patients with both pathologies evidenced by the results obtained in the three tools PHQ9, FIQ and MIDAS point to the need for studies that evaluate both the pathophysiological mechanisms and treatment possibilities of these diseases, in addition to the clinical and psychosocial management of these patients.

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LDMM, AMCF, AFR, BSD, IMLC, PDNM, FACP, Data collect; AFR, BSD, IMLC, PDNM, Writing; MEJ, Guidance and final review



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