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Original

Fibromigraine: a cohort study retrospective

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Objective
To diagnose fibromyalgia in patients with migraine and assess the quality of life of these patients.
Methods
A prospective, cross-sectional study was carried out, comparing groups, in a non-randomized sample, consisting of patients diagnosed with migraine. The sample was evaluated using the Widespread Pain Index (WPI) and Symptom Severity Scale (SSS) questionnaires to diagnose fibromyalgia. Quality of life and level of depression were assessed, respectively, using the Headache Impact Test-6 (HIT-6) and Patient Health Questionnaire-9 (PHQ-9).
Results
We interviewed 100 patients (5 men and 95 women) diagnosed with migraine, with a mean age of 37.1±11.0 years, ranging from 19 to 64 years. Thirty-four patients (34%) had migraine and fibromyalgia concomitantly. Migraine predominated in females, both in the presence and absence of fibromyalgia. In both groups, there was no difference in headache characteristics. In the group with fibromyalgia, there was a predominance of allodynia and a higher PHQ-9 score ($p<0.001$).
Conclusions
Patients with migraine are more predisposed to depression when there is an association with fibromyalgia.

Keywords:
Migraine
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Depression
Quality of life

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Introduction

Fibromyalgia affects 2 to 4% of populations worldwide and is a cause of considerable suffering and functional impairment (1). It is hypothesized that its pathophysiology is a genetic predisposition in the imbalance of neurotransmitters involved in pain modulation, with increased neuronal excitability(2). According to the American College of Rheumatology, the diagnostic criteria are based on the presence of diffuse musculoskeletal pain for at least three months and other variables such as sleep and mood disorders, headache and visceral (3).

It is estimated that 22.2% to 45.1% of patients with migraine have fibromyalgia (1) and that 31.4% of patients with fibromyalgia have migraine (4). The frequent association between these two diseases, called fibromigraine, is still a subject of investigation, but it is believed that there is a common pathophysiological mechanism. The association between fibromyalgia and mood disorders is also well documented, including depression. This condition has been linked to fibromyalgia with prevalences ranging from 12 to 35% (5). Despite the frequent association between fibromyalgia, migraine and depression, studies are still lacking. Therefore, this study aimed to analyze it.

Patients and Methods

Sample size
For the expected prevalence of 31.4%(4), the required sample size was 81 patients, with a margin of error or absolute precision of at least 10% in estimating prevalence and with 95% confidence. This sample size was calculated using the Scalex SP calculator (6). Cohen's d was also used to measure effect size.

Study design and patients
A prospective, cross-sectional study was carried out, with group comparison, in a non-randomized sample, consisting of patients treated in a tertiary neurology service, from January 2021 to January 2022 and diagnosed with migraine. The sample consisted of 100 patients diagnosed with migraine, according to the criteria of the International Classification of Headache Disorders, Third Edition (ICHD-3). The sample was selected among patients treated at a tertiary neurology service, linked to a public university, located in the northeast of Brazil and invited to participate in this research.

Inclusion and exclusion criteria
The study included patients aged between 18 and 65 years, diagnosed with migraine, according to the ICHD-3 diagnostic criteria and who agreed to undergo anamnesis and answer the questionnaires that would be part of the research. Patients diagnosed with migraine associated with another primary or secondary headache, women with headache only during the perimenstrual period, pregnant women and those with cognitive disorders that made it difficult to understand the interview were excluded.

Data collection
Immediately after meeting the inclusion and exclusion criteria, a structured interview followed, carried out by a neurologist specializing in headaches, based on a questionnaire to diagnose migraine. By telephone, a second researcher (the author of the research) evaluated migraine patients using questionnaires to diagnose an association with fibromyalgia. The Widespread Pain Index (WPI) and Symptom Severity Scale (SSS) questionnaires were used to evaluate, respectively, the reported location of muscle pain and the degree of severity of symptoms associated with fibromyalgia. These tests are used to diagnose fibromyalgia. The Headache Impact Test-6 (HIT-6) and Patient Health Questionnaire-9 (PHQ-9) questionnaires were also applied to analyze, respectively, the quality of life and the level of depression in migraine patients with fibromyalgia and without fibromyalgia. Totaling 5 questionnaires.

During data collection, 215 patients diagnosed with migraine were interviewed, but only 100 patients met the inclusion criteria. One hundred and fifteen were excluded for the following reasons: they did not meet the age criteria (n=12), diagnosis of secondary headache (n=1), medical records not found (n=23), no answered the phone (n=52) and refused to participate in the research (n=27).

Statistical analysis
Once the information was organized in a database, the BioEstat program, version 5.0, was used for statistical analysis. The chi-square tests with Yates' correction and Student's t were used for differences in means of unpaired samples, assuming a significance level of 0.05.

Ethical aspects
This research was approved by the Ethics Committee for Research Involving Human Beings of the Universidade Federal do Piauí, CEP-UFPI opinion no. 5076361 and CAAE registration no. 12743813.4.0000.5209. Data were collected from January 2022 to January 2023. All volunteers signed the Free and Informed Consent Form, according to Resolution no. 466/12 of the National Health Council of the Ministry of Health.

It is also worth noting that the risks and benefits were explained to patients. The risk is characterized by the fact that the patient considers complaints that he did not consider important. While the benefits were: offering the patient the possibility of understanding more about the disease. In addition to being able to diagnose fibromyalgia and/or depression, helping with referral to a specialist.

Results

The studied sample consisted of 100 patients, consisting of 5 men and 95 women diagnosed with migraine and characterized by an average age of 37.1±11.0 years, ranging from 19 to 64 years.

Of the 100 patients diagnosed with migraine, 34 (34%) had fibromyalgia as a comorbidity and 66 (66%) had no fibromyalgia, the distribution of which differed according to sex and age, as shown in Table 1. Migraine predominated in females, regardless of the presence of fibromyalgia. This difference was not significant. Regarding age, migraine with fibromyalgia affected patients aged 38.8±11.6 years and migraine without fibromyalgia was diagnosed in younger patients, aged 36.3±10.7 years, these differences being non-significant.

Table 1. Distribution by sex and age, according to diagnosis or not of fibromyalgia.

Variables	Diagnosis		P-value
	Migraine with fibromyalgia (n=34)	Migraine without fibromyalgia (n=66)	
Sexo			0,659*
Male (n; %)	1 (2.9)	4 (6.1)	
Female (n; %)	33 (97.1)	62 (93.9)	
Age (years)			
Average (SD)	38,8 (11.6)	36,3 (10.7)	0,276†
Variation	21-63	19-64	

Note: *P-value based on Fisher test; † P-value based on Student test.

When considering the characteristics of the headache to differentiate patients with migraine associated with fibromyalgia from those without fibromyalgia, it was proven that the two groups were statistically distinct. However, the group diagnosed with migraine associated with fibromyalgia differed significantly from the group without fibromyalgia regarding the presence of allodynia. (p=0.002). The headache characteristics in the two groups are presented in Table 2.

Table 2. Headache characteristics, according to diagnosis or not of fibromyalgia.

Characteristics	Diagnosis		P-value
	Migraine with fibromyalgia (n; %)	Migraine without fibromyalgia (n; %)	
Type			0,288
Episodic	9 (26.5)	26 (39.4)	
Chronic	25 (73.5)	40 (60.6)	
Headache onset			1,000*
< 3 months	0	0	
3-12 months	1 (97.1)	3 (95.5)	
>12 months	33 (2.9)	63 (4.5)	
Pain localization			0,294
Unilateral	13 (38.2)	34 (51.5)	
Bilateral	21 (61.8)	32 (48.5)	
Pain quality			0,879
Tightness/pressure	10 (29.4)	17 (25.8)	
Pulsatile	24 (70.6)	49 (74.2)	
Pain intensity			0,100*
Mild (VAS 1–4)	1 (2.9)	22 (33.3)	
Moderate (VAS 5–7)	7 (20.6)	6 (9.1)	
Intense (VAS 8–9)	26 (76.5)	38 (57.6)	
Worsens with routine physical			0,875
Sim	29 (85.3)	54 (81.8)	
Não	5 (14.7)	12 (18.1)	
Aura			0,352
Yes	12 (35.5)	16 (24.2)	
No	22 (64.7)	50 (75.6)	
Allodynia			0,002
Yes	33 (97.1)	45 (68.2)	
No	1 (2.9)	21 (31.8)	
Associated symptoms			
Nausea	30 (88.2)	47 (71.2)	0,096
Photophobia	30 (88.2)	58 (87.9)	1,000
Phonophobia	29 (85.3)	50 (75.7)	0,395
Osmophobia	29 (85.3)	44 (66.7)	0,080
Absent	0 (0.0)	2 (3.0)	-
Pain triggers			
Stress	31 (91.2)	44 (66.7)	0,015
Prolonged fasting	22 (64.7)	43 (65.1)	0,859
Sleep deprivation	28 (82.3)	51 (77.3)	0,740
Menstruation	24 (70.6)	30 (45.4)	0,030
Alcohol intake	7 (20.6)	15 (22.7)	0,992
Absent	0 (0.0)	4 (6.1)	0,296

Note: Visual Analogue Scale (VAS); P-value based on Chi-square test, comparing: *>3 months/3-12 months versus > 12 months; †mild/moderate versus intense.

The diagnosis of fibromyalgia was based on the WPI and SSS questionnaires, which quantified the extent of widespread pain throughout the body (Table 3).

Table 3 – Study measures means in fibromyalgia variables and group comparisons

Variables	Diagnosis		P-value	Cohen's d
	Migraine with fibromyalgia (n=34)	Migraine without fibromyalgia (n=66)		
Symptoms Severity Scale (SS)			<0.0001	1.84
Average (SD)	10,0 (1.7)	5,7 (2.6)		
Variation	7-12	1-11		
Widespread Pain Index (WPI)			<0.0001	2.06
Average (SD)	8,9 (4.9)	2,4 (1.7)		
Variation	3-15	0-6		

Note: P-value based on Student test.

The investigation of quality of life and depression levels according to the diagnosis of fibromyalgia were evaluated in table 4.

Table 4 – Analysis of quality of life and depression, according to the diagnosis of fibromyalgia.

Variables	Diagnosis		P-value
	Migraine with fibromyalgia (n=34)	Migraine without fibromyalgia (n=66)	
Headache Impact Test-6 (HIT-6)			0,806
Average (SD)	65,8 (10.3)	64,1 (7.9)	
Variation	44-78	26-78	
Patient Health Questionnaire-9 (PHQ-9)			<0.001
Average (SD)	14,0 (7.5)	7,1 (5.8)	
Variation	2-27	0-26	

Note: P-value based on Student test.

Discussion

There was a prevalence of females in patients with migraine (19:1), whether or not they had fibromyalgia. This sex was also more prevalent when taking into account, in addition to migraine, the presence of fibromyalgia (33:1), but without statistical difference (p=0.659). However, other studies found a predominance of females in patients with fibromyalgia and migraines, concomitantly (p=0.031)(1). The predominance of these two diseases among women is justified by pathophysiological bases associated with the antinociceptive and anti-inflammatory effects of estrogen and progesterone(7).

Aiming to identify probable factors that could predict the association between fibromyalgia and migraine, the characteristics of headache in migraine patients, with and without fibromyalgia, were compared. Although statistical significance was not obtained, it was observed that when patients had fibromyalgia, the headache was located bilaterally (61.8%). We did not find anything in the literature that would justify such data. Likewise, in this study, no significant differences were observed in relation to the frequency and duration of pain, while other studies have demonstrated that headache frequency can be a strong predictor of musculoskeletal pain and fibromyalgia(4).

The data of a limited number of literature tends to support that there is not an association between migraine aura and fibromyalgia(1). In our study, the presence of aura was not significant (p=0.352).

Increasing evidence indicates that peripheral tissues are relevant consumers for the input of the painful impulse and can initiate or maintain central sensitization(8).This finding can be explained by the fact that allodynia was more frequently found in patients with fibromyalgia. (p=0.002).

Migraine is usually accompanied by marked neurovegetative symptoms, such as nausea and vomiting(3). However, no data were found in the literature that explains the fact that these manifestations are more present in patients with fibromyalgia and migraines when compared to the group that only has migraines.

Patients with migraines associated with depression are more likely to have fibromyalgia. These psychic phenomena may justify the fact that stress is a triggering factor for headache attacks and is more prevalent in the group with migraine and fibromyalgia when compared to the group with migraine without fibromyalgia (p=0,015).

In the criteria for diagnosing fibromyalgia, scores from the WPI and SSS scales are used, which can determine which parts of the body are painful and the severity of the associated symptoms, respectively. This study observed higher scores in the group of patients with migraine who had associated fibromyalgia, with a significant difference. However, these values were already those expected by the factor already explained above. The effect size, measured by Cohen's d, for the migraine with fibromyalgia and migraine without fibromyalgia groups was, respectively, 1.84 and 2.06, indicating a large effect.

Fibromyalgia and migraine are debilitating pain disorders in which one can increase the morbidity of the other when associated, causing a major negative impact on patients' quality of life (9). In this study, we evaluated the quality of life of patients with migraine who had fibromyalgia using the HIT-6. This is a validated scale that uses criteria such as frequency of severe pain and degree of limitation in daily activities. However, no significant difference was observed between the two samples (p=0.806).

Depression and anxiety disorders have been identified as crucial secondary symptoms of fibromyalgia (8). When patients present these diseases together, they have a worse prognosis with compromised quality of life. In this study, depression was assessed using the PHQ-9 and was found to be more frequent in patients with migraines and fibromyalgia (p=<0.001). Prospective studies in migraine patients could be done to assess whether they are predisposed to depression when associated with fibromyalgia.

Conclusion

The study allowed us to conclude that headache complaints are common in patients with fibromyalgia. With migraine being the most common primary headache found. It was also noticed that patients who have more headache attacks per month, being considered chronic, were those who had a worse grade of depression. As well as a worse quality of life.

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References

1. Onder H, Hamamci M, Alpua M, Ulusoy EK. Comorbid fibromyalgia in migraine patients: clinical significance and impact on daily life. *Neurological Research*. 2019;41(10):909-15.Doi 10.1080/01616412.2019.1630164
2. Grayston R, Czanner G, Elhadd K, Goebel A, Frank B, Üçeyler N, et al. A systematic review and meta-analysis of the prevalence of small fiber pathology in fibromyalgia: Implications for a new paradigm in fibromyalgia etiopathogenesis. *Seminars in Arthritis and Rheumatism*. 2019;48(5):933-40.Doi 10.1016/j.semarthrit.2018.08.003
3. Affaitati G, Costantini R, Tana C, Cipollone F, Giamberardino MA. Co-occurrence of pain syndromes. *Journal of Neural Transmission*. 2019;127(4):625-46.Doi 10.1007/s00702-019-02107-8
4. Yilmaz V, Aras B, Erturk FA, Cakcı FA, Umay E. Migraine in patients with fibromyalgia and outcomes of greater occipital nerve blockage. *Clinical Neurology and Neurosurgery*. 2019;181:54-7.Doi 10.1016/j.clineuro.2019.04.004
5. Calandre EP, García-Leiva JM, Ordoñez-Carrasco JL. Psychosocial Variables and Healthcare Resources in Patients with Fibromyalgia, Migraine and Comorbid Fibromyalgia and Migraine: A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*. 2022;19(15).Doi 10.3390/ijerph19158964
6. Naing L, Nordin RB, Abdul Rahman H, Naing YT. Sample size calculation for prevalence studies using Scalex and ScalaR calculators. *BMC Medical Research Methodology*. 2022;22(1).Doi 10.1186/s12874-022-01694-7
7. Singh L, Kaur A, Bhatti MS, Bhatti R. Possible Molecular Mediators Involved and Mechanistic Insight into Fibromyalgia and Associated Co-morbidities. *Neurochemical Research*. 2019;44(7):1517-32.Doi 10.1007/s11064-019-02805-5
8. Penn IW, Chuang E, Chuang T-Y, Lin C-L, Kao C-H. Bidirectional association between migraine and fibromyalgia: retrospective cohort analyses of two populations. *BMJ Open*. 2019;9(4).Doi 10.1136/bmjopen-2018-026581
9. Whealy M, Nanda S, Vincent A, Mandrekar J, Cutrer FM. Fibromyalgia in migraine: a retrospective cohort study. *The Journal of Headache and Pain*. 2018;19(1).Doi 10.1186/s10194-018-0892-9