BrJP. 2024, v.7:e20240051 ORIGINAL ARTICLE

# Patients' perception on stressful events for fibromyalgia development

A percepção dos pacientes sobre eventos estressores no desenvolvimento da fibromialgia

Ana Julia Campi Nunes de Oliveira<sup>1</sup>, Thaís Di-Giovanni<sup>1</sup>, Cassiano Henrique Giovanini Vanzelli<sup>1</sup>, Bruno de Mendonça Moraes Arauio<sup>1</sup>. Reinaldo José Gianini<sup>2</sup>. José Eduardo Martinez<sup>1</sup>

https://doi.org/10.5935/2595-0118.20240051-en

## **ABSTRACT**

**BACKGROUND AND OBJECTIVES**: Fibromyalgia syndrome (FM) is a rheumatic disease with the following characteristics: generalized chronic pain, fatigue, non-restorative sleep and cognitive disturbances. It is often associated to distress followed chronic and acute stressors exposures. The objective of this study was to determine the patients' perception if stressful events influence the development of FM. The secondary objective was to evaluate the impact of acute stress in determining the future severity of FM.

**METHODS:** A cross-sectional study was carried out for the primary objective and a case-control study for the secondary objective. We used questionnaires on demographic data and instruments for assessing the severity and impact of FM (Fibromyalgia Index - FI, and Revised Fibromyalgia Impact Questionnaire - FIQr), instruments for assessing emotional aspects (PHQ-9 and GAD-7), and a questionnaire on patients' perception of stressful events.

**RESULTS**: Sixty-one patients were evaluated. About 59% reported the presence of acute stress as an aggravating factor. Pa-

Ana Júlia Campi Nunes de Oliveira – ©https://orcid.org/0000-0002-3408-1211;
Thaís Di-Giovanni – ©https://orcid.org/0009-0005-3660-4257;
Cassiano Henrique Geovanini Vanzeli – ©https://orcid.org/0000-0001-5990-6729;
Bruno de Mendonça Moraes Araújo – ©https://orcid.org/0000-0003-0288-0024;
Reinaldo José Gianini – ©https://orcid.org/0000-0002-7046-7306;
José Eduardo Martinez – ©https://orcid.org/0000-0002-3864-6822.

- 1. Pontifical Catholic University of São Paulo, Clinics, Sorocaba, SP, Brazil.
- 2. Pontifical Catholic University of São Paulo, Public Health, Sorocaba, SP, Brazil.

Submitted on April 30, 2024.

Accepted for publication on June 25, 2024.

Conflict of interests: none - Sponsoring sources: PIBIC CNPq - scientific initiation scholarships for the authors Ana Júlia Campi Nunes de Oliveira and Thaís Di-Giovanni.

## HIGHLIGHTS

- The article emphasizes the importance of distress and exposure to stressors to fibromyalgia patients;
- Distress is essential at fibromyalgia impact on quality of life;
- Doctors shall consider distress when approaching the patient's symptoms.

Associate editor in charge: Luciana Buin ©https://orcid.org/0000-0002-1824-5749

Correspondence to: José Eduardo Martinez E-mail: jemartinez@pucsp.br tients mentioned grief for a close relative, financial problems, family conflicts, and being a victim of violence as aggravating events. There was a significant association between the presence of stressful incidents, FI and FIQr (p<0.05). The presence of aggravating circumstances increased the FIQr score by 2.72.

**CONCLUSION**: It was observed a significant association between aggravating stressful events and higher index FM scores and their impact on the patients.

**Keywords**: Fibromyalgia, Psychological distresse, Quality of life.

## **RESUMO**

JUSTIFICATIVA E OBJETIVOS: A síndrome da fibromialgia (FM) é uma doença reumática com as seguintes características: dor crônica generalizada, fadiga, sono não restaurador e distúrbios cognitivos. Ela é frequentemente associada à angústia após exposições a estressores crônicos e agudos. O objetivo deste estudo foi determinar a percepção dos pacientes se os eventos estressantes influenciam o desenvolvimento da FM. O objetivo secundário foi avaliar o impacto do estresse agudo na determinação da gravidade futura da FM.

**MÉTODOS**: Foram realizados um estudo transversal para o objetivo primário e um estudo de caso controle para o objetivo secundário. Foram utilizados questionários sobre dados demográficos e instrumentos de avaliação da gravidade e impacto da FM (Índice Fibromiálgico - FI, e *Revised Fibromyalgia Impact Questionnarie* - FIQr), instrumentos de avaliação de aspectos emocionais (PHQ-9 e GAD-7), e um questionário sobre a percepção dos pacientes em relação aos eventos estressores.

**RESULTADOS:** Sessenta e um pacientes foram avaliados. Cerca de 59% relataram a presença de estresse agudo como um fator agravante. Os pacientes mencionaram o luto por um parente próximo, problemas financeiros, conflitos familiares e serem vítimas de violência como eventos agravantes. Houve associação significativa entre a presença de incidentes estressantes, FI e FIQr (p<0,05). A presença de circunstâncias agravantes aumentou o escore do FIQr em 2,72.

**CONCLUSÃO:** Foi observada associação significativa entre eventos estressantes agravantes e pontuações mais altas do índice de FM e seu impacto sobre os pacientes.

Descritores: Estresse psicológico, Fibromialgia, Qualidade de vida.



This is an open-access article distributed under the terms of the Creative Commons Attribution License.

## INTRODUCTION

Fibromyalgia (FM) syndrome is a rheumatic disease that comprises widespread chronic pain, fatigue, unrefreshing sleep, and cognitive disturbances. It is frequently associated with other functional syndromes such as irritable bowel, migraine, regional pain syndrome, depression, anxiety, etc<sup>1</sup>.

FM is considered the second most prevalent rheumatic disease after osteoarthritis. Its worldwide prevalence is at around 2.5%, with the big female predominance<sup>1</sup>. In Brazil, the prevalence varies between 0.66 and 4.4%, mainly in the 35-60 age group. FM affects people of working age, causing a substantial impact on work and costs for society<sup>2,3</sup>. It is a major factor in reducing patients' quality of life<sup>4</sup>.

Although the diagnosis could be based exclusively on clinical observation, the American College of Rheumatology Preliminary Criteria for the Diagnosis of Fibromyalgia (ACR), published in 2010, may be an ancillary resource for the subject. ACR 2010 is composed by 2 scores: the Generalized Pain Index (GDI) and the Symptom Severity Scale (SSS). Symptoms must be present for at least three months and the patient must not have any other disease that could explain the pain<sup>5</sup>. In 2011, the criteria suffered a small modification with a reduction in the number of somatic symptoms at the SSS. Also, the authors proposed an index based on the sum of the GDI and SSS called the Fibromyalgia Symptom Scales (FS) that ranges from 0 to 3, which provides valuable tools for monitoring<sup>6</sup>.

In 2016, a new modification restores the concept of generalized pain as a prerequisite for using the criteria, maintaining the scores as long as pain be present in 4 out of 5 established body areas<sup>7</sup>.

FM is multifactorial and the known aspects of its mechanism are central sensitization (accompanied by amplification of the perception of the painful stimulus) and distress<sup>8</sup>. The FM natural history can vary from patient to patient. For example, exposure to stressors, previous musculoskeletal disorders, illnesses, physical and emotional trauma can all represent FM aggravating events.

The frequent exposure to stressors during the life is a known fact for FM patients. A study<sup>9</sup> published a meta-analysis that showed association between the FM status with physical abuses, sexual abuse, smaller medical trauma, other stressors and emotional abuses. It was concluded that "stressors are likely to be one of many risk factors for FM which we argue is best approached from a biopsychosocial perspective".

The reaction to day-to-day life situations is influenced by the way patients consider these events stressful or not. A study recently proposed a theory to explain the emotional imbalance present at the FM patients. They consider that there is an overactive "threat" neural system and an inhibited "soothing" system<sup>10</sup>.

Distress related dysautonomia is a known feature of FM etiopathogenesis. So, it is essential to know how patients face daily life stressors to consider this aspect when dealing with their suffering. The stress has a close relation to other physiological process such as pain processing. Treating pain syndromes requires that doctors consider this relation role at these patients lives.

The main objective of this research was to determine the patients' perception of stressful events influencing the development of FM. The secondary objective was to assess the impact of acute stress in determining the future severity of FM.

## **METHODS**

It was performed an analytical cross-sectional observational study for the primary objective and a case-control for the secondary objective. Data were collected in 2020 at the FM outpatient clinic of Sorocaba Hospital Complex (*Conjunto Hospitalar de Sorocaba* - CHS) from questionnaires given to patients and analysis of medical records.

## Research subjects

Inclusion criteria: adult patients who met the criteria of ACR 2010, modified in 2016<sup>7</sup>.

Exclusion criteria: patients with cognitive impairment and those with incomplete medical records.

Groups: patients were divided in two groups according to the report or denying an aggravating stressful event along the evolution of the FM.

## Applied questionnaire

A - Questionnaire on demographic data clinical data and comorbidities: gender, age, marital status, occupational status, condition of diagnosis, time form diagnosis, symptom intensity and presence of associated diseases.

B - A direct question on the presence of a stressful event that have aggravated FM symptoms during its development.

C - FS: based on the sum of the scores of that make up the ACR 2010 and modified in 2011. It ranges from 0 to 31 where 0 is the best clinical condition, and 31 is the worst<sup>6</sup>.

D - FIQr: questions about daily tasks challenges, occupational difficulties, and intensity of symptoms. The total score ranges from 0 (no impact) to 100 (worst possible impact)<sup>11</sup>.

E - PHQ9: questionnaire that assess the presence of depressive symptom. The frequency of each symptom in the last two weeks is evaluated on a scale from 0 to 3 corresponding to the answers "not at all", "several days", "more than half of the days", and "almost every day", respectively<sup>12</sup>.

F - GAD-7: Instrument developed by a study (2007) for the assessment, diagnosis, and monitoring of anxiety. It consists of seven items, arranged on a four-point scale: 0 (never) to 3 (almost every day). The total score ranges from 0 to  $21^{13}$ .

## **Ethical aspects**

This research project was submitted to and approved by the Research Ethics Committee of Pontifical Catholic University of São Paulo (*Pontificia Universidade Católica de São Paulo* – Campus Sorocaba) under the opinion number CAAE: 30537620.2.0005373.

## Statistical analysis

Sampling was done by convenience. Descriptive statistics were used to present demographic variables and clinical data. The

T-test was used for associations and the Chi-square and Fisher's Exact tests for categorical variables between groups.

## **RESULTS**

Sixty one patients were evaluated. The majority were female patients (96.72%), with an average age of 50.38±9.5 years. Most were married or in a stable relationship (73.7%). More than half had a professional activity (54.10%), and 19.67% of patients were retired or receiving sick pay. As for the educational level, 44.26% had incomplete primary education, 16.39% had completed primary education, 34.43% had completed secondary education and only 4.92% had completed higher education.

The majority of patients (80.33%) were diagnosed by rheumatologists and the rest by doctors from other specialties. As for the time of diagnosis, 26.23% had been diagnosed less than a year before the survey, 59.02% more than a year and less than 10 years, and 14.75% more than 10 years before the survey. Eighteen percent had a previous diagnosis of psychiatric illness and 81.96% had somatic comorbidities. Only 24.6% of the patients had a family history of FM.

Regarding the intensity of symptoms measured by FS, the average was 24.1±5.14, and the impact, measured by FiQr, was 70.08±19.68. In emotional aspects, it was observed that the intensity of depression by PHQ9 was 16.23±6.30, and anxiety measured by GAD-7 was 13.77±4.92.

In relation of the patients' perception of stressful events that aggravated FM, about 59% reported the presence of acute stress during the evolution. Among the aggravating factors, the most prevalent was the death of a close relative, followed by family conflicts, financial problems and be a victim of violence.

It was not found a significant difference between the groups with and without stressful events for the age and PHQ-9 and GAD-7 scores. There was a significant association between the presence of aggravating stressful events, and FS (p<0.05) and FIQr, as seen at the table 1.

There was also a significant association with FIQr and the presence of aggravating episodes (p<0.05). The presence of aggravating events increases the FIQr score by 2.72 (IRR= 2.729885, Std Dev = 1.278386, z=2.14, p=0.032, 95% confidence interval 1.090267 and 6.835275).

As for the categorical variables, there was no significant difference between the groups with and without stressful events for gender, skin color, religion, education, marital status, and professional activity.

**Table 1.** Results on the aggravating impact of stressful events on fibromialgia follow up parameters

| Categories | Presence of stres-<br>sful events | Absence of stres-<br>sful events | p-value |
|------------|-----------------------------------|----------------------------------|---------|
| FS         | 25.4 =/- 4.0                      | 22.7 =/- 5.5                     | 0.04 *  |
| FIQr       | 78.23 +/-12.78                    | 63.2 +/- 22.0                    | 0.0002* |
| PHQ9       | 15.3 +/- 6.1                      | 17.8 +/- 5.9                     | 0.10    |
| GAD-7      | 12.7 +/- 4.8                      | 14.4 +/- 4.7                     | 0.09    |

FS = Fibromyalgia index; FIQr = Revised fibromyalgia impact index; PHQ9 = Patient health questionnaire 9; GAD-7 = General anxiety disorder 7.

## DISCUSSION

FM is a syndrome that affects between 0.66% and 4.4% of the Brazilian population. The sample in this study showed an epidemiological profile with a predominance of women aged between 35 and 60, which is in line with the literature<sup>2</sup>. With regard to educational and professional data, only 39.35% of the patients had completed high school and only three patients had completed higher education. With regard to occupation, 54.1% of the patients were employed, 23.6% were "housewives" and 19.67% were retired or on sick leave. This population was cared by the public service, which treats low-income patients. These data are similar to those recently published by a study on gender, age, marital status and occupational aspect. There is a difference in the level of education, with a low number of people with completed higher education in the sample of this research<sup>14</sup>.

As for the assessment of the FM symptoms, the average FI score (0 to 31) was 24.13±5.14. The average FiQr index was 70.08±19.68, scores. Both being considered as severe<sup>15</sup>. This research was developed at a tertiary health care unit, which may explain this patients' profile. The Brazilian Registry on Fibromyalgia (*Estudo Epidemiológico da Fibromialgia no Brasil* - Epifibro) showed similar data on these evaluation tools (FS – 22,19 =/-5,8; FIQr – 68±17.1)<sup>16</sup>.

Concerning patients' mental health, the average PHQ9 was 16.23±6.30, indicating moderate to severe depressive disorder. The mean GAD-7 was 13.77±4.92, also suggesting anxiety moderate to severe 17. Thus, this group presents severe symptoms such as depression, and anxiety that can contribute to a greater impact on life quality, interpersonal relationships, and work capacity. As for the PHQ9, a study found equivalent scores associated to moderate and severe symptoms measured by FIQr. It shall be considered that the studied patients have been followed at a tertiary care medical center 18.

Assessing quality of life through questionnaires has been recognized as an important tool for the knowledge in healthcare. In this sense, it is possible to evaluate subjective factors, as these questionnaires allow a more objective assessment<sup>13,14</sup>. Patients with chronic diseases, including FM, tend to have a worse quality of life<sup>14</sup>. According to the American Anxiety and Depression Association<sup>15</sup>, around 20% of chronic pain patients also have a mood disorder. In this research, 18.03% of patients had a previous diagnosis of anxiety and depressive disorders.

When questioning the presence of acute stressful events in the patients' experience, it was observed that such factors influence both the symptoms of intensity and the evolution of FM. It was observed that reporting the presence of stressors was considered important by patients. An important aspect is that patients' reports of aggravating stressful events during the course of their FM increased their FIQr scores. Family members grief stood out as the most frequently mentioned stressor. One of the most cited stressors in the literature was physical abuse during childhood<sup>19</sup>. This study's design based on interviews may have contributed to the absence of reports regarding childhood trauma, considering that there is reluctance among many patients to mention these situations. Also, case-control studies may differ

from prospective cohorts in results due to the memory of the patients interviewed<sup>20</sup>.

In relation to the positive points of this research, the importance of the topic addressed was highlighted and that its knowledge brings good opportunities in terms of medicine to deal with stress management. The limitation of this research is its methodology. A positive cohort study would value the findings. Another negative aspect is that this study, carried out in a tertiary healthcare environment, might not represent the entire population of patients with FM. Newer research with a larger number of patients and at a primary care setting may amplify this knowledge.

The most obvious conclusion is that, from a neurobiological point of view, stress mechanisms override the mechanisms responsible for the pathophysiology of the symptoms that make up the FM syndrome<sup>21</sup>.

## CONCLUSION

There is a significant association between aggravating stressful events and higher scores of FM assessment indexes and their impact. The main stressors mentioned were financial difficulties, family grief and accompanying clinical illnesses.

## **AUTHORS' CONTRIBUTIONS**

Ana Julia Campi Nunes de Oliveira

Research

Thaís Di-Giovanni

Research

Cassiano Henrique Giovanini Vanzelli

Data Collection, Writing - Preparation of the Original

Bruno de Mendonça Moraes Araujo

Data Collection, Research

Reinaldo José Gianini

Statistical Analysis, Research, Methodology

José Eduardo Martinez

Conceptualization, Writing - Review and Editing, Supervision

## **REFERENCES**

- Heymann RE, Paiva ES, Martinez JE, Helfenstein JR, Rezende MC, Provenza JR, Souza EJ. Novas diretrizes para o diagnóstico da fibromialgia. Rev Bras Reumatol. 2017;57(Supp 2):S467-S476.
- Freitas RPA, Andrade SC, Spyrides MHC, Micussi MTABC, Sousa MBC. Impacto do apoio social sobre os sintomas de mulheres brasileiras com fibromialgia. Rev Bras Reumatol. 2017;57(3):197-203.

- Marques AP, Santo ASE, Berssaneti AA, Matsutani LA, Yuan SLK. A prevalência de fibromialgia: atualização da revisão de literatura. Rev Bras Reumatol. 2017;57(4):356-63.
- Martinez JE. Fibromialgia: impacto na qualidade de vida, medidas de desfecho e acompanhamento clínico. In: Ranzolin, A, Chiuchietta FA, Heymann RE. Dores musculoesqueléticas difusas e localizadas. 2ª Ed. São Paulo, Planmark. 2010; 76-82p.
- Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB, Yunus MB. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken). 2010;62(5):600-10.
- Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia. J Rheumatol. 2011;38(6):1113-22.
- Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, Mease PJ, Russell AS, Russell IJ, Walitt B. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016;46(3):319-29.
- Paiva ES. Fisiopatologia da Fibromialgia. In: Ranzolin, A, Chiuchietta FA, Heymann RE. Dores musculoesqueléticas difusas e localizadas. 2ª Ed. São Paulo, Planmark. 2010 54-64p.
- Kaleycheva N, Cullen AE, Evans R, Harris T, Nicholson T, Chalder T. The role
  of lifetime stressors in adult fibromyalgia: systematic review and meta-analysis of
  case-control studies. Psychol Med. 2021;51(2):177-93.
- Pinto AM, Geenen R, Wager TD, Lumley MA, Häuser W, Kosek E, Ablin JN, Amris K, Branco J, Buskila D, Castelhano J, Castelo-Branco M, Crofford LJ, Fitzcharles MA, López-Solà M, Luís M, Marques TR, Mease PJ, Palavra F, Rhudy JL, Uddin LQ, Castilho P, Jacobs JWG, da Silva JAP. Emotion regulation and the salience network: a hypothetical integrative model of fibromyalgia. Nat Rev Rheumatol. 2023;19(1):44-60.
- Paiva ES, Heymann RE, Rezende MC, Helfenstein JM, Martinez JE, Provenza JR, Bennett RM. A Brazilian Portuguese version of the Revised Fibromyalgia Impact Questionnaire (FIQR): a validation study. Clin Rheumatol. 2013;32(8):1199-206.
- Santos IS, Tavares BF, Munhoz TN, Almeida LS, Silva NT, Tams BD, Patella AM, Matijasevich A. Sensitivity and specificity of the Patient Health Questionnaire-9 (PHQ-9) among adults from the general population. Cad Saude Publica. 2013;29(8):1533-43.
- 13. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-7.
- Fors EA, Wensaas KA, Helvik AS. Prevalence and characteristics of fibromyalgia according to three fibromyalgia diagnostic criteria: a secondary analysis study. Scand J Pain. 2024;24(1):20230143
- Salaffi F, Di Carlo M, Bazzichi L, Atzeni F, Govoni M, Biasi G, Sarzi-Puttini P. Definition of fibromyalgia severity: findings from a cross-sectional survey of 2339 Italian patients. Rheumatology. 2021;60(2):728-36.
- Martinez JE, Paiva ES, Rezende MC, Heymann RE, Helfenstein M Jr, Ranzolin A, Provenza JR, Ribeiro LS, Souza EJR, Feldman DP, Assis MR. EpiFibro (Brazilian Fibromyalgia Registry): data on the ACR classification and diagnostic preliminary criteria fulfillment and the follow-up evaluation. Rev Bras Reumatol Engl Ed. 2017;57(2):129-33.
- Gaskin ME, Greene AF, Robinson ME, Geisser ME. Negative affect and the experience of chronic pain. J Psychosom Res. 1992;36(8):707-13.
- Singh R, Rai NK, Pathak A, Rai J, Pakhare A, Kashyap PV, Rozatkar AR, Mishra S, Mudda S. Impact of fibromyalgia severity on patients mood, sleep quality, and quality of life. J Neurosci Rural Pract. 2024;15(2):320-6.
- Kaleycheva N, Cullen AE, Evans R, Harris T, Nicholson T, Chalder T. The role of lifetime stressors in adult fibromyalgia: systematic review and meta-analysis of casecontrol studies. Psychol Med. 2021;51(2):177-93.
- Santos AMB, Assumpção A, Matsutani LA, Pereira CAB, Lage LV, Marques AP. Depressão e qualidade de vida em pacientes com fibromialgia. Rev Bras Fisioter. 2006;10(3):317-24.
- Van Houdenhove B, Egle U, Luyten P. The role of life stress in fibromyalgia. Curr Rheumatol Rep. 2005;7(5):365-70.