

Persistent musculoskeletal presentations post-chikungunya fever: a case series in a state in northeast Brazil

Apresentações musculoesqueléticas persistentes pós-febre chikungunya: uma série de casos em um estado do nordeste brasileiro

Presentaciones musculoesqueléticas persistentes posfiebre chikungunya: una serie de casos en un estado del noreste de Brasil

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Abstract

Chikungunya fever (CF) is an arbovirolosis caused by the Chikungunya virus (CHIKV). The main characteristic of CF is joint pain and more than half of infected patients experience chronic conditions. This case series study evaluated the persistent musculoskeletal presentations of CF in a sample of 72 patients with persistent symptoms (≥ 1 month) after CF confirmed by laboratory tests (detection of CHIKV by polymerase chain reaction [PCR] and/or immunoglobulin [Ig]M and/or IgG). The patients were followed up for 12 months after treatment at the outpatient clinic of the University Hospital of the Federal University of Sergipe (*Hospital Universitário da Universidade Federal de Sergipe - HU/UFS*). They were evaluated at admission and after 1 month, 2 months, and then every 3 months for up to 12 months. Painful and/or swollen joints, periarticular symptoms, other important findings on physical examination, and visual analogue pain scale (VAS) were evaluated during all consultations. Main results: Among the patients evaluated, 84.7% were

female, the mean age was 53.8 years, and the mean duration of musculoskeletal complaints was 6 months. Comorbidities were present in 61.1% of patients and previous musculoskeletal disease was present in 69.4%. The most frequent presentation on admission was polyarticular, which occurred in 76.4% of cases. The most affected joints were the hands, knees, ankles, and feet. VAS on admission was intense in 66.7% of patients. Tenosynovitis was present in 44.5% of patients and was more frequently reported in the ankles. Corticosteroids and chloroquine were administered to 65.3% and 31.98% of patients, respectively. The findings indicated that persistent musculoskeletal presentations occur frequently after CF. These results provide a better understanding of patient profiles, musculoskeletal involvement, and CF progression, and may guide effective strategies for therapeutic management.

Keywords: Arbovirose; Arthralgia; Chikungunya fever.

Resumo

A febre Chikungunya (FC) é uma arbovirose causada pelo vírus Chikungunya (CHIKV). A principal característica da FC é a dor nas articulações e mais da metade dos pacientes infectados apresentam condições crônicas. Este estudo de série de casos avaliou as apresentações musculoesqueléticas persistentes de FC em uma amostra de 72 pacientes com sintomas persistentes (rsimês) após FC confirmada por exames laboratoriais (detecção de CHIKV por reação em cadeia da polimerase [PCR] e/ou imunoglobulina [Ig]M e/ou IgG). Os pacientes foram acompanhados por 12 meses após o tratamento no ambulatório do Hospital Universitário da Universidade Federal de Sergipe (Hospital Universitário da Universidade Federal de Sergipe - HU/UFS). Eles foram avaliados na admissão e após 1 mês, 2 meses e depois a cada 3 meses por até 12 meses. Articulações dolorosas e/ou edemaciadas, sintomas periarticulares, outros achados importantes no exame físico e escala visual analógica de dor (EVA) foram avaliados durante todas as consultas. Principais resultados: Entre os pacientes avaliados, 84,7% eram do sexo feminino, a média de idade foi de 53,8 anos e a duração média das queixas musculoesqueléticas foi de 6 meses. Comorbidades estavam presentes em 61,1% dos pacientes e doença musculoesquelética prévia em 69,4%. A apresentação mais frequente na admissão foi a poliarticular, que ocorreu em 76,4% dos casos. As articulações mais acometidas foram as mãos, joelhos, tornozelos e pés. A EVA na admissão foi intensa em 66,7% dos pacientes. A tenossinovite esteve presente em 44,5% dos pacientes e foi mais frequentemente relatada nos tornozelos. Corticosteróides e cloroquina foram administrados a 65,3% e 31,98% dos pacientes, respectivamente. Os achados indicaram que as apresentações musculoesqueléticas persistentes ocorrem frequentemente após a FC. Esses resultados fornecem uma melhor compreensão do perfil dos pacientes, do envolvimento musculoesquelético e da progressão da FC, e podem orientar estratégias eficazes para o manejo terapêutico.

Palavras-chave: Arbovirose; Artralgia; Febre Chikungunya.

Resumen

La fiebre chikungunya (FQ) es un arbovirus causado por el virus Chikungunya (CHIKV). La característica principal de la FQ es el dolor en las articulaciones y más de la mitad de los pacientes infectados tienen condiciones crónicas. Este estudio de serie de casos evaluó las presentaciones musculoesqueléticas persistentes de la FQ en una muestra de 72 pacientes con síntomas persistentes (rsimes) después de la FQ confirmada por laboratorio (reacción en cadena de la polimerasa [PCR] detección de CHIKV y/o inmunoglobulina [Ig]M y/o IgG). Los pacientes fueron seguidos durante 12 meses después del tratamiento en la consulta externa del Hospital Universitario de la Universidad Federal de Sergipe (Hospital Universitario de la Universidad Federal de Sergipe - HU/UFS). Se evaluaron al ingreso y después de 1 mes, 2 meses y luego cada 3 meses hasta 12 meses. Articulaciones dolorosas y/o inflamadas, síntomas periarticulares, otros hallazgos importantes en el examen físico y la escala analógica visual del dolor (EVA) fueron evaluados durante todas las visitas. Principales resultados: Entre los pacientes evaluados, el 84,7% eran del sexo femenino, la edad media fue de 53,8 años y la duración media de las molestias musculoesqueléticas fue de 6 meses. Las comorbidades estaban presentes en el 61,1% de los pacientes y la enfermedad musculoesquelética previa en el 69,4%. La presentación más frecuente al ingreso fue la poliarticular, que se presentó en el 76,4% de los casos. Las articulaciones más afectadas fueron las manos, rodillas, tobillos y pies. La EVA al ingreso fue intensa en el 66,7% de los pacientes. La tenosinovitis estuvo presente en el 44,5% de los pacientes y se notificó con mayor frecuencia en los tobillos. Se administraron corticoides y cloroquina al 65,3% y al 31,98% de los pacientes, respectivamente. Los hallazgos indicaron que las presentaciones musculoesqueléticas persistentes ocurren con frecuencia después de la FQ. Estos resultados proporcionan una mejor comprensión del perfil de los pacientes, la afectación musculoesquelética y la progresión de la FQ, y pueden orientar estrategias eficaces para el manejo terapéutico.

Palabras clave: Arbovirus; Artralgia; Fiebre Chikungunya.

1. Introduction

Chikungunya fever (CF) is an arbovirose caused by the Chikungunya virus (CHIKV), which is transmitted by the bite of female *Aedes aegypti* and *Aedes albopictus* mosquitoes. The name derives from a Makonde word and describes the stooped posture of people with severe arthralgia (Weaver & Lecuit, 2015).

In Brazil, the first CF case was confirmed in September 2014 in Oiapoque, Amapá, with almost simultaneous cases reported in Feira de Santana, Bahia. Since then, CF cases have been reported in different states of Brazil (Silva, 2018).

In 2016, Sergipe had the highest incidence rate of CF in northeastern Brazil (108.2 cases/100,000 inhabitants) (4). In 2020, Sergipe ranked second among states in the northeast, with an incidence rate above 100 cases/100,000 inhabitants (165.9 cases/100,000 inhabitants), second to the state of Bahia, with 273.1 cases/100,000 inhabitants (Brasil, 2020). The higher incidence in northeastern states is attributed to the favorable weather, the presence of the vector, and the deficient basic sanitation conditions in the region, which increase mosquito proliferation and disease spread (Cunha & Trinta, 2017).

Acute CHIKV infection is symptomatic in most (approximately 80%) of cases. After the acute phase, patients can progress to subacute (≥ 30 days to 3 months) or chronic (≥ 90 days) phases (Simon et al., 2015).

The prevalence of chronic rheumatologic conditions after CF infection ranges from 14.4% to 87.2% (Marques et al., 2017). The patterns of chronic joint involvement include persistent (20-40%) or recurrent (60-80%) complaints. Up to 72% of patients presenting significant initial improvement may have recurrences, with intervals ranging from 1 week to several years (Javelle et al., 2015).

In the chronic phase, the most frequently affected joints are the knees, ankles, and small distal joints of the upper and lower limbs (Vairo et al., 2019). However, greater proximal (elbows, shoulders, and hips) and axial (neck) involvement has been reported (Nisar & Packianathan, 2017). Evidence indicates the development of chronic rheumatic diseases after CHIKV infection, with the main rheumatic presentations of CHIKV infection including arthritis and arthralgia (Benjamanukul et al., 2021).

In Brazil, no studies have yet reported the monitoring of patients with persistent musculoskeletal presentations after CF and there are few protocols guiding its conduct and treatment. The present study was conducted in a region with a high incidence of CF and assessed the persistent musculoskeletal presentations in CHIKV-infected patients followed up for 12 months.

2. Methodology

Study design. This case series study included a sample of 72 patients with musculoskeletal complaints for at least 1 month after CF diagnosis from an outpatient clinic and who were followed up at a University Hospital in northeastern Brazil for 1 year.

This study evaluated patients aged over 18 years who presented joint and/or periarticular pain associated or not with joint edema at the onset or significant subsequent worsening (if previous rheumatologic disease) of confirmed CF (IgG and/or IgM serology and/or CHIKV polymerase chain reaction [PCR]) progressing for at least 1 month, who agreed to participate in the study. Patients with a new joint condition or worsening of an existing condition justified by another infectious or neoplastic disease were excluded.

2.1 Ethical aspects

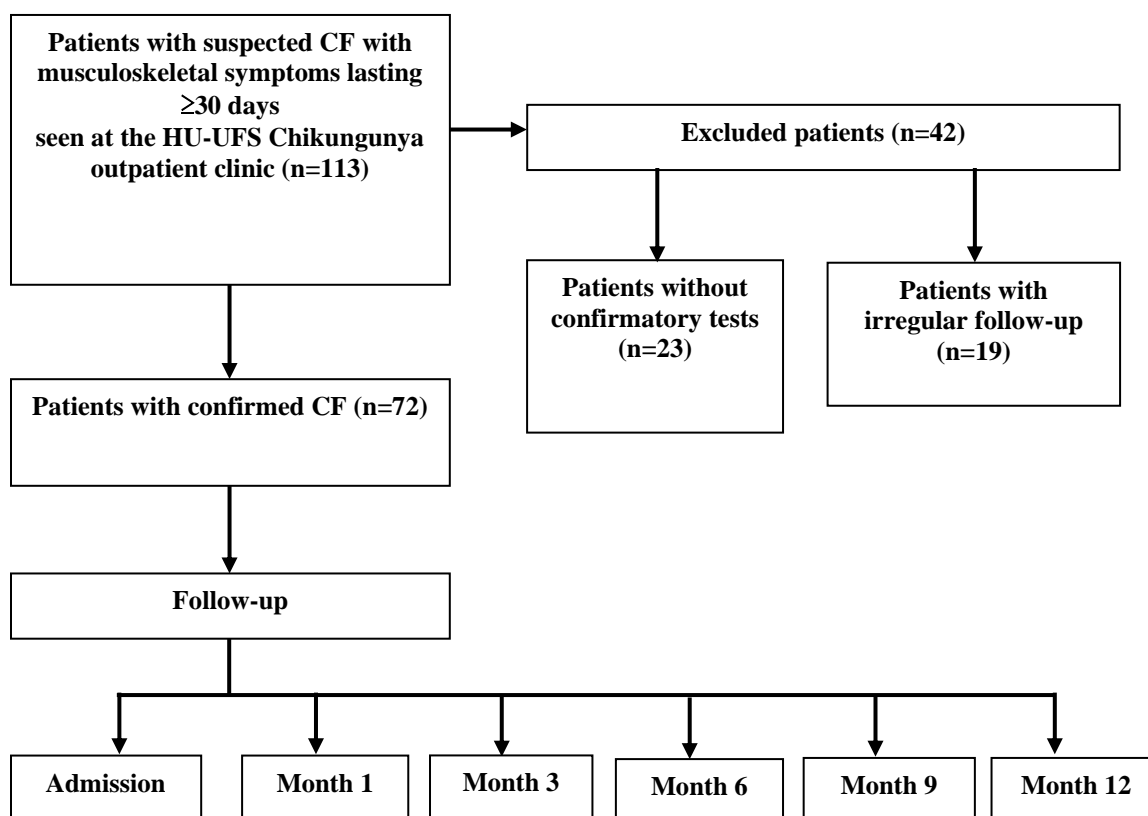
The study was approved by the Research Ethics Committee of the Federal University of Sergipe (*Comitê de Ética em Pesquisa envolvendo seres humanos da Universidade Federal de Sergipe - CEP-HU/UFS*) and met the recommendations of Resolution No. 466/2012 of the National Health Council, opinion number 1.486.302 and CAAE number 54835916.2.0000.5546. Data collection started after approval by the CEP-HU/UFS and included patients who agreed to participate by signing the Informed Consent Form (ICF).

2.2 Data collection and patient follow-up

Patients referred from other outpatient clinics of the same hospital underwent an initial assessment. Only those meeting the clinical-epidemiological criteria for suspected CF were followed up. The inclusion criteria were a sudden onset of fever $>38.5^{\circ}\text{C}$, severe arthralgia or acute onset of arthritis not explained by other conditions, a resident or having visited endemic or epidemic areas up to 2 weeks before symptom onset, and having epidemiological association with a confirmed case (Brasil, 2015).

After admission, the patients were followed up in subsequent consultations after 1 month, 2 months, and then every 2 months until for a total of 12 months. Anamnesis and physical examination were always performed by the same examiner. After 1 year of follow-up, the asymptomatic patients were discharged. The patients with persisting musculoskeletal symptoms continued to be monitored at the rheumatology outpatient clinic or were referred to other specialties, if necessary, at the HU/UFS.

Flowchart 1 - Flowchart of the study participants.



Source: Authors (2021).

The data were cataloged in Excel, version 2013. Relative and absolute frequencies were used for qualitative data while central tendency (mean) and dispersion (standard deviation) measures were used for quantitative data. Chi-square and Fisher's exact tests were used to compare qualitative variables. Analysis of variance (ANOVA) was used to compare quantitative variables and qualitative variables with normal distributions, while Kruskal–Wallis tests were used for comparisons of variables with non-normal distributions. The normality of the distributions was verified using Shapiro–Wilk tests. McNemar and Stuart Maxwell tests were used for longitudinal evaluations. R version 3.6.0 was used for statistical analysis, with significance set at 5% for all tests.

3. Results

Among a total of 113 patients in the outpatient clinic, this study included 72 patients with persistent musculoskeletal symptoms after CF confirmed by laboratory tests. Their sociodemographic and clinical characteristics are described in Tables 1 and 2, respectively.

Table 1 – Patient sociodemographic characteristics.

Variable	Category	No.	%
Sex	Female	61	84.7
	Male	11	15.3
Age in years (mean and standard deviation)		53.8 ± 13.5	
Origin	Aracaju, Sergipe	53	73.6
	Inland cities	18	25
	Other state	1	1.4
Marital status	Married	40	55.5
	Not married	20	27.8
	Widower	10	13.9
	Separated	2	2.8
Variable	Category	No.	%
Education	Illiterate	7	9.7
	Incomplete elementary education	9	12.5
	Complete elementary education	16	22.2
	Incomplete high school education	2	2.8
	Complete high school education	27	37.5
	Incomplete higher education	2	2.8
	Complete higher education	9	12.5
Family income	≤1 minimum salary	54	75
	≥1 minimum salaries	18	25

Source: Authors (2021).

Table 2 – Patient sociodemographic characteristics on admission.

Variable	Category	No.	%
Time from symptom onset until presentation at the clinic (months, mean and standard deviation)		6 ± 4.6	
Visits to the Emergency Room before arriving at the appointment (mean and standard deviation)		1.4 ± 0.9	
Disease stage at admission	Subacute	20	27.8
	Chronicle	52	72.2
Non-rheumatological comorbidities	Present	44	61.1
	Absent	28	38.9
Types of comorbidities	SAH	28	38.9
	DLP	10	13.9
	DM	8	18.2
	Psychiatric illness	2	2.8

	Heart disease	2	2.8
	Hypothyroidism	2	2.8
	Psoriasis	2	2.8
	Asthma	1	1.4
	Multiple sclerosis	1	1.4
	Inflammatory bowel disease	1	1.4
	Alcoholism	0	0.0
	Smoking	0	0.0
Initial joint condition	Monoarticular	10	13.9
	Oligoarticular	7	9.7
	Polyarticular	55	76.4
Morning stiffness	Absent	45	62.5
	<1h	14	19.4
	≥1h	13	18.1
Number of painful joints (mean and standard deviation)		10.3 ± 8	
Number of swollen joints (mean and standard deviation)		3.1 ± 5	
VAS	No pain	1	1.4
	Mild (1, 2, 3)	5	6.9
	Moderate (4, 5, 6)	18	25
	Severe (7, 8, 9, 10)	48	66.7
Tenosynovitis	Ankles	29	40.3
	Fists	3	4.2
	Absent	40	55.5
Plantar fasciitis	Present	7	9.7
	Absent	65	90.3
Hand paresthesia	Present	58	80.5
	Absent	14	19.5
Axial pain (cervical, thoracic, and lumbar spine)	Present	18	25
	Absent	54	75
Previous rheumatic disease	Present	50	69.4
	Absent	22	30.5
Worsening of the rheumatologic condition after CF	Yes	49	98
	No	1	2
Serology and CHIKV PCR	IgM only	7	9.7
	IgG only	37	51.4
	PCR only	24	33.3
	IgM + IgG	2	2.8
	PCR + IgM	1	1.4
	PCR + IgG	1	1.4
	PCR + IgM + IgG	0	0

Initial inflammatory tests	No increase	64	88.9
	ESR only	3	4.2
	CRP only	1	1.4
	ESR + CRP	4	5.5
Serology for hepatitis B, C, and HIV	Present	0	0
	Absent	72	100
Radiographic changes	Present	34	47.2
	Absent	38	52.8

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; PCR: polymerase chain reaction; SAH: systemic arterial hypertension; DM: diabetes mellitus; DLP: dyslipidemia. Source: Authors (2021).

The patients had experienced musculoskeletal complaints for a mean of 6 months before presenting to the outpatient clinic. On admission, 52 (72.2%) and 20 (27.8%) patients were in the chronic (≥ 3 months) and subacute (≥ 30 days) phases of the disease, respectively. Among the patients admitted during the subacute phase, 13 (65%) developed chronic disease. Comorbidities were present in 44 patients (61.1%), most commonly systemic arterial hypertension (SAH), diabetes mellitus (DM), and dyslipidemia (DLP). Among these 44 patients, 32 (44.4%) had only one comorbidity, four (5.6%) had two, seven (9.7%) had three, and one (1.4%) had four comorbidities.

Previous rheumatologic diseases (previous history and/or changed radiography on admission) were absent in 22 patients (30.5%) and present in 50 (69.5%). Among those with previous rheumatologic diseases, 98% reported a worsening of symptoms after CF.

The onset of the joint condition was mostly polyarticular and present in 55 patients (76.4%). Tenosynovitis was reported in 32 patients (44.5%) and occurred more frequently in the ankles. Hand paresthesia occurred in 58 patients (80.5%).

Increased levels of inflammatory markers (erythrocyte sedimentation rate [ESR] and/or C-reactive protein [CRP]) were present in eight patients on admission (11.1%). Of these, five had normalized levels in the third month and two in the sixth month, while one maintained high levels of inflammatory markers (ESR and CRP) until month 12. Three patients (4.2%) were positive for rheumatoid factor (RF).

Radiographic changes were present in 34 patients (47.2%), with knee osteoarthritis the most frequent finding, followed by calcaneal enthesopathy, and hand osteoarthritis. No patient with progression of the joint condition lasting for more than 3 months had erosive lesions on the hands, wrists, feet, and/or ankles.

The most prevalent treatments prescribed during the follow-up were analgesics (90.3%) and prednisone (65.3%) (Table 3).

Table 3 - Treatments prescribed during treatment for CF.

Treatment	N	%
Analgesics	63	90.3
Opioids	12	18.1
NSAIDs	35	48.6
Prednisone	47	65.3
Chloroquines	23	31.9
Methotrexate	8	11.1
Leflunomide	1	1.4
Glucosamine sulfate and chondroitin	8	11.1
Colchicine	1	1.4

NSAIDs: nonsteroidal anti-inflammatory drugs. Source: Authors (2021).

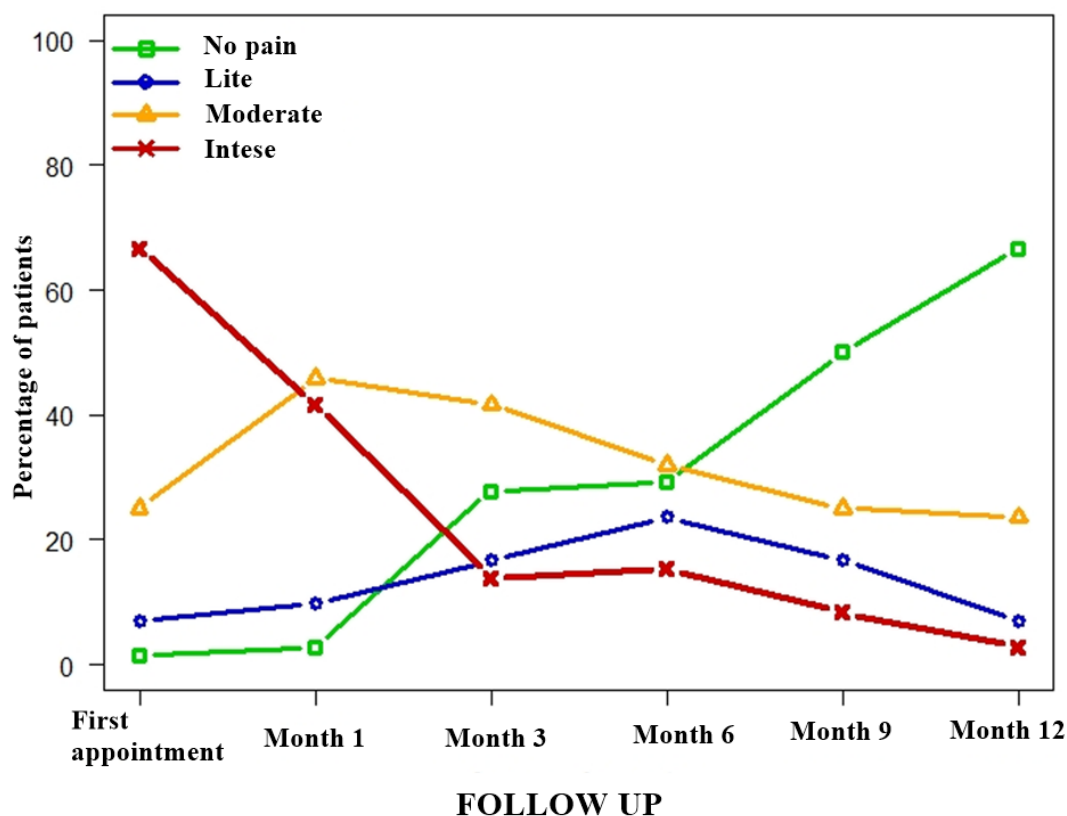
Sixty-eight patients (94.4%) had already used corticosteroids by prescription from another doctor or on their own before admission. At the clinic, prednisone was prescribed to 47 patients (65.3%). At the last evaluation (month 12), six patients (8.3%) continued low-dose prednisone (5 mg/day).

Among disease-modifying antirheumatic drugs (DMARD), chloroquine (chloroquine diphosphate 250 mg/day or hydroxychloroquine 400 mg/day) was the most often prescribed (23 patients, 31.9%). While physical therapy was prescribed to 68 patients (94.4%), only 22 (30.5%) were able to perform it regularly.

The monitoring of the musculoskeletal condition of the patients included three time points for comparisons (months 0, 6, and 12), in which pain was evaluated by VAS and the presence of painful and swollen joints on physical examination.

On admission (month 0), 71 of 72 patients were in pain, 48 of whom showed severe pain (VAS ≥ 7). In the last month of follow-up (month 12), 48 patients had no pain and 24 had some degree of pain (Figure 1). There was a statistically significant improvement in pain ($p < 0.001$) during follow-up.

Figure 1 - Pain assessment in patients.



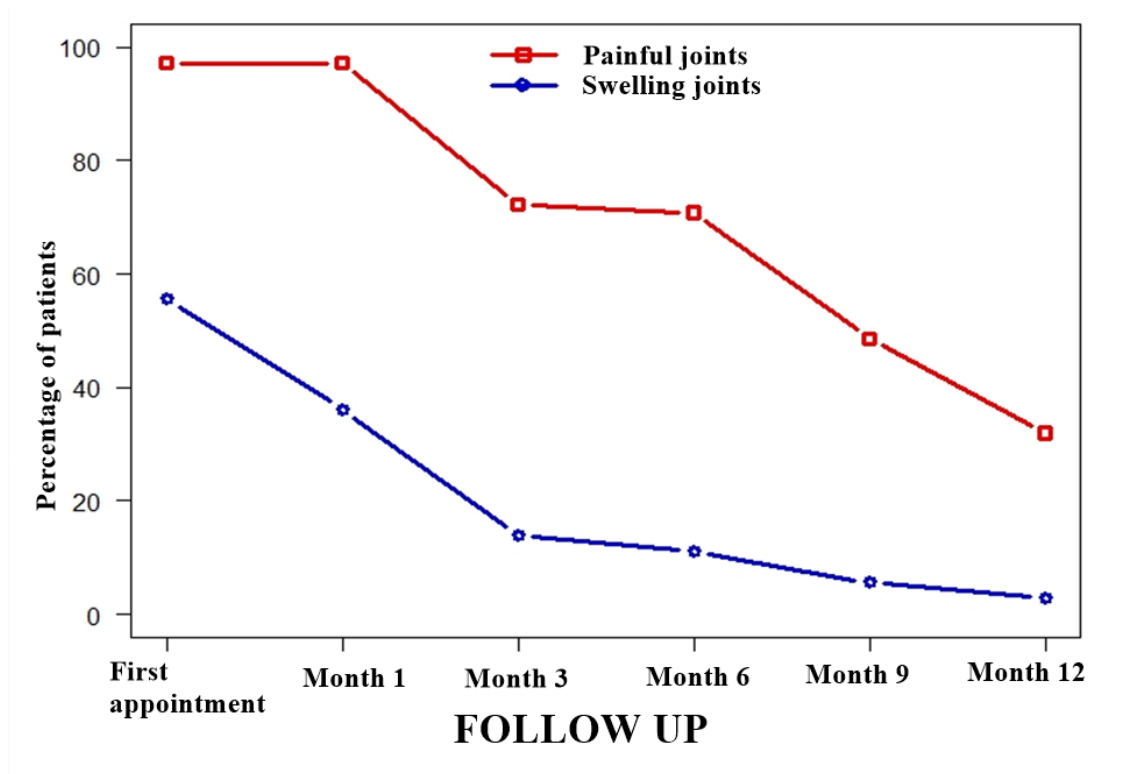
Source: Authors (2021).

The evaluation of painful joints showed a significant improvement during follow-up ($p < 0.001$), with a decreased number of painful joints. Of the 70 people with painful joints at the beginning of treatment (month 0), 20 had no painful joints at month 6. Moreover, among the 51 people with painful joints at month 6, 28 improved while 23 still felt pain on joint palpation at the end of follow-up (month 12) (Figure 2).

The evaluation of swollen joints also showed a significant improvement ($p < 0.001$). Of the 40 patients with swollen joints at the beginning of treatment, 32 had no swollen joints in month 6. Moreover, of the eight people with persisting swollen joints at month 6, six had improved at month 12, while two showed remaining joint swelling on physical examination at the end of follow-up (Figure 2).

Thirteen patients (18%) showed a cyclical progression of the joint condition and pain, with improvement and worsening during follow-up.

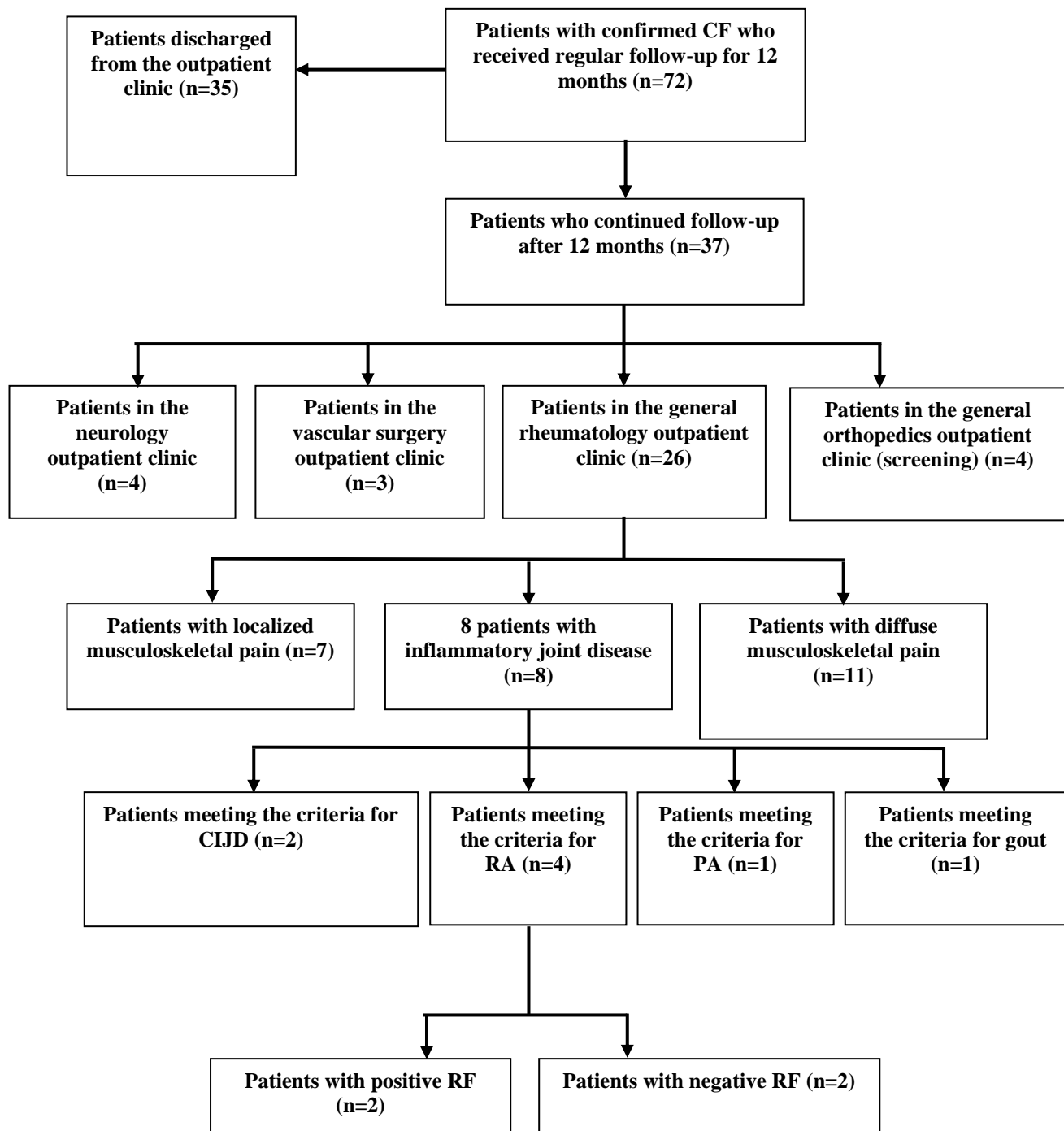
Figure 2 - Presence of painful and swollen joints during the follow-up period.



Source: Authors (2021).

Twenty-three patients (31.9%) were referred for continued follow-up in general rheumatology, four in orthopedics (5.5%), four in neurology (5.5%), one in vascular surgery (1.4%), two in rheumatology and vascular surgery (2.8%), and one in rheumatology and neurology (1.4%). Of the 26 patients referred to the rheumatology clinic, 11 (42.3%) had diffuse musculoskeletal pain, seven (26.9%) had localized musculoskeletal pain, and eight (30.8%) had chronic inflammatory joint disease. Among those with chronic inflammatory joint disease, four (50%) met the criteria for rheumatoid arthritis (RA), one (12.5%) for psoriatic arthritis (PA), two (25%) for post-Chikungunya chronic inflammatory joint disease (CIJD), and one (12.5%) for gout.

Flowchart 2 - Of patient progression and referrals to other specialties after 12 months of follow-up.



Source: Authors (2021).

4. Discussion

This study was motivated by the first CF outbreak in Brazil in 2016, when there were more reported cases in the country and in Sergipe, with an increasing number of new cases in the last 5 years.

The mean duration of musculoskeletal symptoms until the patients presented to the Chikungunya outpatient clinic was 6 ± 4.7 months, with two patients reporting joint complaints that had lasted for 2 years. No previous studies in Brazil have described the characteristics or monitored the progression of musculoskeletal presentations after CF over time. However, several studies, mostly retrospective studies, have also reported the persistence of joint complaints (Essackjee et al., 2013 and Huits et

al., 2018). One of the largest retrospective studies on patients infected with CHIKV, conducted in the Réunion Islands, reported the persistence of symptoms in patients more than 6 years post-CF (Arroyo & Vilá, 2015).

In the present study, the most frequent comorbidities were SAH, DM, and DLP. Patients with previous rheumatologic disease were defined as those with a previous rheumatologic history and/or previous joint damage on admission radiography. Most patients showed previous rheumatologic disease, with a predominance of worsening of the joint condition after CF (Runowska et al., 2018).

We observed no association between the presence of comorbidities and/or rheumatologic history and a more intense condition at the beginning of the follow-up. Regarding the characterization of the joint condition, the most frequent presentation was polyarticular, most often affecting the hands (wrists, proximal interphalangeal, and metacarpophalangeal joints), knees, ankles, and feet, consistent with previous studies (Marques et al., 2016 and Essackjee et al., 2013), indicating that polyarthralgia, especially distal, showed the most frequent presentation in acute, subacute, and chronic phases.

Finger paresthesia was observed in 80.5% of patients. Electroneuromyographical assessment was not possible in these patients, even when requested, due to difficulties in scheduling this test. However, a case series with a population also from Sergipe by Neves and Nunes (Neves & Nunes, 2018) of 29 patients with hand paresthesia after CF reported that 93% of the studied median nerves showed carpal tunnel syndrome in the electrophysiological studies.

In the present study, CHIKV was confirmed by laboratory tests, as it was the first outbreak of the disease, to confirm that the persistent musculoskeletal complaints were attributed to CF. Then, the 72 patients had CHIKV confirmation by serology and/or viral PCR.

Of the 72 patients, 26 were positive for CHIKV by PCR even 1 month after experiencing CF. We cannot conclude that these patients had persisting virus in the blood or had previously been infected by other viruses, confusing the condition with CF. There may also have been an error in the dates reported by patients regarding their symptom onset.

Inflammatory tests (ESR and CRP) were increased on admission in eight patients (11.1%), being normalized during follow-up. Only one patient maintained high ESR and CRP until the end of follow-up, meeting the criteria for RA. The literature describes increased inflammatory tests as a frequent finding in CF patients (Vu et al., 2017 and Hibel et al., 2021). The low frequency found in this study could be associated with the previous use of corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs) in patients before starting follow-up.

The radiographs of the hands, wrists, ankles, and feet of the 51 patients in the chronic phase of the disease showed no joint lesions typical of RA (cysts, bone erosions, and juxta-articular osteopenia). In contrast, radiographs of the affected joints of patients with suspected osteoarthritis showed degenerative changes typical of osteoarthritis (subchondral sclerosis, osteophytosis, and reduced joint space) in 34 of the 72 patients, with a predominance of knee osteoarthritis and spondylarthrosis.

In the clinic setting, the therapeutic approach was based on the recommendations of the Brazilian the Ministry of Health and Brito et al. (2016). Most patients (90.3%) reported oral or injectable steroid use on their own or prescribed by another physician for short periods before presenting to the outpatient clinic. In general, patients reported short-term steroid use (5–7 days), mainly in the subacute phase of the disease, with joint pain and inflammation worsening after discontinuation who highlighted the risk of a rebound effect in arthralgia, arthritis, and tenosynovitis (Page, 2012).

At the outpatient clinic, 65.3% of the patients were prescribed prednisone (20 mg/day), with progressive weaning for 30 days until discontinuation. When necessary, prednisone was repeated in short cycles with efforts to gradually wean off treatment. At the last evaluation (month 12), six patients were under low-dose prednisone therapy.

Chloroquines were the most commonly prescribed synthetic DMARDs in the outpatients setting. Methotrexate (MTX) was prescribed in eight patients with chronic musculoskeletal complaints who met the criteria for inflammatory joint disease.

One patient meeting the criteria for RA was prescribed leflunomide (LFN) associated with MTX. No studies have reported on the use of LFN in the treatment of joint symptoms after CF (Simon, 2015 and Marques, 2017).

As mentioned above, while physical therapy was indicated for most patients (94.4%), only 30.5% were able to undergo therapy due to scheduling difficulties in the public health system in Brazil. Similarly, while physical activity was recommended for all patients, it was not possible to assess the response, as no pattern of physical activity was followed.

The literature is consistent regarding the prescription of physical therapy, as it has shown positive results in patients in the subacute and chronic stages of CF. However, the therapeutic protocols of most studies do not include the details of the therapy (Page, 2012; Oliveira & Silva, 2017).

5. Conclusion

The monitoring of musculoskeletal conditions showed a statistically significant improvement in pain, as assessed by VAS, as well as a decreased number of painful and swollen joints. However, even with regular follow-up and treatment, 37 patients (51.4%) maintained some complaints, and 33.3% showed persisting musculoskeletal pain, most commonly diffuse musculoskeletal pain.

The results of this study provide a better understanding of the patient profile, musculoskeletal involvement, and progression of CF; furthermore, they may guide effective strategies for therapeutic management.

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