

Prevalence, affected joints and intensity of the arthralgias in individuals in the chronic phase of Chikungunya fever

Prevalência, articulações acometidas e intensidade das artralguas em indivíduos na fase crônica da febre Chikungunya

Joselanny Ferreira de Lemos¹, Letycia Monteiro Cavalcanti Araújo¹, Vinícius José Guimarães do Carmo¹, Edeilson Junior Amaral Cardoso¹, Maria Cristina Falcão Raposo², Renato de Souza Melo^{1,3}

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ABSTRACT

BACKGROUND AND OBJECTIVES: Chronic arthralgias caused in patients affected by Chikungunya fever bring repercussions that negatively impact the lives of these individuals. The primary objective of this study was to observe the prevalence, affected joints and intensity of the arthralgias in individuals in the chronic phase of Chikungunya fever. The secondary objective was to identify the factors associated with the presence of the arthralgias in these individuals.

METHODS: Cross-sectional study that evaluated 80 volunteers, of both genders, with age range between 20-80 years, with clinical and/or laboratory diagnosis of Chikungunya fever. The arthralgias were assessed using the Nordic Questionnaire of Musculoskeletal Symptoms and pain intensity using the visual analog scale.

RESULTS: 91% (n=73) of the sample reported recurrent arthralgias, at approximately 34.7±2.20 months, with a greater predominance in the morning (50.7%). The joints that showed the highest prevalence of pain were knees (68.8%), followed by the ankles (66.3%) and wrists (63.8%). Knees (4.81±0.40), ankles (4.66±0.42) and metacarpophalangeal (4.33±0.43) were the joints with greatest pain intensity. In addition to that, overweight was associated with the presence of arthralgias (p=0.002).

CONCLUSION: A high prevalence of arthralgias was observed, of a recurrent character and a greater predominance in the morning. The joints most affected by pain were knees, ankles and the wrists and arthralgias were more intense in the knees, ankles

and metacarpophalangeal joints. Overweight was a factor associated with the presence of arthralgias in individuals affected by Chikungunya fever.

Keywords: Ankle, Chikungunya fever, Chronic pain, Knee, Overweight, Wrist.

RESUMO

JUSTIFICATIVA E OBJETIVOS: As artralguas crônicas observadas em pacientes acometidos pela febre Chikungunya trazem repercussões que impactam negativamente a vida desses indivíduos. O objetivo primário deste estudo foi avaliar a prevalência, as articulações acometidas e a intensidade das artralguas em indivíduos na fase crônica da febre Chikungunya. O objetivo secundário foi identificar fatores associados à presença das artralguas nesses indivíduos.

MÉTODOS: Estudo de corte transversal, que avaliou 80 voluntários, de ambos os sexos, com faixa etária entre 20-80 anos e diagnóstico clínico e/ou laboratorial de febre Chikungunya. A avaliação das artralguas foi realizada por meio do *Nordic Questionnaire of Musculoskeletal Symptoms* e a intensidade das dores pela escala analógica visual.

RESULTADOS: 91% (n=73) da amostra relataram artralguas persistentes, a cerca de 34,7±2,20 meses, com maior predomínio pela manhã (50,7%). As articulações que apresentaram maior prevalência das dores foram joelhos (68,8%), tornozelos (66,3%) e os punhos (63,8%). Joelhos (4,81±0,40), tornozelos (4,66±0,42) e as metacarpofalangeanas (4,33±0,43) foram as articulações com maior intensidade das dores e o sobrepeso foi um fator associado à presença das artralguas (p=0,002).

CONCLUSÃO: Foi observada uma elevada prevalência das artralguas, de caráter recorrente e maior predomínio pela manhã. As articulações mais acometidas pelas dores foram joelhos, tornozelos e os punhos e as artralguas foram mais intensas nos joelhos, tornozelos e metacarpofalangeanas. O sobrepeso foi um fator associado à presença das artralguas nos indivíduos acometidos pela febre Chikungunya.

Descritores: Dor crônica, Febre de Chikungunya, Joelho, Punho, Sobrepeso, Tornozelo.

INTRODUCTION

Chikungunya fever (CF) is a disease caused by the Chikungunya virus, an alpha virus, transmitted by the bite of infected female *Aedes aegypti* and *albopictus* mosquitoes¹. Since the first outbreak

Joselanny Ferreira de Lemos – <https://orcid.org/0000-0003-3630-608X>;
Letycia Monteiro Cavalcanti Araújo – <https://orcid.org/0000-0002-0508-4181>;
Vinícius José Guimarães do Carmo – <https://orcid.org/0000-0002-5707-8277>;
Edeilson Junior Amaral Cardoso – <https://orcid.org/0000-0003-0204-9513>;
Maria Cristina Falcão Raposo – <https://orcid.org/0000-0001-7000-3168>;
Renato de Souza Melo – <https://orcid.org/0000-0002-6776-3606>.

1. Integration Faculty of Sertão, Physiotherapy Course, Serra Talhada, PE, Brazil.
2. Federal University of Pernambuco, Department of Statistics, Recife, PE, Brazil.
3. Federal University of Pernambuco, Department of Physiotherapy, Recife, PE, Brazil.

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Correspondence to:

Renato de Souza Melo
Rua Avelino Cândido, 32 – Salgado
55018-070 Caruaru, PE, Brasil.
E-mail: renatomelo10@hotmail.com

of CF, reported in Tanzania around 1953², the disease has seen an increasing rise in countries in Asia^{3,4} and Africa^{5,6}. In Brazil, the first cases occurred in 2014 and, since then, there has been a significant increase in the number of CF notifications, confirmed throughout the country, either by laboratory or clinical criteria⁷. Clinically, CF has three phases: the acute phase, in which symptomatic patients report an abrupt onset of the disease, characterized by high fever, fatigue, edema, nausea, vomiting, headache, back pain, and polyarthralgia. These symptoms last from 4 to 7 days and may persist for up to three months, characterizing the subacute phase; after this period, the chronic phase begins and the arthralgias stand out as the main symptom, presenting frequent and long duration, lasting for weeks, months, and sometimes years⁸⁻¹⁰.

The duration of the arthralgias is still unknown, but it seems that these symptoms show reduction over time¹¹. The time for full recovery is also unknown, and some patients may remain symptomatic for six to eight years after the infection. In addition to arthralgias, the chronic phase has been associated with physical disabilities and worsening of quality of life in individuals after CF^{13,14}, making the clinical and functional evaluation of these patients essential for planning prevention and treatment strategies¹⁵.

There are few studies on the prevalence of arthralgia and which joints are more affected, and these data are important to guide public health measures and the clinical management of individuals affected by CF. Therefore, the primary objective of this study was to observe the prevalence, affected joints and intensity of arthralgia in individuals after CF; the secondary objective was to identify factors associated with the presence of arthralgia in these individuals.

METHODS

Cross-sectional study developed according to the recommendations of STROBE (Strengthening the Reporting of Observational Studies in Epidemiology)¹⁶⁻¹⁸.

Initially, research was conducted in the epidemiology sector of the Health Department of Serra Talhada, Pernambuco, Brazil, to identify individuals affected by CF. Then, with the help of community health agents, a visit was made to their homes to clarify the characteristics of the study and invite them to participate, as long as they fit the eligibility criteria. The inclusion criteria were to present, through a medical report, a CF clinical/laboratory diagnosis of at least three months, to have functional independence and to be between 20 and 80 years old. The exclusion criteria were: history of joint or rheumatic disease, history of recurrent joint pain prior to CF, osteoarticular or neurological diseases and being pregnant.

To confirm the eligibility criteria data, the volunteers' health data were consulted in the basic health units' registries and an interview with the volunteers' family members, as well as a physical evaluation, were performed. Those who met the eligibility criteria signed the Free and Informed Consent Term (FICT), agreeing to participate in the study.

An assessment form was used in order to obtain the volunteers' personal data, the Nordic Questionnaire of Musculoskeletal Symptoms (NQMS)¹⁹ for the evaluation of arthralgia, and the visual analog scale (VAS)²⁰ to quantify the intensity of arthralgia.

The evaluation of arthralgias was carried out in the volunteer's residence, in a reserved place, where only the participants and the researchers were present, in order to avoid constraints.

After collecting personal data, the volunteers were asked if they still felt any joint pain, in which period of the day the arthralgias were more frequent and how long they had been feeling the joint pain.

Next, arthralgias were assessed by the NQMS, an instrument duly validated for the Brazilian population¹⁹, which is based on dichotomous choices of the presence or not of osteomuscular symptoms in the following body regions: cervical spine, shoulder, arm, forearm, wrist and hand, thoracic spine, lumbar spine, hip, thigh, knee, leg, ankle and foot. The NQMS evaluates several osteomuscular symptoms and provides data on these symptoms at different periods, however, in the present study, the only assessed osteomuscular symptom was the joint pain that occurred in the last seven days.

The instrument was adapted for the present study, including the elbow, hands and feet divided in metacarpophalangeal, interphalangeal, metatarsophalangeal and interphalangeal joints. Although not a synovial joint, the spine was included in the evaluation as it could be a location of pain in individuals affected by CF.

Volunteers were questioned regarding joint pain in the last seven days and, if so, in which joints it was present and which was its intensity, assessed by the VAS scale. This scale consists of a 10cm horizontal line, listed with a starting point of zero and a final point of 10, zero representing no pain and ten disabling pain²¹.

The data were included in Microsoft Excel 2010 by two independent researchers (double data entry) to avoid typing errors and ensure greater reliability²². Gender, physical activity, age and body mass index (BMI) variables were analyzed as possible factors associated with arthralgia.

This study was approved by the Research Ethics Committee of the Integration Faculty of Sertão (FIS), under opinion number 3.734.172, CAAE: 24359619.6.0000.8267.

Statistical analysis

To test the normality of quantitative variables, the Kolmogorov-Smirnov test was used. The Mann-Whitney test was used to compare the means between two groups for cases of non-normality of data and the Student *t* test for cases compatible with the normal distribution. For the dichotomous variables, the Pearson's Chi-square independence test or Fisher's Exact test were used when necessary. The data were arranged in tables in Microsoft Office Excel, version 2010 and transferred to the Statistical Package for the Social Sciences (SPSS), version 20.0, where all analyses were performed, adopting the statistical significance level of 5%.

RESULTS

Ninety-five CF affected individuals were invited to participate in this survey, which took place between November 2019 and March 2020, however, 9 individuals were excluded because they had joint diseases or other osteoarticular disorders prior to CF. Four pregnant women and two individuals who did not agree to participate were excluded. It's also important to note that social distancing due to the new Corona virus pandemic was an obstacle for sample acquisition. Therefore, a convenience sample of 80 volunteers with clinical/laboratory diagnostic of CF participated, being 62 women and 18 men. Mean age was 49.0 ± 1.98 years, with BMI 26.8 ± 0.55 .

Of the 80 evaluated volunteers, 73 (91%) reported feeling arthralgias during the evaluation, feeling pain for 34.7 ± 2.20

months and that pain was recurrent. Arthralgias had incidence throughout the day being 50.7% in the morning, 35.6% at night, 6.8% in any time, 4.2% in the morning and night and 2.7% in the afternoon.

The joints most affected by pain were knees (68.8%), ankles (66.3%) and wrists (63.8%). The most intense arthralgias were in the knees (4.81 ± 0.40), ankles (4.66 ± 0.42) and metacarpophalangeal joints (4.33 ± 0.43) (Table 1).

There was no association between arthralgias and gender ($p=0.185$), physical activities ($p=0.371$) or age ($p=0.068$). However, there was a significant association between the presence of arthralgias and overweight ($p=0.002$) (Table 2).

DISCUSSION

High prevalence of arthralgias was observed, with recurrent characteristics and greater predominance in the morning. Investigations in Colombia^{23,24} and Roraima-Brazil²⁵ also found similar data regarding the high prevalence of arthralgias, highlighting that arthralgias are a common symptom in the chronic phase of CF.

Volunteers reported feeling arthralgias for 34.7 ± 2.20 months. Data on the duration of arthralgias are still scarce in the literature, but the present data suggest that it's around 20 to 40 months after infection^{23,26}. The morning has been the period of greater occurrence of arthralgias in individuals affected by CF²⁶, as this study showed. This fact could be justified by morning stiffness, common in chronic inflammatory joint diseases²⁷.

The mechanisms involved in chronic CF arthralgias and clinical manifestations that persist in that period are not yet fully understood, nevertheless, some risk factors have been pointed out, such as genetic predisposition, preexisting arthropathy, tissue injury induced directly by the virus, persistence of infection in tissues that present inflammation for prolonged periods and the activation of autoimmune responses in the joints^{28,29}.

As for the joints most affected by pain, this study showed a higher prevalence in knees, ankles and wrists, data also present in other publications. Two Colombian studies^{23,24} concluded that

Table 1. Affected joints and intensity of arthralgias after Chikungunya fever

	Presence of arthralgias		Intensity of arthralgias	CI 95%
	n	(%)	Mean±SD	
Cervical spine	23	(28.8)	2.36±0.43	1.50 a 3.21
Shoulders	40	(50.0)	2.85±0.39	2.06 a 3.64
Elbows	30	(37.5)	2.16±0.35	1.45 a 2.88
Wrists	51	(63.8)	4.08±0.39	3.29 a 4.88
Metacarpophalangeal	48	(60.0)	4.33±0.43	3.46 a 5.19
Interphalangeal (hands)	47	(58.8)	4.32±0.42	3.27 a 4.98
Thoracic spine	10	(12.5)	1.08±0.33	0.41 a 1.75
Lumbar spine	45	(56.3)	4.07±0.45	3.36 a 5.18
Hips	33	(41.3)	2.68±0.41	1.85 a 3.52
Knees	55	(68.8)	4.81±0.40	4.00 a 5.61
Ankles	53	(66.3)	4.66±0.42	3.82 a 5.50
Metatarsophalangeal	03	(4.0)	1.88±0.12	1.78 a 3.20
Interphalangeal (feet)	02	(2.6)	1.35±0.25	0.57 a 1.13

SD = standard deviation; CI = confidence interval.

Table 2. Sample distribution according to gender, physical activity practice and descriptive measures of age and body mass index in individuals with and without arthralgias

	Arthralgias (n=73)		No arthralgias (n=07)		Difference between means (CI 95%)	Effect size	p-value	Test statistics
	n (%)	Mean±SD (CI 95%)	n (%)	Mean±SD (CI 95%)				
Gender								
Female	58 (93.5)		04 (6.5)				0.185 ^a	
Male	15 (83.3)		03 (16.7)					
Physical activity								
Yes	18 (85.7)		03 (14.3)				0.371 ^a	
No	55 (93.2)		04 (6.8)					
Age (years)		50.2±2.01 (46.1 to 54.2)		36.8±7.58 (18.2 to 55.4)	-13.4 (-15.6 to -11.1)	-203.8	0.068 ^b	Z= -1.822
Body mass index		27.2±0.57 (26.1 to 28.4)		22.3±0.59 (20.8 to 23.7)	-4.90 (-5.35 to -4.44)	-344.7	0.002 ^b	Z= -3.082

SD = standard deviation; CI = confidence interval; ^a = Fisher's Exact test; ^b = Mann-Whitney test.

the wrists, ankles and fingers; and ankles, hands and wrists, respectively, were the joints most affected by pain. Another study²⁵, which evaluated 40 Brazilian individuals who didn't develop arthritis after CF, concluded that the fingers, knees and wrists were the locations with the highest incidence of arthralgias.

The reason why distal joints of the upper and lower limbs present the highest prevalence of chronic CF arthralgias is not yet known, however, some evidence may contribute to the understanding of this mechanism. Periarticular CF inflammations include bursitis, tendinitis, tenosynovitis, capsulitis and periostitis^{11,30}, these inflammations occur in structures that are abundant in the distal joints of the limbs, which could justify the higher prevalence of pain in the chronic phase of CF in these joints.

Another aspect that deserves further investigation is the fact that the upper and lower limbs distal joints are regions where individuals affected by CF present edema during the acute phase. These joints and their synovial structures remain immersed in the fluid of this inflammation for some time and that may influence the fact that the distal joints of the limbs are more affected by pain after CF. However, the present study did not analyze that particular hypothesis, remaining to be investigated, proven or refuted by future studies.

Besides the higher prevalence of pain, the distal joints of the limbs also presented higher intensity of pain, highlighting the knee, ankle and metacarpophalangeal joints. However, the studies that investigated this outcome in the literature are scarce, demonstrating the relevance of the present work's data, presenting new information which may contribute to the study and more adequate control of individuals affected by CF, as well as the academic discussions on the subject.

Another important contribution of the study was to analyze factors associated with the presence of arthralgias in individuals affected by CF, as these data are also scarce in the literature. The group with arthralgias presented BMI values compatible with overweight and the group without arthralgias presented adequate values, considered eutrophic, indicating that overweight was a factor associated with the presence of arthralgias. There is no such association in the literature in individuals affected by CF, but there is evidence that overweight and obesity are associated with joint pain in individuals who present other chronic joint diseases, such as osteoarthritis³¹⁻³³.

The high prevalence of chronic arthralgias can have a negative impact on daily life activities, functionality and quality of life of these people, however, these aspects were not analyzed in the present study. Anyway, many volunteers reported functional difficulties during daily and domestic activities that should be investigated in future studies, since there are already reports of difficulties by instruments that evaluate functionality in individuals affected by CF³⁴. In addition to that, worse quality of life and functionality due to the chronic arthralgias have been reported in these subjects³⁵⁻³⁷.

Besides arthralgias, the volunteers also associated CF with alopecia, recurrent edemas, sleep disorders, mood changes, and presence of depressive symptoms, visual disorders, as well as concentration and memory difficulties. These findings show how much individuals affected by CF need treatment and mo-

nitoring by a multiprofessional health team in order to control the physical and psychic disorders resulting from CF.

The control of chronic arthralgias coming from CF, according to the current guidelines, consists in drug and physiotherapeutic treatment. The drug treatment in the chronic phase is based on the use of analgesics, opioids, non-steroidal anti-inflammatory drugs and corticosteroids³⁸. It's important to mention that some patients may develop progressive erosive arthritis, with a rheumatoid or psoriatic arthritis pattern¹¹ and, for these cases, the medication may be modified according to the need and clinical condition presented by the patient.

Physiotherapeutic treatment must be present in the three phases of the disease and has been effective in the control of arthralgias and functional improvement of patients affected by CF³⁸⁻⁴². Some complementary therapies have also been suggested, such as aquatic physiotherapy³⁹ and acupuncture³⁸. Moreover, there is evidence that transcranial electrical stimulation and the Pilates method are effective physiotherapeutic approaches for reducing arthralgia and improving the functionality of CF affected individuals^{43,44}.

The CF is a serious public health problem today, affecting not only Brazil but many Latin American countries⁴⁵ and may become an even more serious problem in the future, including the economic and health burdens related to the chronic condition of this disease and its repercussions on health and well-being of the affected population. Therefore, governments must take adequate prevention and treatment measures in order to control CF and care for the affected population, which presents arthralgias and other chronic signs and symptoms resulting from the disease, affecting their physical and psychic health and social well-being.

CONCLUSION

A high prevalence of arthralgias with recurrent characteristics and higher predominance in the morning was observed in individuals affected by CF. The joints most affected by pain were knees, ankles and wrists. Arthralgias presented higher intensity in the knees, ankles and metacarpophalangeal joints, respectively. Overweight was a factor associated with the presence of arthralgias.

AUTHORS' CONTRIBUTIONS

Joselanny Ferreira de Lemos

Data Collection, Writing – Preparation of the original

Letycia Monteiro Cavalcanti Araújo

Data Collection, Writing – Preparation of the original

Vinícius José Guimarães do Carmo

Data Collection, Writing – Preparation of the original

Edeilson Junior Amaral Cardoso

Data Collection, Writing – Preparation of the original

Maria Cristina Falcão Raposo

Statistical analysis, Writing – Reviewing and Editing

Renato de Souza Melo

Project Management, Writing – Review and Editing, Supervision

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