

Major Article

Evaluation of functional disability after Chikungunya infection

**Cristiane Silvia Panato^[1], Eduardo Durans Figueredo^[1], Daniela Bassi^[1],
Ilana Mírian Almeida Felipe^[1], Wellyson da Cunha Araújo Firmo^[2],
Adriana Sousa Rêgo^[1] and Flor de Maria Araújo Mendonça Silva^[1]**

[1]. Universidade CEUMA, Programa de Pós-Graduação em Gestão de Programas e Serviços de Saúde, São Luís, MA, Brasil.

[2]. Universidade CEUMA, Departamento de Biomedicina, São Luís, MA, Brasil.

Abstract

Introduction: Chikungunya (CHIK) is caused by the Chikungunya virus, which is an Alphavirus of the Family Togaviridae transmitted to humans through female mosquitoes of the genus *Aedes*. **Methods:** A cross-sectional study was conducted involving the administration of a questionnaire addressing sociodemographic and health variables and the Roland-Morris Disability Questionnaire on general pain to patients with CHIK in the City of Imperatriz, Brazil, between January and December 2017. **Results:** Data of a total of 130 patients were evaluated. The mean age was 52 years (standard deviation=13.3); majority of the patients were female (n=120) with a prevalence of 38.0% for functional disability. Statistical differences were noted for marital status (p=0.037), presence/absence of comorbidities (p=0.050), and the use of medications prior to the diagnosis of CHIK (p=0.050), use of methotrexate (p=0.030), use of nonsteroidal anti-inflammatory drugs (p≤0.035), and use of nonhormonal anti-inflammatory drugs (p=0.001). **Conclusions:** Patients in the chronic phase of CHIK present functional disability, thus alerting healthcare professionals to the importance of implementing actions aimed at an adequate treatment in all phases of the disease, mainly related to pain treatment and motor rehabilitation.

Keywords: Chronic Pain. Functional Disability. Chikungunya.

INTRODUCTION

Chikungunya (CHIK) is caused by the Chikungunya virus, which is an Alphavirus of the Family Togaviridae that was isolated for the first time in 1952/1953 during an epidemic in Newala, Tanzania. The virus is transmitted to humans mainly by female mosquitoes of the genus *Aedes*. In Brazil, the main vectors are *Aedes aegypti* and *Aedes albopictus*¹.

CHIK was reported in Brazil in 2014, with the first autochthonous case detected in Oiapoque in the State of Amapá (northern Brazil)². This arbovirus has since spread throughout the entire country, reaching its highest level in 2016 and 2017,

mainly affecting northeastern Brazil. Currently, the southern and central western regions have the largest number of CHIK cases. Up to epidemiological week 30 of 2018, there were 42,476 confirmed CHIK cases³.

CHIK affects all sexes and age groups similarly. Symptoms of CHIK are observed after a mean incubation period of 3-7 days. The majority of infected individuals develop clinical symptoms, which can be observed in three phases of the disease: acute, post-acute, and chronic⁴.

The acute phase lasts 3-10 days with the following symptoms: abrupt high fever accompanied with weakness, muscle pain, intense joint pain (100.0% of cases), and maculopapular skin rash, which can evolve to the post-acute phase with predominantly joint symptoms lasting up to 3 months⁵⁻⁷. The chronic phase is characterized by the persistence of musculoskeletal symptoms for more than 3 months. The prevalence of chronic phase ranges from 12% to 87.2%^{2,8-11}. This heterogeneity is due to the methodological differences in the different studies.

Corresponding author: Cristiane Silvia Panato.

e-mail: cristiane.silvia@terra.com.br

Orcid: 0000-0002-7836-4002

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During the chronic phase of CHIK, polyarthritis, which is most often symmetrical and recurrent, is experienced in 86.0% of cases. It may affect similar joints affected during the acute phase or may affect different joints. This phase may also present with the following symptoms: fatigue, headache, neuropathic pain, tendinitis, bursitis, and depressive disorder. The duration varies, lasting up to 3 years^{4,10}.

Symptoms during CHIK's chronic phase are recurrent and socially debilitating, with significant economic impact. Despite accumulated scientific knowledge on the virus, adequate control of this disease and its propagation has not yet been achieved¹².

Finally, the present study aimed to investigate if patients in the chronic phase of CHIK infection develop functional disability, to specifically estimate the prevalence of functional disability in patients in the chronic phase of CHIK infection, and to evaluate the risk factors associated with this clinical evolution.

METHODS

This analytical, transverse, cross-sectional study was conducted at primary and secondary care services in the City of Imperatriz, which is the most populous city in the countryside of the State of Maranhão, with an estimated population of 254,569 in 2017, according to the Brazilian Institute of Geography and Statistics¹³.

Patients with chronic pain following CHIK were recruited from primary and secondary care services by their assistant physicians. Those who agreed to participate in the study signed a statement of informed consent and were subsequently contacted by telephone to schedule interviews, which were held between January and December 2017.

Male and female patients aged over 18 years with symptoms compatible with the chronic phase of CHIK and a laboratory confirmation of the diagnosis were included in the study. Conversely, patients with symptoms compatible with the chronic phase of CHIK with no laboratory confirmation of the diagnosis and those with symptoms compatible with the chronic phase of CHIK and laboratory confirmation of the diagnosis but who had a previous diagnosis of systemic lupus erythematosus, rheumatoid arthritis, psoriatic arthritis, or fibromyalgia were excluded in the study.

Data collection was performed through telephone interviews using two questionnaires. The first questionnaire contained a clinical record with questions about sociodemographic characteristics, social questions, physical activity, and current health status (use of medications, comorbidities, history of hospitalization, and current clinical complaints).

The second questionnaire was the Roland-Morris Disability Questionnaire for general pain (RMDQ-g), which is composed of 24 items addressing activities of daily living, pain, and function. In 2010, Sarda-Júnior et al.¹⁴ validated the Roland-Morris general pain questionnaire, which was initially developed to measure physical disability in patients with low back pain. Simple, objective statements are presented, and the responses are scored either 1 (respondent agrees with the statement) or

0 (respondent disagrees with the statement). The total score is determined by the sum of the item scores and ranges from 0 to 24 points. The cutoff point for the indication of disability is 14 points, with higher scores denoting greater disability. The version translated and adapted to Portuguese was validated by Sarda-Júnior et al.¹⁴.

The clinical variables, risk factors, treatment, and follow-up of patients with suspected CHIK were defined based on the guidelines of the Brazilian Health Ministry (BHM) and Brazilian Society of Rheumatology (BSR)^{4,15}.

The sociodemographic and health variables were sex, age, marital status, comorbidities (diabetes mellitus and systemic arterial hypertension), time elapsed since the diagnosis of these comorbidities, and previous use of medications.

The following aspects related to CHIK infection were evaluated: symptoms of the acute phase (fever, body pain, skin rash, headache, vomiting, conjunctivitis, time elapsed between the onset of fever and onset of joint point) and which joints were affected in the chronic phase (small joints [joints of the hands and feet], large joints [knees, ankles, shoulders, and elbows], spinal column, or all joints).

Regarding the medications, the drugs indicated by the BHM and BSR for the treatment of CHIK in the chronic phase and products popularly used for pain relief were considered as the variables^{4,15}.

In this respect, the following data were collected: place of first treatment, type of service (public or private), and perceptions regarding the first care, taking into consideration the advice given by the physician regarding the diagnosis and proposed treatment.

Other recommendations included regular medical reevaluations to assess the clinical response to treatment and the use of non-pharmacological measures, such as physical activity and motor physiotherapy⁴. Therefore, we also analyzed current follow-up with the physician, referral to motor physiotherapy, the practice of physical activity, any restrictions to physical activity, and expectations regarding an improvement in the symptoms.

Statistical analysis was performed using Stata 14.0 software (Stata Corp., College Station, Texas, USA). Qualitative variables were presented by absolute and relative frequencies. Descriptive statistics included calculation of absolute and relative frequencies (percentages). For nominal categorical variables, the association between explanatory variables and response was performed using the chi-squared test (χ^2) for independent samples. A significance level (α) of 5.0%, test power of 80.0%, and tolerable error of 4.0%, plus 10.0% of possible losses were used, considering the prevalence of 12.0% of chronic cases.

Initially, 142 patients referred from the outpatient clinics of primary and secondary healthcare were evaluated, and 130 patients were and 130 patients who met the inclusion criteria were selected and were considered sufficient in the sample calculation performed. Of the 130 patients diagnosed with CHIK, 80 of them had no disability and 50 had functional disability.

The factors were associated and tested between the explanatory variable (chronic pain after CHIK infection) and the response variable (disability generated by the chronic phase of CHIK infection), considering the statistical significance ($p \leq 0.050$) and the number of exposed in the sample.

This study was approved by the Human Research Ethics Committee of Ceuma University with certificate number 1.079.961.

RESULTS

Data of 130 patients were evaluated, and the mean age was 52 years (standard deviation [SD]=13.3). The analysis of the RMDQ-g results revealed a prevalence rate of 38.0% for functional disability and significant associations between the following variables: marital status ($p=0.030$), presence/absence of comorbidities ($p=0.050$), use/nonuse of medications prior to the diagnosis of CHIK ($p=0.050$), use/nonuse of methotrexate ($p=0.035$), and use/nonuse of nonsteroidal anti-inflammatory drugs ($p=0.001$).

A total of 120 patients were women; the most frequent age group was 25 to 64 years ($n=84$); 96 had a stable partner; 62 had educational level until high school; 78 had no comorbidities; and 76 did not use any medication prior to the diagnosis of CHIK (Table 1).

The onset of symptoms was observed in the first three months of 2017 in 90 cases. The most frequent symptoms in the acute phase were body pain ($n=126$), rashes ($n=84$), and headache ($n=110$); 98 had fever for at least 5 days, and 112 reported the onset of joint pain 5 days after the onset of fever. Small joints were predominantly affected ($n=48$), followed by all joints ($n=42$). Vomiting ($n=30$) and ophthalmopathies ($n=32$) were less frequent in the sample (Table 2).

Regarding the medications taken for the treatment of pain, whether they were hydroxychloroquine, corticosteroids, nonsteroidal anti-inflammatory drugs, analgesics, and methotrexate, majority of the patients were not taking these medications and also were not using any alternative folk remedies such as herbs and plants (Table 3).

Majority of the patients were first treated at a private hospital ($n=88$) and were satisfied ($n=84$) with the orientation received regarding the diagnosis of CHIK and treatment. Seventy-six patients were not undergoing clinical follow-up for the treatment of pain, and 66 had not been referred to a physiotherapist (Table 4). Eighty-six patients performed regular physical activities, and 90 reported some restriction to performing physical activities. Ninety-six patients had positive expectations regarding symptom improvement (Table 4).

TABLE 1: Distribution of 130 patients with chronic arthralgia after Chikungunya infection according to sociodemographic and health variables. Imperatriz, MA, Brazil, 2017.

Variables	Rolland-Morris		P-value
	Absence of disability n (%)	Presence of disability n (%)	
Sex			0.917
Male	6 (7.5)	4 (8.0)	
Female	74 (92.5)	46 (92.0)	
Age			0.660
18-24	6 (7.5)	2 (4.0)	
25-64	52 (65.0)	32 (64.0)	
≥65	22 (27.5)	16 (32.0)	
Marital status			0.037
Without partner	26 (32.5)	8 (16.0)	
With partner	54 (67.5)	42 (84.0)	
Educational level			0.179
Illiterate	6 (7.5)	-	
Primary school	18 (22.5)	10 (20.0)	
High school	38 (47.5)	24 (48.0)	
University	18 (22.5)	16 (32.0)	
Comorbidity			0.134
No	46 (57.5)	22 (44.0)	
Yes	34 (42.5)	28 (56.0)	
Time with comorbidity			0.050
Not applicable	48 (60.0)	22 (44.0)	
≤ 1 year	6 (7.5)	6 (12.0)	
2 to 4 years	12 (15.0)	16 (32.0)	
≥ 5 years	14 (17.5)	6 (12.0)	
Medication			0.050
No	52 (65.0)	24 (48.0)	
Yes	28 (35.0)	26 (52.0)	

Source: Research data (2017).

TABLE 2: Distribution of 130 patients with chronic arthralgia after Chikungunya infection according to the variables of the presence of disability and clinical manifestations. Imperatriz, MA, Brazil, 2017.

Variables	Rolland-Morris		P-value
	Absence of disability n (%)	Presence of disability n (%)	
Onset of symptoms (2017)			0.589
First semester	54 (67.5)	36 (72.0)	
Second semester	26 (32.5)	14 (28.0)	
Fever			0.623
No	4 (5.0)	2 (4.0)	
< 5 days	58 (72.5)	40 (80.0)	
≥ 5 days	18 (22.5)	8 (16.0)	
Muscle pain			0.108
No	4 (5.0)	-	
Yes	76 (95.0)	50 (100.0)	
Rash			0.384
No	26 (32.5)	20 (4.0)	
Yes	54 (67.5)	30 (6.0)	
Headache			0.249
No	10 (12.5)	10 (20.0)	
Yes	70 (87.5)	40 (8.0)	
Vomiting			0.292
No	64 (80.0)	36 (72.0)	
Yes	16 (20.0)	14 (28.0)	
Ophthalmopathies			0.898
No	60 (75.0)	38 (76.0)	
Yes	20 (25.0)	12 (24.0)	
N° of days after onset of fever for onset of pain			0.108
< 5 days	72 (90.0)	40 (80.0)	
≥ 5 days	8 (10.0)	10 (20.0)	
Joint pain			0.249
Small joints	32 (40.0)	16 (32.0)	
Large joints	24 (30.0)	14 (28.0)	
Spinal column	-	2 (4.0)	
All joints	24 (30.0)	18 (36.0)	

Source: Research data (2017).

DISCUSSION

Data of 130 patients were evaluated in the present study, and the main finding of the study is that most patients had no functional disability; however, those with functional disability manifested the presence of characteristic signs and symptoms of CHIK, such as fever, muscle and joint pain, cramps, headache, vomiting, and ophthalmopathies. The mean age of the patients was 52 years (SD=13.3), and majority of the patients were female. These findings are consistent with the data described by Marques et al.¹⁶ who studied 122 Brazilian patients with a clinical and epidemiological diagnosis of CHIK and Rios et al.¹⁷ in a cross-sectional study involving 101 patients in the Municipality of Feira de Santana in the State of Bahia.

In a prospective study conducted in Saint-Pierre on Reunion Island, France, 180 patients diagnosed with CHIK were followed up for 3 years and more than 60.0% of the patients had highly incapacitating joint pain that affected their activities of daily living, professional life, and recreational activities. In the present investigation, the prevalence of functional disability was 38.0%, but was probably underestimated because this was a cross-sectional study involving patients at different points of the chronic evolution of the disease¹⁸.

In the present study, it was observed that patients without comorbidities and who did not previously take medications had less functional disability than patients with comorbidities and who previously took medications. Schilte et al.¹⁸ studies

TABLE 3: Distribution of 130 patients with chronic arthralgia after Chikungunya infection according to the variable of medications used. Imperatriz, MA, Brazil, 2017.

Variables	Rolland-Morris		P-value
	Absence of disability n (%)	Presence of disability n (%)	
Hydroxychloroquine			0.157
No	66 (82.5)	36 (72.0)	
Yes	14 (17.5)	14 (28.0)	
Corticosteroid			0.305
No	52 (65.0)	28 (56.0)	
Yes	28 (35.0)	22 (44.0)	
Nonhormonal anti-inflammatory drugs			0.001
No	68 (85.0)	32 (64.0)	
Yes	12 (15.0)	18 (36.0)	
Analgesic			0.386
No	60 (75.0)	34 (68.0)	
Yes	20 (25.0)	16 (32.0)	
Methotrexate			0.035
No	76 (95.0)	42 (84.0)	
Yes	4 (5.0)	8 (16.0)	
Use of alternative treatment (herbs and plants)			0.863
No	50 (62.5)	32 (64.0)	
Yes	30 (37.5)	18 (36.0)	

Source: Research data (2017).

TABLE 4: Distribution of 130 patients with chronic arthralgia after Chikungunya infection according to the variables of first care and patient follow-up. Imperatriz, MA, Brazil, 2017

Variables	Rolland-Morris		P-value
	Absence of disability n (%)	Presence of disability n (%)	
First care setting			0.138
Private hospital	58 (72.5)	30 (60.0)	
Public hospital	22 (27.5)	20 (40.0)	
Satisfaction with first care			0.104
Satisfied	56 (70.0)	28 (56.0)	
Dissatisfied	24 (30.0)	22 (44.0)	
Currently in follow-up			0.001
No	56 (70.0)	20 (40.0)	
Yes	24 (30.0)	30 (60.0)	
Underwent physiotherapy			0.001
No	48 (60.0)	18 (36.0)	
Yes	32 (40.0)	32 (64.0)	
Performs physical activity			0.265
No	30 (37.5)	14 (28.0)	
Yes	50 (62.5)	36 (72.0)	
Restriction to physical activity			0.186
No	28 (35.0)	12 (24.0)	
Yes	52 (65.0)	38 (76.0)	
Expectation regarding symptom improvement			0.001
No	14 (17.5)	20 (40.0)	
Yes	66 (82.5)	30 (60.0)	

Source: Research data (2017).

identified that diabetes mellitus was a risk factor for long-term arthralgia. Moreover, in this study, it is observed that a larger number of patients were affected in the first semester, probably because this period receives more rainfall in the region, increasing the proliferation of mosquitoes and, consequently, the transmission of the disease.

Short-term fever (n=98), muscle pain (n=126), headache (n=110), and skin rash (n=84) were the most frequent symptoms in the acute phase of the disease, whereas vomiting (n=30) and ophthalmopathies (n=32) were less frequent. These findings are consistent with the data described in the literature^{4,15}.

Chronic arthralgia affecting small joints was noted in 48 of the patients studied. Essackjee et al.¹⁹ found that 5.0% of patients with CHIK met the criteria of the American College of Rheumatology for rheumatoid arthritis. This demonstrates that CHIK can cause rheumatic symptoms, and a differential diagnosis is necessary. In its guidelines for the diagnosis and treatment of CHIK, the BSR recommends investigating rheumatoid factor and the anti-cyclic citrullinated peptide for patients who have persistent synovitis in one or more joints despite adequate treatment.

In its recommendations for the treatment of CHIK, the BSR suggests the administration of methotrexate in the chronic phase of the disease or (considering withdrawal difficulty from this corticosteroid) the administration of a nonsteroidal anti-inflammatory drug for the treatment of musculoskeletal pain refractory to analgesics²⁰. In the present study, majority of the patients were not taking any medication despite experiencing pain, which may be related to the lack of medical follow-up with a skilled professional for the treatment of this illness.

According to the guidelines of the BHM⁴ regarding the clinical management of CHIK and BSR regarding the treatment of the disease¹⁵, non-pharmacological treatment is recommended in the acute and chronic phase of CHIK to alleviate the pain, avoid antalgic postures, and maintain joint function^{4,15}. Majority of the patients in the present study did not undergo motor physiotherapy (n=64) and were not undergoing medical follow-up (n=54), which may be due to the difficulties that patients encounter in finding healthcare services that treat chronic pain, insufficient information on the possible motor consequences, and possible self-medication.

A total of 96 patients had positive expectations regarding symptom improvement. Such an optimistic view is not expected in patients with chronic pain. A study conducted on Reunion Island in 2005 and 2006 reports a high incidence of depression in patients with chronic pain following CHIK¹⁸ and sleep disorders, memory problems, and depression in patients with significant joint pain. The patients in the present study may have experienced more intense pain in the acute phase, leading them to expect an increasingly favorable evolution until the resolution of the symptoms.

It was not possible to include the 162 patients required based on the sample size calculation due to the difficulty the patients had in undergoing the confirmatory laboratory exam

for CHIK infection. This exam is not offered by the public healthcare system in the city where the study was conducted and is necessary in differential diagnosis during the chronic phase of the disease.

Thus, the patients still need better clinical follow-up and non-pharmacological therapies in the chronic phase of the disease. Most of them were not under medical supervision and did not undergo motor rehabilitation, resulting in self-medication to control pain, hence developing disease sequelae.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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