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BRIEF REPORT

# Brief report: the disability of chronic chikungunya arthritis

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## Abstract

In 50% of patients, chikungunya fever (CHIKF) is followed by arthritic pain that is often chronic, painful, and disabling. To better define the spectrum of pain and disability in chronic CHIK arthritis (CCA), we evaluated 35 consecutive CCA patients seen in a Brazilian rheumatology clinic, using a pain Visual Analog Scale and the Health Assessment Questionnaire Disability Index. In our patients, pain and disability levels were of the same magnitude as are seen in other serious rheumatic diseases. The mean score for 19 patients with moderate disability was 1.42± 0.20 (median 1.37). The median HAQ-DI score for the entire group was 1.25. These findings underscore the morbidity imposed by CCA and the urgent need for improvements in management.

**Keywords** Chronic chikungunya arthritis · Disability · Health Assessment Questionnaire Disability Index (HAQ-DI) · Visual Analog Scale (VAS)

## Introduction

Chikungunya fever (CHIKF) is caused by chikungunya virus (CHIKV), a small, single-stranded RNA alphavirus. Human transmission occurs by *Aedes* mosquitoes, *Aedes aegypti*, and *Aedes albopictus*. Most infected individuals develop high fever, arthralgia/arthritis, maculopapular rash, headache, myalgias, nausea, vomiting, and diarrhea [1]. Less frequently, CHIKF causes neurological diseases, including meningoencephalitis, encephalopathy, seizures, sensorineural abnormalities, and Guillain-Barré syndrome, or cardiac diseases, including myocarditis, pericarditis, heart failure, and/or arrhythmias [2]. Following acute infection, approximately 50% of patients recover within a few weeks, but the other 50% develop chronic inflammatory rheumatism that can last for weeks, months, or sometimes years [3, 4].

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Until CHIKV was isolated in Tanzania in 1952, the disease was often misdiagnosed as dengue [1]. During the twentieth century, CHIKF epidemics occurred in Africa and Asia, followed by varying inter-epidemic periods. There was a major epidemic in Kenya (2004) followed by outbreaks in other Indian Ocean countries, including the French island of La Réunion (2005) and then Italy (2007) [4]. CHIKV reached the Western Hemisphere in 2013 and since then, has spread regionally with more than 2 million cases reported in the Americas [1].

Treatment of acute CHIKF includes supportive care, hydration, and pain management. Although fever is usually present, aspirin or NSAIDs are not recommended if there is concern about co-infection with dengue. During the acute phase of CHIKF, when patients have high levels of viremia, corticosteroids, although effective at controlling symptoms, should also be avoided [5].

Why some patients develop chronic arthralgia/arthritis is not well understood. CCA may be a post infectious, inflammatory disorder [6]. For this reason, when arthritis persists for more than 3 months, disease modifying anti-rheumatic drugs including hydroxychloroquine (HCQ), sulfasalazine (SSZ), methotrexate (MTX), and biologics, alone or in combination, have been used [7].

CCA is not only persistent, it is also painful and disabling. Several studies have assessed rheumatic morbidity, quality of life impairment, and disability related to CHIKV infection [8–10].

We have observed persistent pain and disability in CCA patients that we are caring for in a Brazilian epidemic that began in 2014 [11]. We believe that it is important to fully characterize patterns of disability in CCA patients. In this report, we describe the loss of function seen all too commonly in this emerging epidemic.

## Methods

This cross sectional study was conducted in the state of Pernambuco in northeastern Brazil, We included 35 patients seen between January and April 2018 with CHIKF (diagnosed by clinical and epidemiological criteria, and specific anti-CHIK IgG serology by ELISA, kit EUROIMMUN) and arthritis of more than 12 weeks duration, with painful and swollen joints.

Demographic data, including past medical history, and rheumatic disease history was recorded for all patients. Previous treatment for CCA was also assessed. Patients were questioned about the time between acute CHIKF and their first visit to the rheumatologist.

Patients were evaluated using the Health Assessment Questionnaire Disability Index (HAQ-DI), a well validated and widely used outcome measure in rheumatic diseases [12], to measure disability from CCA during the first visit. The eight categories assessed by the HAQ-DI were (1) dressing, (2) standing up, (3) eating, (4) walking, (5) hygiene, (6) reaching, (7) grip, and (8) everyday activities. For each of these categories, patients typically reported difficulty in performing two or three specific activities. Qualifying statements such as SOME, MANY, or USUAL were deliberately not defined; patients were instructed to respond in their own words. The time frame for the disability questions was the patient's status during the LAST WEEK. Since pain is a significant component of our patients' disability, the Visual Analog Pain Scale (VAS) [13], included in the HAQ-DI, was used to quantify self-reported pain. Pain was scored between 0 (no pain) and 10 (most severe pain).

Descriptive statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp, Armonk, NY).

## Results

Among the 35 patients studied, there were 33 (94%) women and 2 (6%) men. The mean age was 56.8 years. All patients had CHIK infection confirmed by CHIKV-specific IgG serology.

The mean time elapsed between the onset of CHIKF and evaluation in our clinic was 21.6 ± 2.85 months. During the initial visit, 27 patients (77%) reported severe pain (VAS 7–10), seven (20%) had moderate pain (VAS 4–6), and only one (3%) reported mild pain (VAS 1–3). Mean pain level for the entire group was 8.02 ± 1.82.

Patients were asked about the presence of previous rheumatic disease which might contribute to their degree of pain. Eleven patients (31.4%) reported osteoarthritis and four (2.8% each) reported gout, fibromyalgia, shoulder bursitis, or low back pain. Thirty-two (91.4%) were using some form of pain medication, including common analgesics (paracetamol or dipyrone) (80%), nonsteroidal anti-inflammatory drugs (NSAIDs) (17.4%), glucocorticoids (62.85%), and codeine (2.85%) (Table 1).

HAQ-DI scores demonstrated that 19 patients (54.3%) had moderate disability (score 1.01–2.00). The mean score for those with moderate disability was 1.42 ± 0.20 (median 1.37). The global median HAQ-DI score was 1.25.

## Discussion

Because CHIK causes chronic disabling pain in widespread epidemics, it has become a major public health problem. CCA limits functional capacity, affecting employment, leisure, family relations, and mood. In this respect, CCA mimics rheumatoid arthritis (RA) in which joint pain often impairs activities of daily living and pain perception correlates with the degree of disability [14].

Quality of life assessments provide important insights about the impact of rheumatic diseases [13]. The Health Assessment Questionnaire (HAQ) evaluates a patient's

**Table 1** Demographic profile, previous treatment, and rheumatic diseases, and HAQ-DI in patients with chronic chikungunya arthritis

| Variables | *N* (%) |
|---|---|
| Number of patients | 35 |
| Age (years) | 56.8 |
| Median (range) | 55 (IQR 21–88) |
| Female | 33 (94) |
| Prior treatment | |
| Paracetamol/dipyrone | 28 (80) |
| NSAIDs | 6 (17) |
| Corticosteroids | 22 (62.85) |
| Opioids | 1 (2.85) |
| Previous rheumatic diseases | |
| Osteoarthritis | 11 (31.4) |
| Fibromyalgia | 1 (2.85) |
| Gout | 1 (2.85) |
| Other musculoskeletal disorders* | 2 (5.7) |
| HAQ-DI score | |
| Median | 1.25 |
| Mean | 1.0 |
| SD | 0.40 |

*Shoulder bursitis or low back pain

ability to perform various activities of daily living during the past week. The first part of the questionnaire, the Disability Index (DI), includes items that assess fine movements of the upper extremities, locomotion of the lower extremities, and activities that involve both the upper and lower extremities [12]. The full version of the HAQ includes the analogue scale assessment of disease and pain activity, questions about extra-articular symptoms, comorbidity, previously applied treatment and its effects, and questions about the costs associated with treatment [15].

Several reports evaluate pain and disability in CCA (Table 2). The highest baseline HAQ scores were reported by Ganu and Ganu [16]. In this study, the functional status of 16 CCA patients with symptoms lasting more than 3 months despite NSAIDs and HCQ therapy was evaluated. Following combination therapy with MTX, SSZ, and HCQ, HAQ scores improved from 2.18 ± 0.63 at baseline to 0.97 ± 0.39 after 2 years of therapy. Conversely, the lowest baseline HAQ scores were reported by Bouquillard and colleagues, with a mean HAQ score of 0.44 ± 0.5 and moderate functional impairment in 307 CCA patients 32 months after their disease onset [17]. The mean HAQ score across the five available studies was 1.59 ± 0.46 [16–20].

Ravindran and Alias measured disability in 72 patients with persistent CHIK arthritis (confirmed by laboratory and epidemiological criteria). Half were treated with triple therapy (MTX 15 mg per week, SSZ 1 g daily, and HCQ 400 mg daily) and half received HCQ monotherapy. Although disability improved significantly in the combination therapy cohort compared to monotherapy (HAQ 1.4 ± 0.31 vs. 1.88 ± 0.47, $p < 0.0001$), the scores remained high for both groups. This study suggested that chronic CHIK disability could persist despite improvements in pain. At 24 weeks, pain VAS was significantly less in the combination therapy group compared to monotherapy (46 ± 6.13 vs. 60.8 ± 11.6, $p < 0.0001$) [20].

In our study, the mean ± SD and median HAQ-DI scores were 1.0 ± 0.40 and 1.25 respectively, and the median VAS pain level was 8. These HAQ-DI scores were at the lower end of the ranges reported among other CCA cohorts. However, in our patients, elevated VAS pain scores were not always correlated with marked disability. Some patients reported a VAS ≥ 8, but had lower overall disability HAQ-DI scores. Other patients had less pain, but more disability. Disability may thus be influenced by biopsychosocial factors other than pain in the context of rheumatic disease [21].

Disability and pain in our patients were similar to the levels seen in RA and other rheumatic diseases. In 2998 arthritis patients, Carmona found mean HAQ-DI scores in RA (1.75), low back pain (1.27), knee osteoarthritis (OA) (1.29), hand OA (1.24), and fibromyalgia (1.30) similar to our study [22]. In another group of 198 patients with OA of the hip, knee, and spine, mean HAQ-DI scores were 1.10 ± 0.92 [23].

Importantly, the levels of pain and disability observed in our patients were worse than HAQ scores considered tolerable for independence in activities of daily living. Among 9000 RA patients, Maska and colleagues determined that those identifying as independent in activities of daily living had mean scores of 0.38 ± 0.45. Likewise, those who were very satisfied with their health reported HAQ scores of 0.42 ± 0.53 [21]. The higher scores for HAQ-DI seen in our patients and the high scores for pain measured by VAS underscore the disability burden imposed by CCA and the urgent need for improvements in management of this disease. Although our sample size is smaller than some other CCA cohorts, our results resemble those of other studies in classifying the majority of patients with CCA with moderate disability. This is the first chikungunya disability study in a Brazilian population, despite the outbreaks of CHIKF in the country since 2014. We

**Table 2** Disability in chronic chikungunya arthritis using HAQ-DI score

| Author, year, country | Study design | No. of patients, No. of male/female, mean/median age | Results (mean HAQ) |
|---|---|---|---|
| Pandya, 2008, India [18] | Prospective | $N = 305$, 82/223, mean 49 years | Mean HAQ 1.6 ± 0.58 |
| Ganu and Ganu, 2011, India [16] | Prospective | $N = 16$, 7/9 | Mean HAQ 2.18 ± 0.63 (initial); mean HAQ 0.97 ± 0.39 (after 2 years) |
| Blettery, et al., 2016, France [19] | Prospective | $N = 128$, 46/82, median 64.1 years | Mean HAQ 1.4 ± 0.9 |
| Ravindran and Alias, 2017, India [20] | Prospective | $N = 72$, 24/48, mean 54.1 ± 6.7 years<br>Mean 56.6 ± 7.6 years | Mean HAQ 1.94 ± 0.08 vs. 1.97 ± 0.08 (initial)<br>Mean HAQ 1.54 ± 0.63 vs. 1.97 ± 0.57 (8 weeks)<br>Mean HAQ 1.33 ± 0.48 vs. 1.9 ± 0.08 (16 weeks)<br>Mean HAQ 1.14 ± 0.31 vs. 1.88 ± 0.47 (24 weeks) |
| Bouquillard et al., 2018, France [17] | Prospective | $N = 307$, 52/255, mean 54 ± 12.6 years | Mean HAQ 0.44 ± 0.5 |

believe our disability data is relevant to a much larger population of CCA patients in Brazil and elsewhere.

## Conclusion

Disability caused by CCA may be as severe as that caused by OA, RA, or fibromyalgia. This is particularly important because CHIKF outbreaks can occur throughout the world over the wide distribution of the *Aedes* mosquito vectors. A large number of people infected with CHIKV will progress to a chronic rheumatic disease, and most of them develop disability.

Our study showed that CCA disability measured using HAQ-DI represents a burden for patients for which as yet there is no satisfactory treatment. We recommend both further studies on CCA disability using other measurement tools as well as studies on the treatment of this emerging and disabling disease.

### Compliance with ethical standards

**Disclosures** None.

## References


1. Silva LA, Dermody TS (2017) Chikungunya virus: epidemiology, replication, disease mechanisms, and prospective intervention strategies. J Clin Invest 127(3):737–749. https://doi.org/10.1172/jci84417
2. Ferreira-Sarmiento S, Lastra-Terán KP, De la Rosa D, Viasus D (2015) Severe chikungunya virus infection. Salud Uninorte 31(3): 631–641. https://doi.org/10.14482/sun.31.3.7352
3. Schilte C, Staikovsky F, Couderc T, Madec Y, Carpentier F, Kassab S, Albert ML, Lecuit M, Michault A (2013) Chikungunya virus-associated long-term arthralgia: a 36-month prospective longitudinal study. PLoS Negl Trop Dis 7(3):e2137. https://doi.org/10.1371/journal.pntd.0002137
4. Yactoyo S, Staples JE, Millot V, Cibrelus L, Pardo PR (2016) Epidemiology of chikungunya in the Americas. J Infect Dis 214(5):441–445. https://doi.org/10.1093/infdis/jiw390
5. Simon F, Javelle E, Cabie A, Bouquillard E, Troisgros O, Gentile G, Leparc-Goffart I, Hoen B, Gandjbakhch F, Rene-Corail P, Franco JM, Caumes E, Combe B, Poiraudeau S, Gane-Troplent F, Djossou F, Schaerverbeke T, Criquet-Hayot A, Carrere P, Malvy D, Gaillard P, Wendling D, Société de pathologie infectieuse de langue francaise (2015) French guidelines for the management of chikungunya (acute and persistent presentations). November 2014. Med Mal Infect 45(7):243–263. https://doi.org/10.1016/j.medmal.2015.05.007
6. Chang AY, Martins KA, Encinales L, Reid SP, Acuña M, Encinales C et al (2018) Chikungunya arthritis mechanisms in the Americas. Arthritis Rheum 70(4):585–593. https://doi.org/10.1002/art.40383
7. Amaral JK, Sutaria R, Schoen RT (2018) Treatment of chronic chikungunya arthritis with methotrexate: a systematic review. Arthritis Care Res 70:1501–1508. https://doi.org/10.1002/acr.23519
8. Marimoutou C, Ferraro J, Javelle E, Deparis X, Simon F (2015) Chikungunya infection: self-reported rheumatic morbidity and impaired quality of life persist 6 years later. Clin Microbiol Infect 21(7):688–693. https://doi.org/10.1016/j.cmi.2015.02.024
9. Ramachandran V, Malaisamy M, Ponnaiah M, Kaliaperuaml K, Vadivoo S, Gupte MD (2012) Impact of chikungunya on health related quality of life Chennai, South India. PLoS One 7(12): e51519. https://doi.org/10.1371/journal.pone.0051519
10. Soumahoro M, Gérardin P, Boëlle P, Perrau J, Fianu A, Pouchot J et al (2009) Impact of chikungunya virus infection on health status and quality of life: a retrospective cohort study. PLoS One 4(11): e7800. https://doi.org/10.1371/journal.pone.0007800
11. Amaral JK, Schoen RT (2018) Chikungunya in Brazil: rheumatologists on the front line. J Rheumatol 45(10):1491–1492. https://doi.org/10.3899/jrheum.171237
12. Bruce B, Fries JF (2003) The Stanford health assessment questionnaire (HAQ): a review of its history, issues, progress, and documentation. J Rheumatol 30(1):167–178
13. Cunha-Miranda L, Barcelos F, Miguel C, Silva C, Santos H, Fernandes S, Borges J, Trinca R, Vicente V, Aguiar P (2014) AB1071 the use of visual analogue scale in rheumatic disease: validation of an electronic version: table 1. Ann Rheum Dis 73(Suppl 2):1155.2–1155. https://doi.org/10.1136/annrheumdis-2014-eular.5384
14. Holm MB, Rogers JC, Kwoh CK (1998) Predictors of functional disability in patients with rheumatoid arthritis. Arthritis Care Res 11(5):346–355. https://doi.org/10.1002/art.1790110506
15. Jankowska-Polańska B, Polański J (2014) Review methods of evaluation of the quality of life in rheumatic diseases. Reumatologia/Rheumatology 1:69–76. https://doi.org/10.5114/reum.2014.41453
16. Ganu MA, Ganu AS (2011) Post-chikungunya chronic arthritis—our experience with DMARDs over two year follow up. J Assoc Physicians India 59:83–86
17. Bouquillard E, Fianu A, Bangil M, Charlette N, Ribéra A, Michault A, Favier F, Simon F, Flipo RM (2018) Rheumatic manifestations associated with chikungunya virus infection: a study of 307 patients with 32-month follow-up (RHUMATOCHIK study). Joint Bone Spine 85(2):207–210
18. Pandya S (2008) Methotrexate and hydroxychloroquine combination therapy in chronic chikungunya arthritis: a 16 week study. Indian J Rheumatol 3(3):93–97. https://doi.org/10.1016/s0973-3698(10)60125-2
19. Blettery M, Brunier L, Polomat K, Moinet F, Deligny C, Arfi S, Jean-Baptiste G, De Bandt M (2016) Brief report: management of chronic post-chikungunya rheumatic disease: the martinican experience. Arthritis Rheum 68(11):2817–2824. https://doi.org/10.1002/art.39775
20. Ravindran V, Alias G (2016) Efficacy of combination DMARD therapy vs. hydroxychloroquine monotherapy in chronic persistent chikungunya arthritis: a 24-week randomized controlled open label study. Clin Rheumatol 36(6):1335–1340. https://doi.org/10.1007/s10067-016-3429-0
21. Schoenfeld-Smith K, Petroski GF, Hewett JE, Johnson, JC, Wright GE, Smarr KL, Walker SE, Parker JC (1996) A biopsychosocial model of disability in rheumatoid arthritis. Arthritis Care Res 9(5): 368–375
22. Carmona L (2001) The burden of musculoskeletal diseases in the general population of Spain: results from a national survey. Ann Rheum Dis 60(11):1040–1045. https://doi.org/10.1136/ard.60.11.1040
23. Wysocka-Skurska I, Sierakowska M, Kułak W (2016) Evaluation of quality of life in chronic, progressing rheumatic diseases based on the example of osteoarthritis and rheumatoid arthritis. Clin Interv Aging 11:1741–1750. https://doi.org/10.2147/cia.s116185