

Clinical and Epidemiological Follow-up of Patients with Arthralgia Post Probable Chikungunya Referred to a Rheumatology Clinic at a Tertiary Hospital in Trinidad and Tobago

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ABSTRACT

Objective: To describe the arthralgia post Chikungunya (ChikV) infection in patients referred to a rheumatology clinic at a tertiary hospital in Trinidad.

Methods: Patients referred for arthralgia and prior probable ChikV-infection were surveyed. Probable ChikV-infection was defined as a clinically compatible case as reported by the patient or the healthcare provider, absence of a more likely explanation and a positive ChikV specific enzyme-linked immunosorbent assay (ELISA) for immunoglobulin (Ig) G.

Results: Fifty-two patients referred between October 2015 and May 2016 were recruited, 44 had a positive ELISA ChikV IgG and thus, were included in the analysis. The median recruitment date was 15.5 months post probable ChikV, with an interquartile range (IQR) of 4.5 months. Thirty-four (77.3%) were female, while 10 (22.7%) were male. Median age was 64 years with an IQR of 14.5 years. In the acute episode, 75.0% reported fever and 93.2% severe joint pain. The joints most affected were knees, 27.6%, shoulders, 18.4% and wrists, 15.7%. The involvement was bilateral, 70.6% more so than unilateral, 29.4%; 77.3% of patients felt that their symptoms negatively affected their daily activities, this was attributed to pain, 29.4% or pain and stiffness, 50.0%.

Conclusion: These data show that patients referred to a rheumatology clinic for arthralgia post ChikV-infection, are likely to be females more than 45 years of age. The joints most involved are the knees, shoulders, wrists and ankles, in a symmetrical distribution. Patients with persistent arthralgia post ChikV perceive that these symptoms negatively affect their daily activities.

Keywords: Arthralgia, Chikungunya, epidemiology, joint

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INTRODUCTION

Chikungunya (ChikV) viral infection has three clinical stages that account for clinical variations over time (1). These stages are not seen in all patients. The acute phase can last up to three weeks, the post-acute phase one to three months and the chronic phase months to years (1). Follow-up of patients six years after the La Reunion Island outbreak in 2006 showed that morbidity and impaired quality of life in the chronic phase can

persist even up to six to eight years after the acute infection (2). The percentage of patients in this phase wanes with time.

Chronic rheumatological sequelae is one of the features in the chronic phase. Over fifty per cent of patients reported rheumatic symptoms 15 months post ChikV viral infection from the La Reunion island outbreak and age greater than 45 years, severe initial joint pain and the presence of underlying osteoarthritis co-morbidity

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were found to be independent risk factors (3, 4). Hoarau *et al* found that the chronic group consisted mainly of patients over age 60 years and patients who had higher viral load (up to 10 viruses per mL of blood) during the acute phase (5). These patients typically report symmetrical polyarthralgia that is highly incapacitating (6). Subsets of these patients with chronic polyarthralgia also have chronic inflammatory rheumatism.

The ChikV outbreak in the Americas began in December 2013 and there have been over two million cases (7). Rodriquez-Morales *et al* reported that at least half of the patients with post ChikV in La Virginia, Risaralda, Colombia, developed chronic rheumatological sequelae and patients over age 40 years required more medical attention than those less than 40 years old (8). There is need for continuous assessment of ChikV sequelae in the Americas since this could have significant impact on economic and health resources in the region.

The aim of this study is to describe the arthralgia post chikungunya in patients referred to a rheumatology clinic at a tertiary care institution in Trinidad.

SUBJECTS AND METHODS

A cross-sectional study was conducted on patients referred for probable ChikV-related joint symptoms to a rheumatology clinic at Port-of-Spain General Hospital in Trinidad and Tobago. Ethical approval was obtained from the Ethics Committee of The University of the West Indies, St Augustine Campus, The North West Regional Health Authority and the Caribbean Public Health Agency and written informed consent was obtained from each participant prior to enrolment.

Inclusion criteria

Patients referred to the rheumatology clinic at the Port-of-Spain General Hospital with arthralgia post probable ChikV-infection during the period October 1, 2015 to May 31, 2016.

Exclusion criteria

Patients less than 18 years old and those who did not meet the criteria for probable ChikV-infection were excluded from the study.

Definitions

The definition for probable ChikV-infection is defined by the Center for Disease Control and Prevention Arboviral Diseases, Neuroinvasive and Non-neuroinvasive 2015 case definitions as: A clinically compatible case of ChikV was met if fever was reported by the patient

or healthcare provider AND absence of neuroinvasive disease (such as meningitis, encephalitis, acute flaccid paralysis documented by physician) AND absence of a more likely clinical explanation. Probable ChikV-infection was met in our patient study group once the referring physician felt that the patient had met the clinical criteria for probable ChikV, was referred in re ChikV associated arthralgia or persistent joint pains post ChikV and also had a positive ChikV IgG *via* ELISA method, given that the patients in the study were recruited a median of 15.5 months post probable ChikV-infection.

The research team administered a case report form to collect data from participants and a 5 mL sample of blood was obtained from each participant for ChikV IgG ELISA testing. The case report form gathered demographic data, symptomatology including joint involvement, duration of illness and impact of activities of daily living.

Statistical analysis

All data collected was analysed using SPSS version 23. The χ^2 -test was used for qualitative variables and $p < 0.05$ was considered statistically significant.

RESULTS

The study was conducted between October 1, 2015 and May 31, 2016. Fifty-two patients were recruited. These patients were all referred for probable ChikV associated arthralgia or joint pains post probable ChikV. Of this group, 44 patients had positive ChikV IgG serology, two patients had indeterminate and six patients had negative serology. Thus data from the 44 patients formed the study cohort. Of the study group, 77.3% were female with the remaining 22.7% male. The median age was 64.0 years, with an interquartile range (IQR) of 14.5 years. The minimum age of the study cohort was 29 years and the maximum age was 87 years. The most common referring sites were the local health centres, accounting for 59.0% ($n = 27$) of the study group as shown in Fig. 1. The median recruitment date was 15.5 months post probable ChikV-infection, with an IQR of 4.5 months. Co-morbidities and demographic characteristics for the study cohort are presented in Table 1.

The acute ChikV presentation of the study cohort varied. Approximately, 93% of patients required no hospitalization, 75.0% of patients noted a fever, 93.2% reported severe joint pains, and as little as 29.5% noted a rash. Table 2 outlines the symptoms of the cohort during the presumed acute ChikV episode. The joints most affected in the acute and chronic period were:

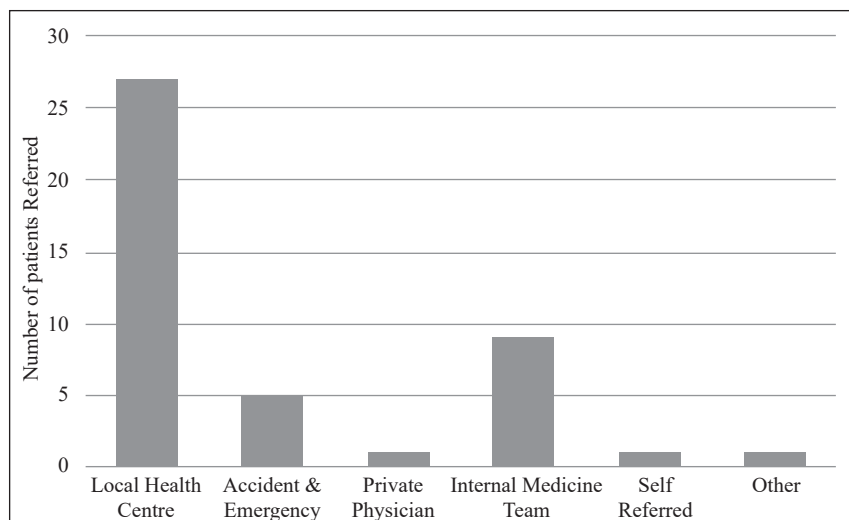


Fig. 1: Referring sites.

Table 1: Characteristics of patients referred to a Rheumatology clinic for persistent arthralgia post probable ChikV-infection

Variables	Study group
Number of patients	44
Median age in years (IQR)	64 years (14.5)
Sex ratio M/F	10/34 (22.7%/77.3%)
Chronic heart disease	4 (9.0%)
Chronic lung disease	3 (6.8%)
Diabetes	5 (11.3%)
Hypertension	13 (29.5%)
History of previous RMSD	17 (38.6%)
Blood transfusion in preceding months	0 (0.0%)
Median time from probable ChikV to recruitment (mths) (IQR)	15.5 (4.5)

RMSD: rheumatic musculoskeletal disorder; IQR: interquartile range; M: male; F: female

knees 27.6%, shoulders 18.4%, wrists 15.7% and ankles 13.1%. Bilateral joint involvement was present in 70.6% of patients, while unilateral joint involvement was seen in 29.4% of patients as shown in Table 3.

Of the patients presenting with persistent arthralgia post ChikV, various characteristics were noted. Ninety-seven per cent of patients who went on to have chronic arthralgia, had arthralgia during the acute episode. Of the patients reporting a previous rheumatologic condition, osteoarthritis was the most common in 29.5% (n = 13) of patients. For the treatment of persisting joint pains, 71.8% of patients reported the use of some form of treatment, the majority using conventional medications, 63.5%. The treatment history of the study cohort is shown in Fig. 2.

Of the patients reporting a previous rheumatologic condition, osteoarthritis was the most common in 29.5%

Table 2: Symptoms reported at presumed acute ChikV episode in patients referred to a Rheumatology clinic for persistent arthralgia post probable ChikV-infection

Variables/ Symptoms	Study group n (%)
Fever	33 (75)
Severe joint pain	41 (93.2)
Mild joint pain	3 (6.8)
Headaches	18 (40.9)
Nausea	9 (20.5)
Vomiting	9 (20.5)
Rash	13 (29.5)
Muscle pain	28 (63.6)

Table 3: Characteristics of rheumatism in patients referred to a rheumatology clinic for persistent Arthralgia post probable ChikV-infection

Characteristics	Prevalence in study group n (%)
Site of arthralgia at disease onset	
Hand	8 (10.5)
Wrist	12 (15.7)
Shoulder	14 (18.4)
Neck	1 (1.3)
Back	2 (2.6)
Hip	3 (3.9)
Knee	21 (27.6)
Ankle	10 (13.1)
Generalized joints	5 (6.6)
Number of joints involved at disease onset	
1	3 (6.8)
2-4	22 (50)
5 or more	19 (43.2)
Incidence of symmetry with joint involvement	
Unilateral joint involvement	20 (29.4)
Bilateral joint involvement	48 (70.6)

(n = 13) of patients. For the treatment of persisting joint pains, 71.8% of patients reported the use of some form of treatment, the majority using conventional medications, 63.5%. The treatment history of the study cohort is shown in Fig. 2. Of the patients using treatment, 75.0% (27/36) found the treatment to have some form of effectiveness. Persons despite this, perceived that these symptoms had a negative impact on their daily activities due to persistent arthralgia, 77.3 % (n = 34). The majority of the perceived negative impact was thought to be due to pain or pain and stiffness, an approximate 79.4%; this is delineated in Fig. 3.

DISCUSSION

The major findings coming out of this study, show that women more so than men are likely to be referred to a rheumatology clinic with symptoms of arthralgia

post ChikV-infection. The joint involvement is bilateral more than unilateral, with the knees and shoulders most commonly affected. No significant association was noted between premorbid conditions and the number of joints affected, ($p > 0.05$). A majority of patients (77.3%) perceived that the persistent arthralgia had a negative impact on their daily activities.

Importantly though, this study has similar observations as that gleaned in other studies on ChikV arthralgia. The study by Javelle *et al*, in Reunion Island found that patients affected with rheumatic disorders post ChikV were predominantly females older than 45 years and that done by de Andrade *et al* similarly showed a female predominance, 75%, reporting persistent arthralgia post ChikV (9, 10). The work done by Sissoko *et al* showed that persistence of joint pains occurred in an older age group, this our study also found, with a median age of 64 years (3). This study, like others done by Clementine Schilte *et al*, Essackjee *et al* and Emilie Javelle *et al*, found the joint involvement to be mostly symmetrical, with our study showing the incidence of bilateral involvement to be 70.6% (6, 9, 11).

The study done by Clementine Schilte *et al* found hands, wrists, ankles and knees to be most affected (6). Our study however found the latter three, in addition to the shoulder joint being predominantly involved. The shoulder joint was the second most affected joint accounting for 18.4% of joints involved in our study cohort. The percentage of patients that perceived a negative impact on their daily activities due to arthralgia was significant, 77.3%, and in resource limited areas such as the Caribbean, this has important implications on the anticipated demands on the social support services and

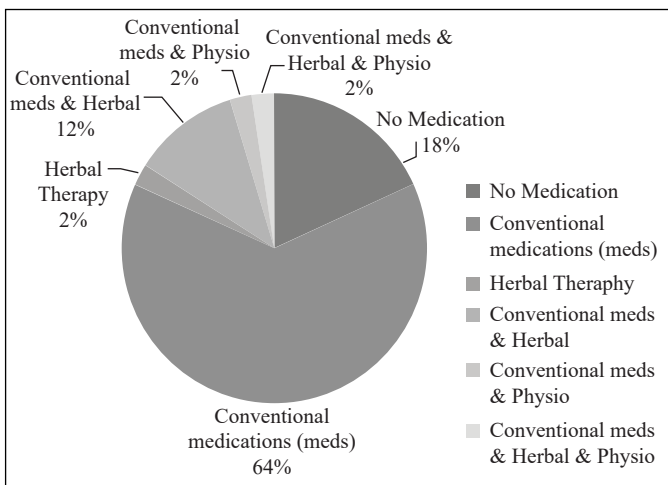


Fig. 2: Treatment history for the Arthralgia.

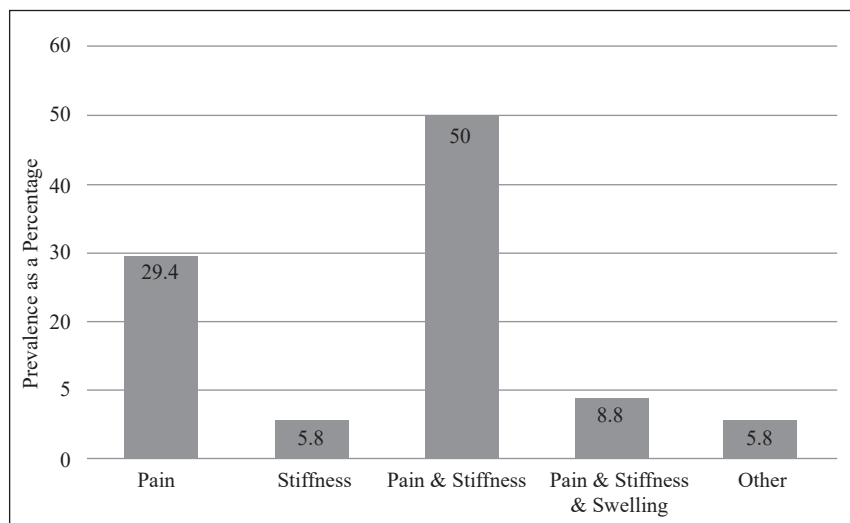


Fig. 3: Main symptoms experienced.

physiotherapy services should the arthralgia persist or progress in the ensuing years post infection. Other studies like ours, had > 50.0% of the patients affected by rheumatologic disease post ChikV reporting a reduction or negative impact upon their activity of daily living. Emilie *et al* reported that 68.0% of persons had their activities of daily living affected and in a study by Giandrea *et al* almost half of the patients reported a negative effect or impact on everyday activities (4, 9, 12).

In review of this study, a few limitations can be cited. Firstly, the number included in the study limits the initial generalizability of the information, but given the descriptive rather than comparative nature of the study design, valuable information can still be observed or inferred. Given that Trinidad and Tobago is endemic for dengue, it would have been beneficial to test the blood samples for this, given the cross reactivity of dengue and ChikV during serologic testing. This may limit causality; however, the joint pain complaint was noted to have started in direct association with a typical acute probable ChikV presentation, which occurred at the time of the ChikV epidemic in Trinidad and Tobago. The patients enrolled into our study are part of a group that were already diagnosed with chronic arthralgia from their referring physician, with the median time of recruitment from the acute ChikV episode being 15.5 months.

Importantly, this study adds to the body of data much needed by policymakers, physicians and other healthcare workers on chronic arthralgia associated with ChikV in the Caribbean and the Americas, a region presently afflicted with emerging arboviral epidemics. Future study on chronic or persistent arthralgia post chikungunya infection in the Caribbean and Americas should follow-up the patients for 24 to 36 months to delineate the percentage of patients that have a longer persistence of the arthralgia.

CONCLUSION

Our data show that patients referred to a rheumatology clinic for arthralgia post ChikV-infection, are likely to be females more than males, over 45 years. The joints most involved are the knees, shoulders, wrists and ankles, in a symmetrical distribution. Patients with persistent arthralgia post ChikV perceive that these symptoms negatively affect their daily activities. Further long term follow-up of this cohort will better delineate this and the long term impact on economic and health resources.

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