



Rapidly evolving outbreak of a febrile illness in rural Haiti: The importance of a field diagnosis of Chikungunya virus in remote locations

Ruth L Bush ^{*1}, Ian T McGraw ¹, Naila Dhanani ¹, Lee A Ray ¹, Regina M Bentley ¹, David M Vanderpool ¹

ABSTRACT

Although rarely fatal, Chikungunya virus (CHIKV) infection can lead to chronic debilitating sequelae. We describe the outbreak of suspected CHIKV in 93 subjects who presented voluntarily over 2 months to a remote rural Haitian general medical clinic staffed by international healthcare providers. Diagnosis was made on clinical signs and symptoms, as no serum analysis was available in this remote rural site. The subjects were 18.0 ± 16.2 (median \pm standard deviation) years of age and were of similar gender distribution. The presenting vital signs included a temperature of $102.3^\circ \pm 0.6^\circ\text{F}$ with fever lasting for 3.0 ± 0.7 days. Symptoms mainly consisted of symmetrical polyarthralgia in 82.8%, headache in 28.0%, abdominal pain in 17.2%, cough in 8.6%, maculopapular rash in 30.0%, and extremity bullae in 12.9%. In 84.9% of subjects, symptoms persisted for 7.1 ± 8.3 days with 16.1% having ongoing disability due to persistent pain (≥ 14 day's duration). There were no deaths. In Haiti, especially in remote, rural regions, the risk for CHIKV spread is high given the shortage of detection methods and treatment in this tropical climate. Preventative efforts are similarly lacking. Implications for a global public health impact are likely with outbreak extension and spread to neighboring countries.

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¹Texas A&M Health Science Center
College of Medicine, Bryan, TX, USA

*Corresponding Author:

Ruth L Bush

Texas A&M Health Science Center, MS
1359 8447 State Highway 47, HPEB 3060,
Bryan, TX 77807-3260

rbush@medicine.tamhsc.edu

Telephone Number: 9794360223

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INTRODUCTION

Chikungunya virus (CHIKV), from the family *Togaviridae* and genus *Alphavirus*, is a single-stranded positive-sense RNA arbovirus with an icosahedral capsid and lipid envelope that is spread by the *Aedes* mosquito.¹ CHIKV is an emerging concern in the Americas since the first documented case of autochthonous transmission in the Caribbean in December of 2013. Since then, the virus has spread to South America and throughout the Caribbean with more than 700,000 suspected autochthonous cases, more than 10,000 confirmed cases, and now, with 11 confirmed autochthonous cases in the United States.² The virus garnered interest in the 1960s and 1970s following its discovery in Tanzania in 1952. Without documented autochthonous cases outside of

endemic regions, interest dwindled until the recent outbreaks beginning in 2004.¹ With the recent documented case of autochthonous transmission in Florida, local spread of the virus in the United States is likely to continue.^{3,4} *Aedes aegypti* and *Aedes albopictus*, the known vectors for CHIKV, have been documented in Haiti.^{5,6} The presence of CHIKV in Haiti further adds to the arthropod-borne diseases already prevalent in the region.

Without definitive diagnosis of CHIKV viremia by polymerase chain reaction (PCR), seroconversion, viral isolation, or antibody tests, suspected cases are defined by presenting symptoms. The clinical syndrome consists of high fever ($>38.5^\circ\text{C}$) with severe



arthritis or arthralgia in the absence of other potential causative etiologies. Symptoms usually appear approximately 2 to 7 days after infection.^{1,4} Patients with CHIKV have a higher propensity than other arbovirus-infected patients to seek medical care due to the disabling nature of the symptomatology, particularly joint pain.^{1,7} Following acute infection, common manifestations of CHIKV include polyarthralgia in a peripheral bilateral distribution, as well as headache, myalgia, conjunctivitis, nausea, vomiting, and maculopapular rash. There is also a high incidence of lymphopenia in presenting patients, as well as other nonspecific laboratory findings such as thrombocytopenia, elevated C-reactive protein and hepatic transaminases.⁸ The disease is usually self-limiting, and typically shows resolution of symptoms within a week. Although rarely fatal, CHIKV infection can lead to chronic debilitating sequelae and severe manifestations such as severe arthralgia, atypical neurologic symptoms, retinitis, hepatitis, nephritis, and/or meningitis.^{1,7-12} There have been 14 confirmed cases in Haiti at the time of this outbreak description. However, without the ability to definitively diagnose CHIKV, the overwhelming majority are diagnosed clinically based on the suspected syndrome criteria.^{2,4} Currently, there are no effective vaccines or definitive treatments for CHIKV, therefore care for presumed cases is limited to supportive measures.¹

The first confirmed cases of CHIKV on Hispaniola was in the Dominican Republic, in April 2014.¹³ The exact date that CHIKV spread to Haiti is confounded by the lack of testing and health statistics available for this country, as well as lack of access to healthcare facilities. Also known as *Kase Le Zo* in Haitian Creole (kreyòl ayisyen), or “break the bones”, CHIKV has rapidly spread and added further to the chronic disease burden that exists in Haiti. We describe the presentation of suspected cases of Chikungunya virus infection diagnosed via patient presentation and symptom manifestation and duration at a remote outpatient rural health clinic over a two-month period.

MATERIAL AND METHODS

Study location and participants

This study was approved by the Texas A&M University Institutional Review Board. Data utilized were prospectively collected during a suspected outbreak of CHIKV in a remote rural Haitian general medical clinic staffed by international healthcare providers and then analyzed in a retrospective manner. Participating medical teams consisted of physicians, physician assistants, nurse practitioners, and registered nurses who received two hours of general training in tropical medicine and local medical issues, including management of several vector-borne diseases. The evaluation and treatment of subjects took place at the LiveBeyond Medical Clinic, located in the Ouest Province in the arrondissement of Thomazeau approximately 40 km northeast of Port-au-Prince. The surrounding rural area is a poor agrarian society with limited or no access to medical care, food, security, or clean water. This region has an approximate population of 300,000 persons though exact census data is not available.

Subjects from the surrounding areas presented voluntarily to the clinic over a two month time frame. The index case was seen on May 22nd, 2014 and the last case seen during data collection on July 21st, 2014. A standard clinical history was obtained and physical parameters measured including height or length, weight, and temperature. Blood pressure was measured in non-pregnant subjects over 18 years of age. The subjects were referred to medical teams for further evaluation. Patients were followed from presentation to clinic until August 9th, 2014 at one-week intervals.

Diagnosis and treatment

A medical doctor or nurse practitioner examined each patient. The medical director of the clinic is a medical doctor who is licensed in both the United States and Haiti. A symptom-specific history and physical exam was performed on each patient. A diagnosis determined and recorded in the medical record. The patients were treated on an outpatient basis and were followed at one-week intervals for progress and symptoms. The charts were reviewed and analyzed by the medical team.



Diagnosis of CHIKV infection was made on clinical signs and symptoms, as no serum analysis is currently available in this remote rural site. Fever and polyarthralgia has been shown to be the strongest clinical indicators of CHIKV infection, with a sensitivity and specificity of 84% (95% CI: 79%-87%) and 89% (95% CI: 86%-91%) respectively during a 2006 outbreak of the East-Central-South-African lineage rather than the Asian lineage responsible for the current Caribbean outbreak.¹⁴⁻¹⁷ There is potential for different sensitivities and specificities accounting to the different genotype, population, and the potential for other endemic arboviruses to mimic CHIKV.¹⁴ But with the published precision of clinical diagnosis alone¹⁴, barring other coinfections, field diagnosis is considered to be accurate. In remote and rural conditions, with high levels of mosquito infestation, CHIKV and Dengue fever must be prominent in differential diagnosis.

Dengue virus is endemic to Haiti, and its symptoms can closely mimic those of CHIKV.¹⁸⁻²¹ Due to the lack of definitive diagnosis through serological testing, the possibility of coinfection with both dengue fever and CHIKV secondary to the presence of *Aedes aegypti* was considered. Due to the increased bleeding risk with dengue fever, treatment was limited to pain management with acetaminophen and supportive care. Acetaminophen was the medication of choice, as opposed to non-steroidal anti-inflammatory agents which might increase bleeding tendency.^{5,6,21,22} Adults were treated with acetaminophen 500 mg as needed for pain and fever.

Children were treated with acetaminophen, 10mg/kg as needed for pain and fever greater than 101.8°F. Persistent, lingering symptoms were treated similarly. Pediatric patients did not have the persistent symptoms resulting in disability that adults experienced. Patients were counseled to stay adequately hydrated and rest as much as possible. They also received education on preventative measures to decrease mosquito bite exposure.

RESULTS

An analysis was performed of 93 subjects (5.3% of total persons seen in clinic) presenting with symptomatology consistent with CHIKV infection. Descriptive data are presented in Table 1. The subjects were an average of 21.8 ± 16.2 years of age (range 0 to 65 years; median 18 years) and were of similar gender distribution. The presenting vital signs included a temperature of 102.3 ± 0.6 F and BMI (weight/height²) of 19.0 ± 4.8 . At the initial presentation, symptoms had been present for 2.0 ± 0.6 days and included moderate to severe symmetrical polyarthralgia and swollen joints (See Figure 1) in 82.8%, headache in 28.0%, abdominal pain in 17.2%, cough in 8.6%, maculopapular rash in 30.0%, and bullae on the hands or feet in 12.9%. Interestingly, all bullae occurred on children under the age of 10 years (range 0-8 years of age). Fever lasted for 3.0 ± 0.7 days. In 84.9% of subjects, symptoms persisted for 7.1 ± 8.3 days (range 3-30 days) with 16.1% being defined as having persistent symptomatology (≥ 14 day's duration). There were no deaths during the data collection period.

Table 1 Demographics of Patient Cohort (Median \pm Standard Deviation or Percent)

	N=93
Mean age (years)	18.0 \pm 16.2
Temperature (°F)	102.3 \pm 0.6
BMI	19.0 \pm 4.8
Number of days with symptoms	7.1 \pm 8.3
Polyarthralgias	82.8%
Headache	28.0%
Abdominal pain	17.2%
Maculopapular rash	30.0%
Bullae on hands and feet	12.9%



Fig 1: Painful swollen knee in a male with clinically diagnosed Chikungunya infection

DISCUSSION

Demographics

Tropical infections such as CHIKV, malaria, typhoid, and Dengue fever present as febrile illnesses. We acknowledge that differentiating between the diseases may be difficult without laboratory diagnosis. However, the recent spread of confirmed CHIKV demonstrates the globalization of infectious diseases. With the lack of laboratory diagnosis in remote regions of Haiti, it is vital that practitioners be knowledgeable of the disease characteristics and treatment options, as well as the possibility of chronic disabling symptoms. CHIKV can be differentiated from other febrile-illnesses often based upon symptom characteristics. The pain is more intense and concentrated in a bilateral distribution in joints.

CHIKV affects all ages and both genders with similar distributions. Multiple outbreaks have been described in the literature and the series presented herein is comparable. However, the location of the disease outbreak in a very impoverished nation with a marginal chance for laboratory diagnosis or future treatment is a cause for concern. The prevalence was 5.3% among the patients in this study and all diagnoses were made by clinical means with physical exam and presenting symptoms in the absence of

costly laboratory confirmation. We acknowledge the possibility of inaccuracy of field diagnosis alone. However, without serum confirmation and with similarity of cases, prompt recognition and treatment as well as follow-up were prudent and instituted. The relatively low prevalence in this cohort may exist due to the health care access barriers. Furthermore, the symptoms alone may make travel to this healthcare facility challenging for affected persons. Many more persons may have been suffering at home. Also concerning is the lack of preventative efforts underway in Haiti considering the rapid manner in which the virus has spread throughout the region.^{2,4,15}

Currently there is no vaccine to prevent possible CHIKV infection. Chronic recurring arthralgia or musculoskeletal pains may occur with a corresponding decrease in quality of life. The symptoms alone may limit a parent or guardian's ability to provide for the family. Preventative measures include removing sources of standing water, using insect repellent, and using window and door screens to prevent mosquito entry.^{23,24} However, these measures have not been found to be widely available or implemented in the Thomazeau region.

Most patients presented soon after fever onset and



none were referred to a distant hospital. Studies have documented the acute onset ranging from 2 to 7 days after the infective mosquito bite.^{3,4,7} Also described has been a group of persons who have asymptomatic disease, ranging from 5 to 10% of those with serum documentation. Unfortunately, this region in Haiti has no way of knowing the actual numbers of those with possible CHIKV infection, symptomatic or asymptomatic, due to lack of reporting standards, centralized data collection, or serum analysis. High fever and symmetric musculoskeletal symptoms that are progressive, indicative of probable CHIKV infection, were common in this cohort. Peripheral joints are usually swollen with pain occurring with both passive and active range of motion. Inflammatory joint effusions have also been described. Attention should also be given to bullae that appear on the extremities, particularly in young children. The diagnosis of CHIKV should be considered. No current treatment exists beyond pain medication and non-steroidal anti-inflammatory agents. This clinic chose to give acetaminophen to affected individuals to avoid any potential bleeding risk, which could occur with aspirin.

Impact

The most common presentations in this cohort were febrile polyarthralgia or very high fever alone. The risk of a chronic debilitating arthralgia could potentially pose a further economic burden on an already impoverished Haitian economy. Infectious diseases in the developing world are predominant factors for poor health status and poverty. The recent CHIKV epidemic most likely has negatively impacted the working population. Therefore it is imperative to continue efforts aimed at diagnosing, controlling, and educating the general public on febrile illnesses including CHIKV. Education to the surrounding population on signs and symptoms as well preventative measures are necessary. The CHIKV epidemic has not been limited to Haiti. Autochthonous cases have been documented in the United States as well as imported cases from tourists, missionaries, and aid workers.

There are several limitations to this study. First, this is a retrospective chart review with its inherent limitations particularly with the language and

education barrier. Second, the lack of definitive serological testing adds a large potential for confirmation bias and misidentification, especially with other endemic illnesses having similar presentation (e.g. Dengue fever). Third, there is a limitation in evaluating chronic sequelae in the relatively short follow-up times for the patients that presented near the end of the data collection period.

CONCLUSION

This cohort highlights the importance of clinical diagnosis CHIKV infection in remote field conditions. The clinical features described herein of polyarthralgia, especially when combined with fever, are reasonable for a field diagnosis of CHIKV in the absence of serological testing. Patients with a presumptive diagnosis should be followed for development of chronic recurring and disabling arthralgia. Persistent disabling symptoms may lead to devastating economic impact in an impoverished society. Developing countries with lacking healthcare infrastructure have difficulties coping with high caseloads, which highlights the need for surveillance, vector control, laboratory confirmation, and communication, none of which have been readily available. International healthcare providers need to heed preventative measure to avoid global importation of CHIKV.

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