

Outbreak

Outbreak of Chikungunya in the Republic of Congo and the global picture

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Abstract

Chikungunya fever is a crippling disease caused by an arthropod-borne virus (arbovirus) transmitted to humans through mosquitoes. Although Chikungunya virus is not often associated with mortality, the effects of virus outbreaks are often devastating, causing significant economic loss due to the strain on health care. Chikungunya is quickly spreading globally as a result of viral genetic mutations leading to the adaptation of new vector hosts and insecticide resistance. The recent outbreak of Chikungunya fever in the republic of Congo has reported thousands of people affected. Here we review the past Chikungunya fever epidemiology and new reports aimed at therapeutic intervention of this disease.

Key words: Chikungunya; virus; arbovirus; outbreak; Congo; cytokine

J Infect Dev Ctries 2011; 5(6):441-444.

(Received and Accepted 02 July 2011)

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Introduction

It is becoming clear that Chikungunya virus is not the virus we thought it was. Chikungunya fever (CHIKF) in humans is caused by infection of the chikungunya virus (CHIKV) which is transmitted by mosquitoes to people (arthropod-borne virus; arbovirus) [1]. It has historically been thought of as a mild disease not associated with mortality. The defining symptom of CHIKF is severe joint pain and as the severe joint pain increases the patient often takes a bent posture [2]. *Chikungunya*, a word originating from the Tanzanian and Mozambique region meaning *that which bends up*, describes this distorted posture [3]. First identified in the 1950s [2], recently CHIKV has caused severe outbreaks associated with mortality in the Indian Ocean region. The virus has also spread from its tropical origins to temperate regions by adapting to a new mosquito vector. Chikungunya is now a global concern.

June 2011 Outbreak of Chikungunya in the Republic of Congo

It was reported by IRIN on 15 June 2011 that a large outbreak of possible Chikungunya fever (CHIKF) is affecting the Republic of Congo (<http://www.irinnews.org/Report.aspx?ReportID=92989>) [4]. In Brazzaville, the Republic of Congo's largest city, an estimated 1,000 cases of CHIKF were suspected in the first half of June. Testing of patients

who presented with CHIKF symptoms in the Republic of Congo resulted positive for the CHIKV.

By the end of June (28 June) an IRIN representative reported that approximately 8,000 people were affected with CHIKF with no associated deaths [5]. The virus has now spread from affecting only Brazzaville to the region of Pool and testing has shown that the virus is being carried by both the *Ae. albopictus* and *Ae. albopictus* mosquitoes [5].

CHIKF not only a disease of the tropics

Historically CHIKV was found only in tropical regions. In 2007, an outbreak of CHIKV occurred in the Emilia Romagna region of Northern Italy. The Italian outbreak of CHIKV spread through communities surrounding the city of Ravenna during August to October of that year and also involved the major Italian city of Bologna [6,7]. It was determined that 254 people were infected with CHIKV which was transmitted by *Ae. albopictus* mosquito. The *Ae. albopictus* mosquito, a mosquito that inhabits temperate regions, has been found in the Emilia Romagna region since 1990 [8-10]. The virus was brought to the Emilia Romagna region by a traveller returning from a CHIKV affected country. The virus was of the Central/East African virus genotype [8,9] and genomic sequencing showed that the amino acid sequence included a substitution mutation in the E1 envelope protein (E1-A226V)

[11]. This mutation has been shown to be important for viral entry into host cells. Specifically, this mutation was acquired during the large 2005-2006 Indian Ocean CHIKV outbreak and enabled the virus to infect the *Ae. albopictus* mosquito when previously it only infected the *Ae. aegyptii* [12]. Importantly, this outbreak showed that temperate regions are also susceptible to the CHIKV infections and not only tropical regions. CHIKV is now of global health concern since expansion of mosquito vectors has created the potential for the Chikungunya virus to spread to temperate areas as *Ae. albopictus* inhabits regions in North America and Europe [13,14].

History of CHIKV and previous CHIKV outbreaks

Chikungunya was identified in East Africa in the early 1950s and since then has caused epidemics in continental Africa, the Indian Ocean region, and countries of Southeast Asia such as India where an estimated 1.39 million cases (since 2006) have been identified [15-19]. Previously the only reported outbreak outside these areas was in Italy in the Emilia Romagna region in 2007. However, small non-epidemic imported cases have been reported in other regions such as North America, France and Japan, which were caused by travellers returning from affected areas [20-22].

La Reunion Island

When CHIKV was first identified, the virus was only transmitted by the *Ae. aegyptii* mosquito [3,23]. Importantly, now CHIKV has been shown to infect and be transmitted by two species of mosquitoes: *Ae. aegyptii* and *Ae. albopictus* mosquitoes. During the epidemic on La Reunion Island, the CHIKV acquired a genetic mutation permitting the *Ae. albopictus* mosquito to carry the CHIKV.

The epidemic which occurred on La Reunion Island, Indian Ocean, in 2005-2006 was a devastating CHIKV outbreak where over one-third of the population was affected [23]. It has been estimated that CHIKV infected over 266,000 individuals [2] and included cases presenting with severe clinical manifestations of the disease such as neurological symptoms, mother-to-foetus virus transfer, and mortality [24,25].

CHIKV in India

Although CHIKV had been reported previously in India in 1963 in Calcutta [26,27], in 2005-2006 CHIKV emerged in epidemic proportions. Frequent

outbreaks were reported in India between 1963 and 1973 but subsequently to these dates there were no major CHIKV outbreaks reported until 2006. Since 2006 there is estimated to be 1.39 million cases in India [15-18]. This epidemic has affected 12 states in India, and was found to be caused by the African genotype of the virus. Analysis of this epidemic showed a 1.2:1 distribution of males to females and a fever lasting a mean of four days where 10% of the patients had persistent joint pain [28].

CHIKV in Africa

CHIKV was initially identified in 1953 in the Africa country of Tanzania [29]. Since then, the virus has moved through a reported 24 countries in continental Africa [30]. Smaller epidemics have been seen in Africa between 2006 and the present, affecting approximately 15,000 individuals per outbreak [11]. Interestingly, the Republic of Congo has previously experienced an emergence and re-emergence of the CHIKV after a gap of 39 years [31].

CHIKV clinical manifestations

Other symptoms of CHIKF include sudden appearance of high fever, rash, headache, nausea, vomiting, myalgia and arthralgia or severe joint pain. Symptoms start four to seven days following infection, which defines the acute phase of CHIKF. Importantly, while the acute phase lasts approximately two weeks, joint pain can persist for months or years following initial infection [7,8,30]. Neurological symptoms have been reported in some outbreaks [2,24].

CHIKV treatments

Currently, the immune response for CHIKV infection remains largely uninvestigated and there is no specific treatment available. As reported in 2010, R. Ravichandran and M. Manian investigated the use of the antiviral agent ribavirin in patients suffering from severe joint pain attributed to CHIKV infection [32]. The ribavirin-treated patients had a faster resolution of joint pain and joint inflammation compared to a control patient group.

Cytokines have also been investigated as possible therapeutic drug targets and/or biomarkers for CHIKF [33,34]. Importantly, Cytokines are immune mediators that direct immune responses during infection. Ng and colleagues found that IL-1, IL-6 and RANTES were correlated with the severe acute phase CHIKF during the Singapore 2007 CHIKV

outbreak [34]. These cytokines need further investigation to be validated as possible biomarkers and/or drug targets for CHIKV.

Chikungunya virus phylogenetics

Chikungunya virus (CHIKV) is a single-stranded positive-sense RNA virus of approximately 11.7 kb long. There are three genotypes (African, Asian and West African) of the virus that all belong to the *Alphavirus* genus in the *Togaviridae* family [13,30].

Conclusions

In recent years the characteristics of CHIKV have changed significantly where parallels can be drawn from the epidemiology of West Nile Virus [35,35]. Chikungunya virus mutation, adaptation to new vectors, and spread to temperate regions signifies the seriousness of CHIKV as a global threat.

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Conflict of interests: No conflict of interests is declared.