

# Vector-Borne Diseases & Treatment

## Chapter 2

### Chikungunya: A Neglected Re-Emerging Disease

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#### Abstract

Chikungunya virus (CHIKV) is a re-emerging arthropod borne virus transmitted by *Aedes* species of mosquitoes that causes major outbreak in more than 60 countries in Asia, Africa and more recently Europe and American continents. The re-emergence of chikungunya poses major public health burden worldwide, mostly affecting low and middle income countries. The outbreak is relatively uncommon; sporadic and affects all age groups. It is a febrile disease characterized with debilitating polyarthralgia lasting for weeks to months. Although chikungunya infection has caused millions of cases, still it is poorly documented without specific preventive and therapeutic interventions. This chapter summarizes our current knowledge about the epidemiology and clinical significance of chikungunya virus, mosquito vector, prevention and control measures.

**Keywords:** *Aedes* mosquitoes; Alphavirus; Arthropod-borne disease; Chikungunya; Vaccine

#### 1. Introduction

Chikungunya infection is considered as a neglected debilitating disease caused by chikungunya virus. The word “chikungunya” is used for both the virus and the disease, which was derived from Makonde word meaning “to walk bent over” [1]. Chikungunya virus is an arthropod-borne virus and belongs to the genus *Alphavirus* within the family *Togaviridae* that is predominantly found in tropical and subtropical regions [2]. Since its first outbreak in Tanzania in 1952, the virus poses serious threats to humans for the last few decades. The virus was first isolated from human sera in 1953 [3]. The chikungunya outbreaks are infrequent, sporadic

and known to cause major epidemics across the globe [4]. During epidemics, humans serve as the major reservoir for the virus, whereas during non-epidemic period, monkeys, rodents and birds serve as the reservoirs. Although chikungunya is not a life threatening disease, mortality was reported in some cases [5]. The US National Institute of Allergy and Infectious Diseases (NIAID) in 2008 categorized chikungunya as ‘Category C Priority Pathogen’ because of the associated potential risk [6,7].

*Togaviridae* family comprised of two genera viz., *Alphavirus* and *Rubivirus*. The genome of chikungunya virus consists of a single stranded, linear, positive sense, ribonucleic acid of about 11.8Kb and comprised of two open reading frames encoding structural (C, E2, E3, E1) and non-structural polyproteins (nsP1, 2, 3 and 4). The structural proteins undergo post-translational modifications to form two major capsid proteins namely E1, E2 and two minor proteins called E3 and 6K [8,9]. The trimers of E1 and E2 heterodimer cover the viral surface and form the spike region. The structural proteins are involved in viral encapsidation and budding during infection. The non-structural proteins are translated from 5’ region of the viral genome which is essential for viral replication and processing [10].

## 2. Outbreaks of Chikungunya

The chikungunya virus circulates in tropics and the primary source for pathogen transmission to humans is mainly through day biting *Aedes* mosquito viz., *Aedes aegypti* (the yellow fever mosquito) and *A. albopictus* (the Asian tiger mosquito) [11]. However, maternal–fetal transmission has also been reported in the recent epidemic [12]. The regional distribution of mosquito vector indicated the predominance of *A. albopictus* in Europe and *A. aegypti* in India. The *Aedes albopictus* is diurnal with wide geographic prevalence and the mosquito’s eggs can resist desiccation. All these characteristics contribute towards the efficiency of the vector in sustaining the virus and thus spreading the disease [13].

Since 2000, chikungunya has expanded its geographic range and it has now been identified in over 60 countries in Asia, Africa, Europe and American continents [14]. In Asia, CHIKV was first reported in Bangkok, Thailand in 1958. In 1963, it was reported first time in Kolkata, India, followed by Pondicherry and Vellore (1964), Barsi (1973) [15,16]. In 2005, India has witnessed a massive outbreak of chikungunya after 32 years. The southern and central parts of India were heavily affected with more than one million cases [17]. Almost one third of the population was affected in the La Reunion outbreak in 2006. The global expansion of *Aedes albopictus* caused emergence of chikungunya cases in Europe for the first time during 2007 [18]. In 2013, the first local chikungunya case in America was diagnosed in Saint Martin. Recently, in 2015, several countries in American continent were affected and about 1.1 million cases were reported [18-20].

### 3. Symptoms

Usually, onset of illness occurs between 2-6 days, after the humans get an infected mosquito bite. CHIKV has an incubation period of 2-4 days and often clinical symptoms are similar to dengue infection. In many cases, dengue is misdiagnosed as chikungunya [21], however, unlike dengue, chikungunya is rarely fatal [22]. Chikungunya causes severe health burden to affected populations causing severe joint pain, rashes, fever, headache, nausea and fatigue. Severe arthralgic syndrome was reported in many cases including joint pain that may last for weeks to months [23]. Other symptoms including fatigue, asthenia, peripheral edema and conjunctivitis are also reported occasionally [24-28]. The clinical manifestations are highly variable and the treatment is purely symptomatic. The infected persons are given non-salicylate analgesics and non-steroidal anti-inflammatory drugs to alleviate viremia symptoms [29].

### 4. Status of Chikungunya Vaccine Development

Since 1952, CHIKV cases appear intermittently across the globe calling for the need of an effective vaccine development at earliest. During the last few years, several approaches have already been explored and substantial progress is achieved for chikungunya vaccine development. Although many vaccines are in the pipeline, still there is no effective anti-viral treatment available so far [30]. Considering these facts and the dismal figures related to disease incidence, the demand for an effective, safe and cost-effective vaccine is highly recognized.

Potential candidate CHIKV vaccines are under development and some are in clinical trials. Live-attenuated vaccines, chimeric alphavirus vaccine, DNA vaccine candidates, whole-inactivated, subunit vaccines and virus-like particle (VLP) approaches are employed to develop a safe and potent vaccine [31-37]. Among these, three vaccine candidates have shown promising results in animal models. For instance, the live-attenuated vaccine (CHIKV/IRES) projected for phase I trial protects mice from animal challenge experiments and elicits strong neutralizing antibody response. The VLP based vaccine (VRC-CHKVLP059-00-VP) has shown strong immunogenicity in animal challenge experiments. Then live attenuated measles virus-based vaccine (MV-CHIK) expressing CHIKV structural proteins elicit both humoral and cellular immune response in CHIKV challenge in mice. The Phase-I trials of the two latter vaccines have successfully completed in 2014 and 2015 respectively. However, none of the vaccine has been directly tested in humans as yet [18, 38].

### 5. Conclusion

Chikungunya is rapidly re-emerging as a major public threat which causes significant mortality and economic burden in affected countries. The early detection and appropriate management of infected vectors could possibly reduce the extent and range of infection. Although preventive measures including mosquito vector control strategies are implemented on priority,

there is no treatment or prophylactic vaccine available to prevent the transmission of virus. The recent chikungunya outbreaks across the globe highlight an increasing trend in the disease severity and its geographical range. The authors encourage to continue such epidemiological studies to generate baseline data of disease burden in distant geographical regions and prioritize the allocation of deliberate health resources and support for the ongoing vaccine initiatives.

## 6. Acknowledgements

The authors are very thankful to The Department of Biotechnology, Bharathiar University, Coimbatore, Tamil Nadu, India for supporting this research through DST-FIST (SR/FST/LST-299/2006 Dt: 31-01-2007) and UGC-SAP (F. No. 3-9/2007 (SAP-II) February 2007).

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