

COMMENTARY

Chikungunya Fever

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ABSTRACT:

Chikungunya fever is caused by the chikungunya virus (CHIKV), a mosquito-borne emerging pathogen, which was first revealed on the borders of Mozambique and Tanzania in 1952. Currently it is stretched over 40 countries globally. It is an arthropod-borne virus endemic in Africa, Southeast Asia and India. *Aedes aegypti* and *Aedes albopictus* are the mosquito vectors which spread this virus. Blood, saliva and urine are the samples for investigation. Since there is no definite treatment available, identifying ways to abolish mosquito populations is the most useful strategy to control the disease. As the virus has facility for global spread, there is need to take preventive measures as well as rapid diagnostic tests to improve identification of Chikungunya patients.

Keywords: *Aedes* mosquito, Chikungunya fever, IgM antibody, Severe sepsis, Vector-borne infections.

INTRODUCTION:

Chikungunya fever is caused by the chikungunya virus (CHIKV), a single stranded (+) RNA virus, belonging to the genus Alpha virus of the *Togaviridae* family. The word Chikungunya, comes from the Bantu language of Makonde people of northern Mozambique and southeast Tanzania, meaning, "That which bends up", ascribing to the stooped posture which develops due to arthritic symptoms.¹ First identified on the borders of Mozambique and Tanzania in 1952, it has now been classified as grade C priority pathogen, because of its spread to over 40 countries worldwide.² It is transmitted by mosquitoes, predominantly *Aedes aegypti*, and *Aedes albopictus*.¹

Both CHIKV and Dengue virus are disseminated by same pattern. The infected mosquitoes bite throughout the day, with spikes in early morning and late afternoon. The *Aedes albopictus* mosquito breeds in a wider range of water-filled breeding sites than *aegypti* mosquito, which includes coconut husks, cocoa pods, bamboo stumps, tree holes and rock pools. The assorted habitats help to explain the abundance of *Aedes Albopictus* in rural and periurban areas.²

EPIDEMIOLOGY:

Historic accounts indicate the emergence of (CHIKV) as early as 18th century in Indonesia and America, by sailing ships which carried susceptible humans and peri-

domestic mosquito vector, *Aedes aegypti* for on-board circulation. Next to its discovery in 1952, the first documented CHIKV emergence provoked urban outbreaks in India and Southeast Asia, the second one was found in coastal Kenya in 2004³ which dispersed independently into islands in the Indian Ocean and to India, via infected air travelers. Subsequently, autochthonous transmission occurred in Italy and France, drafted by infected travelers from India.

Twelve cases of travel-associated CHIKV have been reported in USA, while France and UK have reported 850 and 93 cases respectively. More CHIKV-infected travelers have also been identified in Australia, Belgium, Canada, Czech Republic, French Guiana, Germany, Hong Kong, Italy, Japan, Kenya, Malaysia, Martinique, Norway, Switzerland, and Sri Lanka.⁴

The latest outbreaks were documented in Reunion, the Seychelles and India. The virus emerged in Africa, Mauritius, India and coastal Italy as well in October 2013. It has scoped to at least 45 countries and territories.⁵ CHIKV has come a long way, with several mutations assimilated. In India, approximated 1.3 million people across 13 states were reported to be infected. The increased spread is put down to an increase in global travel. Recently, risk of CHIKV to non-endemic regions has been highlighted. These cases have been archived in European countries, Australia, Asia, and United States.⁶

INCUBATION PERIOD:

The incubation period of can range from 2-12 days, most commonly between 3-7 days.

CLINICAL PRESENTATION:

Clinical course is divided into two phases: an acute phase and a chronic phase. Acute infection presents with polyarthralgia, high fever, asthenia, headache, nausea, vomiting, rash, insomnia and myalgia with joint swelling.⁷ These symptoms usually persist for weeks (Table 1). Iridocyclitis, uveitis, and retinal lesions may also occur. On skin involvement, 50% of patients may exhibit maculopapular rash. Facial edema, bullous eruptions with sloughing; localized petechiae and bleeding gums are less common skin manifestations. Newborns and older adults (≥ 65 years) have risk of

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more severe disease. Presence of hypertension, diabetes and heart disease also relate with severity of infection. In chronic stage of infection, poly-arthritis lasts for weeks to years longer than the acute stage.²

COMPLICATIONS:

Even though chikungunya usually has a mild course, severe life-threatening complications can develop. It can be complicated by multiple organ failure which leads to death. Very recently, the first cases of severe sepsis and septic shock that could be attributed to CHIKV infection were reported.⁸ Further potential long-term or severe complications include prolonged myalgia and fatigue, gastrointestinal upset, encephalitis, depression, lung, kidney and heart dysfunction.⁹

LAB INVESTIGATIONS:

The useful test within first 7 days is RT-PCR, which is very specific and sensitive, as it detects viral RNA when patient is in the acute phase of infection. Unfortunately its cost contributes to a decrease in extensive use. The second diagnostic tool is serologic assay like ELISA immunofluorescence, complement binding, and haemagglutination inhibition. Enzyme-Linked Immunosorbent Assays (ELISA) may test both anti-Chikungunya virus Immunoglobulin, IgM and IgG. They are the most economical and easy to perform, which makes them useful diagnostic tests.²

Within first week after the symptoms appear, saliva can be used for the molecular detection of CHIKV, but it has a lower sensitivity compared to blood. So blood remains the sample of choice.¹⁰ A positive serum sample along with presence of clinical signs and symptoms of

infection makes a conclusive diagnosis.

PREVENTION:

Chikungunya fever is confirmed by: isolation of the virus, molecular methods, detection of IgM antibody, and demonstration of a rising titer of IgG antibody.¹¹ Till now, no specific antiviral agent or vaccine is available against the infection, however, most would agree that the best weapon against CHIKV is prevention. The live recombinant measles-virus-based chikungunya vaccine is safe and has good immunogenicity.¹² Although live CHIKV vaccines are still under trial, one way to achieve the target is to construct a consensus-based DNA vaccine, as it can have a greater safety profile as compared to live or attenuated vaccine, and produced more rapidly than protein-based vaccines. The most effective is one which has an ability to induce both humoral and cellular immune responses.¹³

TREATMENT:

Treatment is supportive, involving rest, proper diet, movement and mild exercise.⁶ In order to minimize the spread of virus, preventative measures should be taken like, vector-control, sleeping with long-sleeved shirts and long pants and sleeping with mosquito nets covering the bed. Sleeping with air conditioning cooling system can also help to reduce transmission. These measures are prescribed as they are effective and easy to execute.² Pain relief medication, such as naproxen, ibuprofen or paracetamol may also alleviate fever and aches.⁶ Adaptive immunity has a decisive role in controlling and beating CHIKV after initial IFN-a/b and other innate immune responses have been abated. In this respect Abs could have the prime impact in anti-CHIKV immunity.^{14,15}

Table: 1
Clinical presentation of patients with Chikungunya Virus & Dengue Virus

| Clinical Features | Chikungunya Virus (CHIKV) | Dengue Virus (DENV) | Reference |
|-----------------------|---|---------------------|--------------------|
| 1) Fever, asthenia | Common | Common | [6,8] |
| 2) Myalgia | Possible | Very common | [6] |
| 3) Polyarthritits | Very Common, edematous | None | [56] |
| 4) Tenosynovitis | Yes | None | [57] |
| 5) Leukopenia | None | Yes | [58] |
| 6) Thrombocytopaenia | None | Yes | [59] |
| 7) Rash | Days 1-4, important skin edema | Days 3-7 | [6,35,58] |
| 8) Retro-orbital pain | Rare | Common | [60] |
| 9) Hypotension | Possible | Common, Days 5-7 | [60,61] |
| 10) Minor bleeding | Chronic polyarthritits up to 1 year | Common | [17,56] |
| 11) Second stage | Possible; Tenosynovitis at M2-M3 Raynaud's syndrome at M2 -M3 | Fatigue up to 3 mo | [6,56,57,58,62,63] |

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CONCLUSION:

Chikungunya has spread to over 40 countries worldwide since its emergence and globally there have been severe outbreaks which remain predominantly limited to Southeast Asia and Central Africa. Chikungunya fever must be considered in travelers who develop fever and

arthritis after traveling to areas affected by an ongoing epidemic; in this regard Public health global initiatives should be alerted on these areas in an attempt to reduce the spread of the virus to neighboring continents. Travelers to areas of epidemicity should be informed of the risk of infection and of adequate preventive

measures, such as protection against mosquitoes. To reduce contact with vectors, it is essential to develop outbreak control plans, including educational efforts for the public.

REFERENCES:

1. Taubitz W, Cramer JP, Kapaun A, Pfeffer M, Drosten C, Dobler G, et al. Chikungunya Fever in Travelers: Clinical Presentation and Course. *Clin Infect Dis*. 2007; 45(1)
2. Sanyaolu A, Okorie C, Badaru O, Wynveen E, White S, Wallace W, et al. Chikungunya Epidemiology: A Global Perspective. *SM J Public Health Epidemiol* 2016; 2(2): 1028
3. Weaver SC. Arrival of Chikungunya Virus in the New World: Prospects for Spread and Impact on Public Health *PLoS Neg Trop Dis*. 2014; 8(6): 2921
4. Thiboutot MM, Kannan S, Kawalekar OU, Shedlock DJ, Khan AS, Sarangan G, et al. Chikungunya: A Potentially Emerging Epidemic? *PLoS Neg Trop Dis*. 2010; 4(4):623
5. Bloch D, Roth NM, Caraballo EV, Muñoz-Jordan J, Hunsperger E, Rivera A, et al. Use of Household Cluster Investigations to Identify Factors Associated with Chikungunya Virus Infection and Frequency of Case Reporting in Puerto Rico. *PLOS Negl Trop Dis*. 2016; 10(10):1371
6. Mohan A, Kiran DH, Manohar IC, Kumar DP. Epidemiology, clinical manifestations, and diagnosis of Chikungunya fever: lessons learned from the re-emerging epidemic. *Indian J Dermatol*. 2010; 55:54-63
7. Sepúlveda DJ, Vera LO, Jara L, Murillo KT, Gonzalez RS, Trampe AL, et al. SAT0495 Chikungunya Viral Arthritis in Mexico: Inflammatory Biomarkers, Disability and Disease Activity Index May Be Predictors of Chronic Arthritis. *Ann of the Rheum Dis*. 2016; 75(2); 1136
8. Tsuboi M, Kutsuna S, Kato Y, Nakayama E, Shibasaki K-I, Tajima S, et al. Autochthonous Chikungunya Fever in Traveler Returning to Japan from Cuba. *Emerg Infect Dis*. 2016; 22(9):1683-5
9. Andrade DC, Jean S, Clavelou P, Dallel R, Bouhassira D. Chronic pain associated with the Chikungunya Fever: long lasting burden of an acute illness. *BMC Infect Dis*. 2010; 10: 31
10. Musso D, Teissier A, Rouault E, Teururai S, Pina J-JD, Nhan T-X. Detection of chikungunya virus in saliva and urine. *J Virol*. 2016; 13(1): 102
11. Hassan R, Rahman MM, Moniruzzaman M, Rahim A, Barua S, Biswas R, et al. Chikungunya an emerging infection in Bangladesh: a case series. *J of Med Case Rep*. 2014; 8(1): 67
12. Ramsauer K, Schwameis M, Firbas C, Müllner M, Putnak RJ, Thomas SJ, et al. Immunogenicity, safety, and tolerability of a recombinant measles-virus-based chikungunya vaccine: a randomized, double-blind, placebo-controlled, active-comparator, first-in-man trial. *The Lanc Infect Dis*. 2015; 15(5):519-27
13. Diallo M, Dia I, Diallo D, Diagne CT, Ba Y, Yactayo S. Perspectives and Challenges in Entomological Risk Assessment and Vector Control of Chikungunya. *The Jour of Infect Dis*. 2016; 214: 459-65
14. Lum F-M, Teo T-H, Lee WWL, Kam Y-W, Renia L, Ng LFP. An Essential Role of Antibodies in the Control of Chikungunya Virus Infection. *J Immunol*. 2013; 190 (12):6295-302
15. Andrade DC, Jean S, Clavelou P, Dallel R, Bouhassira D. Chronic pain associated with the Chikungunya Fever: long lasting burden of an acute illness. *BMC Infect Dis*. 2010; 10:31

