

Editorial

Chikungunya fever: clinical manifestations & management

The recent epidemics of Chikungunya fever and the return of dengue fever in India reflect the tenacity and survival capability of mosquitoes that continue to be man's deadliest foes¹⁻³. Chikungunya fever caused by Chikungunya virus (family *Togaviridae*, genus *Alphavirus*) is transmitted by the bite of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes (that also transmit dengue and yellow fevers)^{4,5}. Historical accounts of epidemics of fever, arthralgias/arthritis and rash, resembling what we now call as "Chikungunya fever" have been recorded as early as 1824 in India and elsewhere⁶. In modern times, Chikungunya fever was first described in 1952^{7,8}, following an outbreak on the Makonde Plateau, along the border between Tanganyika and Mozambique. The word "Chikungunya" translates to "that which bends up" in reference to the stooped posture developed due to the rheumatological manifestations of the disease. For a long time, it was erroneously reported both in reputed medical journals⁹ as well as in lay press and the media that the word "Chikungunya" was derived from the "Swahili" language. However, it has been suggested that the word "Chikungunya" is derived from the *Makonde* language, spoken by an ethnic group in southeast Tanzania and northern Mozambique from the root verb "kungunyala", meaning "to dry up or become contorted", and signifies the cause of a contortion or folding^{8,10}.

Chikungunya fever epidemics are characterised by explosive outbreaks interspersed by periods of disappearance that may last from several years to a few decades. A complex interaction between various factors such as the susceptibility of humans and the mosquito vectors to the virus; conditions facilitating mosquito breeding resulting in a high vector density,

ability of the vector to efficiently transmit the virus, all are thought to play a role. Increasing globalization can also facilitate the introduction of the virus from other endemic areas (*e.g.*, international travel)¹¹. The natural cycle of the virus is human-mosquito-human. We do not know how the virus is maintained in the wild in Asia. Unlike dengue virus, there is no evidence for transovarial transmission of Chikungunya virus in mosquitoes. Variations in the geographical strains of *Aedes* mosquitoes regarding their susceptibility to infection and ability to transmit the virus may be crucial factors in determining endemicity of Chikungunya virus in a given region⁴. Vertical maternal-foetal transmission has been documented in pregnant women affected by Chikungunya fever¹².

Following the report from Tanganyika in 1952^{7,8}, Chikungunya epidemics have been reported from several countries in Africa, Asia, and elsewhere. In Asia, epidemics have been documented in India, Sri Lanka, Myanmar, Thailand, Indonesia, the Philippines, Cambodia, Vietnam, Hong Kong and Malaysia^{4,5}. Since 2003, there have been outbreaks in the islands of the Pacific Ocean, including Madagascar, Comoros, Mayotte the Seychelles, and Mauritius⁶. The outbreak which began in 2005 in Reunion Island (French overseas district in the Indian Ocean) is currently ongoing⁶.

Since the first Indian report from Kolkata (Calcutta then) in 1963¹³, several outbreaks of Chikungunya fever have been documented from different parts of India including Vellore¹⁴, Chennai (then called Madras) and Pondicherry¹⁵ in Tamil Nadu, Visakhapatnam, Rajahmundry, and Kakinada in Andhra Pradesh¹⁶⁻¹⁸, Nagpur¹⁹ and Barsi²⁰ in

Maharashtra. Occasional cases were recorded in Maharashtra State between 1983 and 2000²¹.

Keeping with the character of the disease, it reemerged after nearly 32 yr in October 2005^{1,17,18}. Phylogenic analysis based on partial sequences of NS4 and E1 genes showed¹⁷ that the current isolates were African genotype while all earlier isolates (1963-1973) were Asian genotype. As on October 28, 2006, 1364135 cases suspected to be Chikungunya fever have been recorded from several parts of the country²², which is now showing a downward trend²³.

Chikungunya fever affects all age groups and both sexes are equally affected. The incubation period ranges from 3-12 days (usually 3-7 days)⁴⁻⁸. In susceptible populations, Chikungunya fever can have attack rates as high as 40 to 85 per cent. The onset is usually abrupt and sudden with high grade fever (usually 102-105 °F), severe arthralgias, myalgias and skin rash⁴⁻⁸. Prodromal symptoms are rarely reported. During the initial few days, headache, throat discomfort, abdominal pain and constipation are also frequent. There is conjunctival suffusion, persistent conjunctivitis, and cervical or sometimes generalized lymphadenopathy, with maculopapular or petechial rash present usually on the extremities, neck trunk and ear lobes. Swollen tender joints and crippling arthritis is usually evident. The viral polyarthropathy frequently involves the small joints of the hand, wrist and ankles and may also involve the larger joints such as knee and shoulder⁴⁻⁸. The pain may be severe enough to immobilise the patient and interfere with sleeping in the night. Rheumatological manifestations are some what less frequent in children. Paediatric subjects may also experience febrile seizures, vomiting, abdominal pain and constipation.

Unlike dengue fever, haemorrhagic manifestations are uncommon in Chikungunya fever. When present, they are mild and are more frequently encountered in Asian compared with African patients⁴⁻⁸. These manifestations include epistaxis, bleeding from the gums, positive Hess test, subconjunctival bleed and petechial/purpuric rash. Rarely meningoencephalitis has also been described.

The fever is of short duration and usually resolves in three to four days. In some patients, a biphasic pattern of fever has been described with a febrile episode of four to six days, followed by a fever free period of a few days followed by recurrence of fever (usually 101-102 °F) that may last a few days. Chikungunya is a self limiting disease, and the joint pains resolve in one to three weeks. However, in about 12 per cent of the patients, arthritis persisting for up to three years after the onset of illness has been documented^{24,25}.

Indiscriminate use of corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), especially aspirin and antibiotics can contribute to thrombocytopenia, gastrointestinal bleeding, nausea, vomiting and gastritis. This may lead to dehydration, pre-renal acute renal failure, dyselectrolytemia, and sometimes hypoglycaemia. These can indirectly contribute to the mortality due to Chikungunya fever.

In our experience at the Sri Venkateswara Institute of Medical Sciences, Tirupati, a tertiary care referral centre, in Andhra Pradesh, (n=876 Chikungunya suspects) during the period January-September 2006, short abrupt onset fever (100%), severe and crippling arthritis, most frequently involving knees, ankles, wrists, hands, and feet (98%) have been the most significant clinical manifestations. Rare manifestations included meningoencephalitis (1%), fulminant hepatitis (2%). Haemorrhagic manifestations were also relatively uncommon (3%) and have been mild when present (unpublished data).

Various conditions from which Chikungunya fever must be distinguished from other viral haemorrhagic fevers and viral fevers presenting with arthritis and skin rash such as dengue fever, West Nile fever, O'nyong-nyong fever, Sindbis fever; other common problems such as falciparum malaria and leptospirosis. Twin outbreaks of dengue fever and Chikungunya fever are known to occur frequently, as it is happening in several parts of India presently, especially in Andhra Pradesh and it becomes particularly important to distinguish one from the other. In a study published from Thailand²⁶,

it was reported that, compared with patients with dengue haemorrhagic fever, subjects with Chikungunya were more likely to manifest arthralgia/arthritis, maculopaular rash and conjunctival injection. However, laboratory testing is essential to distinguish Chikungunya fever from the other conditions.

In endemic areas, like for example, at our centre at Tirupati, even during the peak of the Chikungunya fever epidemic, and the resurgence of dengue fever, there has been no respite from the load of falciparum malaria and leptospirosis. The gold standard for the diagnosis of Chikungunya fever is viral culture³⁻⁷, which is seldom routinely done due to lack of adequate facilities. It has the advantage of detecting a wide range of viruses. Reverse transcription-polymerase chain reaction (RT-PCR) has also been found to be a useful molecular tool for the rapid diagnosis²⁷. More frequently, serodiagnostic methods for the detection of IgM and IgG antibodies against Chikungunya virus in acute and convalescent sera are used. These include indirect immunofluorescent method (IIF), enzyme linked immunosorbent assay (ELISA), haemagglutination inhibition or neutralization techniques⁴⁻⁸.

Treatment of Chikungunya fever is symptomatic and supportive. Ensuring adequate fluid intake, judicious use of paracetamol or NSAIDS for symptom relief can be helpful. Aspirin should be avoided due to its effect on platelets. Some clinicians have used hydroxychloroquine/chloroquine for treating the viral arthropathy of Chikungunya fever²⁸. Published evidence does not support the use of corticosteroids, antibiotics or antiviral drugs in the management of Chikungunya fever and indiscriminate use of these agents can be hazardous. Electrolyte imbalance, pre-renal acute renal failure, bleeding manifestations should be watched for carefully and managed accordingly.

Patients with Chikungunya fever should be advised to avoid being bitten by mosquitoes as the disease can be transmitted to others. Thus, the role

of educating the community and public health officials, and adequate vector control measures at the individual and community levels cannot be over emphasized.

Future requirements

Several areas on Chikungunya fever that merit future research include (i) the reason(s) for mysterious behaviour of dramatic outbreaks interspersed by periods of prolonged absence; (ii) development of an effective vaccine; (iii) affordable, reliable and reproducible indigenously developed, rapid serodiagnostic useful in the field setting; and (iv) a nationwide network of reliable, high quality of virology laboratories and developing a surveillance system for monitoring outbreaks of Chikungunya, dengue and other diseases. A drastic change in the outlook of the community and public health authorities with regard to hygiene and mosquito control measures is essential to stand a chance in the war against the mosquitoes.

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