

Chikungunya Fever: An Emerging Threat to Bangladesh

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Introduction:

Chikungunya fever is a relatively rare form of viral fever caused by an alpha virus that is spread by bite of *Aedes aegypti* mosquito. The name is derived from the Mekonde word meaning 'that which contorts or bends up' in reference to the stopped posture developed as a result of the arthritic symptoms of the disease. From the serum of a febrile human in Tanganyika (Tanzania) in 1953, Chikungunya was first isolated. Between the 1960s & 1980s the virus was isolated repeatedly from numerous countries in Central & Southern Africa, in Senegal & Nigeria in Western Africa including Zimbabwe, Zambia & Congo. During this same period, the virus was also identified in many areas of Asia including India, Sri Lanka, Thailand & Vietnam.

Aetiology:

Chikungunya virus or CHIK virus is a Group IV (+) RNA virus belonging to family *Togaviridae* with Genus *Alphavirus* and species *Chikungunya virus*.¹

Structure of Chikungunya virus:

The complete genome sequences of the Chikungunya virus have been identified from viral isolates obtained from a low number of cell culture passages. The structure has a diameter of about 50nm to 70nm.² Chikungunya virus consists of a single stranded positive sense RNA.³ The "molecular signatures" of Chikungunya virus, which constitute genetic fingerprints, in virus envelope protein E1 have also been found.⁴ The scientists suggest that, this signature may confer an advantage and favour the multiplication of the virus in *Aedes albopictus*, its vector (protein E1 is in fact involved in attaching the virus to the mosquito's cell membranes).

Transmission:

Chikungunya virus is most commonly transmitted to humans through the bite of an infected mosquito, specifically mosquitoes of the *Aedes* genus, usually by *Aedes aegypti* which usually bite during daylight hours.⁵ In Africa, the vector involved in forest area is *Aedes africanus* & in Sudan

the vector is *Aedes luteocephalus*. Various *Culex* species are also involved in urban epidemics in Asia.

Epidemiology:

In Africa, Chikungunya virus is transmitted in the savannah & forests of tropical Africa by *Aedes* mosquito & the vertebrate portion of the cycle is provided by non-human primates such as monkeys or baboons which amplify & maintain virus circulation.⁶ In African villages or rural areas these mosquitoes may then infect humans & the substantial viraemia measure suggest that humans, in appropriate setting may contribute to mosquito infection, leading to further virus amplification.

Transmission in Asia follows a different pattern from that scene in Africa, being primarily transmitted from human to human by *Aedes aegypti* & the human epidemics have all been in urban areas infested with *Aedes* mosquito. CHIK activity in Asia has been documented since its isolation in Bangkok, Thailand in 1958. A series of epidemics usually lasting a single year have been reported from Sri Lanka & Philippines.

Reasons for re-emergence of Chikungunya infection:

- Absence of herd immunity- susceptible population.
- Viral mutation.
- Increased air travel, tourism.
- Virus never disappeared, simple resurgence.

Current scenario in Bangladesh:

Recently an outbreak of Chikungunya fever has been discovered in Dhaka, Dohar & Nababganj of Dhaka district & also in Shibganj of Chapainabganj. According to IEDCR, 250 samples have been collected, among them the virus has been identified in the body of 46 persons. According to the information of Prothom Alo on 24th November, this is the 3rd outbreak in Bangladesh. The 1st one was in Poba upozilla in Rajshahi district affecting 32 people in 2008. The 2nd outbreak was in Shathiya upazilla of Pabna in 2009.

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Natural history of disease:

This disease is biphasic:

1st phase: It consists of fever & severe joint, limb & spine pains. Myalgia & conjunctivitis may also be present. It may last for 6-10 days.

2nd phase: It begins after a febrile period of 2-3 days & is associated with an irritating maculo-papular rash over the body, particularly on extensor surface of the limbs. Joint pain may persist occasionally without fever, for up to 4 months. Petechiae, bleeding from gums & a positive tourniquet test have been seen in many patients & may lead to the infection being mistaken for dengue.⁷

In some cases, myocarditis & peripheral circulatory failure have been seen. Encephalitis & manifestations of neurological involvements are occasionally observed. Some patients may develop a febrile illness without a rash or arthralgia. Most patients recover fully over a few weeks, although 5-10% experience chronic joint symptoms including pain, stiffness & swelling that may persist for years.⁸ The ESR is often mildly elevated in acute & chronic cases. Children who are infected are less likely to develop chronic illness.

Mortality rate is estimated at 0.4% but in patients aged under one year, it is as high as 2.8% & similarly in those aged more than 50 years, death rate increases.

Incubation period: It is usually 2-3 days, with a range of 1-12 days.

Clinical Features:

Chikungunya is an acute infection of abrupt onset, characterized by fever & arthralgia, followed by other constitutional symptoms and rash & lasting for a period of one to seven days.

- 1) **Fever:** fever rises abruptly often reaching 39 to 40 degree centigrade & accompanied by intermittent shaking chills. This acute phase lasts two to three days. The temperature may remit for one to two days, resulting in a 'saddle-back' fever curve.
- 2) **Arthralgia :** The arthralgias are polyarticular, migratory & predominantly affect the small joints of hands, wrist, ankles & feet with lesser involvement of larger joints.

Pain on movement is worse in the morning improved by mild exercise & exacerbated by strenuous exercise. Swelling may occur but fluid accumulation is uncommon. Arthralgia usually accompanied by myalgia & fatigue. Tendonitis & fasciitis may also be clinically evident. Patients with milder articular manifestations are usually symptom free within a few weeks, but more severe cases require months to resolve entirely & may lead to crippling arthritis. Generalized myalgias as well as back & shoulder pain is common.

Chronic joint pains are seen in about 1 in 10 cases of Chikungunya infection. The persistent joint pain may be mistaken for rheumatoid arthritis.

- 3) **Cutaneous manifestation:** They are typical with many patients presenting with a flush over the face & trunk, usually followed by a rash generally described as maculo-papular.⁹ Sometimes rashes are accompanied by severe itching. In many cases rash marks last for a long time (especially the ones on the face). The trunks & limbs are commonly involved but face, palms & soles may also show lesions.
- 4) During the acute disease, most patients will have headache.
- 5) Photophobia & retro-orbital pain may also occur but not severe.
- 6) Conjunctival infection is present in some cases.
- 7) Although rare, the infection can result in meningo-encephalitis especially in newborns & those with pre-existing medical conditions.
- 8) In pregnant woman the biggest risk is the possibility of transfer of virus to the foetus. In addition, delivery becomes complicated if the infection starts late in the pregnancy sometimes requiring caesarean section. The virus is not transmitted through the breast milk.
- 9) Chikungunya can be deadly in the case of very old and in newborns. Patients with poor immune systems may require hospitalization.

Case definition:

- **Suspect case:** An acute illness characterized by sudden symptoms of fever with several of the following symptoms- joint pain, headache, back ache. Photophobia, arthralgia & rash.
- **Probable case:** As above & positive serology (when single serum sample is obtained during acute phase or during the convalescence).
- **Confirmed case :** A probable case with any of the following :
 - 1) Four fold HI antibody difference in the paired serum sample.
 - 2) Detection of IgM antibody.
 - 3) Virus isolation from serum.
 - 4) Detection of Chikungunya with virus Nucleic acid in sera by RT-PCR.

WHO criteria for Chikungunya diagnosis:

- **Clinical criteria:** acute onset of fever >38.5°C and severe arthralgia/arthritis not explained by other medical conditions.
- **Epidemiological criteria:** residing or having visited epidemic areas, having reported transmission within 15 days prior to the onset of symptoms.
- **Laboratory criteria:** at least one of the tests mentioned above.

Difference between Dengue & Chikungunya: Dengue

Aspect	Dengue	Chikungunya
Clinical features	Fever, headache, joint pains (Break-bone fever), retro- orbital pain, lower back pain are the usual features.	Fever, joint pains, myalgia, conjunctivitis and maculo-papular rash are the usual features
Course	In Dengue fever patient apparently improves after 3 to 4 days, around 5 th to 6 th day fever intensifies and the patients' conditions can rapidly deteriorate.	The course is of benign disease which usually heals spontaneously after 1 week
Chronicity	There is no chronicity.	There may be chronicity, the disease may last for week to months.
Subsequent Attack	Patient with Dengue are always in risk of subsequent attack by a different serotype of dengue virus.	Once an attack of Chikungunia gives lifelong immunity.
Complication	It may become fatal. With life threatening bleeding, patient may present with shock.	It is usually non fatal, temporary meningo-encephalitis in young children and new born babies may occur rarely.
Treatment	Classical Dengue fever needs supportive treatment. Fever can be treated with paracetamol. DHF and DSS need good medical care and patient should be treated with right amount of I.V. fluid.	Purely symptomatic treatment with paracetamol or NSAID.

The clinical manifestations of Chikungunya fever resemble those of Dengue fever, laboratory diagnosis is critical to establish the cause of disease & initiate specific public health response.

Three main laboratory tests are used for diagnosing Chikungunya fever:

- Virus isolation.
- Serological tests.
- Molecular diagnosis by Polymerase Chain Reaction.

Collection of samples for serology:

- **Sample:** Blood in plain vial/ serum.
- **Time of collection:**

1st sample: Five days after onset of illness for IgM detection as these antibodies appear at this time.

2nd sample: At least 7-10 days after the 1st sample.

Collection of samples for Isolation & Molecular diagnosis:

- **Sample:** Serum.
Mosquitoes collected in nature.
- **Time of collection:** Within first 5 days of illness.

Laboratory tests:

- 1) **Virus isolation:** It is the most definitive test. Chikungunya virus produces cytopathic effects in a

variety of cell lines including BHK-21, HeLa & Vero cells. The cytopathic effects must be confirmed by CHIK specific antiserum & the results can take between one to two weeks.

- 2) **RT-PCR:** Recently, a reverse transcriptase, RT-PCR¹⁰ technique for diagnosing Chikungunya virus has been developed using nested primer pairs amplifying specific components of three structural gene regions- capsid(C), Envelope E2 & part of Envelope E1. PCR results can be available from within one to two days.
- 3) **Serological diagnosis:** It can be made by demonstration of fourfold increase in antibody in acute & convalescent sera or demonstrating IgM antibodies specific for Chikungunya virus.

A commonly used test is the Immunoglobulin M antibody (IgM) capture enzyme linked immunosorbent assay (MAC-ELISA).¹¹ Results of MAC-ELISA can be available within one day.

Interpretations of results:

- Sero-diagnosis tests on demonstrating a fourfold increase in CHIK IgG titer between the acute & convalescent phase sera. However, getting paired sera is usually not practical. Alternatively, the demonstration of IgM antibodies specific

for Chikungunya virus in acute phase sera is used in instances where paired sera cannot be collected.

- A positive virus culture supplemented with neutralization is taken as definitive proof for the presence of Chikungunya virus.
- PCR results for E1 & C genome either singly or together constitute a positive result for Chikungunya virus.

Treatment:

- There is no specific treatment for Chikungunya. The illness is usually self-limiting & will resolve with time.
- Main purpose of treatment is the management of fever and pain. For treatment of Chikungunya fever, Paracetamol is given in the first few days. It is only required in cases where fever management is essential.
- Other medical conditions if any must be evaluated before taking any medicines. Other non steroidal medicines such as Tramadol may be taken for pain management.
- Non-aspirin & non-steroidal anti inflammatory drugs are recommended. There is no role of antibiotics & antiviral agents.¹²
- Supportive care with rest is indicated during acute joint symptoms. Movement & mild exercise tend to improve stiffness & morning arthralgia, but heavy exercise may exacerbate rheumatic symptoms.
- It is important to maintain a healthy life style to promote early recovery from Chikungunya joint pain. A healthy diet which includes fruits and vegetables and good sleep promotes early recovery.
- In unresolved arthritis refractory to NSAID, Chloroquine¹³ is found to be effective.

Prognosis:

- Chikungunya is rarely fatal. Recovery from the disease varies by age. Younger patients recover within 5 to 15 days; middle-aged patients recover in 1 to 2.5 months. Recovery is longer for the elderly.
- However, the chronic joint pain associated with it can substantially reduce the quality of life for a patient.

Vaccine against Chikungunya:

- Currently there are no vaccines available in the market for preventing Chikungunya disease.^{14,15}
- However scientists have developed a working vaccine for Chikungunya. The experimental Chikungunya vaccine contains noninfectious virus like particles coated with the same protein that enables Chikungunya virus to pass through cell walls.

- However the vaccine particle doesn't contain the proteins that Chikungunya uses for replication and hence is harmless.
- The vaccine looks like Chikungunya virus to the immune system which in turn produces antibodies against it. From the experiments on monkeys it was found that these antibodies can prevent Chikungunya infection.
- Monkeys were injected with the vaccine and then after 15 weeks they were injected with Chikungunya virus. It was found that the vaccine offered 100% protection from the disease. The next step for this vaccine is human testing.
- In the case of Chikungunya, careful evaluation is required before any vaccination is recommended.
- Chikungunya is relatively a low risk infection and hence vaccine side effects must be compared with the actual risk for Chikungunya infection.
- Obviously in areas where the infection incidence is low and where mosquito bites are also low, probably there is no need for a vaccine. So when the Chikungunya vaccine becomes available, it is up to the individuals to take an informed decision.

Prevention & Control:

- There is no vaccine or specific medication available against Chikungunya infection.
- Vector control is thus very important in controlling or preventing Chikungunya transmission. Elimination of breeding sites or source reduction is an effective method of control. *Aedes aegypti* is typically a container habitat species & breeds primarily in artificial container & receptacles.
- The best way is to encourage people to eliminate the mosquito habitats by emptying water containers once a week & keeping the permanent water containers covered with a tight fitting lid. Adoption of these methods can be encouraged through community based programmes.
- Legislation, strong public advocacy & community involvement can also help in vector control.
- Personal protection like long sleeve clothes, covering oneself fully, use of repellents, window nets play limited but useful role.
- Use of standard case management guidelines help in reducing the mortality due to Chikungunya.

Conflict of Interest : None

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