Original Article

Chikungunya – A Review Article

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Introduction:

Chikungunya (also known as chikungunya virus disease or chikungunya fever) is a debilitating, but non-fatal, viral illness. Chikungunya virus, which is classified in the family Togaviridae, genus *Alphavirus,* spread by the bite of infected mosquitoes. These are the same tropical and sub-tropical mosquitoes that carry the dengue virus. Clinical presentation also resembles dengue fever.

Chikungunya occurs mainly in Africa, India, and Southeast Asia. There have been a number of outbreaks in the Philippines and on islands throughout the Indian Ocean. Epidemics are sustained by the human-mosquito-human transmission cycle.

The *Aedes* mosquitoes that transmit chikungunya virus (CHIKV), breed in a wide variety of manmade containers which are common around human dwellings. These containers collect water, and include discarded tyres, flowerpots, old oil drums, animal water troughs, water storage vessels, and plastic food containers. Lack of public health infrastructure and lack of awareness promote uncontrolled mosquito breeding are conducive to outbreaks of chikungunya, or other mosquito borne diseases. During December 2008, an investigation team from the Institute of Epidemiology, Disease Control and Research (IEDCR) and ICDDR,B investigated the first outbreak of Chikungunya fever, a viral mosquito borne disease, in Rajshahi and Chapianawabganj districts of Bangladesh.[1]

In late October 2011, a local health official from Dohar Sub-district, Dhaka District, reported an outbreak of undiagnosed fever and joint pain. Investigation at the time of outbreak confirmed the aetiology, describe the clinical presentation, and identify associated vectors.[2]

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Literally, the word "Chikungunya" translates to "that which bends up" in reference to the stooped posture developed due to the rheumatological manifestations of the disease. In Congo, it has been called "buka-buka", meaning "broken-broken" once again reflecting the incapacitating arthralgias that are common acute manifestations of Chikungunya fever.[3.]

Geographical Distribution of Dengue and Chikungunya

Another important aspect of identifying Dengue and Chikungunya is to be aware of geographical distribution of these diseases. It is very important for doctors to get patient history including their travel history. The following maps show the geographical distribution of Chikungunya and Dengue as of 2015.

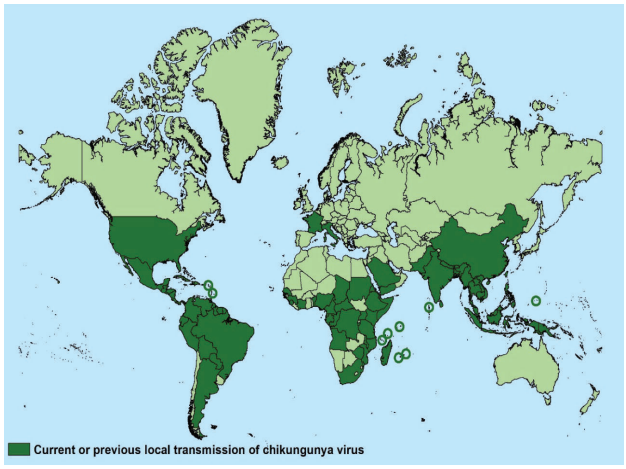

Fig.-1 Geographic Distribution of Chikungunya Fever (2015)

How does Chikungunya virus spread?

During infection, the virus replicates so aggressively, that up to 1 million viruses can be found in a single drop of blood[4]. When a mosquito bites an infected individual, the mosquito gets a stomach full of virus then replicates without killing the mosquito. Next time when the

infected mosquito bites a healthy human or animal, will then be infected with Chikungunya virus. Of the many species of mosquitoes across the globe, two species play critical but distinct roles in the spread of Chikungunya virus: *Aedes aegypti* and *Aedes albopictus* (Figure 2)[5]. One species spreads the virus among wild animals, and the other spread the virus in urban areas among humans.

The incubation period from 4to 8 days but may vary from 2 days to 12 days from the bite of the mosquito and the appearance of clinical features.

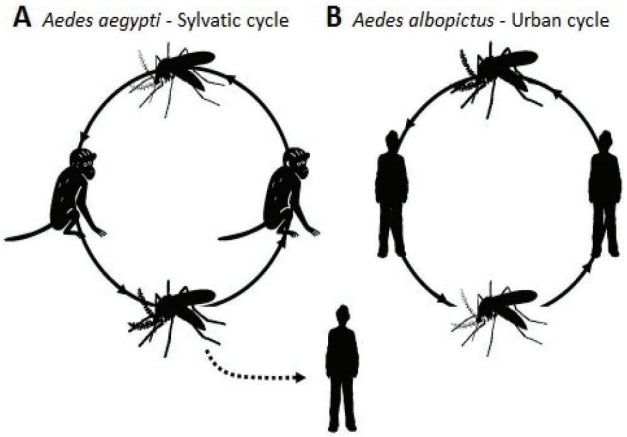

Figure 2 Two cycles of Chikungunya transmission from two species of

A) Sylvatic cycle: *Aedes aegypti* mosquitoes breed in the wild and prefer to feed on primates, rodents, and birds in the wild. Humans traveling in forested areas may be at risk for rare infections.

B) Urban cycle: *Aedes albopictus* mosquitoes that breed in man-made containers in urban areas prefer to feed on humans and carry Chikungunya virus between humans.

Pathophysiology

Following transmission, CHIKV replicates in the skin, and disseminates to the liver, muscle, joints, lymphoid tissue (lymph nodes and spleen) CHIKV spreads rapidly in the body after initial infection. Following inoculation with CHIKV through a mosquito bite, the virus directly enters the subcutaneous capillaries, with some viruses infecting susceptible cells in the skin, such as macrophages or fibroblasts and endothelial cells. Local viral replication seems to be minor and limited in time, with the locally produced virus probably being transported to secondary lymphoid organs close to the site of inoculation. Virus dissemination through the blood and pathological events associated. True arthritis remains a rare event (from 2% to 10%).The pathological events associated with tissue infection are mostly subclinical in the liver (hepatocyte apoptosis) and lymphoid organs (adenopathy), whereas in the muscles and joints are associated with very strong pain, with some of the patients presenting arthritis.[6,7]

Clinical features:

The incubation period of chikungunya disease is from 2-6 days with symptoms usually appearing 4–7 d post-infection.

Children

Chikungunya fever in children resembles that observed in adults with important differences.[8] Common clinical manifestations include abrupt onset of high-grade fever, skin rashes, minor hemorrhagic manifestations, arthralgia/arthritis, lymphadenopathy, conjunctival injection, swelling of eyelids, and pharyngitis. Rare clinical features include neurological manifestations including seizures, altered level of consciousness, blindness due to retrobulbar neuritis, and acute flaccid paralysis. Rheumatological manifestations are somewhat less frequent in children. Pediatric subjects may also experience febrile seizures, vomiting, abdominal pain, and constipation.[8,9]

Clinical features of Chikungunya fever, for better understanding can be divided in 2 phases

Acute Phase

Onset

Prodromal symptoms are rare. In the acute stage, the onset is usually abrupt and sudden with high-grade fever (usually 102-105 °F), severe arthralgias, myalgias, and skin rash. [10] Headache, throat discomfort, abdominal pain, and constipation may also be evident. Conjunctival suffusion, persistent conjunctivitis, cervical, or sometimes generalized lymphadenopathy may be present.

Mucocutaneous manifestations

Several mucocutaneous manifestations, such as morbilliform eruption, scaling, macular erythema, intertrigo, hypermelanosis, xerosis, excoriated papules, urticaria, and petechial spots have been described in patients with Chikungunya fever. [11,12] These are described in detail elsewhere in this issue of the journal.

The virus has been shown to infect epithelial and endothelial cells, fibroblast and monocyte derived macrophages explaining the involvement of muscle, joints and connective tissue.

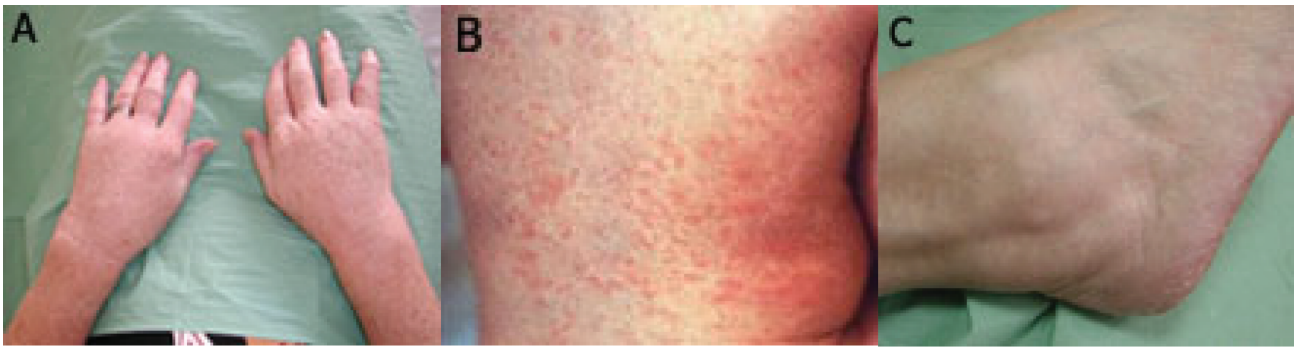

Figure 3 : Chikungunya fever symptoms. A and B: Rash characterized by raised, spotted lesions, C: Joint pain with the presence of swelling (Internet)

Neurological manifestations

Although described in other alphavirus infections, neurovirulence and neuro-invasiveness are not common manifestations of Chikungunya fever.[10] During the present epidemic, several neurological manifestations were documented. Wadia [13] described the following neurological manifestations reported at 5 centres: encephalitis neuropathy myelitis ; entrapment neuropathy and muscle injury . In another Indian report from Kota (Rajasthan) from August to October 2006, [14] altered mental functions, seizures, focal neurological deficit with abnormal computed tomography of head and altered cerebrospinal fluid (CSF) biochemistry, and permanent neurological sequelae have been described. In a study from Nagpur[15] of the 300 patients with Chikungunya fever seen during the June-December 2006, 49 (16.3%; 42 males) had neurological complications. These included encephalitis, predominantly demyelinating type), myelopathy , peripheral neuropathy myeloneuropathy and myopathy In another publication,[16]_neurologic syndromes in 99 cases from Ahmedabad and Pune seen during 2006 included encephalitis encephalopathy and myelopathy or). The report from Andaman Nicobar Islands[17] documented acute flaccid paralysis in four patients with Chikungunya fever.

Ocular manifestations

Nodular episcleritis, acute iridocyclitis, uveitis, and neuroretinitis have been documented as unusual ocular manifestations of Chikungunya fever.[18,19]

Hemorrhagic manifestations

Unlike dengue fever, hemorhhagic manifestations are uncommon in Chikungunya fever. When present, they are mild and more frequently encountered in Asian compared with African patients[10] .

Chronic stage

In a majority of the patients, the joint pains resolve in 1 to 3 weeks. However, the arthritis can persist in about 33% of patients for 4 months, 15% for 20 months, and in 12% for 3-5 years. [20,21] ,

The chronic stage is characterized by unpredictable relapses that include sensation of fever, asthenia, and exacerbation of arthralgias and stiffness. Affected patients may manifest inflammatory polyarthritis, severe subacute tenosynovitis/bursitis (consequently nerve tunnel syndromes) in hands, wrists, and exacerbation of pain on movement in previously injured joints. [22]

Chronic Phase

Most patients recover fully but the chronic stage of chikungunya fever is characterized by polyathritis that can last from weeks to years beyond the acute phase. The word "chikungunya" means "to walk bent"

Occasional cases of eyes like uveitis and retinitis, neurological complication like meningoencephalitis and myocarditis have been reported.

Effect on pregnancy

Chikungunya fever appears to have a direct impact on pregnancy with a higher risk of abortion in the first trimester and mother-to-child transmission in the last trimester.[23,24] In a study from the Reunion Islands outbreak, three out of nine miscarriages before 22 weeks of gestation were attributed to the Chikungunya virus infection documented by positive reverse transcription polymerase chain reaction (RT-PCR) in amniotic fluid. [25]

Clinical and laboratory features of chikungunya virus infections compared with Dengue virus infections

	Chikungunya	Dengue
Fever (>39°C)	+++	++
Arthralgia	+++	+/-
Arthritis	+	-
Headache	++	++
Rash	++	+
Myalgia	+	++
Hemorrhage	+/-	++
Shock	-	++
Lymphopenia	+++	++
Neutropenia	+	+++
Thrombocytopenia	+	+++
Hemoconcentration	-	++

Neonates

Mothers afflicted with Chikungunya fever in the perinatal period (–4 days to +1 days) can transmit Chikungunya fever to neonates by vertical transmission.[26] Intrapartum transmission also contributes; caesarean section does not appear to prevent the transmission.[26,27] Neonatal Chikungunya fever is associated with fever, poor feeding, pain, distal edema, various skin manifestations, seizures, meningo-encephalitis, and echocardiographic abnormalities in the newborn.[26]

How is chikungunya diagnosed?

The confirmation of Chikungunya fever is through any of the followings:

Four fold HI (Haemagglutination Inhibition) antibody difference in paired serum samples. This turns positive within 5 to 8 days of infection.

1 Isolation of virus

2. Detection of virus nucleic acid in serum by RT-PCR. This needs to be conducted within 5 days of infection.

3. Detection of IgM antibody. These antibodies persist upto 6 months of infection

4 . Demonstration of rising titre of IgG antibody

IgM antibodies demonstrable by ELISA may appear within two weeks. In some persons it may take six to twelve weeks for the IgM antibodies to appear in sufficient concentration to be picked up in ELISA

No significant pathognomonic hematological finding is seen. Leucopenia

with lymphocyte predominance is the usual observation. Thrombocytopenia is

rare. Erythrocyte sedimentation rate is usually elevated. C-Reactive Protein is

increased during the acute phase and may remain elevated for a few weeks. A

small proportion of patients have tested positive for rheumatoid factor during and after clinical episode.

WHO Criteria for Chikungunya Diagnosis

1. Clinical criteria: acute onset of fever >38.5°C and severe arthralgia/arthritis not explained by other medical conditions.

2. Epidemiological criteria: residing or having visited epidemic areas, having reported transmission within 15 days prior to the onset of symptoms.

3. Laboratory criteria: at least one of the tests mentioned above.

Treatment of Dengue and Chikungunya

There is no antiviral drug or medicine specific for Chikungunya yet available. But chikungunya is cured by immune system in almost all cases . Treatment usually is for the symptoms and includes sufficient rest, maintain hydration, nutrition and medicines to relieve pain (paracetamol). Rehydration is important in all cases of fever, particularly in hot climates like Bangladesh, where patients should be treated with oral rehydration therapy as required. Patients specially in children when associated with severe anorexia and or with repeated vomiting should be treated with parenteral rehydration. Platelet transfusion never required in chikungunya. Currently there are no vaccines available for Chikungunya. Numbers of vaccines are in clinical trials and we can expect vaccines for Chikungunya will be available in near future.

Usually the disease starts to decrease in intensity after 3 days and it may take up to 2 weeks for recovery. But in elderly the recovery is very slow and may take up to 3 months. In some cases the joint pain can last even up to a year specially in adult.

How can chikungunya be prevented?

There is neither chikungunya virus vaccine nor drugs are available to cure the infection. Avoiding mosquito bites

and to eliminating the mosquito breeding sites is another key prevention measure. To prevent mosquito bites, do the following:

- Use mosquito repellents on skin and clothing
- When indoors, stay in well-screened areas. Use bed nets if sleeping in areas that are not screened or air-conditioned.
- When working outdoors.

Conclusion:

Through the recent epidemics, CHIKV has demonstrated its ability to spread and infect large proportions of the population. There is a very good chance that CHIKV will continue to spread unless measures are taken to improve the recognition of the disease, to control the vectors responsible for the transmission, and to rapidly communicate epidemiological information to vector control experts and other public health officials. Hopefully, timely sharing of accurate information will help control the spread and magnitude of future outbreaks.

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