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# Chikungunya

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#### ABSTRACT

Now a days, Chikungunya has become the principal jolt in the world. Chikungunya is a form of viral fever caused by an Alphavirus that is spread by mosquito bite of the Aedes aegypti mosquito. The condition known as Sandhi jwara in Sanskrit has the similar symptoms to Chikungunya. The symptoms of Chikungunya include sudden fever, joint pain with or without swelling, chills, headache, nausea, vomiting, lower back pain, and skin irritation. Chikungunya spreads from one individual to another through the bite of the mosquito and is generally observed among family members. Chikungunya mainly occurs in the continents of Africa and Asia. Several countries including India have increased surveillance for this disease since 2006. In 2007, limited transmission of Chikungunya virus occurred in Italy. This disease is rarely life-threatening. Epidemics of fever, rash and arthritis, resembling Chikungunya fever have been recorded as early as 1824 in India. However, the virus was first isolated in 1952 from both, human beings and mosquitoes in Tanzania during an epidemic of fever that was considered clinically indistinguishable from dengue. Till date, there is neither any specific anti-viral treatment available for Chikungunya nor any vaccine. The treatment of Chikungunya at present is only symptomatic. Medicines such as naproxen, acetaminophen, or paracetamol are employed to relieve fever and joint pain. Aspirin should be avoided as it increases the risk of bleeding.

Key words : Aedes aegypti, Chikungunya, Chills, Fever

## INTRODUCTION

"One fine morning, I experienced while talking with one of my close friends, a growing pain in my right hand, and the joints of the lower arm, which proceeded step by step upwards to the shoulder and then continued onto all the limbs; so much so that by evening, I was already in my bed with high fever. I often found myself crawling to perform day-to-day household activities, as I was not in a position to stand erect. It has now been three weeks that I have not been able to go out of my home due to severe and continuous pain in my joints, arthralgia, severe fatigue and swelling in my both the ankles. Climbing the stairs up and down has become a terrible task due to stiffness and pain in my feet." These are the wordings of a patient suffering from Chikungunya.

#### **Background:**

The word Chikungunya has no connection for its origin to chickens. The term Chikungunya is derived from the word 'Swahili', which means stooped posture (In Makonde language which is spoken in East Africa). The disease was first described by Marion Robinson and W.H.R. Lumsden (Lumsden, 1955). Chikungunya fever is a viral illness that is spread by the bite of infected *Aedes aegypti* mosquito. It is caused by an insect-borne single stranded RNA virus, called as Chikungunya virus (CHIKV) or Buggy Creek Virus. This virus is an arthropod borne virus (arbovirus), a member of the genus, *Alphavirus*, in the family Togaviridae. This virus is spherical in shape and 60 nm in diameter. A burst of infection occurred in Africa in 2006, through a new species of mosquito called Aedes Albopictus. About 1 million people are infected with Chikungunya annually since 2006 around the Indian Ocean and causes intense joint pain, which can persist for years.

#### History:

The first outbreak of Chikungunya virus infection (CHIKV) occurred in Tanzania of East Africa in 1952. Soon thereafter, epidemics were noted in the Philippines (1954, 1956, and 1968), Thailand, Cambodia, Vietnam, India, Burma, and Sri Lanka. In 1999, an outbreak had occurred in Port Klang of Malaysia. Since 2003, there have been outbreaks in the islands of the Pacific Ocean, including Madagascar, Comoros, Mauritius, and Reunion Island, with a surge in numbers of cases after the December 2004 Tsunami. In January 2006, over ten thousand cases have been reported in an epidemic on

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Reunion Island. It is suspected that many cases of Chikungunya are either misdiagnosed or go unreported. Subsequent epidemics have been reported from Zimbabwe, South Africa, West Africa, Central Africa, Southeast Asia, and the Indian subcontinent mainly in Pakistan and Southern India. The first documented Asian outbreak was in 1958. The Aedes mosquitoes that transmit Chikungunya breed in a wide variety of man-made containers, which are common around human dwellings. In India, the first outbreak was reported in 1963 in Calcutta (Shah et al., 1964). After a gap of about 42 years, the infection re-emerged in India in 2005 (Chhabra et al., 2008). In India, the states affected by Chikungunya are Karnataka, Maharashtra, Tamil Nadu, Kerala, Andhra Pradesh, Madhya Pradesh, Gujarat, Andaman and Nicobar Island, Delhi, Haryana, Rajasthan, Pondicherry, and Goa. The recent epidemic started in 2006, affecting a large population in southern and central India. Over 2,000 cases of CHIKV fever were reported from Malegaon town in Nasik district of Maharashtra between February and March 2006. Several countries have increased surveillance for this disease, and cases continue to be reported throughout the continents of Asia and Africa. In Malaysia alone, more than 4,000 cases of Chikungunya fever were reported by the Ministry of Health in 2009. However, no deaths were reported due to Chikungunya fever. During 2009, more than 49,000 cases of Chikungunya fever were reported in Thailand. There were an additional 900 victims of Chikungunya in Indonesia and India recently in May, 2010.

#### Spread of Chikungunya:

Chikungunya is a benign form of viral infection caused by a RNA-virus and is relatively rare. Chikungunya virus is highly infective and disabling. CHIKV is primarily transmitted through the bite of mosquitoes, specifically the species Aedes aegypti and Aedes albopictus, also known as the Asian tiger mosquito. It exists most notably in Africa, Asia and Europe. The bite of a female Anopheles mosquito introduces the virus into the bloodstream of the host. The virus will then fuse to the plasma membrane of permissive cells in the host. If the Aedes aegypti mosquito bites an infected person, then the virus gets transferred into its body. The virus does not affect the mosquito itself; but on the contrary, the mosquito aids the virus to become stronger within its body. Now, when the mosquito bites a healthy person, the strengthened virus is now transferred into the body of that person. Monkeys, and possibly other wild animals, may also serve as reservoirs of the virus. Aedes aegypti (the yellow fever mosquito), an aggressive daytime biter, which breeds in household containers is primarily

responsible for Chikungunya fever seen in humans. *Aedes albopictus* (the Asian tiger mosquito) may also play a role in human transmission in Asia. Various forest-dwelling mosquito species in Africa have also been found to be infected with the virus. Chikungunya is not a contagious disease as the transmission of infection cannot occur directly from human to human in the absence of mosquito bite. A pregnant lady carries the risk of transmitting Chikungunya to her foetus.

#### **Pathophysiology:**

The exact pathophysiology of human CHIKV infection is still unknown. It was found from animal experiments that CHIKV mainly targets fibroblast cells, which are responsible for tropism of muscles, joints, and skin (Ziegler *et al.*, 2008). Even hepatic and myocardial tropism was found in patients with severe disease, which demonstrate the presence of virus in liver mainly in Kupffer cells and myocytes. Two critical factors influencing viral replication are i) neonatal age and ii) defective type-I interferon (IFN) signaling. Even after the disappearance of virus in the muscles of legs was observed.

#### Symptoms:

CHIKV infection (whether clinical or silent) is thought to confer life-long immunity. The incubation period for Chikungunya usually ranges from 2–12 days. Chikungunya typically lasts a few days to 2 weeks. However fatigue may last for several weeks in some patients.

Symptoms of Chikungunya	
Fever with very high temperature about	Persistent
40°C (104 °F)	headache
Chills	Nausea and
	vomiting
Arthralgia (Severe pain all over the body)	Conjunctivitis
Arthritis ( pain in the joints along with	Slight
inflammation)	photophobia
Myalgia (muscular pain)	Loss of taste
Maculopapular rashes mainly on limbs and	Mouth ulcers
trunk	
Fatigue, lethargy and weakness	Neutropenia
Cardiovascular and neurological disorders occur in rare cases	

#### **Diagnosis:**

#### Enzyme-linked immunosorbent assays (ELISA):

It is a serological test used to confirm the presence of IgM and IgG anti-Chikungunya antibodies. Three to five weeks after the onset of illness, IgM antibody levels are the highest and persist for about two months. The IgM specific response against CHIKV is detectable starting from two to six days after the onset of symptoms by ELISA/ immunofluorescence (IIF), and could persist for several weeks up to three months. Presence of IgM antibody distinguishes the disease from dengue fever. (Hundekar *et al.*, 2002)

## **RT-PCR:**

Various reverse transcriptase–polymerase chain reaction (RT–PCR) methods are available but are of variable sensitivity. RT–PCR is used for genotyping of the virus, which allows comparison of samples of virus from various geographical sources.

### Virus isolation:

This technique involves exposing specific mammalian cell lines (Vero cells) to samples from whole blood or by culturing in mice and identifying Chikungunya -specific responses. It provides the most definitive diagnosis but takes 1–2 weeks for complete diagnosis. This test is sensitive during the viremic phase only, which usually last up to 48 hours after the bite.

#### Plaque neutralization test in vitro:

It is a confirmatory test though time-consuming. It can be routinely performed by third party laboratories.

#### **Treatment:**

CHIKV infection is a self-limiting illness. The treatment of Chikungunya at present is only symptomatic. Medicines such as acetaminophen or paracetamol are employed to relieve fever and joint pain. Aspirin and ibuprofen should be avoided as they are known to increase the risk of bleeding. Non-steroidal anti-inflammatory drugs like naproxen and chloroquine phosphate (250 mg/day) have given promising results. Chloroquine inhibits the entry of virus by making the entry site basic in pH.

#### Homeopathic treatment:

Homeopathy has very effective treatment for Chikungunya fever and is also equally effective in post-Chikungunya complaints like stiffness in joints, muscle pain, weakness, etc. Colchicum, Eupatorium Perfoliatum, Lycopodium, Sulphur, Arnica, Ledum Pal, Ruta are some of the examples of homeopathic drugs given according to the symptoms of the patients. These homeopathic drugs also help in sufferings due to Chikungunya. Eupatorium Perfoliatum Q (tincture, 3 to 5 drop dose) will remove the debilitating joint pains and cut short the intensity and duration of the disease. It is also claimed that the medicine Eupatorium perf. can also prevent Chikungunya infection.

#### Ayurvedic treatment for Chikungunya:

Ayurveda treats Chikungunya as a vata dosha disorder. Vata is the air component of our body, which represents the air that we breathe in and the dissolved gases in our blood. In a healthy person, there is a proper balance of the vata dosha with pitta dosha and kapha dosha. But, when this balance is impaired, the disease marks its beginning. There are some Ayurvedic herbs that can reduce the symptoms of Chikungunya by restoring the balance of these doshas.

 Dry, seedless grapes mixed with cow's milk is a good medicine, which gives relief from several Chikungunya symptoms

 Taking raw carrot is an excellent medicine as it increases resistivity of body against Chikungunya symptoms

- Tulsi leaves, which reduce fever, are taken as a medicine.

- Recently an Ayurvedic medicine, Triphala (composition of 3 fruits namely harada, amla and behada) has been found to be effective in Chikungunya. In Cochin, Ayurvedic doctors generally prescribe powdered sunflower seed taken along with honey, which is a good supplement. This mixture must be taken about 3 times a day along with your regular medicines to get relief from joint pains.

- Drinking lots of water will also help in reducing the pain and suffering from this disease.

#### Complications due to Chikungunya:

Various neurological complications include myeloneuropathy, myeloradiculitis, meningo-encephalitis, myelitis, Guillain-Barre' (GB) syndrome, external opthalmoplegia, facial palsy, sensorineural deafness, and optic neuritis. Optic nerve involvement in CHIKV infection include papillitis, retrobulbar neuritis, and neuroretinitis. Encephalitis appears to represent the most common clinical manifestation and occurs either simultaneously or within few days of the onset of systemic symptoms, during the period of viremia. Chikungunya can have problems in elderly people as their body resistance is already weak. Chikungunya in elderly patients may show cerebral complications like dementia, paralysis and kidney disorders. Similarly, Chikungunya is more critical in children than adults, since children are not able to identify the symptoms exactly (Chandak et al., 2009).

#### **Prevention of Chikungunya:**

No vaccine is available against this virus infection at

present. Prevention is entirely dependent upon taking steps to avoid mosquito bites and elimination of mosquito breeding sites.

#### Prevention from mosquito bites:

– People affected with Chikungunya should wear full sleeve clothes and long dresses to cover the limbs. Bright colored clothes are preferred in order to repel mosquitoes. For greater protection clothing may also be sprayed with repellant containing permethrin or any other Environmental Protection Agency (EPA)-registered repellant.

 Mosquito coils, insect repellants (DEET, picaridin, IR3535), electric vapour mats and mosquito nets should be used.

- Curtains (cloth or bamboo) can also be treated with insecticide and hung at windows or doors.

#### Avoid breeding of mosquitoes:

The *Aedes* mosquitoes usually breed in a wide variety of man-made containers, which are common around human dwellings. These containers include old oil drums, water troughs, discarded tires, water storage vessels, flowerpots, and plastic food containers, which collect rainwater. To get rid of mosquito breeding:

- Empty coolers, when not in use.

- Drain standing water from tanks, barrels, coolers, buckets and drums, etc.

- Change the water in pet dishes and replace the water in bird baths frequently.

- Keep away plant saucers, flowerpots, which have water collected in them.

– Introduce larvivorous fish namely *Gambusia* and Guppy in aquaria, garden pools, etc

- Cooperate with public health authorities in antimosquito measures.

#### **Diet for Preventing Chikungunya :**

- Leafy vegetarian food should be taken, as it is easily digestible.

– Ample fluids like soups, gravies, pulses should be taken in the food.

– Eat fruits like apples and plantains.

- Oil intake should be less, as it could aggravate cough.

- Take Ayurvedic preventive medicines such as Inthukantham Kashaya and Vilvadi Gulika, which enhance the immunity of the body.

#### **Concluding Remarks:**

Chikungunya fever is a viral illness transmitted

through the bite of infected Aedes mosquitoes. This illness not only resembles dengue fever but also co-occurs with dengue fever. Therefore, it is often misdiagnosed. Usually, the disease subsides in intensity after 3 days and it may take up to 2 weeks for recovery. But in elderly patients, 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! Indian systems of medicine, particularly homeopathy and ayurveda provide some beneficial symptomatic treatment for the management of Chikungunya. Despite the gravity of its infectious potency and the fear of it being a potential biological weapon, there is no vaccine for Chikungunya till date. Therefore, the best way to prevent Chikungunya is to take measures towards keeping mosquitoes away. Realizing the urgent need of a vaccine for this deadly disease, earnest efforts need to be under taken to prevent the cause and further spread of Chikungunya.

## REFERENCES

Chandak, N.H., Kashyap, R.S., Kabra, D., Karandikar, P., Saha, S.S., Morey, S.H., Purohit, H.J., Taori, G.M. and Daginawala, H.F. (2009). Neurological complications of Chikungunya virus infection. *Neurology*, **57**: 177-180

Chhabra, M., Mittal, V., Bhattacharya, D., Rana, U.V.S. and Lal, S. (2008). Chikungunya fever: A re-emerging viral infection. *Indian J. Med. Microbiol.*, **26**: 5-12.

Hundekar, S.L., Thakare, J.P., Gokhale, M.D., Barde, P.V., Argade, S.V. and Mourya, D.T. (2002). Development of monoclonal antibody based antigen capture ELISA to detect Chikungunya virus antigen in mosquitoes. *Indian J Med Res.*, 115: 144-48.

Lumsden, W.H. (1955). An epidemic of virus disease in Southern Province, Tanganyika Territory, in 1952-53. II. General description and epidemiology. *Trans. R. Soc. Trop. Med. Hyg.*, **49**: 33–57.

Shah, K.V., Gibbs, C.J. Jr and Banerjee, G. (1964). Virological investigation of the epidemic of haemorrhagic fever in Calcutta: Isolation of three strains of Chikungunya virus. *Indian J. Med. Res.*, **52**:676-83

Ziegler, S.A., Lu, L., da Rosa, A.P., Xiao, S.Y. and Tesh R.B. (2008). An animal model for studying the pathogenesis of Chikungunya virus infection. *American J. Trop Med. Hyg.*, **79**: 133-139.

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