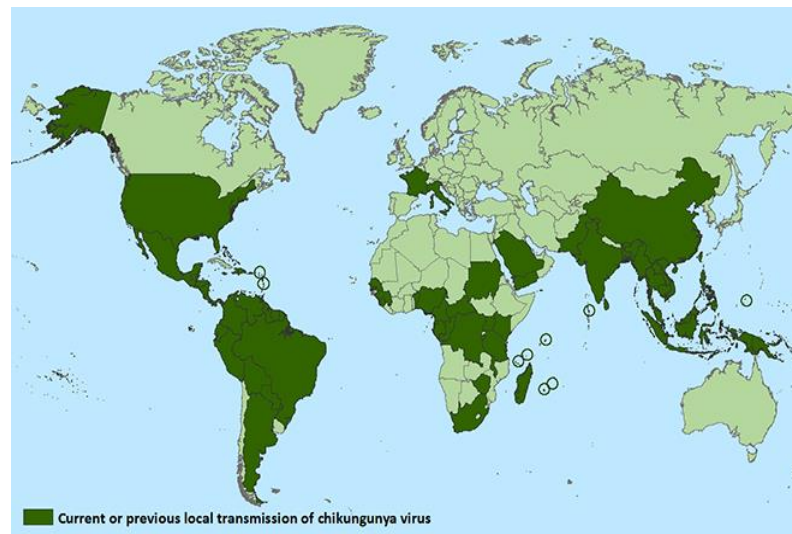
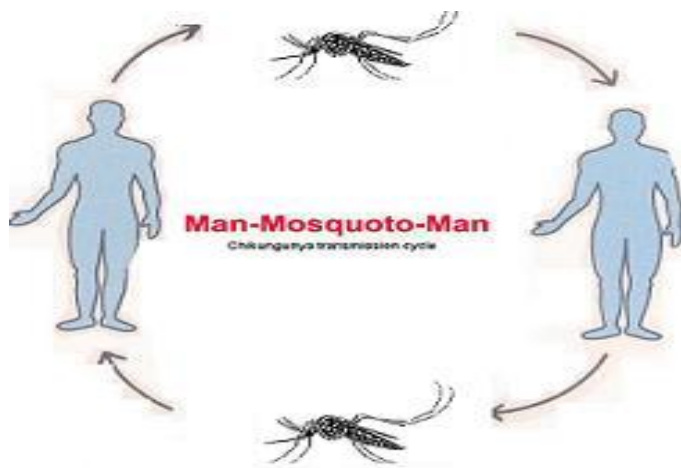




NATIONAL GUIDELINE ON CLINICAL MANAGEMENT OF CHIKUNGUNYA FEVER



Disease Control Division,
Directorate General of Health Services,
Ministry of Health & Family Welfare

National Guideline on Clinical Management of Chikungunya Fever

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List of Abbreviation and Acronyms

CDC, DGHS	: Communicable Disease Control, Directorate General of Health Services
DGHS	: Directorate General of Health Services
DRRT	: District Rapid Response Team
HEB	: Health Education Bureau
Icddr.b	: International Center for Diarrheal Disease Research, Bangladesh
IEDCR	: Institute of Epidemiology, Disease Control and Research
IHR	: International Health Regulation 2005
IHR NFP	: National Focal Point for International Health Regulation 2005(Director, DC, DGHS)
IPC	: Infection Prevention and Control
IPH	: Institute of Public Health
IPHN	: Institute of Public Health Nutrition
LD CDC	: Line Director, Communicable Disease Control
NIPSOM	: National Institute of Preventive and Social Medicine
NNS	: National Nutrition Services
NRRT	: National Rapid Response Team
OIE	: Office International des Epizooties (World Organization for Animal Health)
PHEIC	: Public Health Emergency of International Concern
PoE	: Port of Entry
RRT	: Rapid Response Team
SOP	: Standard Operating Procedure
URRT	: Upazila Rapid Response Team
UNICEF	: United Nations Children's Fund
WHA	: World Health Assembly
WHO	: World Health Organization
ZIKV	: Zika Virus

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Introduction

Chikungunya fever (CF) is a viral illness caused by an arbovirus transmitted by the *Aedes* mosquitoes. The disease was documented first time in the form of an outbreak in Tanzania. The name is derived from the ‘makonde’ dialect which means ‘that which bends up’, indicating the physical appearance of a patient with severe clinical features. The fever locally also named as ‘LangraJor’ (ল্যাংড়া জ্বর).

Chikungunya fever is caused by virus of Chikungunya virus (CHIKV) which is an RNA virus that belongs to the *Alphavirus* genus of the *Togaviridae*, the family that comprises a number of viruses that are mostly transmitted by arthropods. The virus was first isolated in 1952-1953 from both man and mosquitoes during an epidemic of fever that was considered clinically indistinguishable from dengue fever in Tanzania. It is a single stranded RNA virus, heat labile and sensitive to temperatures above 58⁰ C. Three lineages with distinct genotypic and antigenic characteristics have been identified: two phylogenetic lineages from Africa and one from Asia. Chikungunya virus strains isolated in India during the 2004-2006 outbreaks are closely related to strains isolated from Réunion islands.

Epidemiology

In the South-East Asia region, Chikungunya virus is maintained in the human population by a human-mosquito-human transmission cycle that differs from the sylvatic transmission cycle described on the African continent. A high vector density is seen in the post monsoon season that enhances the transmission. Chikungunya fever epidemics display cyclical and seasonal trends. There is an inter-epidemic period of 4-8 years (sometimes as long as 20 years). Outbreaks are most likely to occur in post-monsoon period when the

vector density is very high. Human beings serve as the Chikungunya virus reservoir during epidemic periods. During inter-epidemic periods, a number of vertebrates have been identified as reservoirs. These include monkeys, rodents, birds, and other vertebrates. The exact nature of the reservoir status in South-East Asia Region has not been documented. After an extensive outbreak during the beginning of current millennium in the French territory of Reunion Islands in the Indian Ocean, the disease has been reported from almost 40 countries from various WHO regions including South-East Asia. The spread of the disease in South India from 2004 has affected millions of people and left many with crippling disabilities. The disease continues to cause epidemics in many countries in the region. There is no significant sex predilection and the virus causes illness in almost all age groups. As this is an illness not sufficiently covered in medical curriculum, it has become necessary to develop new guidelines, based on the limited clinical experience from managing patients in the region.

Vector

Chikungunya virus is transmitted by *Aedes* mosquitoes (*Ae. aegypti* & *Ae. albopictus*) which breed in clean water collections in containers, tanks, disposables, junk material in domestic and peri-domestic situations besides natural habitats like tree holes, plantations etc. Like Dengue its transmission is also related to rainfall and temperature. In recent years, it has been observed that during the period of monsoon and post-monsoon there is an upsurge in the cases because population of the vector fluctuates with rainfall and its life span is influenced by temperature and humidity. A high vector density in the post-monsoon season enhances virus transmission. *Aedes aegypti* is the main vector of transmission of Chikungunya in Bangladesh. However, *Aedes albopictus* has

also been found to be playing a part in some areas. They are principally day biters. Eggs of these vectors have the ability to withstand desiccation for more than a year. This could result in the virus to remain in nature for long periods and cause outbreaks. Flight range of these vector mosquitoes are less making the outbreaks to occur in clusters, especially in congested localities. Recently, it has also been shown that viraemia are quite high and infected mosquitoes could transmit the disease to more than one person since small amounts of blood in the proboscis still carry large quantity of virus. *Aedes* mosquitoes take multiple feeds per day and it would also result in small focal outbreaks. In the initial part of outbreak, individual population is not protected which could result in larger outbreaks.

Transmission Cycle

The human infections are acquired by the bite of infected *Ae. aegypti* /*Ae. Albopictus* mosquitoes, which are day biters and epidemics are sustained by human-mosquito-human transmission. The incubation period (time from infection to illness) can be 2-12 days, but is usually 3-7 days. Acute Chikungunya fever typically lasts a few days to a couple of weeks, but some patients have prolonged fatigue lasting several weeks. Additionally, some patients have reported incapacitating joint pain, or arthritis which may last for weeks or months. The prolonged joint pain associated with CHIKV is not typical of dengue. Co-circulation of dengue fever in many areas may mean that Chikungunya fever cases are sometimes clinically misdiagnosed as dengue infections, therefore the incidence of Chikungunya fever could be much higher than what has been previously reported. No deaths, neuro-invasive cases, or hemorrhagic cases related to CHIKV infection have been conclusively documented in the scientific literature.

Case definition

Chikungunya Fever should be suspected when a person develops sudden onset of fever, joint manifestations and rash.

Cases are to be categorized as:

- a) **Possible case:** a patient meeting only clinical criteria
- b) **Probable case:** a patient meeting both the clinical and epidemiological criteria
- c) **Confirmed case:** a patient meeting the laboratory criteria, irrespective of the clinical presentation

Criteria for the Identification of Chikungunya Infection

Clinical criteria

- acute onset of fever $>38.5^{\circ}\text{C}$
- 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 following tests in the acute phase:

- Virus isolation by Cell Culture
- Presence of viral RNA by real Time RT-PCR (Within 5 days of onset of Illness)
- Presence of viral specific IgM antibody in single serum sample collected within 5 to 28 days of onset Fever
- Four-fold Rise of IgG antibody in samples collected at least three weeks apart (1st sample after 7 days)

Clinical Presentation

Table 1: Clinical features of Chikungunya fever

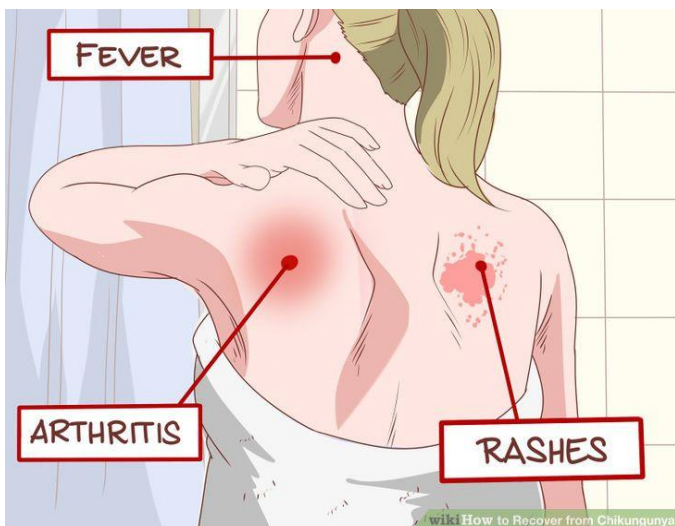
Common	Infrequent	Rare in adults but seen in children
Fever	Stomatitis	Photophobia
Arthritis/	Oral ulcers	Retro-orbital pain
Arthralgia	Exfoliative dermatitis	Vomiting
Backache	Photosensitive	Diarrhoea
Headache	hyperpigmentation	Mental confusion
Rash		Signs of meningeal irritation

Fever

The fever varies from low grade to high grade, lasting usually for 24 to 48 hours. Fever rises abruptly in some, reaching 39-40⁰C, with chills and rigor, no diurnal variation, usually subsides with use of antipyretics.

Joint manifestation

The joint symptoms usually start with arthralgia or arthritis. Involvement is symmetric and often ankles wrists and small joints of the hand are the worst affected. Migratory polyarthritis with effusions may be seen, but resolves in the majority. Larger joints like knee and shoulder and spine were also involved. Pain tends to be worse in the morning, relieved by mild exercise and exacerbated by aggressive movements. The pain may be relieved for 2-3 days and then reappear in a saddle back pattern. There is a tendency for early and more significant involvement of joints with some trauma or degeneration. The classical bending phenomenon was probably due to the lower limb and back involvement which forced the patient to stoop down and bend forward.



MucoCutaneous manifestation

Transient maculopapular rash is commonly seen, usually disappear within 48 hours. Other skin lesion may appear in the form of vesiculobullous eruption, angiomatous lesions and fewer had purpuras. Epidermolysis bullosa is also seen in children. Most skin lesions recovered completely except in cases where the photosensitive hyperpigmentation persisted. Stomatitis and oral ulcers also observed.

Neurological manifestation

Neurologic manifestations of meningo-encephalitis, encephalitis, acute encephalopathy Guillain-Barré syndrome and myelitis were reported.

Ocular manifestation

Neuro-retinitis and uveitis in one or both eyes may occur. The main ocular manifestation associated with the recent epidemic outbreak of chikungunya virus infection in South India included granulomatous and nongranulomatous anterior uveitis, optic neuritis, retrobulbar neuritis, and dendritic lesions. Majority of the patients recover with good vision.

Clinical Classification of Chikungunya Fever

Chikungunya fever is classified into three categories based on severity of clinical presentation.

Mild

- Low grade fever
- Mild arthralgia
- Mild focal myalgia
- General weakness
- Skin rash/itching

Moderate

- Low to high grade persistent fever
- Moderate arthralgia /arthritis
- Generalized myalgia
- Hypotension
- Mild bleeding
- Retro-orbital pain
- Oliguria

Severe

- Persistent high grade fever
- Severe arthralgia/Arthritis
- Persistent vomiting / Diarrhoea
- Altered sensorium
- Bleeding (GI bleeding due to use of drugs e.g. analgesics)
- Shock due to persistent vomiting and diarrhoea

High Risk group

Chikungunya infection with one of the following conditions may be considered as high risk.

a) Co-morbid condition

Hypertension, Diabetic, CAD/CVD, Geriatric age, Pregnancy, COPD,

b) Co-infection

Dengue, Tuberculosis, Enteric fever, Pneumonia, HIV, Malaria

Clinical course and outcome

- Acute symptoms typically resolve within 7–10 days

- Some patients might have relapse of rheumatologic symptoms (e.g., polyarthralgia, polyarthritis, tenosynovitis) in months following acute illness
- In variable proportions of patients, joint pain may persist for months to years.
- Rare complications include
 - uveitis, retinitis, myocarditis, hepatitis, nephritis, bullous skin lesions, hemorrhage, meningoencephalitis, myelitis, Guillain-Barré syndrome, and cranial nerve palsies may develop

Differential diagnosis

Some of the diseases which can be considered in differential diagnosis are:

- (1) **Dengue fever:** Severe back pain with purpuras or active bleeding might suggest dengue fever. Confirmatory laboratory diagnosis is possible.
- (2) **Reactive Arthritis:** In general, any arthritis that follows a febrile gastrointestinal or genitourinary infection (triggering microbes) is considered a reactive acute inflammatory arthritis if it lasts less than six months. The hallmark feature is enthesitis where collagenous structures such as tendons and ligaments insert into bone are involved. Oral mucosal ulcers are seen.
- (3) **Serum sickness illness:** Polyarthritis may be associated with a serum sickness type reaction caused by vaccine, medication or other viral infections
- (4) **Rickettsial disease** can present with fever, rash and joint pains. Confirm by serology.
- (5) **Rheumatic fever:** More common in the children and presents with fleeting (migratory) polyarthritis predominantly affecting the large joints. Modified

Jones criteria should be the basis for diagnosis. Raised ASO titre and a history of recurrent sore throat are other points to be noted.

(6) **Malaria:** patient can present with high fevers and may also complain of joint pains. Periodicity of fever and alteration of consciousness / seizures should prompt a diagnosis for malaria

(7) **Leptospirosis:** Severe myalgia localized to calf muscles with conjunctival congestion/ or subconjunctival haemorrhage with or without oliguria or jaundice in a person with history of skin contact to contaminated water would suggest Leptospirosis

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	-	++

Chikungunya and dengue

- Difficult to distinguish chikungunya and dengue based on clinical findings alone
- Chikungunya and dengue viruses transmitted by the same mosquitoes
- The viruses can circulate in the same area and cause occasional co-infections in the same patient
- Chikungunya virus more likely to cause high fever, severe polyarthralgia, arthritis, rash, and lymphopenia
- Dengue virus more likely to cause neutropenia, thrombocytopenia, hemorrhage, shock, and death
- **Patients with suspected chikungunya should be managed as dengue until dengue has been ruled out**
- Proper clinical management of dengue reduces the risk of medical complications and death
- Aspirin and other NSAIDs can increase the risk of hemorrhage in patients with dengue

Principles of Management

Mild and moderate cases can be managed at home. Severe cases should be managed at hospital.

A. Home Management

- Consume plenty of water with electrolytes (approximately 2 litres of home available fluids with salt in 24 hours).
- Take paracetamol tablets during periods of fever (up to 1000 mg tablets four times daily), in persons with no preexisting liver or kidney disease . Children may be given 50-60 mg per kg body weight per day in divided doses.
- Adequate rest in a warm environment

- Cold compresses may help in reducing joint damage. Heat may increase/worsen joint pain and is therefore best to avoid during acute stage.
- Refrain from exertion. Mild forms of exercise and physiotherapy are recommended in recovering persons.
- Avoid self medication with aspirin or NSAIDs.
- Antihistamines can be used for itching.

B. Admission criteria

1. If the person is hemo-dynamically unstable (frequent syncopal attacks, hypotension with a systolic BP less than 90 mmHg or a pulse pressure less than 30 mmHg),
2. oliguria (urine output less than 500 ml in 24 hours),
3. altered sensorium
4. bleeding manifestations
5. persons not responding or having persistent joint pain or disabling arthritis even after three days of symptomatic treatment
6. persons above sixty years
7. infants (below one year of age)
8. Pregnancy
9. High risk Group

C. Hospital management

- Assess for dehydration and institute proper rehydration therapy. (5% DNS, Normal Saline, & baby saline for paediatric cases)
- Take paracetamol tablets during periods of fever (up to 1000 mg tablets four times daily), in persons with no preexisting liver or kidney disease. Children may be given 50-60 mg per kg body weight per day in divided doses.
- Antibiotics can be used to treat secondary bacterial infection.

- Antihistamines can be used for itching.
- Cold compresses may help in reducing joint damage. Heat may increase/worsen joint pain and is therefore best to avoid during acute stage.
- Refrain from exertion.
- Mild forms of exercise and physiotherapy are recommended in recovering persons.
- Aspirin or NSAIDs should be avoided during first 10 days. NSAIDs can be used in Chikungunya only when Dengue fever is adequately excluded.
- Cutaneous manifestations with topical or systemic drugs, and neuro-psychiatric problems with specialist care and drugs).
- Steroid has no role in acute stage.
- In cases with ophthalmic symptoms complications, consult with ophthalmologists.

Treatment of serious complications

- Bleeding disorders with blood components- platelet transfusions in case of bleeding with platelet counts of less than 50,000 cells per cu mm., fresh frozen plasma, or Vitamin K injections if prothrombin time INR is more than 2.
- Hypotension with fluids/ inotropics, acute renal failure with dialysis, contractures and deformities with physiotherapy/surgery,
- Patients with myo-pericarditis or meningoencephalitis may require intensive care with regular monitoring, inotropic support, ventilation etc.
- Anti-neuralgic drugs (Amitriptyline, Carbamazepine, Gabapentin, and Pregabalin) may be used in standard doses in disturbing neuropathies.

- Use hydroxychloroquine 200 mg orally once daily or chloroquin phosphate 300 mg orally per day for a period of four weeks in cases where arthralgia is refractory to other drugs.
- Hyperpigmentation and papular eruptions may be managed with Zinc oxide cream and/or Calamine lotion

Special Situation

Effect on pregnancy

Chikungunya fever **appears to have a direct impact on pregnancy** with rare reports of spontaneous abortions and mother-to-child transmission in perinatal period.

Effect on neonates

Mothers afflicted with Chikungunya fever in the perinatal period (−4 days to +1 days before/after delivery) can transmit Chikungunya fever to neonates by vertical transmission. Caesarean section does not appear to prevent transmission. Neonatal CHIK fever is associated with fever, poor feeding, pain, distal edema, various skin manifestations, seizures, meningoencephalitis, and echocardiographic abnormalities in the newborn. No infants are found to be infected with chikungunya virus through breast feeding. Mothers are encouraged to breast feed their infants.

Laboratory Diagnosis

Preferred Specimen:

- 1) Blood or Serum
- 2) CSF (if neurological features present)

Routine Laboratory Investigations

- CBC
 - Leucopenia (Decreased WBC)
 - Thrombocytopenia: rare
 - ESR: Usually Elevated
- C-Reactive Protein: Increased during the Acute Phase and may remain elevated for a week
- SGPT: Elevated

Specific Laboratory Investigations: at least one of the following tests in the acute phase:

- Virus isolation by Cell Culture
- Presence of viral RNA by real Time RT-PCR (Within 5 days of onset of Illness)
- Presence of viral specific IgM antibody in single serum sample collected within 5 to 28 days of onset Fever
- Four-fold Rise of Ig G antibody in samples collected at least three weeks apart (1st sample after 7 days)

N.B.:

1. Diagnostic validity of currently available ICT kit for the detection of IgM and IgG for Chikungunya virus is very poor.
2. RT-PCR for Chikungunya is performed only at IEDCR.

Public Health Measures

Patient when infected can spread the infection by spreading the infection through mosquitoes. It is important to break this transmission by minimizing

the vector density by community participation and taking appropriate control measures in the hospital setting by following measures.

- Minimizing transmission of infection: This can be done in the following ways:
 - Risk communication to the household members
 - Minimize the vector population
 - Minimize the vector-patient contact (Aedes mosquitoes bite during day time, mostly in the morning and late afternoon)
 - Reporting to the nearest public health authority/ or the DPMO

Risk communication to the household members:

Chikungunya is a disease that is transmitted by mosquitoes. House hold members may also come down with Chikungunya infection as they also share the same environment. Hence, there is no need to isolate the patient or to segregate the patient. It is important to reduce the vector population in the house hold

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1. Weekly epidemiological record (WER) No. 47, 2007, 82, 409–416.
2. Geographical distribution of Chikungunya cases 2001-2007 (data are presented as reporting period followed by estimated number of cases, where data are available)
3. Guidelines on Clinical Management of Chikungunya Fever (Ministry of Health, India)

