NATIONAL GUIDELINE
for
CLINICAL MANAGEMENT OF CHIKUNGUNYA

2016

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Chapter 1

INTRODUCTION

Chikungunya fever is a viral disease transmitted to humans by the bite of infected *Aedes aegypti* mosquitoes. Chikungunya virus (CHIKV) is a member of the genus Alphavirus, in the family *Togaviridae*. CHIKV was first isolated from the blood of a febrile patient in Tanzania in 1953. Since then it has been identified repeatedly in west, central and southern Africa and many areas of Asia, and cited as the cause of numerous human epidemics in those areas. The virus circulates throughout much of Africa, with transmission, thought to occur, mainly between mosquitoes and monkeys. In 'Swahili' language, Chikungunya means that which contorts or bends up or illness of the bended walker. This refers to the contorted (or stooped) posture of patients who are afflicted with the severe joint pain (arthritis), a most common feature of the disease. It is a debilitating, but non-fatal viral illness.

Since 1960, the outbreaks of the disease in South Eastern Asia were reported from India, Sri Lanka, Myanmar, Thailand, Indonesia, Philippines and Malaysia. Chikungunya outbreaks typically result in large number of cases but deaths are rarely encountered. Chikungunya cases start appearing in post-monsoon season period that is in the month of May onwards with a peak between the month of July and August as during this period vector density remains very high.

In the Indian sub-continent, first isolation of the virus was done in Calcutta during 1963. Subsequently, there have been several reports of Chikungunya virus infection during 60's in different parts of India viz: Kolkata, Pondicherry and Chennai in Tamil Nadu, Rajamundry, Vishakapatnam and Kakinada in Andhra Pradesh, Sagar in Madhya Pradesh and Nagpur in Maharashtra.Thereafter, sporadic cases also continued to be recorded specially from Maharashtra. The last outbreak of Chikungunya infection in 20th century occurred in India during 1973. Thereafter, after a quiescence of 2-3 decades during 2006 reports of large scale outbreaks of fever caused by Chikungunya in several parts of India have confirmed the re-emergence of this virus in the country with 13.9 million clinically suspected and 2001 laboratory confirmed cases (www.nvbdcp.gov.in;Chhabra M *et al,* 2008). Since then transmission is continuing in various parts of the country. The re-emergence of Chikungunya may be due to a variety of social, environmental, behavioral and biological factors. Lack of herd immunity may have probably led to its rapid outbreak across several states of India.

During 2006, the disease re-appeared in the country, affecting millions of people in 16 States/UTs and incapacitating many of them with crippling disabilities for varied period. Since 2007 cases of clinically suspected cases of Chikungunya are being reported from many states and UT's in the country. During 2015, a total 27,553 clinically suspected case of Chikungunya have been reported from 22 states and 3 UT's.

Currently in 2016, big upsurge/epidemic due to Chikungunya is being going on in the capital city of Delhi and reporting case from other States/UT's too. Till, 11th September, 2016 a total of 14656 clinically suspected cases (including 1724 in Delhi) from 18 states and 2 UT's have been reported.
Though, so far no mortality directly due to Chikungunya has been reported so far from any part of the country and elsewhere, however, due to media report of suspected deaths due to Chikungunya and associated diseases in elderly people by two private hospitals namely Sir Gagna Ram Hospital and Apollo Hospitals in Delhi necessitated the revision of guidelines on situation to alarmed the public health system and treating physicians in the country. Against such back drop, a need was felt to revise and formulate uniform guidelines for management of acute Chikungunya cases and post Chikungunya sequlae.

Chapter 2

Chikungunya: Status & disease burden

2.1. Transmission & trends

In the South-East Asia Region, Chikungunya virus is maintained in the human population by a human-mosquito-human transmission cycle. 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 and accentuates the transmission. Human beings serve as the Chikungunya virus reservoir during epidemic period. During inter-epidemic periods, a number of vertebrates have been implicated as reservoirs in African region. These include monkeys, rodents and birds. However, the reservoir status in South-East Asia Region has not been documented yet. The agents contributing to Chikungunya fever i.e., virus and vector and host are described at **Annexure 1.**

2.2. Global situation

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 disease continues to cause epidemics in many countries in the region. The history of this disease epidemic was known since 1952 with its first ravage in East Africa followed by numerous epidemics in Asia, including the Philippines (1954,1956, and 1968), Thailand, Cambodia, Vietnam, India, Burma, and Sri Lanka. In India, the first Chikungunya outbreaks were recorded during 1963-65 and later in 1973 and again the disease reappeared in 2006 after a gap of almost 3 decades. A distinctive feature of Chikungunya virus is that it causes explosive outbreaks, before apparently disappearing for a period of several years to decades.

The re-emergence of the disease was documented in Kinshasa, Democratic Republic of the Congo during 1999-2000 after more than 39 long years with an estimated infection of 50,000 persons. Since then, epidemics were noticed in Java (2001-2003) and in the islands of the South Western Indian Ocean during the end of 2004. Then outbreaks were accounted from Comoros islands during January- March 2005 with 5,000. Later, the virus got circulated in other islands of Indian Ocean, i.e., Mayotte, Seychelles, Reunion, Mauritius. Of all the islands in the Indian Ocean, Réunion with a total population of 770,000 was the most infected with an estimated 258,000 cases by May 2006. The infection was thought to be imported from the Comoros islands. According to the *Eurosurveillance 2006*, imported cases from these countries are approximated to be nearly 307 in France, 197 in Italy, 17 in Germany, 9 in United Kingdom, 12 in Belgium and 1 each in Czech Republic and Norway. (Source : eurosurveillance 2008).

2.3. Chikungunya in India (Past & present)

In India a major epidemic of Chikungunya fever was reported during the last millennium viz.; 1963 (Kolkata), 1965 (Puducherry and Chennai in Tamil Nadu, Rajahmundry, Vishakhapatnam and Kakinada in Andhra Pradesh; Sagar in Madhya Pradesh; and Nagpur in Maharashtra). After the outbreak of Chikungunya infection in India during 1971, sporadic cases continued to be recorded during 1973 in Barsi, Solapur district Maharashtra state. The activity of CHIKV appeared to decline and no outbreak was reported from India until 2005. A study carried out in Calcutta (Kolkata) in 1994 showed 4.3% sero prevalence of Chikungunya virus out of 389 sera tested. The highest sero-positivity was observed in the age group of 51-

55 years and no Chikungunya antibody was detected in young and young adults. The findings suggested Chikungunya virus disappearing from the Calcutta population. (Neogi S *et al,* 1995).

During 2005, the outbreak in India was started in the end of year when cases of suspected fever were reported from some parts of Andhra Pradesh and Karnataka. Initially the disease was thought to be Dengue. The incapacitating arthralgia raised the doubt and in January 2006, the outbreak was confirmed as Chikungunya with laboratory findings. Subsequently, World Health Organization also confirmed re-occurrence of Chikungunya fever in India. The outbreak had an attack rate of 4–45%. (Source : WHO).

During 2006, total 13,90,322 clinically suspected cases of Chikungunya were reported from 16 States/UTs in the country. The affected States/UTs were Andhra Pradesh, A&N Islands, Karnataka, Maharashtra, Tamil Nadu, Madhya Pradesh, Gujarat, Kerala, Delhi, Rajasthan, Puducherry, Goa, Odisha, West Bengal, Lakshadweep and Uttar Pradesh, Karnataka reported maximum number of suspected cases (7,62,026) followed by Maharashtra (2,70,116), Gujarat (75,419) and Kerala (70,731). Thereafter, total 59,535 suspected Chikungunya cases in 2007; 95,091 in 2008; 73,288 in 2009; 48,176 in 2010; 20,402 in 2011; 15,977 in 2012; 18,840 in 2013; 16,049 in 2014 and 27,553 in 2015 suspected Chikungunya cases were reported respectively.

The numbers of suspected Chikungunya fever cases reported by States/UTs during 2006 and 2014-15 are as below:

Chikungunya fever Cases in the Country during 2006, 2014 & 2015							
Sl. No.	**Name of the State**	**2006**		**2014**		**2015**	
		No. Suspected Chikungunya cases	**No. of confirmed cases**	**No. Suspected Chikungunya cases**	**No. of confirmed cases**	**No. Suspected Chikungunya cases**	**No. of confirmed cases**
1	Andhra Pd.	77535	248	1359	119	817	83
2	Arunachal Pd.	0	0	0	0	35	6
3	Assam	0	0	0	0	0	0
4	Bihar	0	0	0	0	3	1
5	Goa	287	2	1205	49	561	32
6	Gujarat	75419	225	574	114	406	42
7	Haryana	0	0	3	1	1	1
8	Jharkhand	0	0	11	0	21	0
9	Karnataka	762026	298	6962	992	20763	2099
10	Kerala	70731	43	272	265	175	152
11	Madhya Pd.	60132	106	161	59	67	11
12	Meghalaya	0	0	0	0	78	15
13	Maharashtra	270116	804	1572	222	391	207
14	Odisha	6461	34	10	1	81	46
15	Punjab	0	0	2	0	180	18
16	Rajasthan	102	24	50	50	7	7
17	Tamil Nadu	64802	116	543	543	329	329
18	Telangana	0	0	1687	78	2067	149
19	Tripura	0	0	34	0	180	7
20	Uttar Pradesh	4	4	4	4	0	0
21	Uttrakhand	0	0	0	0	0	0
22	West Bengal	21	21	1032	19	1013	61
23	A&N Island	1549	0	161	31	68	3
24	Chandigarh	0	0	0	0	1	1
25	Delhi	560	67	8	8	64	64
26	D&N Haveli	0	0	0	0	0	0
27	Lakshadweep	35	0	0	0	0	0
28	Puducherry	542	9	399	16	245	8
Total		**1390322**	**2001**	**16049**	**2571**	**27553**	**3342**

Chapter 3

Laboratory diagnosis of Chikungunya fever

As the clinical manifestations of Chikungunya fever resemble those of dengue and other fevers caused by arthropod borne viruses of the *Alphavirus* genus, laboratory diagnosis is critical to establish the cause of diagnosis and initiate specific public health response.

3.1 Types of Laboratory tests available and specimens required:

Laboratory criteria include a decreased lymphocyte count consistent with viremia. However a definitive laboratory diagnosis can be accomplished through three main laboratory tests: virus isolation, serological test and molecular technique of Polymerase Chain Reaction (PCR). Specimen is usually blood or serum but in neurological cases with meningo-encephalitic feature, CSF (cerebro-spinal fluid) may also be sent.

3.1.1. Virus isolation

Virus isolation provides the most definitive diagnosis, but takes one to two weeks for completion and must be carried out in biosafety level III laboratories to reduce the risk of viral transmission. The technique involves exposing specific cell lines to samples from whole blood and identifying chikungunya virus-specific responses. The isolation process is time-consuming and the degree of success is dependent on a number of complicating factors, for example, time of collection, transportation, maintenance of cold chain, storage and processing of samples.

3.1.2 Serological diagnosis

Serological diagnosis requires a larger amount of blood than the other methods, and uses an ELISA assay to measure chikungunya-specific IgM levels in the blood serum. Chikungunya antibody tests are generally appropriate after the first week of symptom onset and onward. Serum obtained from 10-15 ml of whole blood is required. An acute phase serum must be collected immediately after the onset of illness and the convalescent phase serum 10-14 days later. The blood specimen is transported at 4° Celsius and not frozen for immediate transfer to the laboratory. Only if the testing cannot be done immediately, the serum specimen should be separated and then stored and shipped frozen. ELISA test is quite specific with very little cross reactivity with related alphaviruses.

Serologic diagnosis can be made by demonstration of four-fold rise in antibody titre in acute and convalescent sera or by demonstrating IgM antibodies specific for CHIK virus. A commonly used test is the Immunoglobulin M Antibody (IgM) capture enzyme-linked immunosorbent assay (MAC-ELISA). Results of MAC-ELISA can be available within same day.

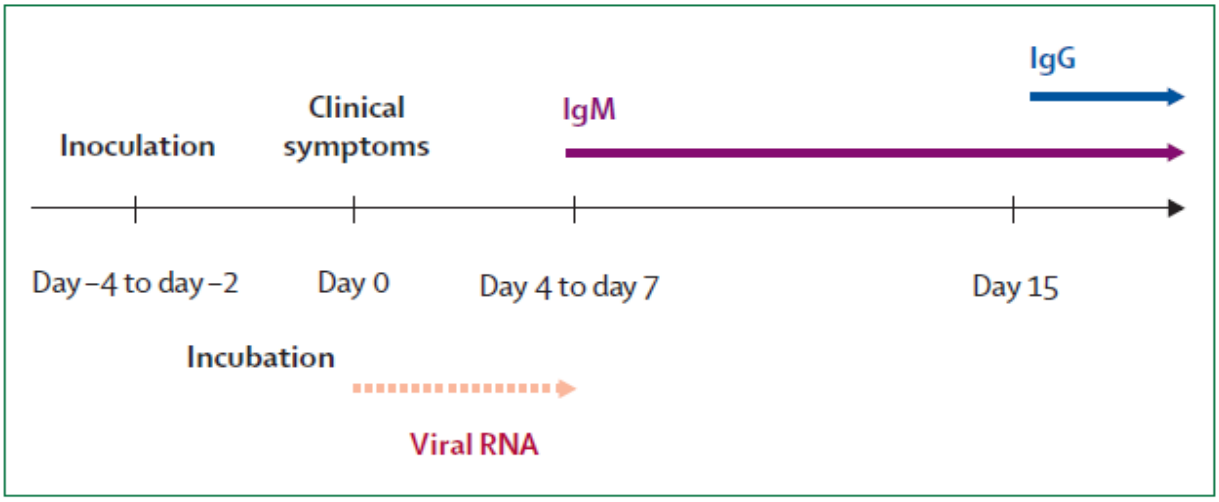
3.1.3. RT-PCR

Reverse Transcriptase, (RT) PCR technique using nested primer pairs is used to amplify several Chikungunya-specific genes from whole blood, generating thousands to millions of copies of the genes in order to identify them.The Chikungunya virus reverse transcriptase (RT)-PCR assay is appropriate in the early days of symptom onset, since CHIKV RNA can be detected during the acute phase of illness (≤8 days after symptom onset). RT-PCR can also be used to quantify the viral load in the blood. Using RT-PCR, diagnostic results can be available in one to two days.

The technique is used for diagnosing CHIK virus using nested primer pairs amplifying specific components of three structur0al gene regions, Capsid (C), Envelope E-2 and part of Envelope E1. A specimen for PCR is exactly similar to the one for virus isolation i.e. heparinized whole blood.

3.2. Interpretation of results:

Sero-diagnosis rests on demonstrating a four-fold increase in CHIK IgG titer between the acute and 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 the definitive proof for the presence of Chikungunya virus. Positive PCR result for E1 and C genome either singly or together from the specimen (serum, cerebro-spinal fluid, etc) also constitutes a positive evidence of Chikungunya virus infection.



No significant pathogenomonic haematological finding is seen. Leucopoenia 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.

3.3 NVBDCP Laboratory Network:

Directorate of National Vector Borne Disease Control Programme, GOI has identified a network of laboratories (Sentinel Surveillance Hospitals and Apex Referral Laboratories) for surveillance of chikungunya fever cases across the country since 2007. Numbers are increasing every year to augment the diagnostic facilities in all endemic areas. Numbers of SSHs has been increased from 110 in 2007 to 137 in 2008 to 170 in 2009 to 182 in 2010 to 311 in 2011, 347 in 2012, 394 in 2013, 439 in 2014, 521 in 2015 and 542 in 2016. They are linked with 15 Apex Referral Laboratories (ARLs) with advanced diagnostic facilities for back up support. For details, please refer to NVBDCP website www.nvbdcp.gov.in.

These laboratories receive the samples, diagnose and regularly send the report (line list) to districts/municipals health authorities for implementation of preventive measures to interrupt the transmission.

Chikungunya IgM ELISA Test kits (1 Kit= 96 tests) are provided to the identified laboratories through National Institute of Virology (NIV), Pune since 2007. Cost is borne by GOI. Buffer stock is also maintained at NIV, Pune to meet any emergency in case of outbreak in new areas and to avoid stock out.

3.4 Laboratory confirmation in case of Chikungunya outbreak

(*Outbreak criteria: One or more cases in an area where no case was reported before*). For the Public Health action, it is not necessary to confirm the diagnosis of each and every suspected Chikungunya case. Remedial measures for containment of the diseases, and symptomatic treatment of the suspected Chikungunya fever cases should be started immediately on the basis of Epidemiological diagnosis of the disease. However, Laboratory confirmation of the suspected cases would be required to validate the clinical diagnosis of the suspected cases. Confirmation of few cases would be enough to identify the cause of fever outbreak. Out of the reported suspected Chikungunya fever cases, 5-10% blood samples should be randomly collected for Laboratory test.

In case, any blood sample is found positive serologically for Chikungunya IgM antibody the respective area (sub-center/ Ward) should be declared as having confirmed outbreak of Chikungunya. There is no need for taking additional blood samples for laboratory diagnosis of Chikungunya from that sub-centre area/Ward and clinically suspected cases should be treated as Chikungunya.

Chapter 4

Case definition and differential diagnosis

Chikungunya should be suspected when epidemic occurs with the characteristic of abrupt onset of fever, arthralgia and myalagia, with or without rash.

4.1 Case definition

Probable or suspected case: a patient meeting the clinical criteria only

Confirmed (definitive) case: a patient meeting both the clinical and laboratory criteria,

Clinical criteria:

- Acute onset of fever and severe arthralgia / arthritis with or without skin rash and residing or having left an epidemic area 15 days prior to onset of symptoms

Laboratory criteria:

- At least one of the following tests done in the acute phase of illness

Direct evidence

- Virus isolation / Presence of viral RNA by RT-PCR

Indirect evidence

- Presence of virus specific IgM antibodies in single serum sample collected in acute or convalescent stage.
- Four-fold increase in IgG values in samples collected at least three weeks apart.

Cases are to be categorized for the purpose of epidemiological reporting.

4.2. Differential diagnosis

Fever with or without arthralgia is a very common manifestation of several other diseases. Some of the diseases which can be considered in differential diagnosis are:

- Dengue Fever
- Malaria
- Leptospirosis
- Enteric Fever
- Rheumatic Fever
- Reactive arthritis
- Serum sickness illness
- Rickettsial disease

(1) **Dengue fever:** Severe low 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.

Few common features for DD of Chikungunya fever from Dengue are as follows:

Sl. No.	**Features**	**Chikungunya**	**Dengue**
1.	Fever Onset Duration	Acute 2-4 days	Gradual 5-7 days
2.	Rash	Maculopapular	Petechiae maculopapular
3.	Arthralgia Frequency Duration	 Frequent May last longer than a month	 Less common Short duration
4.	Hypovolaemic shock	Rare	Common
5.	Leukopenia	Common	Infrequent
6.	Thrombocytopenia	Infrequent	Common
7.	Haematocrit	Normal	High

Chapter 5

Clinical manifestation of Chikungunya

5.1 Incubation period

CHIK virus causes an acute febrile illness with an incubation period of 3-7 days (can be 2-12 days,). Viraemia persists for upto 5 days from the onset of symptoms. Fever and arthralgia are the hallmark of Chikungunya fever.

5.2. Clinical Features:

Clinical presentation of Chikungunya is divided in to three phases. In Chikungunya mostly symptoms have an abrupt onset with high grade fever, single or multiple joint pains, skin rashes, headache and myalgia. Clinical presentation of Chikungunya usually follows 3 phases which are as follows:

a) Acute phase : Less than 3 weeks
b) Sub-acute phase : > 3 weeks to 3 months
c) Chronic phase : > 3 months

Clinical presentation may be mild, moderate or severe and most of the symptoms subside within 3 weeks from the onset of symptoms. Some of the symptoms may persist for 3 months and even more. Usually 10 – 15 % of the patient those who present with severe Chikungunya progress to Sub-acute or chronic phase.

Common

- Fever
- Arthralgia/Arthritis
- Backache
- Headache
- Skin rash/Itching

Rare in adults but seen sometimes in children

- Photophobia
- Retro-orbital pain
- Vomiting
- Diarrhea
- Meningeal syndrome
- Acute encephalopathy

Course of illness:

- Symptoms and signs are generally self-limiting among most of the patients. Some of the signs and symptoms progress to Sub acute or chronic phase.
    - Arthralgia
    - Myalgia
    - Arthritis
    - Persistent Joint stiffness
    - Restricted joint movement
    - Painful joint movement
    - Enthesopathy
    - Tendinnitis
    - Skin pigmentation
    - Skin rash

5.3 Clinical Classification of severity of Chikungunya:

Based on clinical presentation severity of Chikungunya is classified in to three categories, However this category may vary over time during the course of illness.

Mild:

Low grade Fever
Mild Artharlgia
Mild focal Myalgia
General weakness
Skin rash/itching

Moderate:

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


Wrist oedema and arthritis

Severe:

1. Persistent high grade fever
2. Severe Joint pain
3. Persistent vomiting / Diarrhoea
4. Altered sensorium
5. Bleeding (GI bleeding due to use of Analgesics)
6. Shock due to persistent vomiting and diarrhoea

5.4 High Risk group:

Chikungunya infection with one of the following conditions may be considered as high risk group patients as they likely to develop severe manifestation and adverse outcome.

Co-morbid condition:

Hypertension
Diabetic
CAD/CVD
Geriatric age
Pregnancy
COPD
Hypothyroid

Co-infection:

Tuberculosis
Enteric fever

Pneumonia
HIV
Malaria
Dengue

5.5 **Fever:** The fever varies from low grade to high grade usually lasting for 24 to 48 hours. It has an abrupt onset usually responds to antipyretics.

5.6 **Arthralgia/Arthritis:** Arthralgias are polyarticular and usually involve peripheral joints. The joint pain tends to be worse in the morning which gets better with mild physical activity. The pain may remit for 2-3 days and then reappear in a saddle back pattern in some patients. It is usually polyarticular, symmetrical involving predominantly small joints of hands and feet. Ankles, wrists and small joints of the hand are the worst affected. Larger joints like knee and shoulder may also be involved. There is a tendency for early and more significant involvement of joints with some previous trauma or degeneration.

Source of photo: Dr. Ashutosh Biswas, AIIMS, New Delhi

SYMPTOMS	ANDHRA PRADESH, INDIA, 2006*	KERALA, 2007*	MAHARASTRA 2006 *	WEST BENGAL 2007*	REUNION OUTBREAK,2005-06**	MALAYSIAN OUTBREAK, 1998**
FEVER	100	100	100	100	100	100
ARTHRALGIA/ ARTHRITIS	98	99.4	100	96	100	78
RASH	NA	80.8	31	94	39	50
MYALGIA	NA	99.4	-	80	60	50
HEADACHE/ BACKACHE	NA	97.5	55.17	70	70/NA	50/50
NUMBER	876	354	87	321	504	51

**** Outbreak investigation report of NVBDCP***
***** Published documents***

There are reports that fever rash commonly appear within five days of onset of the disease while a small proportion of cases may develop diarrhoea at the end of the week. Most of the scarring (exfoliation of skin in the children and residual althralgia in adults) develop mostly around 6th to 10th day of the infection.

5.7. Back ache

One of the commonest symptom of Chikungunya giving a typical posture. In initial phase of the disease back ache could be very severe.

5.8. Headache

One of the prodromal symptom and could persist during the 1st week of illness.

5.9 Rash:

Transient maculopapular rash is seen in up to 50 % patients. The maculopapular eruption persists for more than 2 days in approximately 10% of cases. Nasal blotchy erythema and photosensitive hyperpigmentation are more frequently observed. Exfoliative dermatitis affecting limbs and face was seen in around 5% cases. Epidermolysis bullosa was an observation in children. Most skin lesions recovered completely except in cases where the photosensitive hyperpigmentation persisted. Intertriginous aphthous-like ulcers and vesiculbullous eruptions were noticed in some. A few persons had angiomatous lesions and fewer had purpuras.

5.10. Stomatitis and oral ulcers :

Usually seen in the acute phase mainly as a result of hyperpyrexia.

5.11. Hyperpigmentation

Though not common it may be encountered in the acute phase of the disease mainly on the shin and cheeks.

5.12. Exfoliative dermatitis

Usually encountered among pediatric

5.13. Retrobulbar pain

Though commonly seen in dengue cases it may be encountered in few cases of Chikungunya.

5.14. Neurological manifestations

Meanigeal syndromes and encephalopathy are not common signs of chikungunya. However, some times may present with neck rigidity and up going toes. Similarly, very few cases may present with unconsciousness due to encephalopathy. These are usually transient in nature.

5.15 Occular manifestations

Neuroretinitis and uveitis in one or both eyes have been observed. Anterior uveitis, optic neuritis, retrobulbar neuritis, and dendritic lesions are also seen. The visual prognosis generally is good.

5.16 Chikungunya in Children

Clinical manifestations in children are very variable ranging from asymptomatic to severe disease. Children can have minor haemmhoragic manifestations, lymphadenopahty swelling of eyelids, and pharangitisInfants may have watery stools. Unusal clinical features include sezizures, altered sensosrium and blindness due to retroblbar neuritis and acute flaccid paralysis. Infants can ahave constitional symptoms like, lethargy, irritability and excessive crying in addition to fever. Sometimes acrocyanosis and superficial vessico bulluos lesion can also be seen.

The most characteristic feature of the infection in infants was acrocyanosis and symmetrical superficial vesicobullous lesions were noted in most infants. Erythematous asymmetrical macules and patches were observed which later progressed to morbiliform rashes. The face and oral cavity was spared in all observed patients.

Unusual clinical features include: neurological manifestations including seizures, altered level of consciousness, blindness due to retrobulbar neuritis and acute flaccid paralysis. Viruse may be detected in cerebro spinal fluid. Watery stools may be seen in infants.

During a prospective study of all children with suspected central nervous system (CNS) infections admitted to a hospital in rural southern India, there was an unseasonal increase in admissions. This increase occurred at the same time as the CHIKV outbreak in southern India, during the outbreak period from January 2006 through October 2006, this study found that CHIKV was responsible for 14% of suspected CNS infections.

5.17 Impact of Chikungunya in Pregnancy & Neonates

Pregnant woman can get Chikungunya infection at any stage of pregnancy. Chikungunya virus can also be transmitted from the mother to the child. The time of greatest risk of Chikungunya virus transmission from a mother to a fetus appears to be during birth. Various preliminary studies showed that such a contamination is “rarely serious” when the babies were infected during birth, signs of infection appeared around Day 4. and more than 90% of the infected newborns recovered quickly without sequelae. Immunoglobulin M [IgM], an antibody, generally appears between 4 and 7 days after the onset of clinical signs. IgM, however, does not pass through the placental barrier. The body starts producing Immunoglobulin G [IgG] around Day 15 and pass it through the placenta and confer immunity to the fetus. Fever, in general, can trigger uterine contractions, miscarriages or fetal deaths.

The chances of passing the infection to fetus is very less even though a recent research study in the French Reunion islands demonstrated for the first time the maternal-fetal transmission of Chikungunya virus, if the pregnant woman is infected at the time of delivery, the virus can be transmitted to the new born child. So it is important to ensure that in Chikungunya areas pregnant woman is protected from mosquito bite. Neonatal cases observations in French Reunion island outbreak in 2005 suggest possible fetal transmission during pregnancy. These study further revealed that though fetal contamination risks appear to be rare before 22 weeks of gestation, they are potentially dangerous. After 22 weeks gestation, newborns infection occurs if the mother is viremia positive at delivery. Transplacental transmission is suspected, but the pathogenic mechanism remains unknown. As per the available literature there is no impact of Chikungunya infection on pregnancy outcomes except for the number of prenatal hospitalizations. There is no evidence to suggest that Chikungunya virus is transmitted through breast milk. (Langlet Y *et al*, 2006 ; Ramful D. *et al*, 2007, Gerardin P *et al*, 2008)

5.18 Chikungunya in Elderly

Chikungunya is more dangerous for elderly people because their bodily resistances are already weak due to which any underlying medical condition may be exacerbated. Elderly persons take a longer time to recover from Chikungunya infections and it could be severe and may present with oedema. Chikungunya in elderly people could cause cerebral problems like dementia and paralysis and kidney disorders. Correspondingly, Chikungunya is more deadly in children as compared to adults because children cannot express exact symptoms and it may take time to diagnose the disease. Elderly patients with co-morbidities may have more complications and psychological sequelae than patients belonging to other age groups.

5.19. Chikungunya Co infection with Dengue

During the current outbreak from 2006-2009, there are reports of co-infection of Dengue and Chikungunya received from various States. This is not very unusual as both Dengue and Chikungunya are arboviral diseases, transmitted by the same *Aedes* mosquitoes. Available literature also confirm co-infection of Dengue and Chikungunya virus. Infact, it was observed

in Thailand in the earlier outbreaks during 60s. Nimmannitya S, 1969 while dealing DHF cases in Thailand, observed other non-specific constitutional symptoms such as anorexia, vomiting, headache, and muscle or joint pains and subjected the samples to Chikungunya serology as well. She has documented the *n*on-specific constitutional symptoms observed in haemorrhagic fever patients with dengue and Chikungunya virus infection*s* as follows:

Symptom	Chikungunya fever (%)	DHF (%)
Injected pharynx	90.3	98.9
Vomiting	59.4	57.9
Constipation	40.0	53.3
Abdominal pain	31.6	50.0
Headache	68.4	44.6
Generalized lymphadenopathy	30.8	40.5
Conjunctival injection	55.6	32.8
Cough	23.3	21.5
Restlessness	33.3	21.5
Rhinitis	6.5	12.8
Maculopapular rash	59.6	12.1
Myalgia/arthralgia	40.0	12.0
Exanthema	11.1	8.3
Abnormal reflex	0.0	6.7
Diarrhoea	15.6	6.4
Palpable spleen (in infants<6 months)	3.1	6.3
Coma	0.0	3.0

5.20 Sequelae:

Chikungunya is a self limiting disease however in severe form of the disease sequelae can be seen. It has been observed that 90% joint symptoms resolve completely. However, some have either

- episodic stiffness and pain
- persistent stiffness without pain and
- persistent painful restriction of joint movements.

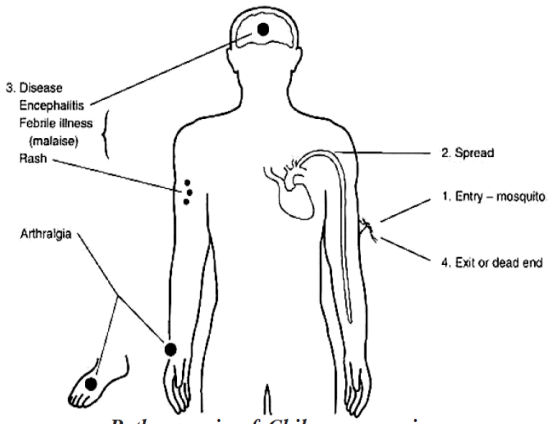
Enthesopathy and tendinitis of tendoachilles has also been observed in upto 53% of those who had musculoskeletal involvement. Older patients,(>45yrs) patients with severe initial joint pain symptoms and presence of osteoarthritis increase the sequelae of Chikungnya fever. Neurological, emotional and dermatologic sequelae are also described in Chikungunya infection.

5.21 Mortality

Chikungunya is a usually nonfatal disease and death is very rare. In the outbreak of Chikungunya in the Reunion Island epidemic, there were 237 cases of deaths with case fatality rate of 1/1000 cases. However, it was not sure whether the mortality was directly associated with Chikungunya or co- existing morbidities worsened with Chikungunya infections (Jessaron L *et al*, 2006; Ledroms M *et al*, 2007). Chikungunya infections may increase the morbidity as well as mortality due to coexisting infections. In India no report of death due to Chikungunya received in 2006-2009. (www.nvbdcp.gov.in)

5.22 Pathogenesis

At present, not many detailed studies are available on the pathogenesis of the Chikungunya fever. In humans, the bite of an infected mosquito leads to deposition of Chikungunia virus (CHIKV) in the subcutaneous tissue resulting in viremia. A febrile response signals viral replication with release of inflammatory cytokines. Lymphocytic perivascular cuffing and extravasation of erythrocytes from capillaries are seen in biopsies of the cutaneous rash. Animal studies on related flaviviruses have shown that replicating virus in the synovial fluid, endosteum and periosteum of the affectedbones induce complement activated immune complex mediated arthritis (Rulli NE *et al.,* 2007).



Pathogenesis of Chikungunya virus

In the later stages, involvement of synovial joint spaces leads to frank arthritis. There is no synovial lymphocytosis, bone or cartilage destruction. Neurovirulence and neuro invasiveness (neurotropism) of other alpha virus has been established. CHIKV can also cause CNS manifestations in the form of encephalitis, encephalomyelitis and optic neuritis (Ramful *et al.,* 2007).

Chapter 6

Clinical management of Chikungunya cases

6.1 Guiding principles of clinical management

(1) Management during Acute and sub-acute phase of the illness and (2) Management during Chronic phase or Sequelae.

- There is no antiviral drugs against CHKV
- Most of the signs and symptoms are self-limiting.
- Treatment for Chikungunya is purely symptomatic - supportive care and rest and nutrition
- Analgesics, antipyretics and fluid supplementation are important aspects in managing this infection.
- Supportive or Palliative Medical Care With Anti-inflammatories
- Supportive care with rest is indicated during the acute joint symptoms.
- Movement and mild exercise tend to improve stiffness and morning arthralgia, but heavy exercise may exacerbate rheumatic symptoms.
- *There Is No Vaccine Currently Available.*

Disabling peripheral Arthritis/ Artropathy refractory to NSAID:
Short term corticosteroid may be used.
Long term anti-inflammatory therapy
Physiotherapy
Chloroquine phosphate
Management of Chikungunya with High risk group:
Proper management of Co-morbid condition and co-infection.

6.1.1 Acute stage:

Clinical Management of CF during acute stage can be in ambulatory settings. Hosptialisation is rarely indicated.

(a) Domiciliary (Home care)
(b) Hospital based

6.1.2 Domicilary (Home Based)

- Adequate rest or activity as tolerated
- Paracetamol 500 mg TDS/QID (dose not to exceeds 3 Gm24 hours)
- Antacids like PPI/H2 blocker to counter gastritis
- Antihistaminics, if required in consultation with doctors
- Tepid water sponging for high fever
- Ensure adequate intake of water orally to maintain urine output at least more than a litre per day
- Cold compresses to involved and painful joints. Avoid hot fomentation in acute stages as it can worsen the joint symptom.
- Physiotherapy in form of mild exercises in recovering patients.
- Avoid self-medication particularly antibiotics, steroids, and other painkillers specially over dosing
- Avoid Aspirin

6.1.2.1 When to seek medical help (community health worker refers to PHC)

- Fever persisting for more than five days
- Intractable joint pain

- Altered sensorium
- Postural dizziness, cold extremities
- Decreased urine output
- Any bleeding under the skin or through any orifice
- Incessant vomiting
- Jaundice

*Refer sooner at extreme of age, pregnancy and significant comorbid illness.

6.2. Hospital based

- At the primary level or point of first contact (PHC/CHC level)
- At the secondary level (District Hospital)
- At the tertiary level (Teaching hospital situations / infectious diseases specialists/ advanced care centres.)

6.2.1. At the point of first contact (PHC/CHC level)

All fever cases must be seen by a medical officer and differential diagnoses of dengue fever, malaria and other relevant illnesses excluded by history, clinical examination and basic laboratory investigations. If a clinical diagnosis of Chikungunya fever is made (probable case) the patient may be treated symptomatically with paracetamol.

If the pain is intractable then NSAIDS like ibuprofen (400 mg three times daily), naproxen (250 mg twice daily),diclofenac (50 mg twice daily) and other NSAIDS. Parcetamol needs to be continued. To minimize gastric intolerance , H2 blockers ranitidine 150mg bd or proton pump inhibitor like Omperazole 20 mg od may be used. There is no definite role of steroid in management of CF including athralgia.
During pregnancy only paracetamol or mefenamic acid are safe to use, avoid NSAIDS in 3rd trimester.

If the patient is dehydrated then patient should be rehydrated according to the degree of dehydration.

6.2.1.1 Criteria for referal to a seccondary centre

1. If the person has hemodynamic instability (frequent syncopal attacks, hypotension with a systolic BP less than 100 mmHg or a pulse pressure less than 30 mmHg),
2. Oliguria (urine output less than 500 ml in 24 hours),
3. Altered sensorium or
4. Bleeding manifestations,
5. It may be advisable to refer persons above sixty years and infants (below one year of
6. Severe incapacitating arthritis not responding to paracetamol or NSAIDS for more than 15 days.

6.2.2. At the secondary level (district hospital)

All fever cases with joint or skin manifestations must be evaluated by a physician. Rule out other causes for fever and joint pains.

Collect blood for Chikungunya ELISA test
Treat the conditions as they warrant

Collect blood samples for serology (IgM – ELISA). As an alternative, blood test for IgG may be done — to be followed by a second sample after two to four weeks.
In severe cases following vital signs must be thoroughly monitored. :

- Sensorium

- BP charting
- Urine output
- Development of rash/mucous membrane bleed
- Laboratory parameters- platelets, total leukocyte count, differential count, Haemoglobin, serum creatinine, Urea, electrolytes and liver functions)

If the case has already been treated with paracetamol, start an NSAID (as per recommendations). Monitor for adverse effects from NSAID use. Cutaneous manifestations like hyperpigmentation can be managed with topical agents like zinc oxide cream. And itcing may be relieved by antihistaminics cetrizine or chlorpheniramine maleate. Maintain oral hygiene and prevent oral ulcers

6.2.2.1 Criteria for referral to a tertiary care

Refer cases with any of the following to a higher healthcare centre:

1. Renal failure requiring dialysis,
2. Refractory Hypotensin requiring invasive and intensive monitoring.
3. Multiorgan system failure
4. Refractroy thrombocytopenia wit bleeding
5. Neurological syndromes like ncephalitis, Acute infectious polyneuritis

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6.2.3. At the tertiary care level

All the patients must be admitted in the tertiary care. Care must be individualised. Steroids can be used when there are neurological conditions. The role of disease modifying agents in treatment of CHK arthritis is not proven.

6.3. Guiding principles for managing chronic pain

6.3.1 Management ofChronic Chik Arthritis

Since an immunologic etiology is suspected in chronic cases, a short course of steroids may be useful. Nonweight bearing exercises may be suggested. Contractures and deformities with physiotherapy/surgery

- NSAIDS
- Short course of steroid (In case of refractory to NSAID after 2-3 weeks))
- HCQS (During sub-acute stage)
- Physiotherapy
- Surgery

Chloroquine phosphate was found to be improving both Ritchie artricular index and morning stiffness in post Chikungunya arthritis. (Brighten SW 1984). However, the study was based only on 10 cases.

6.4 Summary

- Management is mostly symptomatic for this self limiting illness.
- Paracetamol and NSAIDs are commonly used for symptomatic relief
- Avoid acetyl samino salycilic acid (Aspirin)
- During epidemic, every patient clinically suspected need not to undergo serological testing.
- Promptly refer the case to higher centres as and when indicated (cited above)
- Protect against mosquito bite during febrile phase for prevention for transmission (mosquito net, mosquito repellent etc.).
- Systemic manifestation is rare
- Relapse or reinfection is not seen.

- Co-infection with Dengue and malaria can occur concurrently.
- No specific antiviral drug is available.

Chapter 7

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.

7.1. 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

7.1.1 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***

7.1.2 Minimizing vector population

- Intensify efforts to reduce larval habitats in and around the houses; remove stagnant water from all junk items lying around in the household and in the peri-domestic areas
- Stagnating water in flower pots or similar containers should be changed daily or at least twice weekly.
- Introduce larvivorous fish in aquaria, garden pools, etc
- Weeds and tall grasses should be cut short to minimize shady spaces where the adult insects hide and rest during hot daylight hours
- Drain all water stagnating after rains
- Fogging and street sanitation with proper waste management (fogging does not appear to be effective, yet it is routinely implemented in epidemic situation)

7.1.3. Minimize the vector-patient contact

- Insecticide sprays: bed rooms, closets and crevices, bathrooms, kitchens, nooks and corners; alternatively, coils, mats, vaporizers, etc
- Have the patient as well as other members of the household wear full sleeves to cover extremities, preferably bright coloured clothes
- Wire-mesh/ nets on doors and windows

7.1.4 Involvement of various community group in prevention and control of Chikungunya

Involvement of the community to achieve successful and sustainable environmental conditions for prevention and control of Chikungunya is of paramount importance. Various groups which could play important role in this effort.

7.1.5 Vector Control and Source reduction for Chikungunya vector in Hospital setup

- Chikungunya is transmitted and spread by *Aedes* mosquitoes. Both *Ae. aegypti* and *Ae. albopictus* can transmit the disease.

- *Aedes* mosquitoes breed in various type of domestic /per domestic container holding water. Vector mosquito breed indoor , rest indoor and feed indoor in and near vicinity of human dwellings
- Adult could be identified by characteristic white and black band on legs and abdomen.(Known as tiger mosquito).
- The probable potential breeding sites where water could accumulate and acts as breeding place for *Aedes* in the hospital setting are –

1. **In side hospital**
   Water coolers , AC ducts, flower pots , artificial containers having ornamental plants, money plants in OPD , over head / water tanks in wards and sometimes in operation theaters also, toilets/cisterns , canteens /cafeterias

2. **Over the roof**
   Over head water tanks, unused hardware material including condemned furniture and other articles which may accumulate water in rainy seasons

3. **In the campus/compound**
   Unused receptacles (Bottles/tins/buckets/drums), flower pots, cement tanks,

4. **In hostels**
   The probable places are in boys/girls/nursing/training hostels situate in the campus-Coolers/water tanks etc. Kitchens of the hostel are also potential breeding places.

5. **Residential houses (Officers/Servant quarters /staff quarters) –** House hold containers /coolers etc.

6. **Construction sites within hospital campus –**
   Articles kept for water storage and unused hardware articles kept in the open

7. **Tea shops/Dhabas in compound**
   Water storage containers and other discarded thrown away articles

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The Virus

Chikungunya (CHK) is caused by an arbovirus that belongs to the genus *Alphavirus* under the Togaviridae family. It has a single-stranded RNA genome, a 60-70 nm diameter capsid and a phospholipids envelope (Fig.3). It is sensitive to temperatures above 58° Celsius and also to desiccation. Believed to be enzootic throughout much of Africa, CHK virus probably spread to other parts of the world from this origin.

Fig. 4. Electron microscopic view of Chikungunya Virus

African and Asian strains are reported to differ biologically with distinct lineages. Three lineages with distinct genotypic and antigenic characteristics have been identified: east-central southern, west African groups from Africa and Asian phylogroup. Isolates from the recent outbreak that started in the Indian Ocean islands belong to a distinct clad within the large east-central-southern African phylogenetic group and the isolates from the on-going outbreaks in India are closely related to this. The different geographical genotypes exhibit differences in their transmission cycles. In Asia, the virus appears to be maintained in an urban human-mosquito-human transmission cycle with vectors namely, *Aedes aegypti* and *Aedes albopictus*.

Analysis of the recent outbreak has suggested that the increased severity of the disease may be due to a change in the genetic sequence, altering the virus' coat protein, which potentially allows it to multiply more easily in mosquito cells.

Genotype of Chikungunya virus:

The definition of a Chikungunya genotype is based on the identification of well defined phylogenetic clusters that its origin has been associated to a given geographic region. Chikungunya Virus (CHIKV) epidemics have been described in Africa, the Middle East, Europe, India, and Southeast Asia. CHIKV being an RNA virus is susceptible to high mutation rates which may help the virus to evade the immune response and thus adapt efficiently. Three phylogenetically distinct groups of CHIKV with distinct antigenic properties have been identified, namely, *the Asian geno-type, the West African genotype, and the East/Central/ South African (ECSA) genotype*.
CHIKV strains with an Asian genotype of E1 gene were reportedly detected during the 1963–73 outbreaks in India. It was prevalent in Thailand, Malaysia and Indonesia as well during the period. In 2006 outbreak East Central South African genotype was isolated. The same genotype had been

isolated from samples collected from 2010 to 2014. The East Central South African genotype was circulating in the Delhi region during 2010–2014 (Singh, P. *et al*, 2016).

Vector

Chikungunya 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 accentuates virus transmission.
Aedes aegypti is the main vector of transmission of Chikungunya in India. 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 each feed 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* mosquitoes, which are day biters and epidemics are sustained by human-mosquito-human transmission.

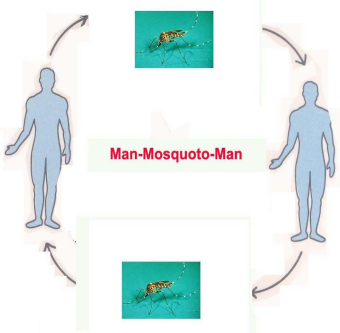

Fig. 5. : Transmission cycle of Chikungunya

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.

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