Review Article

Oral Manifestations of Chikungunya and its Comparison with Dengue Fever : A Literature Review with an Indian Perspective

Sandeep Singh Sihmar[1], Karthikhan Ramalingam[2], Sandeep Goyal[3], Shalini Rathi[4]

[1]Postgraduate student; [2]Professor and Head of the Department; [3]Reader, Department of Oral Pathology and Microbiology; [4]Postgraduate student, Department of Oral Medicine and Radiology, Surendera Dental College and Research Institute, Sriganganagar, Rajasthan.

ABSTRACT

Chikungunya and dengue outbreaks currently affect thousands of individuals all over the world since the past decade. Both are arthropod-transmitted disease but dengue is the most prevalent mosquito-borne infection worldwide.These diseases are debilitating and if inadequately treated increases the chance of mortality. Recurrent epidemics of chikungunya and dengue, which are *Aedes* mosquito-borne viral diseases, represent a significant health problem in over a hundred tropical countries. With the re-emergence of the chikungunya virus (CHIKV) and dengue virus (DENV) cases have also been reported in parts of Europe and other parts of the Asian subcontinent. This review focuses on the oral manifestations of these diseases with relevant data from the Indian perspective. The objective of this review is to educate dental practitioners on the oral manifestations of both CHIKV and DENV which may help in the early diagnosis and prompt management of these viral diseases.

INTRODUCTION

Chikungunya (CK) literally means "that which bends up" in the Makonde language, probably coined because of the severe, prolonged, incapacitating arthritis associated with this disease. Chikungunya fever (CF) is caused by Chikungunya virus (CHIKV) (Family -Togaviridae, Genus - Alphavirus) and is transmitted by the bite of infected mosquitoes (*Aedes aegyptii* and *Aedes albopictus*). The first description of CF was made during the outbreak on the Makonde plateau along the border between Tanganyika and Mozambique in the year 1952 and the virus was isolated from both mosquito and humans.[1] In Swahili language, the word Chikungunya means "the illness of the bended walker".[2] During the past 50 years, numerous CHIKV re-emergences have been documented in both Africa and Asia, with irregular intervals of 2–20 years between outbreaks. The absence of serological surveillance means that precise numbers of individuals infected during these outbreaks can only be estimated.[3]

Dengue fever (DF) is a febrile disease and a major public health problem in tropical countries. It is caused by virus serotypes of the genus Flavivirus, family Flaviviridae (that also includes the West Nile and Yellow Fever viruses), Group IV ssRNA. The transmission of dengue to humans is by the mosquito *Aedes aegypti*.[4] The viral etiology of DF has been established since the 1940s and the history of dengue-like diseases can be tracked back more than 200 years.[5]

This review is a novel attempt to describe the pathogenesis of CK and DF along with its epidemiology stressing on the Indian scenario and summarize the clinical findings in general and oral manifestations in detail.

Etiopathogenesis

With reference to the data published by Centers for Disease Control and Prevention, CHIKV is transmitted to people through bites of *Aedes aegypti* and *Aedes albopictus* mosquitoes.[2] In contrast to Africa where sylvatic cycle is maintained between monkeys and wild mosquitoes, in Asia the cycle continues between humans and the *Aedes aegypti* mosquito.[6] It was noted that most alpha viral infections in humans and domesticated animals are considered a 'dead end'- the virus cannot be transmitted to a new host, so the evolutionary pressures

driving viral diversification may be linked to their true host species. For CHIKV, a thorough exploration of other zoonotic viral reservoirs has not been carried out. From a clinical perspective, the two groups of alpha viruses are subdivided into those associated with encephalitis (predominantly New world viruses) and those associated with polyarthritis and rash (predominantly Old world viruses)[3]. There are 6 entities under the arthritic virus group - O'nyong-nyong virus, Semliki forest virus, Ross River virus, Sindbis virus, Mayaro virus and CHIKV.[7]

Habit of *A. albopictus* mosquitoes is to lay their eggs in dry areas in anticipation of heavy rainfall. The abnormally high rainfall in the third week of January 2006 witnessed a sharp increase in the *A. albopictus* population 1-2 weeks later and this preceded the onset of the explosive epidemic of February/March 2006.[8] These mosquitoes get infected when they feed on a person already infected with CHIKV. Infected mosquitoes can then spread the virus to other people through bites. These are the same mosquitoes that transmit other mosquito-borne viruses like dengue virus and they bite during day and at night.[9] Their biting activity could be noted throughout daylight hours, though there may be peaks of activity in the early morning and late afternoon. Both species are found biting outdoors but *A. aegypti* will also readily feed indoors and are often found living around buildings in urban areas. After the bite of an infected mosquito, onset of illness occurs usually between 4 to 8 days but can range from 2 to 12 days. The risk of a person transmitting the virus to a biting mosquito or through blood is highest when the patient is viremic, usually during the first 2-6 days of illness. Maternal-fetal transmission has been documented during pregnancy; the highest risk occurs when a woman is viremic at the time of delivery.[10]

The genus Alphavirus contains approximately 30 members and can be broadly divided into New world and Old world viruses. These two groups have evolved distinct ways of interacting with their respective hosts and differ in their pathogenicity, tissue and cellular tropism, cytotoxicity and interference with virus-induced immune responses. Some alphaviruses are not pathogenic to humans, whereas others are highly infectious, with the associated clinical diseases ranging from mild to severe.[3,7] The CHIKV genome is a linear, positive sense RNA with a capsid diameter of 60-70 nm and a phospholipid envelope. The molecular pathogenesis of CK bears a large similarity to the Ross River virus that also causes polyarthritis and cutaneous manifestations.[11]

A cell-mediated immune response where CD8+T cells are inactive has been suspected to cause this chronic disease. Toxic chemokines are reported to be the cause for tissue/cell destruction with an antibody-dependent enhancement mechanism similar to the dengue virus. Unlike dengue, there is no evidence of transovarial transmission of CK. Till date, studies have not found CHIKV in breast milk and no infants have been found to be infected with CHIKV through breastfeeding. Hence, the mothers are encouraged to breastfeed even in areas of CHIKV circulation.[7,11] Blood borne transmission is possible and cases have been documented among laboratory personnel handling infected blood and through aerosol exposure in the laboratory.[10]

CHIKV was found to primarily target muscle, joint and skin fibroblasts, but it was also identified in the epithelial and endothelial layers of many organs, including the liver, spleen and brain. The various tissues that are involved are depicted in Figure 1. Notably, newborn and young mice are highly sensitive to CHIKV infection and represent a valuable model for studying CHIKV pathogenesis. Non-human primates have also been used as models for CHIKV-associated pathology and vaccine testing.[3]

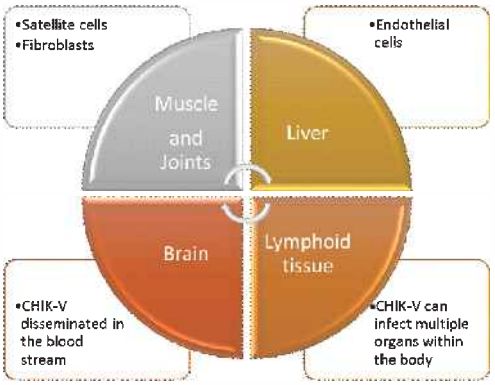

Figure 1: Target cells in human by chikungunya virus.

In a study by Labadie K et al[12], intravenous or intra-dermal CHIKV inoculation of macaques resulted in high viremia, peaking 24–48 hours after infection. Although infection was not lethal, it was associated with a transient acute lymphopenia and neutropenia, an increase in monocytes and a pro-inflammatory response. Infection recapitulated the viral, clinical and pathological features observed in humans. CHIKV targeted lymphoid tissue, liver, central nervous system, joints and muscle during the acute phase. Persistent infection (measured 44 days post-infection) occurred in splenic macrophages and in endothelial cells lining the liver sinusoids. Tissue derived from these animals carried low levels of replication-competent virus.

It will be important to establish whether these animal studies could reflect human disease progression or the effects of viral persistence in the chronic sequelae associated with CF.

The dengue virus belongs to the genus flavivirus of the Flaviviridae family with four serotypes of the dengue virus (DENV 1-4). Three of these encode structural proteins and seven encode non structural ones. Infection by any of them is thought to confer lifelong immunity against variants of the same serotype but only partial and transient cross-protection against infections caused by other serotypes. It is known that the DENV enters the host organism via the skin when an infected mosquito takes its blood meal. However, the most severe clinical presentation during the infection course is not accompanied by a high viral burden. These symptoms occur following the rapid clearance of the virus from the host organism, suggesting that the humoral, cellular, and innate immune responses of the host are associated with the pathogenesis of dengue infection.[13]

The immunopathogenic events of dengue infection are usually related to disruptions in endothelial microvascular permeability and thromboregulatory mechanisms, leading to an increased rate of protein and plasma loss. It has been postulated that endothelial cell activation caused by monocytes, T-cells, the complement system and various inflammatory molecules mediate plasma leakage which is linked with useful rather than damaging effects on endothelial cells. Thrombocytopenia may be associated with alterations in megakaryocytopoiesis, elicited by the infection of human hematopoietic cells and impaired progenitor cell growth, which results in platelet dysfunction, destruction or consumption leading to significant hemorrhages.[13]

Epidemiology

CHIKV has been identified in around 45 countries or territories all over the America with more than 1.7 million suspected cases and in the year 2008 it was listed as a US National Institute of Allergy and Infectious Diseases (NIAID) category C priority pathogen.[2] Epidemic re-emergencies were also documented in Kinshasa, the Congo (50,000 estimated cases in 1999–2000), Indonesia (2001–2003), the Indian Ocean islands of Mayotte, Seychelles, Mauritius and La Reunion[11] (300,000 cases in 2005–2006), India (1.4–6.5 million estimated cases in 2006–2007), La Reunion Island, South-west Indian Ocean (2006), and Malaysia and Thailand (3,000 and 42,000 estimated cases in 2009), Caribbean Isle of Saint Martin (2013), France (2014), Spain and Senegal (2015), Argentina, USA (Florida, Rico, U.S Virgin Island) and Kenya (2016) respectively.[2,3] Documented first time from an outbreak in Tanzania in 1952, explosive outbreaks of epidemics of the disease have occurred after periods of long quiescence in different parts of the world.

In the year 2004, CHIKV emerged in Kenya and spread to Comoros, where 5,000 cases were reported. In 2005–2006, the outbreak spread to other islands in the Indian Ocean, including La Reunion, this was the first time that CHIKV had infected an occidental country; strikingly, an estimated 300,000 cases of CHIKV infections and 237 resultant deaths were reported. Viral genetic analysis supported the link between the infections in La Reunion and the outbreak in Kenya in 2004. The epidemic also spread to India and it is estimated that more than 1.5 million people were infected. It was subsequently identified in Europe and the United States, where it is thought to have been imported by infected travelers returning from areas with high incidence rates. Indeed, between July and September 2007 the virus caused the first autochthonous epidemic outbreak in the north-east of Italy with more than 200 human infections, all traced back to the same index case.[3] After an interval of 32 years, India has witnessed a massive epidemic in 2005, which is still ongoing in different parts of the country. The disease has affected millions of people and left many with crippling disabilities.[2] Suryawanshi SD et al in 2009 reported in a study of Maharashtra that mortality in confirmed cases with CF was about 3.4%.[14] According to Arbonet by State of Territory-United State 2016, CHIKV was confirmed in the laboratory for 175 cases (travel-associated cases) and there were no locally transmitted cases.[15]

Geographical distribution of Chikungunya cases in India

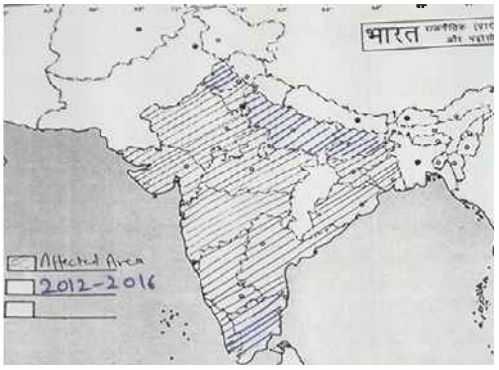

Figure 2: Geographical representation showing the affected areas of India in 2012-2016.[16]

Data are presented as reporting period followed by estimated number of cases (Figure 2)

In India, several outbreaks of CF have been reported with the first outbreak being in Calcutta in 1963. The disease re-emerged in India after a gap of 32 years in 2005 with more than 13 lakhs infected patients. Currently the toll is growing, 12,255 cases of chikungunya had been reported in India till August, 2016 which is near 50% of cases reported in the entire year of 2015. There have been approximately 28,000 cases of dengue and 60 deaths because of dengue hemorrhagic fever. The year 2015 had seen 99,913 dengue cases with 220 deaths. They are being called the twins which are attacking our country with an ever-increasing percentage each year.[2]

Dengue, however is the most common arthropod-transmitted disease seen and is common in more than 110 countries.[1] The incidence of DF has significantly surged in recent years, especially in southern Taiwan during the summer. Globally, approximately 2.5 billion people are estimated to live in dengue-endemic regions and 50 to 100 million people are infected by dengue virus annually. According to Taiwan Center for Disease Control (CDC), approximately 1000 to 2000 people are infected by dengue virus annually. In 2014, Taiwan experienced its large dengue virus outbreak, with more than 10,000 affected patients since 1981.[5]

The first dengue-like illness to be documented in India was in Madras and Calcutta was the first city to report virologicalepidemic of DF. In recent times, the cumulative dengue diseases burden has attained an unparalleled proportion with upsurge in the magnitude of human population at risk. Complex pathophysiological, economic and ecologic problems are highly presented in dengue infections.[13] The increase in the CF and DF is because of rapid urbanization, global warming and growth in population.[11]

Clinical Features

CF affects all the age groups from neonates to old age with the incubation period of 3 to 12 days. Males and females are equally affected.[17] Skin lesions resolved within an average of 7.6 days leaving post-inflammatory hypopigmentation.[18] Table-1 shows the common clinical features.

Riyaz N et al have reported skin pigmentation as the second most common presentation of CF in their study. Macular pigmentation of the nose, melasma-like lesions of the face and peri-orbital melanosis were also noted.[19] In a study conducted by Chandak NH, Kashyap RS et al in Nagpur, a total of 300 patients with CF were evaluated

Table 1: Clinical features of chikungunya fever [10]

Common	Infrequent	Rare in adults but seen occasionally in children
Fever (92%)	Rash	Photophobia
	Stomatitis	Retro-orbital pain
Backache (67%)	Oral Ulcer	Vomiting
Headache (62%)	Hyperpigmentation	Diarrhea
		Meningeal syndrome
	Exfoliative dermatitis	Acute encephalopathy

over seven months, 16.3% of patients had a neurological manifestation such as myelopathy, encephalitis, peripheral neuropathy and myopathy. A rare manifestation that was noted was flaccid paralysis in a patient with CF. Unlike dengue, severe hemorrhagic manifestation is not noted in CF.[20] Jean-Baptiste E et al studied the impact of CHIKV infection on diabetic patients (DPs) and nondiabetic patients (NDPs) and to evaluate its effects on glycemic control among DP in Haiti. They found that arthralgia was more intense in diabetics and took longer to improve. There was also a median increase in fasting capillary glucose after onset of infection. In summary, among DP CHIKV infection has a significant negative impact on glycemic control and compared with NDP, results in greater morbidity. Close clinical and glycemic observation is recommended in DP with CHIKV infection.[21]

Dengue fever in human causes a spectrum of illness from febrile to fatal disease. According to World Health Organization, the dengue virus (DENV) causes three clinical syndromes: dengue fever, dengue hemorrhagic fever and dengue shock syndrome. The incubation period varies from 3-14 days most often being 4-7 days. The disease is characterized with a sudden onset of fever, frontal headache, muscle and joint pain and skin rashes. The mild phase of dengue includes fever, generalized pain, nausea, vomiting and occasionally petechiae. In the severe phase, with the resolution of fever there is fluid accumulation in the chest, abdominal cavity as well as decreased blood supply to vital organs.[1] Differences between CF and DF are given in table 2.

Effect on pregnancy:

CF appears to have a direct impact on pregnancy with rare

reports of spontaneous abortions and mother-to-child transmission in perinatal period.[22] Dengue infection in pregnancy carries the risk of hemorrhage in both the mother and the newborn. There is serious risk of premature birth and fetal death. In case of infection close to term, there is risk of vertical transmission.[4]

Effect on neonates:

Mothers afflicted with CF in the perinatal period (−4 days to +1 days before/after delivery) can transmit CHIKV to neonates by vertical transmission. Caesarean section does not appear to prevent transmission. Neonatal CF is associated with fever, poor feeding, pain, distal edema, acrocynosis, various skin manifestations, vesiculobullous lesions (most common in infant)[22], morbiliform rashes seizures, meningo-encephalitis, and echocardiographic abnormalities in the newborn.[22] Psoriasis could be noted in some cases and recently a case of guttate psoriasis was also observed.[23] In some cases unmasking of undiagnosed Hansen's disease were also observed.[24]

In dengue fever striking feature observed in infant e.g. presence of sever thrombocytopenia in 78% patients, oligohydramnios and low birth weight (LBW) being common in 52% cases.[4]

Table 2: Adapted from Comparison of the Clinical Features of Chikungunya Fever and Dengue Fever[25]

Clinical Features	Chikungunya Fever	Dengue Fever
Fever (> 38.9oC)	70-100%	40-69%
Myalgias	10-39%	40-69%
Arthralgias	70-100%	<10%
Rash	40-69%	10-39%
Bleeding dyscrasias	<10%	40-69%
Shock	0%	<10%
Leukopenia	40-69%	70-100%
Lymphopenia	70-100%	40-69%
Neutropenia	10-39%	70-100%
Thrombocytopenia	10-39%	70-100%

Oral Manifestations:

Both the viral infections are characterized by similar signs such as high fever, headache, pain in the joints and eyes, rashes and lethargy. This is often confused with viral fever and malaria. Mucocutaneous lesions occur in a similar manner in both diseases. But bleeding is more evident in DF and lesions are persistent in CF.[25] Females seems to be more affected than males and severe signs and symptoms were found in patients older than 50 years as compared to those who were younger than 20 years. Table-3 shows data of different studies from various geographical areas of India.

Diagnosis

WHO definition[22] for DF: Recent fever lasting for 2-7 days, occasionally biphasic, hemorrhagic tendencies evidenced by at least one of the following:

- A positive tourniquet test- A blood pressure cuff of the sphygmomanometer on the upper aspect of the arm to apoint midway between systolic and diastolic pressure for about 5 min, if there are more than 20 petechia/2.5cm^2, the test is considered to be positive.[30]
- Petechia or purpura
- Mucosal bleeding
- Hematemesis, melena
- Platelet count ≤100 000/mm.

The confirmation of Chikungunya or Dengue is by performing the following tests[10,15,31]:

Confirmation of dengue infection is done by serology or detection by virus isolation and by reverse transcriptase polymerase chain reaction. The timing of clinical course plays a major role in the laboratory diagnosis of dengue.Virus isolation and identification is a gold standard for diagnosing dengue infections. This procedure can simply be done using infected cell cultures obtained from plasma, serum or WBC and this procedure is consistent, effortless and most rapid. In addition, it allows the recognition of numerous viruses in patients with concomitant infections with above one serotype.

Serological diagnosis

Diagnosis of dengue infection can be performed using five basic serologic tests viz. hemagglutination-inhibition, complement fixation, neutralization test, immunoglobulin M capture enzyme-linked immunosorbent assay (ELISA) and indirect immunoglobulin G ELISA. Serologic diagnosis depends

Table 3: Data from various articles published about oral manifestations of Chikungunya fever from India

Study	Clinical Symptoms	Percentage
Riyaz et al in Kerala, India (Total - 162 patients)[11]	Multiple aphthae, erosion and cheilitis	13.64%
Ketti et al Karnataka, India (Total - 182 patients)[11]	Pain on gingiva	54.32%
	Mucopyrosis	54.32%
	Bleeding on Gingiva	54.32%
	Difficulty in chewing and swallowing	29.1%
	Halitosis	21.34%
	Ulceration	17.46%
	Trismus	11.64%
	Excessive salivation and Distaste	9.7%
	Mobile teeth	0.97%
Suryawanshi et al, Maharashtra, India (Total - 405 Patients)[13]	Lymphadenopathy	0.09%
	Oral ulcers	0.024%
	Bleeding manifestations	0.002%
Ramesh BM, R Yashaswi et al, 2008, Mangalore (Total - 75 patients)[1]	Oral ulcers	16%
Katti R et al Karnataka, India (Total -208 Patients) (97 confirmed CF)[26]	Pain on gingiva (younger-old age)	64.1% -67.85%
	Severe gingivitis	19.58%
	Bleeding on gingiva	96.42%
	Difficulty in chewing and swallowing	39.28%
	Halitosis (more in old age)	28.57%
	Oral hygiene	Poor- 29.9% Fair-70.1%
	Ulceration	17.46%
Mohan et al. Andhra Pradesh, India (Total – 1226 patients)[27]	Oral ulcers	Not described
	Lymphadenopathy	0.3%
	Bleeding manifestations	0.1%
Lakshmi et al. Andhra Pradesh, India (Total – 296 patients)[28]	Oral ulcers	Not described
	Lymphadenopathy	9%
	Bleeding manifestations	Not described
Kannan et al. Kerala, India (n = 354 patients)[29]	Oral ulcers	5%
	Lymphadenopathy	Not described
	Bleeding manifestations	2%
Bandyopadhyay et al. West Bengal, India (n = 321 patients)[17]	Distaste	86.4%
	Skin rashes	22.8%
		1.2%
	Bleeding manifestations	20.2%
	Lymphadenopathy	Not described

upon the increase in the titer of specific antibodies between acute- and convalescent-phase serum samples.

Viral serotypes: Reverse transcriptase-polymerase chain reaction (RT-PCR) provides a rapid serotype-specific diagnosis. This method is rapid, sensitive, simple and reproducible.

Immunofluorescence: Direct immunofluorescence involving the skin shows negative for the deposition of immunoglobulins and complement for the presence of dengue viral antigen.

Differential Diagnosis: DF and CF quite similar, despite this, both the diseases are very much different. Due to sharing quite similar signs, it becomes difficult in identifying the exact problem.

Few differences in CF and DF are [25]:

- Dengue and CHIKV, though carried by the same mosquito type, but are caused by different viruses. While CHIKV is caused by a Togaviridae (alphavirus), dengue is caused by a Flavirideae (flavivirus).
- Dengue in the last few years has become more common and dangerous than CF. However, the joint pain associated with CF can last for years.
- Dengue signs begin to show up within 3 to 14 days after infection whereas , the signs of CF begin to show up with the sudden onset of fever within 2 to 4 days after exposure.
- The incubation period of CF is of 1 to 12 days and the duration varies from 1 to 2 weeks. However, signs such as joint pain persist for a long time. The incubation period for dengue is of 3-7 weeks while it stays from about 4 to 7 weeks.
- Swelling and pain is high in CF as compared to that in dengue.
- CF can create the possibilities of tremendous joint pain whereas dengue can cause bleeding in some cases, breathing problems etc.
- In contrast to CHIKV, DENV infection does not become chronic. The monocytes and macrophages that cause chronicity of CHIKV contribute to the infection control of DENV.

Guiding principles of clinical management

There is no specific antiviral drug against CHIKV and DENV. Treatment is entirely symptomatic. Paracetamol is the drug of choice. If paracetamol does not provide relief, other analgesics like non steroidal anti inflammatory drugs (NSAIDs) may be used. During the acute stage of the disease, steroids are not usually indicated because of the adverse effects. Aspirin is preferably avoided for fear of gastrointestinal and other side effects like Reye's syndrome. Mild forms of exercise and physiotherapy are recommended in recovering persons.Treatment should be instituted in all suspect cases without waiting for serological or viral confirmation. During an epidemic, it is not imperative that all cases should be subjected for virologic/serologic investigations. All suspected cases should be kept under mosquito nets during the febrile period. Communities in the affected areas should be sensitized about the mosquito control measures to be adopted in hospital premises and houses.[32] Lin J et al reported that CHIKV presenting as an intermediate uveitis, subsided with oral corticosteroids.[33]

Future Aspect

CHIKV has also been reported to be infectious via the intranasal route in wild-type mice, with intranasal and aerosol infection. The relevance of non-vector based transmission for enzootic cycles or epidemics is generally likely to be limited, with hemorrhage and deficiencies in IFNα/β response. The safety implications of infectious saliva could be most relevant for dentistry.[34]

Viperin induction in monocytes has played a key role in the innate immune response against viruses like Influenza, West nile virus, HCV, DENV and CHIKV. Viperin inhibits viral replication via different mechanisms. Viperin-mediated antiviral response could be noted in primary fibroblasts, interferon production and interferon stimulated genes (ISG) expression. CHIKV and other RNA viruses are dependent on the host cell machinery to initiate translation of non-structural proteins after infection. Loss of viperin expression is reflected by increased viremia and CHIKV associated joint inflammation. Hence, viperin targeted therapy could help in management of these diseases.[35]

Active immunization against CHIKV is considered to be a cost-effective health intervention as a mass immunization procedure. Various attempts including live-attenuated vaccines, chimeric alpha-virus, adenovirus, pox-virus and DNA-based vaccines, subunit formulations based on recombinant envelope proteins of CHIKV, inactivated VLPs (virus-like particles) have been performed on mice

and non-human primates. VRC-CHKV, MV-CHIK, CHIKV-IRES vaccines have yielded promising efficacy and will be submitted soon for human testing.[36]

Biological confirmation is generally based on detection of viral RNA by RT-PCR or real-time RT-PCR with hydrolysis probes. It requires extensive sample preparation and expensive equipments. Yaren O et al have tested a detection kit for viral RNA with a hand-held visualization apparatus and refrigeration-free sample transport on unprocessed urine and other biological samples to distinguish Zika, CHIKV and DENV. The limits of detection (LODs) were approximately 1.22 pfu for dengue and 38 copies of chikungunya seen by visual examination of three-color coded fluorescence signals.[37] Erguler K et al have proposed a large-scale stochastic spatiotemporal model for analyzing global outbreaks of *Aedes albopictus*-borne chikungunya transmissions. They report that adult vector intervention has high impact but short lived whereas larval intervention has low impact but long lasting in quarantining, infected territories.[38]

PREVENTION

There is no specific vaccination for both CHIKV and DENV. Protection includes prevention against contact with the infected mosquito and other preventive measures such as spraying insecticide should be initiated in areas endemic to the disease. There is no specific treatment but NSAIDs, to provide palliative relief from symptoms such as fever and pain are given for patients with CF. In patients suffering from dengue fever, proper fluid balance is important and blood transfusion is initiated if severe symptoms exist.[11]

CONCLUSION

Oral health is intertwined with systemic health of an individual. Chikungunya and Dengue infections occur worldwide and needs adequate control of the vectors that spread these diseases. Infection can protect subsequent exposure to same phenotype but not against others. Oral ulcers, bleeding manifestations, and taste alteration are consistently reported by Indian investigators along with skin rashes, arthralgia and high fever. Indiscriminate use of corticosteroids, aspirin and antibiotics could lead to secondary complications. Early identification of these oral manifestations by dental professionals can help in prompt referral and management of affected patients. At present, there is no commercial vaccine available for Chikungunya fever in India. Hence, education of the community and public health officials about vector control measures is crucial for containing this epidemic.

REFERENCES

1. Bhat RM, Rai Y, Ramesh A, Nandakishore B, Sukumar D, Martis J, Kamath GH.Mucocutaneous manifestations of chikungunya fever: A study from an epidemic in coastal Karnataka. Ind J Dermatol 2011; 56: 290-294.
2. Chikungunya virus. Available at www.cdc.gov/chikungunya/index.html Accessed on 31-01-2017.
3. Schwartz O, Albert ML. Biology and pathogenesis of chikungunya virus. Nat Rev Microbiol 2010; Jul 8 (7) : 491-500.
4. Agrawal P, Garg R, Srivastava S, Verma U, Rani R. Pregnancy outcome in women with Dengue infection in northern India. Ind J Clin Pract 2014; 24(11):1053-1056.
5. Huang HW, Tseng HC, Lee CH, Chuang HY, Lin SH. Clinical significance of skin rash in dengue fever: A focus on discomfort, complications, and disease outcome. Asian Pacific J Trop Med 2016; 9 (7): 713-718.
6. Chhabra M, Mittal V, Bhattacharya D, Rana U, Lal S. Chikungunya fever: a re-emerging viral infection. Ind J Med Microbiol 2008 ; Jan-Mar; 26 (1): 5-12.
7. Chia YP, Ng LMM, Chu JJH.Chikungunya fever: A review of a re-emerging mosquito-borne infectious disease and the current status. Current Research Technology and Education Topics in Applied Microbiology and Microbial Biotechnology. A. Mendez-Vilas (Ed.) 2010; 597-606.
8. Ramchurn SK, Goorah SSD, Mungla D, Ramsurrun B, Pydiah V, Summun A. A study of the 2006 Chikungunya epidemic outbreak in Mauritius. Internet Journal of Medical Update 2008 ; 3(1):11-21.
10. Staples JE, Hills SL, Powers AM: Chikungunya. Available at www.nc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/chikungunya. Accessed on 31-01-2017.
11. Mobeen N. Oral Manifestation of Chikungunya and Dengue Fever, J Pharma Sci Res 2015 ;Vol. 7 (9) : 769-771.
12. Labadie, K. *et al.* Chikungunya disease in nonhuman primates leads to long-term viral persistence in macrophages. J Clin Invest 2010; 120: 1–13 .
13. Roopashri G, Vaishali MR et al. Clinical and oral implications of Dengue Fever: A Review. J Int Oral Health 2015;7(2):69-73.
14. Suryawanshi SD, Dube AH, Khadse RK et al. Clinical profile of chikungunya fever in patient in a tertiary care centre in Maharashtra, India. Ind J Med Res 2009 ; Apr;129(4):438-41.
15. Laboratory-confirmed chikungunya virus disease cases reported to ArboNET by state or territory - United States, 2016. https://www.cdc.gov/chikungunya/pdfs/2016/2016table.pdf, Accessed on 31-01-2017.

16. Guidelines on Clinical Management of Chikungunya Fever Oct-2008, World Health Organization, Regional Office for South-East Asia. http://www.wpro.who.int/mvp/topics/ntd/Clinical_Mgnt_Chikungunya_WHO SEARO.pdf, Accessed on 31-01-2017.
17. Bandyopadhyay D, Ghosh S K. Mucocutaneous manifestation of chikungunya fever. Ind J Dermatol 2010; Jan-Mar;55(1):64-67.doi: 10.4103/0019-5154.60356
18. Pakran J, George M, Riyaz N et al: Purpuricmacules with vesiculobullous lesions: a novel manifestation of Chikungunya. Int J Dermatol 2011; Jan; 50(1):61-9.doi: 10.1111/j.1365-4632.2010.04644.x.
19. Riyaz N, Riyaz A,Rahima, et al. Cutaneous manifestation of chikungunya during a recent epidemic in Calicut, north Kerala, south India. Ind J Dermatol Venereol Leprol 2010 ; Nov-Dec; 76 (6): 671-6. doi: 10.4103/0378-6323.72466.
20. Chandak NH, Kashyap RS, Kabra D, Karandikar P, Saha SS, Morey SH, Purohit HJ, Taori GM, Daginawala HF. Neurological complications of Chikungunya virus infection. Neurol India 2009 ; 57:177-80
21. Jean-Baptiste E, von Oettingen J, Larco P et al. Chikungunya Virus Infection and Diabetes Mellitus: A Double Negative Impact. Am J Trop Med Hyg 2016; Dec 7; 95 (6): 1345-1350.
22. Information for Health Providers. Chikungunya Fever: Pan American Health Organization and World Health organization.http://www2.paho.org/hq/index.php?option=com_docman&task=doc_download&Itemid=270&gid=23974&lang=en, Accessed on 31-01-2017.
23. Seetharam KA, Sridevi K, Vidyasagar P. Cutaneous manifestation of chikungunya fever, Ind Pediatr 2012; Jan;49(1):51-3.Epub 2011 Aug 15.
24. Inamadar AC, Palit A et al. Cutaneous manifestation of chikungunya fever: observation made during a recent outbreak in south India. Int J Dermatol 2008; Feb; 47(2):154-9.
25. http://www.microbiologynotes.com/differences-between-dengue-and-chikungunya/ March 2017.
26. Katti R, Shahapur PR, Udapudi KL. Impact of Chikungunya virus infection on oral health status: an observational study. Ind J Dent Res 2011;22(4):613.
27. Mohan A, Kiran DHN, Manohar IC, Kumar DP. Epidemiology, clinical manifestations, and diagnosis of chikungunya fever: lessons learned from the re-emerging epidemic. Ind J Dermatol 2010 Jan-Mar; 55 (1): 54-63.
28. Lakshmi V, Neeraja M, Subbalaxmi MV, Parida MM, Dash PK, Santhosh SR, et al. Clinical features and molecular diagnosis of chikungunya fever from South India. Clin Infect Dis 2008;46:1436–42.
29. Kannan M, Rajendran R, Sunish IP, Balasubramaniam R, Arunachalam N, Paramsivan R, Tewari SC, Samuel PP, Tyagi BK. A study on chikungunya outbreak during 2007 in Kerala, south India. Ind J Med Res. 2009 Mar ; 129(3):311-5.
30. Mithra R, Baskaran P, Sathyakumar M. Oral presentation in dengue hemorrhagic fever: a rare entity. J Nat Sc Biol Med 2013; 4:264-7.
31. de Andino RM, Botet MV, Gubler DJ, García C, Laboy E, Espada F et al. The absence of dengue virus in the skin lesions of dengue fever. Int J Dermatol 1985 ;24(1):48–51.
32. Staples EJ, Breiman RF, Powers AM. Chikungunya fever: an epidemiological review of a re-emerging infectious disease. Clin Infect Dis 2009; 49 (6): 942-48.
33. Lin J, Chen RW, Hazan A, Weiss M. Chikungunya. Virus Infection manifesting as intermediate Uveitis. Ocul Immunol Inflamm 2016; 23:1-3.
34. Joy G, Penny A R, Natalie A P et al: Infectious Chikungunya Virus in the Saliva of Mice, Monkey and Humans. PLoS One. 2015; 10(10): e0139481.
35. Teng TS, Foo SS, Simamarta D, Lum FM et al. Viperin restricts chikungunya virus replication and pathology. J Clin Invest 2012; 122(12): 4447-4460.
36. Schwameis M, Buchtele N, Wadowski PP, Schoergenhofer C, Jilma B. Chikungunya vaccines in development. Hum Vaccin Immunther 2016; Mar (3): 716-731.
37. Yaren O, Alto BW, Gangodkar PV, Ranade SR et al. Point of sampling detection of Zika virus within a multiplexed kit capable of detecting dengue and chikungunya. BMC Infect Dis 2017; 17: 293.
38. Erguler K, Chandra NL, Proestos Y, Lelieveld J, Christophides GK, Parham PE. A large-scale stochastic spatio-temporal model for *Aedes albopictus*-borne chikungunya epidemiology. PLoS One 2017; 12 (3): e0174293.

Corresponding author

Dr. Karthikeyan Ramalingam, Professor and Head of Department, Department of Oral Pathology and Microbiology, Surendera Dental College and Research Institute, H.H.Gardens, Sriganganagar, Rajasthan.

email: rk@sgi.org.in