Chikungunya Virus: History, Geographic Distribution, Clinical Picture, and Treatment

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Chikungunya fever (CHIKF) is a re-emerging mosquito-borne disease caused by a virus endemic to Africa and Asia. Due to the ease with which its vectors propagate, the virus has spread to India and Europe, and more recently it arrived to the Caribbean, eventually extending into North, Central, and South America. According to the World Health Organization (WHO), the most common clinical manifestations are abrupt fever, polyarthralgia, headache, maculopapular rash, myalgia, and nausea/vomiting. Severe joint pain and stiffness have been known to incapacitate some patients from a few days to several months after infection. Fatal cases are rare, but some individuals have been known to develop severe forms of the disease that include neurological and cardiac complications and severe cutaneous manifestations. Additionally, there have been reports of infected mothers miscarrying and newborns that were infected in utero being born with congenital illnesses. Advanced age and various comorbidities have been associated with severe or atypical forms of CHIKF. Currently there are no approved vaccines for the chikungunya virus (CHIKV), and treatment aims to alleviate patient symptoms. The re-emergence of the CHIKV and its spread to new places around the globe encourage the development of new preventive, diagnostic, and treatment options. [*P R Health Sci J 2018;37:187-194*]

Key words: Chikungunya virus, Chikungunya fever, Arbovirus

The chikungunya virus (CHIKV) is a single-stranded RNA arbovirus (genus Alphavirus, family Togaviridae) that is transmitted to humans by the bite of infected mosquitoes (1). It causes chikungunya fever (CHIKF), an illness characterized by the sudden onset of fever and severe arthralgia known to cause chronic morbidity. The virus rarely causes a fatal infection; however, it is known to cause great morbidity to those affected, sometimes extending from weeks to years. "Chikungunya" is a word taken from the Makonde language in Tanzania which means "that which bends up" and refers to the bent posture observed in patients and that is caused by the severe pain in their joints (2). The disease was first identified in Tanzania in 1952 by RW Ross. After its discovery, outbreaks of chikungunya typically occurred in Asia and Africa. However, in 2004, the CHIKV reached India and several islands in the Indian Ocean, causing major outbreaks that affected more than 1 million people (3). Since then, the virus has reached new regions, including the Americas and Europe.

It is believed that the CHIKV has been present on the African continent for centuries, from back when science was not capable of identifying it (4). Three distinct CHIKV genotypes have been identified, based on their geographic distribution: the West-African, East/Central/South African (ECSA), and Asian isolates. They are responsible for major epidemics around the world, and the identification of the virus by its corresponding genotype is achieved through gene sequencing (5).

During inter-epidemic periods, the CHIKV is conserved through an enzootic cycle in places where it is endemic (such as Africa and Asia) and an urban cycle when the virus reaches the cities. In the enzootic cycle, continuous transmission of the pathogen occurs between wild animals and vectors. Non-human primates (NHP) serve as the reservoir for the virus, and the mosquitoes from the *Aedes genus* are the vectors responsible for the transmission of the virus. It is known that the CHIKV can use such animals as buffalos, rodents, and birds as hosts, but the critical host for enzootic circulation is not known with certainty (6).

A spillover of the virus can occur when people who live in rural areas close to these virus reservoir cycles are bit by an infected mosquito. If these people then travel to urban areas in which there are viable vectors, more people could almost certainly be infected. In urban areas, the virus is transmitted by mosquitoes of the *Aedes aegypti* and *Aedes albopictus* species. It is preserved and further spread in an autochthonous cycle in which continuous transmission occurs between mosquitoes and humans. In this type of transmission, infected mosquitoes

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transmit the virus to a person, enabling that individual to then contaminate the mosquitoes which feed on his or her blood, thus continuing the cycle (7).

The species *Aedes aegypti* was the principal vector involved in the outbreaks in Africa (8). However, during the outbreaks in Asia, the territories of the Indian Ocean, Europe, and the Caribbean, *Aedes albopictus* was identified as the principal vector. This change in the species of the vector occurred because the virus acquired a new mutation which enhanced its ability to use *A. albopictus* as a vector. This mosquito species, originally from Southeast Asia, has shown a great ability to adapt to other climates, allowing it to spread into places that are non-endemic for the CHIKV (5,9). For this reason, the CHIKV is a latent threat for many countries, and thus new diagnostic and preventive measures are in need.

Disease history and Geographic distribution

Figure 1. Countries and territories where CHIKF cases have been reported. *Note that only locally acquired infections are shown on this map; it does not include imported cases (10).

In 1952, the first CHIKV case was reported in the Makonde Plateaus region in Tanzania (2). The virus was isolated for the first time in 1953 by RW Ross (11). In 1958, the first CHIKV infection in Asia was documented. Since 1960 many countries in Southeast Asia, along with countries located in Central, Southern, and Western Africa, have reported outbreaks.

The outbreak on the island of Reunion (2005–2007), which is located in the Indian Ocean, is of particular interest because 38.8% of the 785,000 habitants were infected (12). The cause of this phenomena was found to be a single acquired A226V mutation in the envelope protein E1 of the ECSA genotype of the CHIKV. The mutation increased the CHIKV infectivity of the island's native mosquitoes (*Aedes albopictus*) and led to a greater dissemination of the infection due to the abundance of the vector (13). Before the introduction of this mutation, the *Aedes aegypti* mosquito was the predominant vector used by the CHIKV. This mutation enabled the genotype to spread with a different vector which is also present in other regions.

Later, in 2007, a CHIKV strain with the same mutation was introduced by travelers into the Emilia–Romagna region in Italy. This was the first CHIKV outbreak in Europe, and it led to at least 205 infections in the area (5,14,15). On December 6 of 2013, the first CHIKV case in America was confirmed in the Collectivity of Saint Martin, an overseas collectivity of France; the outbreak was thought to have been caused by the frequent travel of the residents between the islands of the Caribbean (16). Subsequently, most territories in the Caribbean reported locally acquired CHIKF cases.

The CHIKV found in the Caribbean corresponds to the Asian strain, and its principal vector is the *Aedes aegypti* mosquito (17,18). This genotype, which does not have the A226V mutation in the E1 gene, has been widely reported in both Central America and South America. The introduction of these strains into the Americas could result in a wider spread of the virus, because the *A. albopictus* mosquito is present in most of these regions (4).

The first case of CHIKF in the United States territory of Puerto Rico was reported during May 2014. A total of 28,327 cases were identified using multiple passive surveillance systems, as recommended by government agencies (19). Of these cases, 6,472 patients were tested for the presence of the CHIKV and 4,399 were found to be positive (19). Since there was a substantial weekly increase in the number of suspected cases of CHIKF and because the capacity for laboratory testing by the Puerto Rico Department of Health was overwhelmed, diagnostic testing was not performed on all the suspected cases. For these reasons, diagnostic testing was prioritized for hospitalized patients and for patients from locations in Puerto Rico which had no laboratory-confirmed cases up to that date.

Several months after the CHIKV arrived at the Caribbean, the state of Florida, in the United States, reported 11 autochthonous cases during the summer of 2014 (4). During that year, 243 imported cases were reported in 31 states, Puerto Rico, and the US Virgin Islands (20).

There were 475 imported CHIKF cases reported in countries belonging to the European Union during the period of 2008 to 2012 (21). Most of these imported cases matched the times when outbreaks were occurring in endemic countries. For this reason, the establishment of the CHIKV in the Caribbean poses a great threat to European countries due to the high number of travelers from the latter to the former. This implies that more diagnostic and surveillance measures need to be implemented in regions where the CHIKV could thrive, in order to prevent further outbreaks in new places and regions where the virus has not reached before (22).

Clinical picture

The clinical manifestations of the CHIKV cause severe impacts on the quality of life of those affected. The clinical findings are similar to those of other viral diseases. Thus we have to be aware of the differential diagnosis for the virus (5). Infections that are asymptomatic are possible, but these cases are not frequent and have been observed in only 15% of patients infected with the CHIKV (23). Typical symptoms include abrupt fever, polyarthralgia, headache, maculopapular rash, myalgia, and nausea/vomiting (24). Patients with the CHIKV tend to seek more medical attention due to symptoms than do

the patients of most other mosquito-borne diseases (25). The typical incubation period after being bitten by a mosquito is between 3 to 7 days; however, a range of 1 to 12 days has been observed (26). Currently, the manifestations of the CHIKV are divided into 3 phases, according to the Pan American Health Organization and the Centers for Disease Control and Prevention: the acute phase, the subacute or convalescent phase, and the chronic phase.

Acute phase

The acute phase is characterized by the abrupt onset of high fever and severe joint pain and typically lasts for 3 to 10 days (3,27). Other manifestations or symptoms observed include headache, diffuse back pain, myalgia, nausea, vomiting, rash, and conjunctivitis. This stage is characterized by high levels of the virus in the blood. Consequently, the innate immune system quickly reacts to the viremia to control the infection. Patients will also present high levels of cytokines that cause inflammation as the body fights the virus (28). Finally, the viremia declines quickly during days 1 to 3. Such data are important since these patients are able to infect any mosquitoes that bite them during this time; for this reason, said patients should have some physical or chemical protection against further mosquito bites.

Table 1. Clinical syndromes and laboratory values in 54 laboratory-confirmed CHIKF patients of the 2005–2006 Reunion island outbreak (28).

Clinical syndrome	% Reported
Arthralgia (joints affected)	
Metacarpophalangeal joints	74.1
Interphalangeal joints	68.5
Wrists	72.2
Ankles	68.5
Knees	61.1
Shoulders	48.1
Lumbar	46.3
Feet	42.6
Cervical joints	38.9
Elbows	25.9
Myalgia	46.3
Laboratory values	**% Reported**
Neutropenia (<2,000 cells/mm^3)	22.2
Lymphocytopenia (<1,000 cells/mm^3)	79.6
Thrombocytopenia (<150x10^3 cells/mm^3)	25.9
Elevated liver enzymes (ASAT/ALAT>45IU/L)	22.0

Subacute or Convalescent phase

The subacute or convalescent phase of the disease begins after day 10 of infection and is typically characterized by the improvement of the presenting symptoms (3). Most of the initial symptoms, such as the shivering that is caused by fever, recede by day 7, but more than 40% of the patients in an outpatient study done on the island of Reunion reported persistent arthralgia, asthenia, myalgia, or headache (or a combination of 2 or more of the previous) (28). The virus itself might not be detectable in the patient's blood during this time.

Table 2. Clinical syndromes and laboratory values in 157 laboratory-confirmed CHIKF patients of the 2005–2006 Reunion island outbreak (27).

Clinical syndrome	% Reported
Joint swelling	31.8
Maculopapular rash	40.1
Gastrointestinal symptoms	47.1
Lymphadenopathy	8.9
Aphthous ulcerations	2.5
Laboratory values	**% Reported**
Lymphopenia (lymphocyte <1,000 cells/mm^3)	79.0
Moderate thrombocytopenia (<150x10^3 cells/mm^3)	43.9
Hypocalcemia (<2.25mmol/L)	54.8

Chronic phase

The chronic phase is defined by symptoms that persist for more than 3 months. These symptoms typically consist of persistent arthralgia in the joints that were previously affected during the acute phase of the disease (3). Only a few individuals develop complications from the chronic inflammatory response, which complications include destructive arthropathy and arthritis that resembles rheumatoid or psoriatic arthritis (29). Patients who most commonly reach this phase are older in age, have preexisting joint disease, and display severe symptoms during the acute phase of disease.

It is important to acknowledge that the clinical manifestations observed depend on several factors. Due to acquired mutations, the different CHIKV strains have variations in their infectivity, pathogenicity, observed symptoms, and severity (30). Another point to consider is that the prevalence of CHIKF symptoms will be different in the different populations observed. For these reasons, results from previous outbreak studies about the clinical manifestations of CHIKF must be reviewed in terms of the date and location of the outbreak.

Table 3. Clinical syndromes in 141 laboratory-confirmed CHIKF patients of the 2014 outbreak in Dominica (31).

Clinical syndrome	% Reported
Fever	95
Arthralgia	72
Rash	21

Outbreaks and Clinical manifestations

Reunion Island Outbreak, 2005

Clinical manifestations and laboratory results were studied in outpatients of the CHIKV outbreak of Reunion island in 2006 by Thiberville et al. (28) Cases selected for this study were laboratory confirmed by reverse transcription-polymerase chain reaction (RT-PCR) and seroconversion. The clinical syndromes and laboratory values reported in the study are summarized in Table 1. In the study, arthralgia was the most prevalent manifestation. It typically occurred in small joints such as the phalanges and wrist but also in the ankles and knees (28).

This study developed a clinico-biological score which took into consideration clinical manifestations and lymphocyte count to classify patients as "probable," "possible," and "not probable" in terms of their having the CHIKV. The parameters taken into consideration (wrist pain, metacarpophalangeal pain, minor or absent myalgia, and lymphopenia [<1G/L]) were selected because they were observed in the CHIKV-positive patients. The calculation of the clinico-biological score was done using a formula developed by Thiberville et al., which gave a positive predictive value of 94% in the studied population. These patients were followed up for a period of 300 days in order to assess the persistence of symptoms as a function of time. The results showed that people who had a more severe onset of pain in their joints also reported persistent arthralgia at day 300. Additionally, age represented an independent factor for the outcome of the disease, since most of the patients who reported persistent joint pain at day 300 were significantly older (28). This tendency was consistent with what was found in previous studies in India, where increased age was correlated with atypical presentations and persistent arthralgia.

After the Reunion island outbreak, Borgherini et al. conducted a study with 157 confirmed cases of CHIKF, also from Reunion island after the outbreak of 2005–2006. Cases were laboratory confirmed, using RT-PCR, seroconversion, or positive IgM serologic results. The reported fevers had a mean value of 38.9°C and had an abrupt onset (27). Most of the patients reported arthralgia in more than 1 joint, affecting, mostly, the distal joints of the lower body. Other reported clinical syndromes and laboratory findings are summarized in Table 2. The predominant laboratory findings at admission were lymphopenia and hypocalcemia (27). This same study reported that hospitalized patients had significantly higher levels of creatinine and aspartate transaminase than non-hospitalized patients did; it is believed that this may be caused by drug toxicity in patients receiving antipyretic and analgesic drugs prior to hospital admission. Patients who required hospitalization were older and had more comorbidities than patients who did not require hospitalization. The number of patients with skin manifestations is highly variable in the literature, since the reported results of the affected patients range from 14% to 86% (27). Finally, as reported in this study, hemorrhage is not a common clinical sign in patients with CHIKF.

Dominica, 2014

Ahmed et al. reported information on case surveillance that was taken during the 2014 CHIKV outbreak in Dominica. All the suspected infections were laboratory confirmed using either real-time PCR (rPCR) or IgM detection using ELISA. From December 2013 through July 2014, 3,559 CHIKF cases were reported, from which 141 cases were confirmed by laboratory tests. The principal symptoms documented during the outbreak are reported in Table 3. In this study, 55% of the patients were female. The strain responsible for this outbreak was not specified, but it was reported that one of the first patients had recently traveled from St. Martin, where the Asian genotype was responsible for the outbreak (31).

Italy, 2007

During 2007, the first CHIKV outbreak in a temperate area was reported in the Emilia–Romagna region of Italy. Moro et al. did a cohort study in order to describe the long-term clinical course and outcome after the CHIKV outbreak. Patients were recruited for the study through active and passive surveillance methods. A total of 250 laboratory-confirmed patients who completed the required follow-up interviews were included in the analysis. The symptoms reported during the acute phase are reported on Table 4. After 12 months of patient follow-up, the most common symptom observed was arthralgia (60.8%). As in previous studies, elder patients or those subjects with an underlying rheumatic disease before infection were found to have persistent arthralgia after 12 to 13 months of infection (32).

Table 4. Clinical syndromes in 250 laboratory-confirmed CHIKF patients followed up after the Emilia–Romagna (region of Italy) outbreak of 2007 (32).

Clinical syndrome	% Reported
Asthenia	92
Arthralgia	90
Myalgia	47.4

Southern Thailand, 2008–2009

The CHIKV outbreak involving the ECSA strain re-emerged in southern Thailand during August of 2008. By the end of 2009, 49,069 CHIKF cases had been reported. Chusri et al. conducted a study in which 45 laboratory-confirmed cases were evaluated at different points in time to assess the kinetics on the CHIKV infections. All the subjects had fever and arthralgia (these were the inclusion criteria of the study). The mean fever duration and temperature were 5.9 days and 39.5°C, respectively. The clinical syndromes and laboratory values reported in the study are summarized in Table 5. The mean duration of the arthralgia was 5.8 days. A rash (82%) was typically observed 2 to 3 days after the onset of illness.

Detectable levels of viremia were reported during the first 5 days of the illness. IgM antibodies against the CHIKV were detected at day 3 and persisted in the blood of the patients until day 22 to 23. In some patients, the appearance of IgG was concomitant with the appearance of IgM antibodies, but at day 6, all the patients had detectable levels of IgG antibodies in their serum (33).

Atypical manifestations

During the 2005–2006 outbreak in Reunion, Economopoulou et al. conducted a study to determine the incidence and mortality of atypical CHIKV infection (34). According to the article that resulted, atypical manifestations are classified into 3 categories: exacerbation of underlying medical conditions, deterioration of disorders that had not been discovered, and

Table 5. Clinical syndromes and laboratory values in 45 laboratory-confirmed CHIKF patients of the southern Thailand outbreak of 2008–2009 (33).

Clinical syndrome	% Reported
Arthralgia (joints affected)	
Interphalangeal joints	91
Knees	71
Elbows	67
Wrists	56
Rash	82
Trunk	53
Limbs	52
Gastrointestinal symptoms	
Vomiting	63
Abdominal pain	42
Diarrhea	2
Laboratory values	**% Reported**
Lymphocytopenia (<1,000 cells/mm^3)	47
Leukopenia (<4,000 cells/mm^3)	11
Thrombocytopenia (<150x10^3 cells/mm^3)	13
Elevated liver enzymes (ASAT/ALAT>45IU/L)	33

exaggerated response to the CHIKV infection. Some of the atypical manifestations include neurological symptoms (as meningitis, encephalitis, and Guillain–Barre syndrome), cardiac complications (as pericarditis and myocarditis), and extensive bullous skin lesions (35,36).

During the 2006 outbreak on Reunion island, atypical cases comprised 0.3% of all the CHIKV cases reported (34). Results of this study showed that the incidence of atypical cases and mortality was higher as age increased (34). In addition, 89% of the patients with atypical manifestations had underlying medical conditions. It is important to note that some previously healthy individuals also developed cardiovascular or neurological involvements, indicating that underlying conditions are a risk factor; but there are other variables that are not yet understood and that may lead to these kinds of severe cases (34). Finally, it is important to note that patients with latent respiratory or cardiovascular conditions had a higher risk of developing severe CHIKF symptoms (35). Mortality due to the CHIKV is known to be low; however, severe cases have been reported during outbreaks.

Perinatal Chikungunya infections

It is known that the CHIKV can be transmitted from mother to child during the perinatal period if the mother is infected with the CHIKV (37). Such transmission is more likely to occur in a mother infected a few days before labor. During previous outbreaks, some infected neonates have developed diseases that resulted in hemorrhage, disseminated intravascular coagulation, or cardiac and neurological complications (24). In a study performed with CHIKF patients from hospitals in Santo Domingo, Colombia, and El Salvador in 2014 (Torres et al.), the observed vertical transmission rate was found to range from 27.7% (in laboratory-confirmed cases) to 48.29% (in data obtained from clinically suspected cases of CHIKF) (38). In this study, the most common clinical manifestations in neonates included fever, rash, irritability, hyperalgesia, diffuse limb edema, meningoencephalitis, and bullous dermatitis (38). It is of importance for clinicians to be aware of such manifestations in neonates infected with the CHIKV in order to identify and give the necessary care. Performing C-sections on pregnant mothers infected with the CHIKV has not been shown to reduce vertical transmission. There is also no evidence that the virus can be transmitted to newborns through breast milk (39). Finally, it is important to mention that there is no evidence of teratogenic effects as a result of perinatal CHIKV infection. However, there are cohort studies and case reports which suggest poor neurologic outcome in neonates who are infected in the perinatal period (40).

Diagnostic tests

CHIKF's clinical manifestations are similar to those of such diseases as dengue and malaria as well as to those of other alphaviruses. For this reason, a laboratory diagnosis is essential in order to distinguish the CHIKV from other viruses. Currently, diagnostic tests done to confirm CHIKV infection depend on the time at which the patient seeks medical attention.

For patients in the early days of the disease, virus culture, antigen detection, and nucleic acid amplification tests are the standard diagnostic methods. Currently, the real-time RT-PCR technique is used because it allows for viral load quantification (36). However, these types of test are used during the first 5 to 7 days, when the viral load is sufficiently high in a given patient's blood (24,36). In reality, many patients delay visiting medical facilities until after their symptoms have progressed to the point at which the detection of nucleic acids becomes difficult.

Another method used for the diagnosis of CHIKF is the detection of antibodies in the patient's blood. This type of test is adequate for approximately 1 to 2 weeks after the initial infection. During this time frame, the most common test to confirm the diagnosis of chikungunya is the IgM capture enzyme-linked immunosorbent assay (ELISA) (24).

Efforts have been made to develop rapid detection kits against CHIKV antibodies. While such kits would expedite the diagnostic process, they are flawed, in that they are not able to achieve the sensitivity or specificity of current laboratory methods. For this reason, most of the IgM rapid test kits developed to date are not reliable, and the development of more universal methods is needed.

Treatment

According to the WHO and the CDC, treatment for the CHIKV is currently symptomatic since there is no specific therapy. During the acute phase, treatment should be focused on the symptoms, using antipyretic and antalgic therapies. The medications used should include paracetamol/acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDS) (26,41).

Initially, acetaminophen is preferred over NSAIDs or aspirin, due to the effects of both the latter on platelets; some regions are endemic not only for chikungunya but also for dengue fever infections, and these viral illnesses are difficult to tell apart until laboratory testing is performed. For patients who do not experience relief in their arthralgia with the above-mentioned medications, other therapeutic strategies, such as a short course of opioids, could be implemented, but only after evaluating the potential risks and benefits of the proposed treatment. Finally, it is important to emphasize rest and adequate fluid/electrolyte replacement to these patients.

There are no licensed antiviral drugs to limit CHIKV replication (42). The development of such drugs could help in the improvement of symptoms in the acute phase; some studies have found that a higher viral load during the acute phase has been associated with more severe symptoms in patients. The significance of viral load is still controversial since some studies did not find any correlation between viral load and the development of more severe symptoms (26).

Some patients progress to the subacute and chronic phases of the disease, meaning they might experience chronic joint pain for up to a year after the initial infection. In these cases, pain management can be effected using long-term anti-inflammatory therapy; however, caution must be taken when using aspirin or NSAIDs because of the possibility of gastrointestinal side effects (43). Patients with disabling refractory joint pain after using any of the previously mentioned medications can be started on intra-articular corticosteroids or topical NSAIDs. Finally, physiotherapy might be useful in patients who experience persistent joint pain associated with contractures of or deformities in their extremities.

Vector control measures

Since treatment for CHIKF is currently symptomatic, mosquito control is believed to be the best choice in terms of preventing CHIKV infections. However, this strategy has proven to be difficult to implement, especially in poor countries with limited resources (41). Recently infected people should take the appropriate measures to prevent mosquito bites because their viral loads are sufficiently high during this phase so as to contaminate feeding mosquitoes, which can then go and infect other people. The use of mosquito nets and window screens is recommended in order to prevent spread. Furthermore, the use of air conditioners has been found to make the environment less hospitable for *Aedes* mosquitoes and thus is linked to a lower seroprevalence (44). In case of a possible outbreak, public health measures that encourage the mechanical destruction of breeding places would impede the reproduction of mosquitoes and thus decrease transmission.

A study was conducted in Spain in order to measure the effectiveness of multiple intervention strategies for the control of the *Aedes albopictus* mosquito (45). These strategies consisted of source reduction by eliminating water-holding containers, larvicide treatment of stagnant waters, adulticide treatment (fumigation) of public gardens, and cleaning up uncontrolled landfills. A key component of this study was a home-based intervention to educate citizens in the area about mosquito control measures such as the ones mentioned previously. The study showed that there was a significant reduction in the number of mosquito eggs in the areas under observation (45). Currently, most mosquito control programs rely on chemical interventions (outdoor spraying, impregnated nets, and indoor spraying); however, the efficacy of such interventions is threatened by the resistance developed in the mosquito population to the compounds used (46,47). For this reason, the mechanical destruction of breeding sites should be encouraged in order to control the spread of vectors and consequently stop the CHIKV and other arboviruses from spreading further.

Vaccines

Currently there are no licensed vaccines against the CHIKV available for humans, which fact encourages scientific research in the area. Up to and including the date of this report, only 4 vaccine candidates have reached phase 1 clinical trials.

Conclusion

The CHIKV causes several clinical manifestations, such as abrupt fever, polyarthralgia, headache, maculopapular rash, myalgia, and nausea/vomiting. It is estimated that 15% of infected individuals remain asymptomatic. The most common symptoms recorded during the different outbreaks were fever and arthralgia; in terms of laboratory findings, lymphocytopenia was the most common. The arthralgia was the most prevalent in the phalanges, followed by the ankles and knees. Severe joint pain and stiffness have been known to incapacitate some patients from a few days to several months after infection. Increased age is considered an important determinant for the persistence of symptoms after infection. Although fatal cases are rare, some individuals develop severe forms of the disease, which forms can include, among others, neurological symptoms (meningitis, encephalitis, and Guillain–Barre syndrome), cardiac complications, and in babies infected in utero, congenital illnesses. Due to these complications, patients such as these require special medical attention. Advanced age and various comorbidities have been associated with severe or atypical forms of CHIKF, but it is important to recognize that the complications mentioned above have also been observed in previously healthy individuals.

The re-emergence of the CHIKV and its spread to new places around the globe together encourage the development of new preventive, diagnostic, and treatment options. There are no licensed vaccines for the CHIKV, and the candidate vaccines that have reached phase I clinical trials need to be studied in bigger populations to assess the safety and efficacy of those vaccines. Treatment strategies aim to relieve symptoms, thus the pathogenesis associated with the CHIKV needs to be further assessed in order to develop viable treatment options.

The spread of the CHIKV around the world is dependent on the spread of its vectors and the travel of its human carriers between affected and non-affected areas. Since its introduction into the islands of the Caribbean, the CHIKV has spread to several places in South America, Central America, and North America. Its introduction into new places in Europe has been associated with outbreaks occurring in the Caribbean region. This is possible because of the frequent travel between these locations and the ease with which the vectors (the *Aedes aegypti* and *Aedes albopictus* mosquitoes) propagate in those areas. Climate changes affect the migration patterns observed in Aedes mosquitoes, increasing the populations of these mosquitoes in North America and Europe. For this reason, CHIKV outbreaks are still a threat and new preventive and diagnostic measures must be developed.

Resumen

La fiebre de Chikungunya (CHIKF) es una enfermedad reemergente transmitida por mosquitos que es causada por un virus endémico en África y Asia. Debido a la disponibilidad de sus vectores, el virus se ha extendido a India, Europa y, más recientemente, llegó al Caribe y de ahí se extendió a lugares en Norte, Centro y Sudamérica. Según la Organización Mundial de la Salud, las manifestaciones clínicas más comunes son fiebre abrupta, artralgia, dolor de cabeza, erupción cutánea, mialgia, náuseas y vómitos. El dolor y la rigidez en las articulaciones pueden ser tan severos que incapacitan a las personas afectadas por un tiempo de días hasta varios meses después de la infección. Los casos fatales son raros, pero se sabe que algunas personas desarrollan formas graves de enfermedad que incluyen complicaciones neurológicas, cardíacas, y manifestaciones cutáneas severas. Además, se han reportado muertes fetales espontáneas y enfermedades congénitas en bebés infectados durante el embarazo. La edad avanzada y varias comorbilidades se han asociado con formas graves o atípicas de CHIKF. Actualmente no hay vacunas aprobadas para el Virus de Chikungunya (CHIKV) y el tratamiento tiene como objetivo aliviar los síntomas del paciente. La reaparición de CHIKV y su propagación a nuevos lugares en todo el mundo fomentan el desarrollo de nuevas opciones preventivas, diagnósticas y de tratamiento.

Abbreviations

CHIKF - chikungunya fever, CHIKV - chikungunya virus
ELISA - enzyme-linked immunosorbent assay
RT-PCR - reverse transcription PCR

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