Journal of the Egyptian Society of Parasitology, Vol. 53, No.3, December 2023
J. Egypt. Soc. Parasitol. (JESP), 53(3), 2023: 475 – 489
Online: 2090-2549

CHIKUNGUNYA VIRUS VERSUS AEDES-BORNE OTHER VIRUSES: A REVIEW ARTICLE

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Abstract

Chikungunya virus is an alphavirus transmitted by *Aedes aegypti* and *Ae. albopictus* causes acute febrile polyarthralgia and arthritis. Also, transmission of chikungunya virus can occur via maternal-fetal transmission, blood products and organ transplantation. Chikungunya virus is endemic in West Africa; outbreaks have occurred in Africa, Asia, Europe, islands in the Indian and Pacific Oceans, and recently in the Americas. But, with the climatic changes Chikungunya invaded into new areas, where local transmission occurs if competent mosquitoes are present. *Aedes* vectors are also capable of transmitting Zika virus, Dengue virus and Yellow fever virus.

Currently there is no vaccine to prevent or medicine to treat chikungunya virus infection, and people can protect themselves by avoiding mosquito bites. Eradicating *Aedes* species is a must.

Key words: Chikungunya fever, *Aedes* vectors, Climatic changes, Global spreading, Review.

Introduction

Chikungunya is an arthropod-borne alphavirus transmitted by mosquitoes causing acute febrile polyarthralgia and arthritis (Weaver and Lecuit, 2015). The name chikungunya is derived from an African language meaning "that which bends up" or "stooped walk" because of the incapacitating arthralgia caused by the disease.

Epidemiology: CDC maintains a website summarized chikungunya virus geographic distribution. It belongs to *Togaviridae* family and alphavirus genus transmitted by Aedes (Rougeron *et al,* 2015). Chikungunya virus is endemic in certain parts of West Africa; human serosurveys have identified antibodies to chikungunya virus in 35 to 50% of the population in some areas (Chevillon *et al,* 2008). Outbreaks of chikungunya disease have occurred in Africa, Asia, Europe, and islands in the Indian and Pacific Oceans and more in the Americas, occurred during the tropical rainy season and abate du ring the dry season (Staples *et al,* 2009). Never- theless, outbreaks in Africa have occurred after periods of drought, where open water containers serve as vector-breeding sites and it can cause large risky outbreaks, affecting one-third to three-quarters of the population in areas as virus is circulating (CDC, 2024). The outbreak on Réunion Island in the year 2005 to 2006 had involved about 266,000 individuals; 34% of the island's population (Renault *et al,* 2007).

Review and Discussion

Chikungunya was perceived as a tropical disease until an outbreak in Italy occurred in 2007 (Rezza *et al,* 2007). The first local acquired chikungunya cases of in the Americas were in 2013 in the Caribbean islands (Morens and Fauci, 2014). Since then, chikungunya virus infections have spread widely in the Caribbean and Americas (Fischer and Staples, 2014). The first locally transmitted cases in the United States were in Florida (Kendrick *et al,* 2014). Local transmission was reported widely in Puerto Rico, where sero-surveys found nearly 25% of blood donors were infected (Simmons *et al,* 2016). Chikungunya is transmitted the *Aedes* vectors as Dengue and Zika viruses. The viruses can co-circulate in a geographic region, and

co-infections (Waggoner *et al,* 2016). ZIKA was detected in Egypt, Cameroon, and several Asian Countries (CDC, 2016a).

Chikungunya is transmitted by *Aedes aegypti* and *Aedes albopictus* infecting travelers, who imported chikungunya into new areas (Charrel *et al,* 2007) with *Ae. aegypti* and/or *Ae. albopictus* local transmission follows. This was reported in many Asian and European countries as well as in the Americas and Australia (Gibney *et al,* 2011) by *Aedes* bites, or rarely via maternal-fetal transmission, blood products and organ transplantation. Mosquitoes become infected when they feed on infected patients, which can then spread the virus to other people via biting, after the virus reaches salivary glands (Furuya-Kanamori *et al,* 2016). In endemic areas of Africa, chikungunya virus transmission occurs in cycles involving man, *Aedes* and other mosquitoes, and animals (nonhuman primates and perhaps other animals). Outside Africa, major outbreaks were sustained by mosquito transmission among susceptible humans (Russo *et al,* 2020). They bite primarily during the day but also at night. *Aedes* are also vectors of Zika virus and dengue virus (Caron *et al*, 2012), and yellow fever virus (Waggoner *et al,* 2018).

Ae. aegypti is well adapted to urban settings and is widely distributed in the tropics and subtropics worldwide. It prefers the human host and breeds readily in flowerpots and in trash. A single *Ae. aegypti* mosquito can infect more than one human since this species may feed on another host if its blood meal is interrupted (Wilke *et al,* 2019)

Ae. albopictus (the Asian tiger mosquito) can survive more temperate environments than *Ae. aegypti* so has a wider potential distribution. It has been considered a relatively inefficient vector since it bites a range of animal species, and blood meals from non-susceptible hosts do not contribute to virus transmission, but some populations of *Ae. albopictus* may be more anthropophilic (preferring human blood) than others; in some settings, man may be the most abundant host (Reiter *et al*, 2006). *Ae. albopictus* is competent to transmit a number of arboviruses (inc luding yellow fever, West Nile, Japanese encephalitis, and Eastern equine encephalitis viruses (El-Bahnasawy *et al,* 2013).

Chikungunya virus can spread geographically via travel of infected persons between regions with appropriate season/climate that competent mosquitoes exist for perpetuation of local transmission (Charrel *et al*, 2008). Also, dissemination of mosquitoes can occur via transport of *Aedes* larvae and eggs by ships and air traffic to new areas with suitable environmental and climatic conditions (Tatem *et al*, 2006). Generally, in cool temperatures in temperate areas, a mos- quito may die before the extrinsic incubation period is complete. Also, mutations in some strains of the chikungunya virus may shorten the extrinsic incubation period, allowing more mosquitoes to survive long enough to transmit virus (Tsetsarkin *et al,* 2007). But, the warmer the temperature, the shorter the extrinsic incubation period (between an *Aedes* blood meal from a viremic patient and transmission of the virus to a new host), and the sooner the virus is transmit to a new host (Alomar and Alto, 2022).

Blood products & organ transplantation: Chikungunya transmitted via blood products was reported in France, where a nurse was infected by exposure to blood while caring for a patient infected in Réunion (Bordi *et al,* 2008). Transmission by organ transplantation also occur since chikungunya viremia (may exceed 10^9 RNA copies/ml plasma) was likely prior to onset of symptoms (Brouard *et al,* 2008). Chikungunya virus infects human cornea and might be transmitted via corneal grafts, which were reported in individuals without systemic chikungunya manifestations (Couderc *et al,* 2012).

Maternal-fetal transmission (perinatology): Pregnant women infected with chikungunya virus are not at increased risk for atypical or severe disease. Maternal-fetal chikungunya virus transmission was described, and maternal chikungunya virus infection was associ-

ated with miscarriage (Lenglet *et al,* 2006). Risk of maternal-fetal transmission is highest when pregnant women are symptomatic during the intra-partum period (two days before or after delivery). During this period, vertical transmission occurs in about half of cases; among 39 women in the Réunion outbreak with viremia at the delivery time, vertical transmission rate was 49% and cesarean delivery was not protective against vertical transmission (Gérardin *et al,* 2008). The perinatal infection caused risky complications and potential cognitive impairment (Cardona-Correa *et al,* 2017). The virus neither was detected in the breast milk nor transmitted via breastfeeding. But, Campos *et al.* (2017) in Brazil by RT/PCR detected chikungunya virus in a breastfeeding woman's serum, urine and milk, but her three months old baby was negative.

Acute clinical manifestations of adults and postnatal infected children: Following an incubation period of 3 to 7 days (range 1 to 14 days), clinical manifestations begin abruptly with fever and malaise (Burt *et al*, 2012). Majority of infected individuals have symptoms; asymptomatic seroconversion occurred in <15% of patients (Appassakij *et al,* 2013).

Fever may be high grade (>39ºC); the usual duration of fever is 3 to 5 days (range 1 to 10 days). Polyarthralgia begins two to five days after onset of fever and commonly involves multiple joints; often 10 or more joint groups (Lakshmi *et al,* 2008). Arthralgia is usually bilateral and symmetric and involves distal joints more than proximal ones, affected joints were hands (50 to 76%), wrists (29 to 81%), ankles (41 to 68%), and axial skeleton was noted in 34 to 52% of cases (Goupil and Mores, 2016). Pain may be intense and disabling, leading to immobilization and stiffness up to 40 months after viral infection (Tritsch *et al,* 2021).

Skin manifestations were reported in 40 to 75%of patients (Simon *et al*, 2007). The commonest one is macular or maculopapular rash (usually appearing three days or later after onset of illness and lasting three to seven days). Rash often starts on the limbs and trunk, can involve the face, and may be patchy or diffuse. Pruritus was reported in 25 to 50% of patients (Taubitz *et al*, 2007). Others may include headache, myalgia, facial puffiness, and gastrointestinal symptoms. Atypical dermatologic manifestations include bullous skin lesions (children mainly) and hyperpigmentation (Rajapakse *et al*, 2010) External ear redness may reflect chondroitis, but hemorrhagic manifestations are uncommon (Javelle *et al,* 2008). Silva *et al.* (2018) in Brazil reported that chikungunya virus was distinguished by the rapid onset of fever, short viremia, rash, arthralgia, skin bleeding, hemorrhagic dyscrasia, joint swelling, elevated C-reactive protein, leukopenia, and normal or low platelet count. Physical examination, per-articular edema or swelling was observed in 32 to 95% of cases. Also, large joint effusions were noted in 15% of cases. Peripheral lymphadenopathy (mainly cervical) may be in 9 to 41% of patients (Borgherini *et al,* 2007). Conjunctivitis may occur (Mahendradas *et al,* 2008).

The common laboratory abnormalities are lymphopenia and thrombocytopenia. Hepatic transaminases and creatinine may be elevated. High viral load during the acute illness was associated with poor prognosis in post-acute phase, which duration was usually 7 to 10 days (Jain *et al,* 2017).

Severe complications as respiratory failure, cardiovascular decompensation, myocarditis, acute hepatitis, renal failure, hemorrhage, and neurologic involvement occurred (Robin *et al,* 2008). Meningoencephalitis is the main neurologic complication; others include acute flaccid paralysis, Guillain-Barré syndrome, myelitis, and cranial nerve palsies (Gérardin *et al,* 2016).

Ocular manifestations (iridocyclitis, retinitis, episcleritis, macular choroiditis, uveitis), and sensorineural hearing loss were also reported (Bhavana *et al,* 2008). Extensive skin necrosis of nose was reported in three severely ill adults (Torres *et al,* 2016). The incidence of severe infection in Réunion hospital-

ized patients with complications as respiratory failure, meningoencephalitis, acute hepatitis, or kidney failure) was 17/100,000 population (Economopoulou *et al,* 2009). Vairo *et al.* (2019) in Italy found that after 1 to 12 days incubation period, symptoms were similar to other febrile infections appear, with a sudden onset of high fever, nausea, polyarthralgia, myalgia, widespread skin rash, and conjunctivitis. Serious complications include myocarditis, uveitis, retinitis, hepatitis, acute renal disease, severe bullous lesions, meningoencephalitis, Guillain-Barré syndrome, myelitis, and cranial nerve palsies. The treatment was only supportive.

In Réunion, there were 228 deaths, with mean age of 78 years (Paquet *et al,* 2006). Deaths associated with chikungunya virus infection were reported during outbreaks in Mauritius, Réunion, and India (Beesoon *et al,* 2008). During chikungunya epidemic in Ahmedabad, India, in 2006, about 60,000 cases died; the deaths number during the four months of peak epidemic activity exceeded the average death rate during those months in the previous four years by 3000 (Mavalankar *et al,* 2008). Deaths during chikungunya outbreaks were among <65 years patients and those with chronic medical problems; as most commonly diabetes and cardiovascular disease (Rollé *et al,* 2016).

Persistent or relapsed disease: Some patients have persistence or relapse of signs and symptoms in months after acute illness; manifestations included arthritis/arthralgia, edematous polyarthritis of fingers and toes, morning pain and stiffness, and severe tenosyno vitis; especially of wrists, hands, & ankles (Josseran *et al,* 2006). Carpal tunnel syndromes resulted from hypertrophic tenosynovitis. Besides, patients may report joint or bone pain at previous injury sites (CDC, 2017). Occasionally, sternoclavicular or temporomandibular joints are involved. New-onset Raynaud phenomena in the 2nd or 3th month after infection reported in up to 20% of cases (Jaffar-Bandjee and Gasque, 2012). Cryoglobulinemia was reported in patients with chronic chikungunya symptoms; 90% in one series (Oliver *et al,* 2009).

Chronic manifestations usually involved the joints affected during acute illness and can be relapsing or unremitting and incapacitating. Patients may develop a new chronic inflammatory polyarthritis or may have flares of preexisting joint conditions (whether inflammatory, non-inflammatory, or mechanical) during and post infection (Blettery *et al,* 2016). In a review of about 5700 patients with chikungunya virus infection, about 25 to 35% of them developed chronic joint symptoms (Rodríguez-Morales *et al,* 2016), about half of patients developed chronic inflammatory arthritis (rheumatoid arthritis, nonspecific post-viral polyarthritis, or seronegative spondylitis); other manifestations included arthralgia and other musculoskeletal pain conditions (e.g., fibromyalgia, frozen shoulder, and plantar fasciitis). Symptoms duration varied, among 47 patients with acute chikungunya fever followed in Marseilles, France, 82% had persistent joint symptoms. At one, three, and six months after acute illness, symptoms persisted in 88, 86, & 48% of patients, respectively; at 15 months, 4% remained symptomatic (Thiberville *et al,* 2013). Among 88 acute chikungunya patients in Réunion 18 months, 63% had persi-stent polyarthralgia (Borgherini *et al,* 2008).

Morning stiffness was in 75% of individuals, and almost half reported but without had impact on daily activities. In Réunion, 60% of 180 chikungunya viremic patients, at 36 months, still had arthralgias (Schilte *et al,* 2013). In South Africa, 12% of patients, had arthralgia three years post-acute illness (Brighton *et al*, 1983).

Neonatal infection: Clinical manifestations among neonates in Réunion outbreak were observed within three to seven days after delivery and included fever, poor feeding, rash, and peripheral edema; 89% had thrombocytopenia (Singh *et al,* 2023). Some developed neurologic disease; as meningoencephaalitis, cerebral edema, & intracranial hemorrhage, or myocardial disease. Neurocognit-

ive outcome was in children with perinatal transmission from infected mothers (Gérard-*et al,* 2014).

Laboratory abnormalities included elevated liver function tests, reduced platelet & lymphocytes, and increased prothrombin time. Chikungunya virus infection must be suspected in patients with acute onset of fever and polyarthralgia and epidemiologic exposure as residence in or travel to Aedes-borne chikungunya virus infected area (CDC, 2023).

Chikungunya diagnosis is by detecting viral RNA via real-time reverse-transcription polymerase chain reaction (RT-PCR) or virus serology (CDC, 2016b): 1- For individuals presented 1 to 7 days following symptoms onset, RT-PCR for detection of chikungunya virus RNA must be performed; a positive result establishes a chikungunya virus diagnosis. A negative one must prompt chikungunya virus serologic testing via ELISA or indirect fluorescent antibody (IFA), and 2- For individuals presented ≥8 days following onset of symptoms, chikungunya virus serology as ELISA or IFA must be done. A positive result establishes a diagnosis of chikungunya virus infection. Testing for dengue and Zika virus infections must also be pursued. A single PCR test to evaluate all the three infections is available via CDC and other qualified laboratories (CDC, 2016c).

Chikungunya virus RNA can be detected by RT-PCR during the first five days after symptoms onset with excellent sensitivity and specificity. IgM anti-chikungunya virus antibodies (by direct ELISA) are present start about 5 days (range 1 to 12 days) after symptoms onset and persist for several weeks to three months, IgG antibodies appeared about two weeks after symptoms onset and persist for years (Johnson *et al,* 2016).

Viral culture is generally a research tool with chikungunya virus sensitivity is high in early infection but, drops five days after illness onset(Simon *et al*, 2008). Virus isolation allows strain identification and is important for epidemiologic and research studies.

In endemic areas, chikungunya virus infection may be suspected based on characteristic clinical findings; in areas without laboratory facilities, infection may be undiagnosed. Patients presented with persistent or chronic joint symptoms and relevant epidemiologic exposure must have chikungunya virus confirmation with serologic testing if not yet performed. Also, to evaluate the inflammation level and to screen for other musculoskeletal conditions presence distinct from chikungunya-induced arthropathy must be based on history and clinical data (Imad *et al,* 2021).

Differential diagnosis: Prominent arthralgia, high fever, diffuse rash, without respiratory symptoms can distinguish chikungunya from other illnesses (Singal, 2017).

Mimics of acute infection: Mimics of acute chikungunya virus infection include other viral causing arthritis (tab. 1): 1- Both dengue and chikungunya share many clinical manifestations and of geographic distribution areas. Chikungunya virus infection is more likely to cause high fever, severe arthralgia, arthritis, rash, and lymphopenia, but dengue virus more likely causes neutropenia, thrombocytopenia, hemorrhage, shock, and death, and diagnosed by PCR or serology (El-Bahnasawy *et al,* 2011). 2- Zika and chikungunya viruses share many clinical manifestations and areas of geographic distribution. Symptoms and signs include fever, rash, headache, arthralgia, myalgia, and conjunctivitis. Chikungunya typically presents with higher fever and more intense joint pain than Zika virus infection with overlap in clinical presentations and diagnosed by PCR or serology (Minh *et al,* 2016). 3- Parvovirus infection can present with acute and symmetric arthritis or arthralgia, most frequently involving the small joints of the hands, wrists, knees, and feet. Rash may or may not be present. Canine parvovirus infection is still a worldwide and commonly occurring infectious disease leading to severe morbidity especially in puppies, and diagnosed by serology (Gerlach *et al,* 2020). 4- Rubella (German meas-

les): A mild viral infection that typically occurs in children and non-immune young adults. Clinical pictures include low-grade fever, coryza, conjunctivitis, and lymphadenopathy, as well as macular rash begins on face and spreads to trunk, and arthritis, and diagnosed serology (Leung *et al,* 2019). 5- Ross River virus: Its clinical manifestations of infection include fever, arthritis, and rash. Epidemiologic history can help to exclude Ross River virus infection as it is transmitted only in Australia. Ross River virus diagnosis is typically by serology (Aly *et al,* 2019). 6- Measles (rubella) infects the respiratory tract and then spreads via body. Symptoms include a high fever, cough, runny nose and Koplik spots may precede generalized rash, and diagnosed by serology (CDC, 2020). 7- Leptospirosis (spread by contaminated soil and water during a hurricane) is characterized by fever, rigors, myalgia, and headache. Less common manifestations include cough, nausea, vomiting, diarrhea, abdominal pain, and arthralgia. Conjunctival suffusion and jaundice are suggestive of leptospirosis, but some may be asymptomatic (CDC, 2023b). 8- Malaria is characterized by fever, malaise, nausea, vomiting, abdominal pain, diarrhea, myalgia, and anemia. Fever is often intermittent, but in chikungunya typically persistent and diagnosis by detecting the malaria parasites on peripheral smear (Morsy *et al,* 2023b). 9- African tick bite fever is observed among travelers to Africa and the Caribbean and is characterized by headache, fever, myalgia, solitary or multiple eschars with regional lymphadenopathy, and generalized rash, and diagnosed by serology (Saleh e*t al,* 2016). 10- Relapsing fever is characterized by fever, headache, neck stiffness, arthralgia, myalgia, and nausea; being diagnosed by direct smear and PCR (El-Bahnasawy *et al,* 2012). 11- Meningococcal infection may be associated with meningitis and hemorrhagic rash, and diagnosis is based on cerebrospinal fluid examination (Abdelrahman *et al,* 2016). 12- Enteric fever is a cumulative term of typhoid and paratyphoid fever. Clinical manifestations include fever, bradycardia, abdominal pain, and, infrequently, a rash (rose spots). Enteric fever is typically sub-acute, but chikungunya infection is typically abrupt in onset. Diagnosis is complicated as symptoms overlap with other fevers and early investigations are inconclusive (Kuehn *et al,* 2022). 13- Infectious mononucleosis: It is caused by Epstein-Barr virus, commonly affects youths and adults aged 15 to 24 years. It is transmitted primarily in saliva. Clinical manifestations include fever, malaise, and pharyngitis, also lymphadenopathy and splenomegaly may be present with atypical lymphocytosis. Fatigue may be profound, but tends to resolve within 3 months. Peri-orbital and/or palpebral edema, typically bilateral occur in one-third of patients. Splenic rupture is the high risky complication, and diagnosed by serology (Leung *et al,* 2023). 14- Acute human immunodeficiency virus infection: Clinical manifestations of acute HIV may range from asymptomatic to a severe illness such as fever, lymphadenopathy, sore throat, rash, myalgia/ arthralgia, and headache. Diagnosing acute HIV infection is important for patient care and public health concerns by via immunoassay and/or HIV virology test (Richey and Halperin, 2013). 15- A *Streptococcus* Group (GAS) is classified as gram-positive cocci causing many diseases. GAS can be divided into greater than 100 different subtypes based on their surface M-protein. GAS infections caused acute pharyngitis, impetigo, erysipelas, and cellulitis. Clinical presentations include fever, myalgia, cutaneous manifestations (cellulitis, fasciitis), pharyngitis, and shock, Diagnosed by blood or other tissues positive cultures (Newberger and Braithwaite, 2023). 16- Specific arthritis viruses: Many viruses can cause viral arthritis; the commonest are Parvovirus, alphavirus, rubella, HCV HBV, and flavivirus. Other viruses (EBV, HIV, cytomegalovirus, mumps, & herpes) rarely cause arthritis/arthralgia (Tiwari and Bergman, 2023).

The possibility of dual infection must be

suspected if the clinical course is atypical or fever persisted more than five to seven days (Gould *et al,* 2008). Chikungunya virus outbreaks occurred simultaneously with dengue, Zika outbreaks (Roth *et al,* 2014), and/or yellow fever (Ratsitorahina *et al,* 2008), and co-infection with chikungunya and other pathogens was reported (Nayar *et al,* 2007), chikungunya and yellow fever (Parola *et al,* 2007), chikungunya and ameba (Ezzedine *et al,* 2008) chikungunya and Zika virus (Wichit *et al,* 2021).

Mimics of persistent or relapsed disease include: 1- Seronegative rheumatoid arthritis: Chikungunya viral arthritis can closely resemble seronegative rheumatoid arthritis (Miner *et al,* 2015). Clinical manifestations of seronegative rheumatoid arthritis include inflammatory arthritis involved three or more joints for >6 weeks, with negative rheumatoid factor and anti-cyclic citrullinated peptide (CCP) antibody tests (Choi and Lee, 2018). 2- Reactive arthritis (or Reiter syndrome) refers to arthritis associated with a coexisting or recent antecedent extraarticular infection. Clinical manifestations include at least one of the following: asymmetric oligoarthritis (often affecting the lower extremities), enthesitis (inflammation at the insertion site of ligaments and tendons to bone), dactylitis (inflammation of an entire digit), and inflammatory back pain. Diagnosis is clinically based on the presence of characteristic features with a preceding or ongoing enteric or genitourinary infection, with exclusion of other causes of arthritis (Pennisi *et al,* 2019). 3-Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease that may involve many different organs displaying a variable clinical course. Paients may be characterized by fever, rash, and inflammatory polyarthritis or arthralgias, similar persistent chikungunya infected patients. SLE can be distinguished by absence of serologic evidence for viral disease, presence of antinuclear antibodies and often other systemic pictures or organ system involvemnt SLE characters (Kuhn *et al,* 2015). 4- Chronic infection with HCV or extra-hepatic manifestations are a feature of chronic HCV (include mixed cryoglobulinemia, non-Hodgkin lymphomas, cardiovascular disease, insulin resistance, type 2 diabetes, neurological and psychiatric disease and other rheumatic diseases influencing morbidity, quality of life & mortality of HCV-infected patients). It can be associated with arthralgia or arthritis and various dermatologic manifestations. Dependable serology for chikungunya and HCV, without a history of other virus was diagnostic (Mazzaro *et al,* 2021).

Treatment of acute chikungunya: There is no specific antiviral therapy for acute virus infection. During acute phase treatment consists of supportive care, such as rest, fluids, and acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) to relieve acute pain and fever (Javelle *et al,* 2015). Aspirin and other NSAIDs must not be given to dengue patient until he became afebrile ≥48 hrs without warning signs for risky dengue (abdominal pain, persistent vomiting, mucosal bleeding, pleural effusion or ascites, lethargy, enlarged liver, and increased hematocrit with decrease in platelet count); but important to give the bleeding risk complications associated with dengue infection and to avoid Reye syndrome, the potentially fatal pediatric illness (Trivedi and Chakravarty, 2022). Systemic glucocorticoids and other immunosuppressive medications must generally be avoided in patients during acute infection (Chanana *et al,* 2007).

Persistent or relapsed disease: Management of persistent or relapsed manifestations, particularly joint disease, depends upon the duration of symptoms and results (da Cunha and Trinta, 2017). Symptomatic control with anti-inflammatory drugs and analgesics was appropriate in the several months immediately after the disease acute phase; more longstanding disease, beyond three months after infection onset, may use disease-modified antirheumatic drug (DMARD) therapy; such as methotrexate (MTX).

Post-acute infection: In patients with joint

symptoms persist into post-acute phase (between a month and up to the 3rd month end after infection onset) treatment includes continued analgesia and NSAIDs (Martí-Carvajal *et al,* 2017). Also, analgesic benefit may be provided by neuropathic pain medications (e.g., pregabalin or gabapentin). Physical therapy may also be benefiting (Neumann *et al,* 2021). In NSAIDs resistant patients exhibted inflammatory arthritis, tendinitis, or bursitis, a short course of systemic glucocorticoids (prednisone 10mg daily for 5 days, tapered off over next 10 days) was used; more severely affected patients that required higher doses (0.5mg/kg daily), but patients required up to one to two months of glucocorticoid therapy (Arroyo-Ávila and Vilá, 2015)

Chronic disease: Patients with clinical manifestations persisting three months after infection onset must be referred to a rheumatologist for more diagnosis assistance and to decide if DMARD treatment was indicated (Salem *et al,* 2022). Sulfasalazine was used as in patients with peripheral spondylo-arthritis (Fagerli *et al,* 2014). Treatment was based upon the available case series and expert opinion, without randomized trials comparing DMARDs for this condition (Ganu and Ganu, 2011). Patients with preexisting rheumatic disease on non-biologic and biologic DMARDs, including TNF inhibitors occurred in a small cases to be effectively managed with NSAIDs and rest and to experience a normal infection course without an exacerbation of rheumatic disease were well treated (Brunier *et al,* 2016). Patients with a sustained complete response for several months, suggested that DMARD may be discontinued as symptoms may resolve in some patients (Simon *et al,* 2015).

Vaccination: A virus-like particle vaccine for epidemic Chikungunya virus protected non-human primates against infection (Akah ata *et al,* 2010), But, no licensed vaccine for human chikungunya (Chang *et al,* 2014).

Prevention: This consists of avoiding man mosquito bites (Ramsauer *et al,* 2015). *Aedes* bite primarily during daytime but, also at night; they breed in stagnant water; particularly containers (Jansen and Beebe, 2010).

For control *Aedes* eggs withstand desiccation with about 2-15% egg viability after a year and viability remained < 88% under all conditions by 56 days (Faull and Williams, 2015).

Avoiding bites causes human protection and environmental control measures (Roy *et al,* 2014). Patients may reduce spread to others by avoiding bites during the viremia period, first week of illness (Staples and Fischer, 2014)

Chikungunya virus transmission by breast feeding was not reported, and women may be encouraged to breastfeed in areas with circulating chikungunya virus (CDC, 2016c).

What about Egypt? Details of *Aedes* vector and dengue fever were given (Morsy *et al,* 2023b). Humphrey *et al.* (2017) in Middle East and North Africa reported that seroprevalence studies and outbreaks suggested that urban cycle CHIKV endemic transmission in at least the Red Sea region and Pakistan. They added that a low CHIKV quantity, but sero-epidemiological studies may be unrecognized. Failloux *et al.* (2017) reported that the geographical distribution of mosquito-borne diseases; such as Rift Valley fever, West Nile, Dengue, Chikungunya, and Zika expanded over the last decades. They added that the Mediterranean & Black Sea Regions countries were not spared. Fang *et al.* (2022) suggested that in Egypt there are at least 5 common mosquito-borne viruses (MBVs), including dengue virus, Rift Valley fever virus, West Nile virus, Chikungunya virus, & Sindbis virus. They added that it was indicated to evaluate endemic transmission risk, and to establish an early control for MBVs.

In Saudi Arabia, Hussain *et al.* (2013) reported that chikungunya virus was in Jeddah in 2011 in a positive qRT-PCR 55-year-old woman suffered from very severe arthralgia. Alikhan *et al.* (2014) reported that *Aedes* species populations in the western region of Saudi Arabia, especially in and around Jeddah, were increasing. Al-Tawfiq and Memi-

sh (2018) reported that dengue virus is one viral hemorrhagic fever that exists in Saudi Arabia as well as Alkhurma (Alkhurma) Hemorrhagic Fever, Chikungunya virus, Crimean-Congo hemorrhagic fever, and Rift Valley fever, and dengue was limited to western and south-western regions, where *Ae. aegypti* exists. Hakami *et al.* (2021) reported that 1/40 chikungunya cases showed anti-chikungunya IgG antibodies, but PCR was negative in all.

In Yemen: Zayed *et al.* (2012) found chikungunya virus in *Ae. aegypti* collected during Al Hodayda outbreak, January 2011. Malik *et al.* (2014) in Al-Hudaydah Governorate between 23 & 26 January 2011, WHO team, Yemen MoPH & P and NAMRU-3, detected a chikungunya outbreak.

In Sudan: Lewis (1955) reported that *Aedes* was high adapted and efficiency vector of flaviviruses. Gould *et al.* (2008) in South Kordofan from September to December 2005, reported yellow fever outbreak and IgM chikungunya antibodies in asymptomatic ones, and that chikungunya and yellow fever existed together. Seidahmed *et al.* (2012) along a Red Sea Coastline reported that spatial and temporal patterns of dengue transmission occurred and that in Port Sudan City there was a history of major outbreaks of yellow & dengue fevera with huge mortalities and economic loss. Adam *et al.* (2016) reported chikungunya outbreaks virus with abundance of *Ae. aegypti*. Mohamed *et al.* (2019) in Kassala found that the overall seroprevelance was 73/119 (61.3%), highest positivity was 52/73 (73.1%) chikungunya virus; 29 males and 20 females. Others were Sindbis 20.5% (15/73), and Rift Valley fever 6.8% (5/73). Ali *et al.* (2022) in Kassala reported chikungunya infections in pregnant women associated with miscarriage, preterm birth, thrombocytopenia and leukopenia that led to at high risk of poor obstetric outcomes. Ahmed *et al.* (2022) in four States found 166 larvae, 30% were *Anopheles gambiae* & *An. stephensi* & 117 *Ae. luteocephalus* (39%), *Ae. aegypti* (32%), *Ae. vexans* (9%), *Ae. vittatus* (9%), *Ae. Africanus* (6%), *Ae. metallicus* (3%), and the risky *Ae. albopictus* (3%). Africa CDC (2023) with Republic of South Sudan, Ministry of Health managed a suspected viral hemorrhagic fever outbreak in remote areas of Dukubela, Pacime, & Dajo areas of Longechuck-County, Upper Nile State.

In Libya Amer and Mehlhorn (2006) only detected both *Ae. aegypti* and *An. stephensi.*

Conclusion

Chikungunya begins clinically with high fever. Polyarthralgia begins two to five days after fever involving multiple joints (ten or more joint groups). Arthralgia is usually bilateral and symmetric involving distal joints more than proximal ones. Skin manifestation is macular or maculopapular rash (three days or later after illness onset and lasted three to seven days). Others may include headache, myalgia, and gastrointestinal symptoms. Severe complications were meningoencephalitis, cardiopulmonary decompensation, acute renal failure, and even death very commonly among patients <65 years with chronic medical problems. Some patients have persistence or relapse of signs and symptoms in months after acute illness, such as polyarthralgia, morning stiffness, tenosynovitis, and Raynaud phenomena.

Risk of maternal-fetal virus transmission is highest when pregnant women are symptomatic during intrapartum period (two days before and after delivery). Clinical manifestations occur three to seven days after delivery include fever, rash, peripheral edema, neurologic disease and myocardial disease.

Laboratory abnormalities include elevated liver function tests, reduced platelet, but increased counts of lymphocyte, and of prothrombin time.

Recommendations

Control of *Aedes* adult and immature stages is a must to stop all *Aedes*-borne viruses.

Chikungunya infection must be suspected in patients with acute onset of fever, polyarthralgia with relevant exposure to an endemic chikungunya area, Diagnosis by viral RNA

by RT/PCR or serology. Dengue and Zika virus must also be tested.

Supportive treatment is care and includes rest, fluids, and anti-inflammatory and analgesic agents. In dengue patient, aspirin and other non-steroidal anti-inflammatory drugs must not be used until he is afebrile ≥48 hours without warning signs for severe deng ue. Some chronic arthritis patients may warrant treatment with systemic glucocorticoids or disease-modified antirheumatic drugs, such as methotrexate or other agents.

Tell now no vaccine for chikungunya virus infection; prevention is avoiding *Aedes* exposure. Infected patients must avoid mosquito bites during the first week of illness or viremia window.

Authors' declaration: The authors reported that they neither have conflict of interest nor received any fund. All authors equally shared in this review article,

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Table 1: Clinical features: Zika virus compared with dengue and chikungunya viruses

Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	–	–
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	–	++	–
Shock	–	+	–

Explanation of figures

Fig. 1: CDC Areas at Risk for Chikungunya (Chikungunya virus)
Fig. 2: Chikungunya virus sylvatic/rural cycles and urban one