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Challenges in diagnosis and control of Chikungunya virus infection: A review

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ABSTRACT

Chikungunya virus (CHIKV) infection in humans causing severe musculoskeletal pain, fever and rashes, is transmitted by the bite of infected mosquitoes, primarily *Aedes* (*Ae.*) *aegypti* and *Ae. albopictus*. CHIKV has resulted in 18.7 million cases worldwide till 2020 and after 2004 has spread to Europe, Middle East (Saudi Arabia, Pakistan, Yemen, Egypt, Oman, Iraq, Kuwait, and Iran) and Pacific regions. This rapid spread of CHIKV emphasizes the pivotal need of enforcing control measures and examining new diagnostic methods. As the mosquito vectors (*Aedes*) of CHIKV are evolving, vector control methods are losing its efficacy. Further, existing serological and molecular assays to detect CHIKV show variabilities in sensitivity and specificity, leading to mis-reporting or under-reporting of CHIKV cases in affected regions. In this review article, we start by discussing CHIKV infection, followed by an introduction to currently available control and detection methods. We further highlight the challenges these methods pose and how they can be conquered by employing various easy and sustainable strategies. This review may provide valuable information for the development of novel diagnostic strategies in resource limited settings for mitigating CHIKV disease.

KEYWORDS: Chikungunya virus; Vaccine development; Vector; Neglected tropical disease; Arbovirus; Outbreak; Emerging disease

1. Introduction

Chikungunya is an emerging vector borne infection caused by the Chikungunya virus (CHIKV). It is primarily transmitted by the *Aedes* mosquitoes, mainly by *Aedes (Ae.) aegypti* and *Ae. albopictus*. CHIKV is a positive strand, single stranded RNA virus under the genus *Alphavirus* and family Togaviridae. It was first isolated during an outbreak in 1952 on the Makonde highland (Tanzania) and named after the word: "kungunyala", meaning: "bends up", referring to the posture taken by the patients due to severe joint pain due to CHIKV infection[1]. Later, Chikungunya re-emerged in Kenya in 2004 resulting in half a million cases, followed by Reunion Island in 2005 and India in 2006 with 26600 cases and 1.4 million cases respectively. Since then, Chikungunya virus has been detected in many outbreaks in 114 countries primarily in Asia, Africa, Americas, Europe and Oceania[2]. Recently, on 9th July 2025, a cluster of Chikungunya fever cases were reported from Foshan City of Guangdong Province[3]. As of August 2025, over 10000 confirmed cases were reported making it the largest Chikungunya outbreak in China. Due to global warming and increased human mobility between endemic and non-endemic regions, global spread of viral vectors of CHIKV has increased, thus making it a major public health concern (Figure 1).

As per one of the recent studies on estimating the global burden of Chikungunya from 2011 to 2020, it was reported that CHIKV was responsible for 18.7 million cases in 110 countries with a disability adjusted life years (DALYs) of 19.5 million. During these 10 years, the total economic burden was assessed at 2.8 billion USD and 47.1 billion USD in direct and indirect cost respectively[4]. As Chikungunya affects improvised and marginalised populations residing in the tropical and subtropical regions, World Health Organization (WHO) has placed it under the list of neglected

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tropical diseases (NTDs). Further in its 2022 report, WHO has acknowledged Chikungunya as a major global health challenge and is willing to provide support to regions where outbreaks are reported. This support involves improved surveillance, technical know-how for managing outbreak, vector control guidance and development of new vaccines or antivirals[5]. In spite of its high morbidity and high attack rate compare to other mosquito borne viruses like dengue, Zika or yellow fever, Chikungunya is still being ignored both by epidemiologist and policy makers.

Acute stage of Chikungunya infection is described with symptoms like fever, arthralgia, headache myalgia, nausea and rash. Although a self-limiting disease, it can progress to debilitating chronic outcome like joint pain and other lengthy complicacies which impacts the quality of life of the infected individual. In few patients, Chikungunya infection can show atypical incarnation affecting multiple organ systems like cardiovascular and neurological systems resulting in bad prognosis or even death. Chikungunya can also lead to congenital infection *via* intrapartum fetal infection leading to severe and sometimes fatal disease in the neonates[6]. Acute CHIKV infection can be treated with rest, oral hydration and pain management using analgesics and non-steroidal anti-inflammatory drugs, while the chronic infection can be treated by non-steroidal anti-inflammatory drugs or disease modifying antirheumatic drugs[7]. Various other antivirals and monoclonal antibody-based therapies are under stages of pre-clinical trials, but none have been licensed for human use.

CHIKV has one serotype having four lineages, they are antigenically stable and thus vaccination can be an effective method to mitigate CHIKV disease[8]. Several vaccines options like inactivated vaccines, live-attenuated vaccines, alphavirus chimeras, recombinant vaccines, DNA vaccines, subunit vaccines and more recently virus-like particle (VLP) have been employed to develop an effective vaccine against CHIKV[9-13]. In November 2023, first CHIKV vaccine (Ixchiq-VLA1553) was announced by Valneva SE, which was latter approved by United States Food and Drug Administration (USFDA)[14]. Currently, Ixchiq remains the only approved vaccine for use in the US, while many vaccine candidates are undergoing various stages of clinical trials as shown in Table 1. As this vaccine was approved recently, there is an unmet requirement of CHIKV vaccines in endemic areas where the preventive measures are primarily focused on vector control.

Early laboratory diagnosis of CHIKV remains the foremost need to lower the morbidity associated with CHIKV infection. Currently viral antigen detection is carried out by ELISA, IFA, rapid diagnostic test (RDT), and immune-blot methods. Neutralising antibodies can be detected by plate reduction neutralization tests (PRNT) which remains the gold standard for detection of CHIKV[15]. Molecular methods are used to find the presence of viral RNA by assays like RT-PCR and isothermal amplifications[16]. Due to its similarity in clinical manifestations with other mosquito-borne diseases, which are also prevalent in the similar geographic regions, diagnosis of CHIK remains challenging. Thus, a diagnosis based alone on clinical presentation is difficult and differential diagnosis for a patient with a travel history or living in an CHIKV endemic region is warranted. Even after its discovery for more than five decades ago, CHIKV continues to spread globally generating novel challenges to its disease prevention, surveillance, diagnosis and patient management. In this review, we would like to provide a comprehensive overview of challenges associated with the diagnosis and control of CHIKV and the recent measures available to control this re-emerging human pathogen.

2. Clinical and diagnostic challenges

Accurate diagnostic techniques, which are specific and sensitive, are needed to detect sporadic cases of Chikungunya as well as to detect emerging Chikungunya outbreaks for initiating timely public health response. Chikungunya infection is often presented with high fever and debilitating arthralgia and it is important to clinically and differentially diagnose the disease from other arboviral infections like dengue and Zika using laboratory based assays.

Depending on the kinetics of viral markers of the infection like anti-Chikungunya IgM/IgG antibodies, viral genome and virus-specific antigens, various laboratory diagnosis techniques are available. The detection of Chikungunya-specific antigens is usually done by using various enzyme linked immunosorbent assay (ELISA), immunoblotting techniques, immunofluorescence assays (IFA), and rapid diagnostic tests (RDTs). Molecular detection techniques based on the principle of isothermal amplification like Loop mediated isothermal amplification (LAMP), conventional or standard RT-PCR, qualitative & quantitative real time RT-PCR assays are used to detect the CHIKV genome (Table 1). Plate reduction neutralization tests (PRNT) is considered the gold standard test for serology-based assays. It relies on detecting neutralizing antibodies but is rarely applied routine diagnosis of Chikungunya infection as it relies on trained laboratory personnel and requires the use of recommended biological safety level (BSL) precautions[17-19]. Laboratory detection of Chikungunya is mired with its own challenges, which will be discussed in the forthcoming sections.

2.1. Symptom overlap with other arboviral diseases

The classic triad of symptoms observed in Chikungunya cases includes rapid-onset of fever, severe arthralgia which is debilitating in nature and a rash, commonly maculopapular rash[20]. Headache and gastrointestinal disorders like nausea, vomiting, abdominal discomfort and anorexia are also commonly reported. Clinical

Table 1. List of diagnostic assays for Chikungunya virus.

Test	It detects	Specimen type	Best window from symptom onset	Advantages	Limitations
Virus isolation (cell culture)	Live virus	Serum/Plasma/ CSF/Mosquito sample	Early acute phase	Definitive and enables sequencing/strain typing	Slow; requires high-containment/ specialized facilities; not routinely used for patient care
Plaque Reduction Neutralization Test (PRNT)	Neutralizing antibodies	Serum	Convalescent phase; used after serology screen	Highly specific; reference confirmatory test for positive/equivocal IgM	Labor-intensive; slow; limited to specialized labs; not for routine screening
Antigen detection (ELISA or rapid lateral-flow for E1 antigen)	Viral antigen	Serum/Plasma	Acute phase (first week)	Can be quick and simple; meta-analyses show good specificity; useful where NAAT unavailable	Sensitivity varies by kit/genotype and timing; some assays show modest sensitivity; confirmatory testing often needed
IgM antibody (MAC-ELISA; automated ELISAs exist)	Anti-CHIKV IgM	Serum/Plasma	From day 4-5 onward; can persist for months	Broad availability; detects recent infections after NAAT window	False positives (cross reactivity with other alphaviruses); early samples may be negative; positive IgM should be confirmed by PRNT (as per CDC guidelines)
IgG antibody (ELISA)	Anti-CHIKV IgG	Serum/Plasma	Appears from 7-10 days post infection; persists for a long period	Confirms past exposure; paired sera (acute/ convalescent) showing ≥4-fold rise supports recent infection	Alone cannot distinguish past *vs.* recent infection without paired sera; potential cross-reactivity
RT-PCR/real-time RT-PCR (NAAT)	Viral RNA in serum/plasma (also whole blood/CSF)	Serum/Plasma/ Whole blood/ Urine/ Saliva	Highest yield in the first week (≈ days 0-6/7)	Gold-standard for acute infection; high sensitivity/ specificity; fast TAT; multiplex assays can co-test DENV/ZIKV	Falls off after viremia wanes; needs molecular lab; false negatives if sampled late or below limit of detection.
RT-LAMP (isothermal NAAT)	Viral RNA	Serum/Plasma/ Whole blood/ Urine/ Saliva	Acute phase (similar to RT-PCR)	Rapid, low-cost, minimal equipment; promising field use	Availability varies; performance depends on assay design/sample inhibitors; fewer validated clinical kits than RT-PCR
Multiplex arbovirus RT-PCR panels (*e.g.*, CHIKV/ DENV/ ZIKV)	Viral RNA (multiple targets)	Serum/Plasma/ Whole blood/ Saliva	First week of illness	Efficient triage where co-circulation occurs; performance comparable to single-plex kits in studies	Same timing limits as RT-PCR; kit availability/regulatory status varies by region

diagnosis is not enough to differentiate CHIKV infections from other etiologies *i.e.* flaviviruses like dengue virus and Zika virus (DENV and ZIKV), alphaviruses, non-viral pathogens like *Plasmodium* species, *Rickettsia*, *Leptospira* and *Salmonella*[21]. Due to similar transmitting agent *i.e. Aedes* mosquitoes and occurrence in similar geographical regions favourable for the transmission of the disease, CHIKV co-transmission with DENV and ZIKV is often reported. Thus, it is highly crucial to accurately diagnose CHIKV infection.

Misdiagnosis often masks the spread of Chikungunya infection resulting in large scale outbreaks. The symptoms of CHIKV infection are similar with the acute phase of dengue mono-infection and are often indistinguishable which often delays treatment resulting in neurological manifestations like encephalitis, Guillain-Barré syndrome, neuropathy, retinitis[22] and cardiovascular diseases like heart failure, arrhythmias and pericarditis[23]. Failure or delays in diagnosis based on clinical symptoms or unavailability of reliable diagnostic assays can increase morbidity and mortality in the affected individuals[24]. Establishing a rapid and accurate diagnosis is of paramount importance for treatment and control of spread of infection.

2.2. Laboratory diagnostic limitations

CHIKV can be isolated from clinical samples during the early stages of the infection. Various cell lines of mosquitoes as well as mammals, mosquitoes and cerebra of suckling mice can be inoculating for isolation and culture of CHIKV[25]. However, virus isolation is not used anymore for routine diagnosis as these are expensive, time consuming, technically demanding and not very sensitive compared to modern diagnostic assays[26]. RT-PCR and real time RT-PCR based assays are now more commonly used to detect CHIKV genome in clinical samples, which offer better sensitivity and specificity and are rapid. Molecular detection also includes use of LAMP which is cheap and uses isothermal amplification techniques. But these molecular assays are often restricted to detection of CHIKV only in the acute phase of Chikungunya *i.e.*

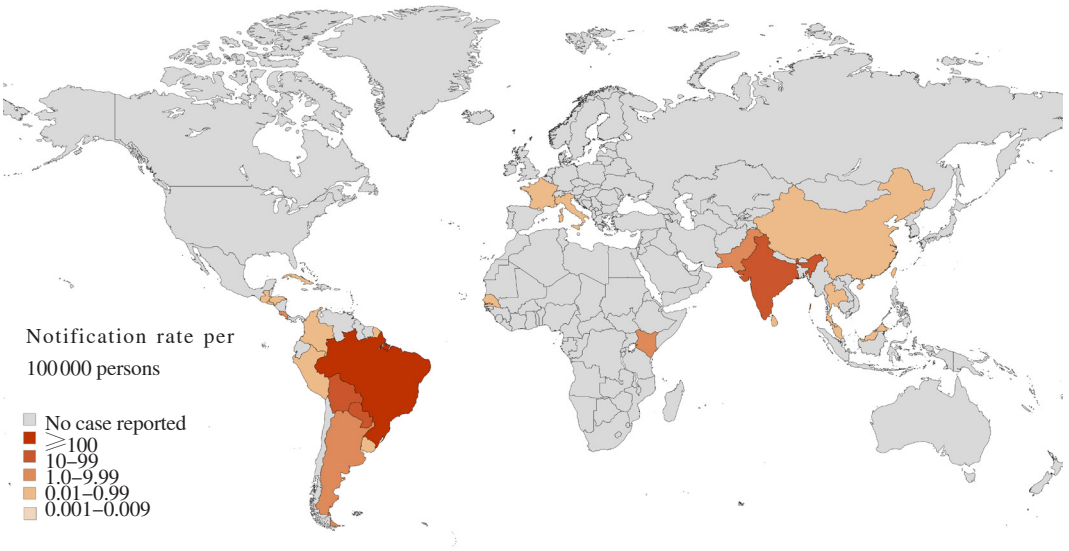

Figure 1. Regions with evidence of Chikungunya virus transmission to humans reported during the last 12 months (September 2024 to the end of August 2025). [Source: Centers for Disease Control and Prevention (CDC, USA) and ECDC, Data collected in August 2025].

within the first few days of onset of symptoms. These methods are comparatively expensive and need expertise. The sensitivity of CHIKV RNA detection in serum sample collected from suspected patient declines between 4 and 7 days of onset and anti-CHIKV IgM becomes detectable. Antibodies against CHIKV can be detected by serological assays like ELISA for IgM and IgG antibodies. But these assays often cross-react with other alphaviruses that include Mayaro virus (MAYV) and O`nyong-nyong virus (ONNV) yielding false positive/negative results (Figure 2)[27]. A significant proportion of dengue-confirmed patients often test positive for Chikungunya IgM antibodies, indicating considerable cross-reactivity or dual infection in the particular region. This further emphasizes the need for accurate differential diagnosis that can be done by using various molecular techniques. Accurate diagnosis of mono- or dual- infection is significant to prevent complications by starting supportive treatment well in time[28]. Lack of rapid and accurate point-of-care diagnostics for CHIKV often delays diagnosis and masks the spread of CHIKV in the community. Delayed diagnosis affects surveillance programs and public health control efforts for Chikungunya.

2.3. Resource-limited settings

Modern diagnostic assays often need experience laboratory personnel for performing and analyzing the results. These assays need high end equipments which are not available in low-middle-income countries and resource-constraint regions. The RNA of CHIKV is highly unstable, it needs proper maintenance of cold chain conditions during transportation. Degradation of viral RNA during transport might also lead to incorrect diagnosis further delaying the initiation of control strategies.

2.4. Chronic manifestations

CHIKV is often confused with other non-viral infections and chronic diseases presenting with persistent joint pain and arthritis-like syndromes. Lack of standardized diagnostic markers in such cases might lead to long-term complications especially in children, senior adults and patients with co-morbidities. Patients of age above 65 years *i.e.* in older adults, the clinical presentation in CHIKV infection is complicated, with higher rates of neurological complaints[29].

2.5. Handling diagnostic challenges

Re-emergence and expansion of CHIKV at an alarming rate comes with the added burden of being established endemically in newer regions where vectors and favorable environmental conditions are available. The global spread of CHIKV in past few years emphasizes the emergency to investigate and employ precautionary as well as control measures to curtail further spread of the disease. This is particularly important in resource-constrained nations due to limited availability of diagnostic tools and other challenges discussed earlier. The prevention and control efforts against CHIKV infection need updating the current available diagnostic methods to enable the reliable detection of early and low CHIKV antigen levels. Further these assays should enable accurate differential diagnosis between CHIKV infections and dengue, Zika, other medically relevant alphaviruses[30]. Development of multiplex assays with multiple pathogen targets using real time PCR will offer simultaneous detection of arboviruses with higher sensitivity and specificity[31]. Expansion of point-of-care molecular tests using isothermal amplification techniques will enable rapid and less-

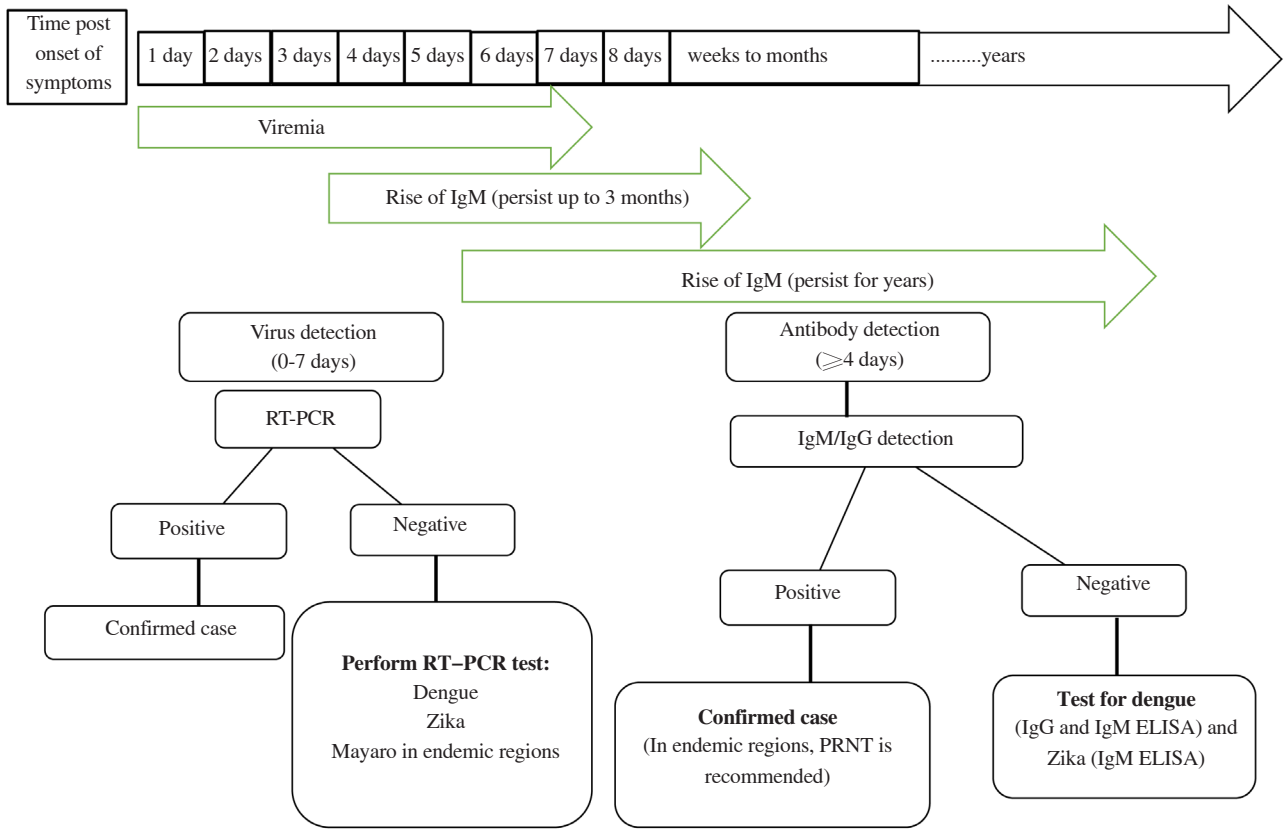

Figure 2. CHIKV infection timeline showing viral and antibody kinetics and protocol for laboratory diagnosis. This image has been modified with permission from article from Soto Graita *et al*, 2018 (https://doi.org/10.1007/s40506-018-0172-x). This reference has been cited in the text as reference [27].

Table 2. Control strategies for Chikungunya virus.

Control strategies		Approved age/Status	Dosage/Remarks	Major limitations
USFDA approved vaccines for Chikungunya	IXCHIQ (Live-attenuated)	U.S.: Adults⩾18 years EU: People⩾12 years Brazil: Adults⩾ 18 years	Single dose	Following adverse cardiac/neuro side-effects, it was suspended in U.S. (Aug 2025), Previously paused in older adults (60+ years), Ban has now been lifted in EU with use only under high-risk situations, UK had temporary restriction for 65+, which is under review. It is contraindicated in immunocompromised individuals; caution advised in pregnant/breastfeeding individuals and those ≥60–65 years old.
	VIMKUNYA (Virus-like particle, recombinant)	U.S.: People⩾12 years	Single dose	Newly licensed (Feb 2025); long-term safety and real-world effectiveness still under observation
Antivirals and other therapies for Chikungunya	Supportive care only	Standard of care	Effective symptom relief	Doesn't alter disease course or viral replication
	Favipiravir (T-705)/ T-1105	Experimental	Reduced severity/ mortality in mice experiments	No human trials; safety/efficacy in humans unknown
	Ribavirin	Experimental	Inhibits CHIKV *in vitro*	Clinical efficacy not demonstrated; Has toxicity concerns
	Harringtonine	Experimental	Very potent inhibitor of CHIKV *in vitro*	No *in vivo* or human data; toxicity profile unclear

expensive detection of CHIKV. Improved surveillance systems for early detection of CHIKV and real time data integration will allow control of CHIKV transmission. Training of healthcare workers and capacity building in differential diagnosing the CHIKV infection and its detection will aid in strengthening surveillance programs and public health control efforts. Designing of diagnostic assays should be done with focus on developing rapid, cheap and affordable, user-friendly tests to accurately track the progression of the CHIKV infection regionally as well as globally enabling policymakers to take appropriate action.

3. Challenges in controlling the infection

Although licensed vaccines are available, access remains limited in many settings and indications for specific population groups are not uniformly defined; clinical management continues to rely primarily on supportive care. Current controlling methods for CHIKV are mainly focussed on vector control and personal protective measures to prevent the bite of *Aedes* mosquitoes. Still these methods have its own limitations and challenges like changing vector behaviour, lack of community engagement in vector control, insecticide resistance and lack of appropriate animal models for developing drugs or vaccines etc are discussed in the forthcoming sections.

3.1. Lack of specific therapeutics and vaccine

Chikungunya is managed by mainly treating the symptoms as there are no approved evidence-based therapies and antivirals for routine and standard clinical use[32] (Table 2). Supportive care mainly helps in managing the symptoms which usually includes drinking enough fluids to stay hydrated, controlling body pain and fever, and using analgesics and physiotherapy to ease persistent joint problems that can last for several weeks or even months after the infection[33,34]. Since there are no approved antiviral drugs that has shown any steady success in patients, research has concentrated on several repurposed agents and antiviral candidates. But so far most of these are at early clinical or preclinical stages and none has become a licensed and approved treatment yet[35].

In recent years, progress in the vaccine development for Chikungunya infection has been quite fast. A live-attenuated vaccine, VLA1553 (IXCHIQ), has successfully completed the advanced development and has become the first Chikungunya vaccine to regulatory approval, reflecting a significant step forward in the efforts to prevent the diseases[36,37]. Apart from live-attenuated vaccines, multiple approaches are actively being evaluated which includes mRNA formulations, virus-like particle constructs, inactivated-virus vaccines, and viral-vectored candidates (*e.g.*, ChAdOx1) and many of these have already shown promising immune responses in human trials (Table 3)[38-40]. Even though trial results look promising they still have few concerns like how well they will work in immuno-compromised individuals and elderly people, how long the protection lasts, whether enough can be produced and distributed in the endemic regions, and how effective they are in real world settings[41,42]. So right now, clinicians mainly rely on supportive care to help patients manage Chikungunya symptoms, while researchers are working to develop an effective and safe antiviral drug that can be widely used to lower the societal and clinical burden of the infection.

3.2. Vector biology and adaptability

Aedes mosquitoes are well adapted to cities and towns because they can easily find small collections of water, such as gutters, water-storage vessels, flower pots, and discarded containers and use

Table 3. Clinical trials of vaccines against Chikungunya virus.

NCT number	Developer/Sponsor	Vaccine	Formulation	Clinical trial Phase/Status	Route of administration	Results
NCT02861586	Themis Bioscience GmbH	MV-CHIK-202	Recombinant MV vectored	2/Completed	Intramuscular	Safe in humans, no side effects, 100% seroconversion, acceptable tolerability
NCT04786444	Valneva Austria GmbH	VLA1553	Live attenuated vaccine	3/Completed	Intramuscular	Data not publicly available as of 10 September 2025
NCT06669208	Najit Technologies, Inc.	HydroVax-005	Inactivated virus vaccine	1/Recruiting	Intramuscular	Data not publicly available as of 10 September 2025
NCT03807843	Themis Bioscience GmbH	V184-006	Live recombinant MV	2/Completed	Intramuscular	Data not publicly available as of 10 September 2025
NCT03992872	Bavarian Nordic	PXVX0317	CHIKV-VLP	2/Completed	Intramuscular	Well tolerated and immunogenic, No adverse effects
NCT06007183	Bavarian Nordic	PXVX0317	CHIKV-VLP	3/Active	Intramuscular	Data not publicly available as of 10 September 2025
NCT04546724	Valneva Austria GmbH	VLA1553	Live attenuated vaccine	3/Completed	Intramuscular	Safe and strong immune response, induced virus neutralizing antibodies by 28 days PV
NCT03101111	Themis Bioscience GmbH	MV-CHIK	Live recombinant MV vector vaccine	2/Completed	Intramuscular	Data not publicly available as of 10 September 2025
NCT03635086	Themis Bioscience GmbH	MV-CHIK	Live attenuated recombinant MV vaccine	2/Complete	Intramuscular	Good immunogenicity, Safe and acceptable tolerability
NCT06928753	Centre Hospitalier Universitaire de la Réunion	IXCHIQ	Live attenuated CHIKV vaccine	4/Recruiting	Intramuscular	Data not publicly available as of 10 September 2025

Table 3 continues in the next page.

Table 3 continued.

NCT number	Developer/Sponsor	Vaccine	Formulation	Clinical trial Phase/Status	Route of administration	Results
NCT03483961	Bavarian Nordic	PXVX0317	CHIKV-VLP	2/Completed	Intramuscular	Safe, no side effects, durable serum neutralizing antibodies till 2 years
NCT02562482	National Institute of Allergy and Infectious Diseases (NIAID)	VRC-CHKVLP059-00-VP	CHIKV-VLP	2/Complete	Intramuscular	Safe, immunogenic and well tolerated, no serious adverse effects; neutralizing antibodies in all dose groups
NCT04566484	International Vaccine Institute	BBV87	Whole virus inactivated vaccine	2/3 Terminated	Intradermal	Data not publicly available as of 13 September 2025
NCT01489358	National Institute of Allergy and Infectious Diseases (NIAID)	VRC-CHKVLP059-00-VP	CHIKV-VLP	1/Completed	Intramuscular	Safe, immunogenic and well tolerated, no serious adverse effects; neutralizing antibodies in all dose groups
NCT04603131	Bharat Biotech International Limited	BBV87	Inactivated CHIKV vaccine	1/Completed	Intramuscular	Data not publicly available as of 13 September 2025
NCT07003984	Bavarian Nordic	Vimkunya	CHIKV-VLP	3/Recruiting	Intramuscular	Data not publicly available as of 13 September 2025
NCT07133178	Valneva Austria GmbH	VLA1553	Lyophilized live-attenuated CHIKV vaccine	3/Active	Intramuscular	Data not publicly available as of 13 September 2025
NCT04838444	Valneva Austria GmbH	VLA1553	lyophilized live-attenuated CHIKV vaccine	3/Active	micro plaque reduction neutralization test	Safe and immunogenic; neutralizing antibodies persisted up to 2 years. No adverse effects
NCT06106581	Valneva Austria GmbH	VLA1553	Live-attenuated CHIKV Vaccine	2/Completed	Intramuscular	Data not publicly available as of 13 September 2025
NCT03028441	National Institute of Allergy and Infectious Diseases (NIAID)	VRC-CHKVLP059-00-VP	MV-CHIK	1/Completed	Intramuscularly	Data not publicly available as of 13 September 2025
NCT05072080	Bavarian Nordic	PXVX0317 (Vimkunya)	CHIKV-VLP	1/Completed	Intramuscular	Safe, self-limited adverse effects, rapid and robust immune response
NCT06973772	Butantan Institute	VLA1555 and Dengue 1,2,3,4 vaccine	Live Attenuated DENV and CHIKV Vaccines	3/Active	Intramuscular	Data not publicly available as of 13 September 2025
NCT06028841	Valneva Austria GmbH	VLA1553	Lyophilized live-attenuated CHIKV vaccine	3/Withdrawn	Intramuscular in moderately immunocompromised adults	Data not publicly available as of 13 September 2025
NCT05349617	Bavarian Nordic	PXVX0317	CHIKV-VLP (Vimkunya)	3/Completed	Intramuscular	Safe and well tolerated in 65 years and older adults, high rate of protection within 2 weeks of PV
NCT03382964	Valneva Austria GmbH	VLA1553	Lyophilized live-attenuated CHIKV vaccine	1/Completed	Intramuscular	Data not publicly available as of 13 September 2025
NCT04650399	Butantan Institute	VLA1553	Lyophilized live-attenuated CHIKV vaccine	3/Completed	Intramuscular	Safe and well tolerated, induced seroprotective titers in all groups; induced neutralizing antibodies in 98% people 28 days PV
NCT05065983	Bavarian Nordic	PXVX0317	CHIKV-VLP	2/Completed	Intramuscular	Data not publicly available as of 13 September 2025
NCT04440774	University of Oxford	ChAdOx1 Chik & ChAdOx1 Zika vaccines		1/Complete	Intramuscular	Data not publicly available as of 13 September 2025
NCT03590392	University of Oxford	ChAdOx1 Chik		1/Complete	Intramuscular	Not available
NCT03325075	Moderna TX, Inc	VAL-181388	CHIKV mRNA vaccine	1/Completed	Intramuscular	Safe, well tolerated, elicited substantial and long-lasting neutralizing antibodies

MV: measles virus vectored; DENV: Dengue virus; ADV: Adenovirus; VLP: virus like particle; mRNA: Messenger RNA; PV: Post vaccination.

these sites as their breeding spots for laying their eggs, allowing mosquito numbers to stay high and making disease transmission common in urban settings[43,44]. Peri-urban areas, where farmland and city houses or open green spaces are present, provides a breeding ground for both rural species such as *Ae. albopictus* and urban adapted species like *Ae. aegypti*. These places are often the hotspots of mosquitoes to breed across artificial containers and also naturally[45,46]. Many of these mosquito breeding sites are small and are easily overlooked. Due to this reason, these sites are usually missed during regular control measures making it difficult to eliminate the vector[47]. Since these breeding spots are often found indoors or on private property and are many in numbers, simple "search-and-drain" drives are not enough. Clearing them requires regular efforts from both local authorities and households, and if either side misses out, leads to rapid re-infestation[43,44]. Taken together and because *Aedes* mosquitoes can thrive in both semi-urban and urban areas, controlling them should be a regular affair along with the involvement of the community. The most effective way is to monitor and target the local breeding hotspots as this will help reduce mosquito populations and risk of transmissions.

3.3. Global expansion of Aedes vectors

The increase in international trade and travel and also because of the climate change, *Aedes* mosquitoes are now spreading to newer regions where they could not survive before, increasing the chance of Chikungunya appearance in places that were previously free of virus. Changes in rainfall patterns and rising temperature make more areas suitable for *Ae. aegypti* and *Ae. albopictus* to breed, which raises the risk of Chikungunya transmission in places that were once unaffected[48,49]. Commercial shipping, human travel, and global trade of items like used plants and tires have helped *Aedes* mosquitoes to reach new places. Once they arrive, they can survive and transmit easily in cities and towns because they can well adjust in human environments and breed in small containers of water. Therefore, repeated introductions by goods and people and increased environmental suitability works together in driving their spread into new regions[50]. Due to the resulting climate change, *Aedes* mosquitoes are spreading into new regions, as the evolving climate conditions are increasingly suitable for their survival. These regions also face the immediate danger of local Chikungunya transmission if the virus is introduced by an infected traveller. Since public health system in these regions often lacks strong surveillance for *Aedes*-borne viruses, rapid response and early disease detection becomes harder[51,52]. As mosquito habitats are expanding, control efforts cannot just rely on local measures like insecticide spraying. Countries must equip their lab for rapid identification of infected cases, faster screening of travellers, and a stronger mosquito monitoring system. Sharing informations between nations and using climate aware risk mappings will help detect new introductions and mitigate future outbreaks. Further, with the rise of globalisation and temperature, a good urban planning and reduction of water-filled containers will limit the mosquitoes breeding sites, thus restricting the spread of infection[53].

3.4. Community participation issues

It is crucial that community awareness programs are carried out to educate people about the various household activities that help in the breeding of *Aedes* mosquitoes[54]. Each household must be motivated to follow these measures regularly and timely. This strategy alone may show only short-term success, but may not bring lasting change[55]. Studies have shown that even when people are aware, they may still continue daily activities like storing water, delayed cleaning of stagnant water and along with these the additional financial burden also prevents them to follow these practices over time[56]. Cultural and social aspects like trust in health officials, their earlier experiences with disease control programs, and people's willingness to get involved in control efforts play a significant part in controlling CHIKV infection. It has been observed that when health messages do not fit with local beliefs and trust on health officials are weak, community participation with regular follow-up tends to decrease[57]. Novel approaches like genetic engineering or *Wolbachia* bacteria can reduce the mosquito populations without people having to take daily preventive steps. However, these methods only work well if the community accepts, stays involved and understands the process. Programs that combine new technologies with clear communication and active participation can achieve the target better with fewer negative reactions[58]. So, for long term mosquito control, we have to address social barriers and involve communities in delivery and planning of strategies[54]. Cost effective and natural solutions should be employed to prevent mosquito-borne diseases like Chikungunya, malaria, and dengue[59]. This initiative must involve community by involving school teachers in application and preparation of the oil, ensuring local ownership and sustainability.

3.5. Insecticide resistance

Surveys from different parts of the world have shown that both *Ae. albopictus* and *Ae. aegypti* are showing resistance to carbamates, pyrethroids, and organophosphates[60]. Resistance in mosquitoes mainly develop in two ways. First genetic changes where mutations in the sodium-channel gene known as *kdr* mutations make mosquitoes resistant to pyrethroid insecticides, making their nerves not getting affected as strongly as intended[61]. Secondly, detoxification, where mosquitoes produce higher levels of enzymes, such as cytochrome P450, which breaks down insecticides before they cause any harm. Thus, these two forms of resistance often occur together and their presence differs across regions[62,63].

Mosquitoes can develop resistance to insecticides, and this

resistance may vary from place to place. Because of this, using only one type of insecticides may not work everywhere and is not reliable in providing a long-term solution. Thus, to keep these control efforts effective, it's important to check resistance patterns regularly at regional levels. This will help the health programs to pick the right insecticides and use different combinations, which will eventually slow down their resistance[64,65]. Biological control of mosquito population can be another effective strategy to deal with the challenge of insecticide resistance. Further various tools are also available to help countries design and track resistance-aware control strategies[65,66].

3.6. Co–circulation with other arboviruses

Chikungunya virus often spreads along with other arboviruses causing dengue, Zika, yellow fever *etc.*, also transmitted by *Aedes* mosquitoes in many subtropical and tropical regions[67]. Due to this reason, people with acute fever show similar symptoms, making the clinical diagnosis difficult thus delaying treatment. Studies from recent outbreaks has also reported that some patients can also be infected with two viruses at the same time, though the number of such cases vary depending on the region and type of tests used for detection[68]. If we only rely on tests or symptoms for just one virus, it can underestimate the true number of cases and fail to detect when another virus becomes more common in the community[69]. The time of sample collection affects assay accuracy and as CHIKV infection produces cross reactive antibodies, antibody tests alone can give incorrect diagnosis in few cases[70]. Health services also face the challenges of preparing for different disease outcomes. For example, dengue can cause bleeding problems while Chikungunya leads to persistent joint pain. These differences make it harder to sort patients, and get clear information for their disease management[71].

3.7. Handling control challenges

To manage these challenges in controlling the CHIKV infection, integrated surveillance system should be made stronger by involving sero-surveys and multiplex molecular testing that can track down past infections in communities and can also check for several viruses at once. Integrated vector management strategies involving biological and genetic engineering should be employed along with traditional methods. In order to mitigate the breeding spots of *Aedes* mosquitoes, environmental management and sustainable urban planning must be incorporated. Practical and clear information must be given to public with strategies involving community mobilisation can go a long way in vector control. Further current labs should be updated and international collaboration must be carried out to build stronger laboratory networks so that the test results are reliable, accurate, and faster[72]. Since *Aedes* mosquitoes can transmit other viral diseases, efforts to lower their numbers can help against multiple diseases at the same time. When combined with better strategies and testing to handle sudden increase in cases, these measures give strong protection during outbreaks that happens together[67].

4. Future perspectives

With the current resurgence of CHIKV infection globally, future of CHIKV diagnosis and control will be driven by rapid, decentralized testing and strengthening vector surveillance and intervention strategies. Advances in biosensor based and clustered regularly interspaced short palindromic repeats-based assays promise sensitive, less-equipment diagnostics, which can be deployed at clinics in resource limiting countries at the time of an outbreak. Further, a faster and validated multiplex molecular panel that detect CHIKV alongside dengue and Zika, will improve the diagnostic accuracy especially in regions, where these arboviruses co-circulate, benefiting clinical care and disease management. Although, vaccine availability has changed the disease landscape, by offering a tool to protect high-risk groups, still its rollout will require careful safety monitoring, age- and risk-targeted strategies, and clear risk-benefit communication. Finally, in order for a significant and sustained reductions in CHIKV transmission, integrated vector management is needed, which include community source-reduction, targeted insecticide use, and biological approaches such as *Wolbachia* releases, combined with climate-informed forecasting and genomic surveillance to detect viral evolution. Together, these advances will propel us to a future where timely diagnostics, smarter vaccination, and resilient vector control will substantially reduce the CHIKV disease burden.

5. Conclusions

Although the CHIKV is spreading rapidly, we are yet to address certain research gaps in understanding its replication, its seasonal occurrence along with dengue and its potential relationship with climate. As we have made significant number of scientific advancements in the field of nanotechnology, more focus should be given to develop rapid, accurate and portable point of care devices that can detect CHIKV in clinical samples. Prevention of not only acute clinical disease, but chronic disease requires a vaccine against CHIKV. Recent approval of CHIKV vaccine by USFDA does represents a significant step towards prevention, but we also have to explore other feasible vaccine platform like mRNA vaccine. Further, smart surveillance methodologies along with AI tools and climate adaptive vector control strategies can go a long way in controlling the global spread of CHIKV.

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Authors' contributions

SK and SS conceived and designed the work, data collection, data analysis, interpretation and critical revision of the article and approved the final draft. NP, RP and DG analyzed the data, figures and tables, drafting the article, and approved the final draft.

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