Comprehensive review of Chikungunya virus infection: Clinical Characteristics, Epidemiology, and its Control Programme, Northern India

Munish Rastogi[1], Dolly Rastogi[2], Yashvi Gupta[3], Anjali Verma[4], Mansi Singh[5], Tushar Sharma[6], Mohit Kumar[7*]

[1,3,4,5,6,] Department of Medical Microbiology, School of Health Sciences, C.S.J.M.U. Kanpur
[2]Professor & Head, Dept. of Physiology (G.S.V.M. Medical College Kanpur)
[7*]Tutor, Department of Microbiology (Government Medical College Kannauj)

***Corresponding author**: Mohit Kumar
*Tutor, Department of Microbiology (Government Medical College Kannauj)

ABSTRACT

INTRODUCTION: Chikungunya fever (CHIKF) is a virus- borne illness conveyed by mosquitoes that's brought on by an alphavirus from the Togaviridae family. In Congo region it's known by the name "Buka-Buka" meaning "broken-broken" describing crippling joint pain.

CLINICAL CHARACTERSTICS: Sudden onset: Fever, joint pain, and swelling develop suddenly. Fever: High-grade fever (102°F-104°F) lasting 2-5 days.

EPIDEMIOLOGY: Chikungunya is a mosquito-borne disease endemic in Africa, Asia, and the Indian Ocean region, with outbreaks reported in the Americas, the Caribbean, and the Pacific Islands. The virus is primarily transmitted through the bite of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes.

PATHOGENESIS: Chikungunya virus (CHIKV) enters the host through mosquito bites, binding to receptors on host cells, and replicates primarily in skin fibroblasts, muscle cells, and joint tissue.

DIAGNOSIS OF CHIKUNGUNYA: Laboratory diagnosis relies upon the discovery of the virus on early samples and/or specific anti-chikungunya virus (CHIKV) IgM and IgG on blood samples.

TREATMENT: Treatment for Chikungunya typically involves managing symptoms and providing supportive care. Over-the-counter pain relievers like acetaminophen (Tylenol) and ibuprofen.

CONTROL PROGRAMME: A comprehensive control program for chikungunya involves a multi-faceted approach. Vector control measures are crucial, including eliminating breeding sites by removing standing water around homes, communities, and public areas. using mosquito nets and screens on windows and doors can also prevent bites.

CONCLUSION: Chikungunya is a mosquito-borne viral disease that has become a significant public health concern globally. Characterized by severe joint pain, fever, and swelling, Chikungunya can lead to chronic arthritis, neurological disorders, and even death.

KEY WORDS: Chikungunya, Pain, RNA, Disease, Aedes species.

INTRODUCTION

Chikungunya fever (CHIKF) is a virus-borne illness conveyed by mosquitoes that's brought on by an alphavirus from the Togaviridae family.[1]This virus is categorized as an enveloped virus with positive-stranded RNA and the primary vectors are *Aedes aegypti* and *Aedes albopictus* mosquitoes.[1] The virus was first isolated from the serum of an infected cases, the first chikungunya virus (CHIKV) outbreak in India was reported from Kolkata (Calcutta), West Bengal, in 1963.[2] The term 'chikungunya' is derived from the root word 'kungunyala' of the Kimakonde mother tongue in the same area which means "to dry up or come contorted", and alludes to the bending posture of patients infected with the contagion due to the rheumatologic manifestations describing the word chikungunya.[3]In Congo region it's known by the name "Buka-Buka" meaning "broken-broken" describing crippling joint pain.[4] Like utmost tropical infections, the Chikungunya virus (CHIKV) is constantly misdiagnosed, underreported, and undervalued; it primarily affects areas with limited resources, like developing nations.[5]It has turn a hazard to public health over the past 20 years, contributing to certain fatalities and substantial disease-associated morbidity.[6] Infection with Chikungunya virus (CHIKV) outcomes in a feverish complication like the Dengue virus (DENV) and causes symptoms similar as high body temperature, muscle and common discomfort, flaccid limb weakness, headache, nausea, exhaustion, puking, conjunctivitis, rash, and is veritably infrequently deadly in humans.[7,8] The crucial genotypes of CHIKV have been classified as Asian, East-Central-South-African (ECSA), and West African, predicated on their Geographical Distributions and all three variants can produce chikungunya fever (CHIKF) in humans.[9] The most significant attribute of CHIK is the prolonged arthralgia pattern that initially affects the peripheral small joints associated with excruciating pain.[10] The disease is generally non-fatal and the acute phase resolves within 3-4 days leaving the arthralgia syndrome carrying on for some further time.[10] Comparing the earlier outbreaks, the recent circumstance was massive, spread at a fast pace to wider areas causing serious

profitable and social impact.[10] Symptoms and complications symptomatic of Chikungunya (CHIK) including deaths were reported.[11] The present review briefly describes the disease in general and highlights the colourful clinico-pathological aspects, observed during the recent outbreak.[11]

Alphaviruses bear all viruses of this family that are carnal pathogens and possess a worldwide geographic distribution grounded on which they're portrayed classically as either Old World or New World viruses.[12] The New World alphaviruses are allocated across the Americas and react encephalitis in steeds and humans.[12] For illustration, the eastern equine encephalitis contagion, western equine encephalitis contagion, and Venezuelan equine encephalitis contagion.[12]

Whereas Old World alphaviruses to which CHIKV belongs, bring fever, rash, and arthritis in humans, other members of the group include Sindbis contagion, o'nyong'nyong contagion, Ross River contagion, Mayaro contagion, Barmah Forest contagion, and Semliki Forest contagion are present in Asia, Europe, Australia, and region of Africa.[12] Utmost alphaviruses are spread by arthropod vectors that presumably control their geographic disbandment and it's likely that several transoceanic exchanges might have reached.[12] The alphavirus chikungunya virus (CHIKV) belongs to the Semliki forestland contagion establishment of the Alphaviruses.[12]

CLINICAL CHARACTERSTICS

- **Sudden onset:** Fever, joint pain, and swelling develop suddenly.
- **Fever:** High-grade fever (102°F - 104°F) lasting 2-5 days.
- **Joint pain and swelling:** Severe pain and swelling in hands, feet, knees, elbows, and wrists.
- **Polyarthritis:** Multiple joints are affected, often in a symmetrical pattern.
- **Skin rash:** Maculopapular rash on trunk, limbs, and face (in 50% of cases).
- **Headache:** Severe headache, often accompanied by photophobia.
- **Muscle pain:** Myalgia, especially in the legs.
- **Fatigue:** Prolonged fatigue and weakness.
- **Nausea and vomiting:** Mild to moderate gastrointestinal symptoms.
- **Duration:** Symptoms last 5-7 days, but joint pain and fatigue can persist for weeks or months.

EPIDEMIOLOGY

Chikungunya is a mosquito-borne disease endemic in Africa, Asia, and the Indian Ocean region, with outbreaks reported in the Americas, the Caribbean, and the Pacific Islands.[13] The virus is primarily transmitted through the bite of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes, with rare instances of human-to-human transmission through blood transfusion, organ transplantation, or vertical transmission.[14]

The incubation period ranges from 2-12 days, with an average of 3-7 days, and high attack rates of up to 50% have been observed in exposed populations.[15] Chikungunya affects both urban and rural areas, with seasonality typically peaking during rainy seasons or periods of high mosquito activity.[16] Large outbreaks have occurred in Africa, Asia, and the Americas, with increased global spread attributed to climate change, urbanization, and travel.[17]

Re-emergence has been reported in areas previously thought to be chikungunya-free, highlighting the need for continued surveillance and control measures.[18] Monitoring mosquito populations and virus circulation, implementing vector control measures, and conducting public awareness campaigns are essential for preventing and controlling outbreaks.[19] Development of vaccines and diagnostic tools is also crucial for addressing the disease.[20]

PATHOGENESIS

Chikungunya virus enters the host through mosquito bites, binding to receptors on host cells, and replicates primarily in skin fibroblasts, muscle cells, and joint tissue.[13] The virus then enters the bloodstream, leading to viremia, which triggers an immune response.[13] The innate immunity is activated, involving neutrophils, macrophages, and dendritic cells, followed by an adaptive immune response, producing antibodies and activating T-cells.[14]

This immune response leads to the release of pro-inflammatory cytokines, causing inflammation, fever, and joint damage.[14] Chikungunya virus infects and damages joint tissue, resulting in Arthritis, Tendonitis, and Muscle involvement, leading to Myalgia and Myositis.[15] In rare cases, Chikungunya virus can cause neurological symptoms like Headache, Confusion, Seizures, and Encephalitis.[15] Eventually, the immune system clears the virus, and symptoms resolve, but some patients may experience persistent Joint pain and Chronic arthritis.[15]

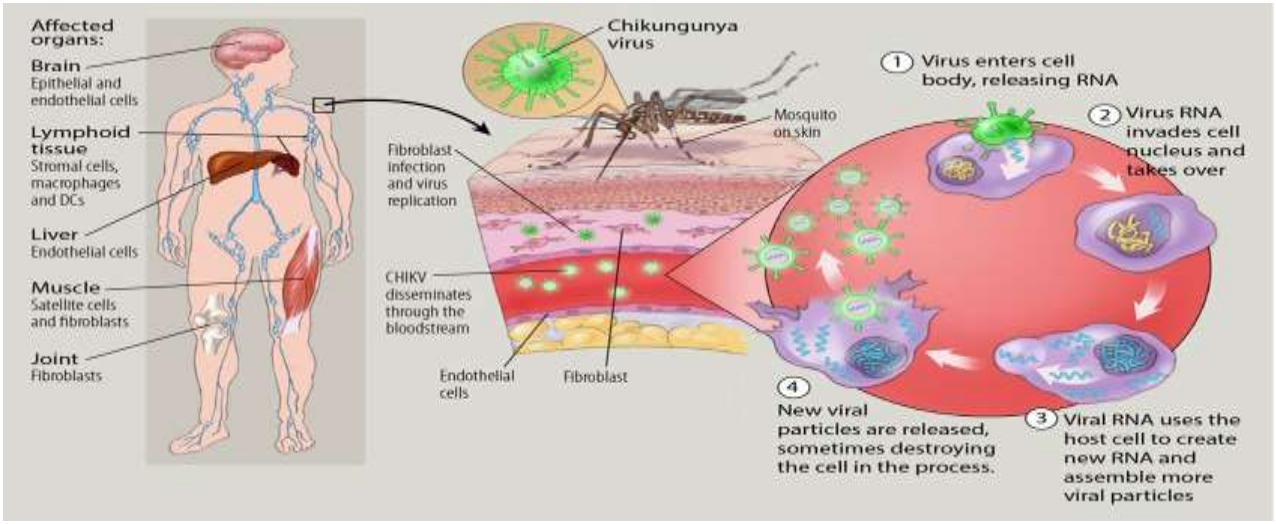

Fig:1 Shows the pathogenesis of Chikungunia Virus.

DIAGNOSIS OF CHIKUNGUNYA

Laboratory diagnosis relies upon the discovery of the virus on early samples and/ or specific anti-chikungunya virus IgM and IgG on blood samples.

Viral Detection

RT-PCR (Reverse Transcription Polymerase Chain Reaction): Detects viral RNA in blood samples during the acute phase of the illness. Viral Isolation: Isolates the virus from blood samples using cell culture techniques

Serological Tests

ELISA (Enzyme-Linked Immunosorbent Assay): Detects IgM and IgG antibodies against Chikungunya virus. IFA (Indirect Immunofluorescence Assay): Detects IgM and IgG antibodies against Chikungunya virus. ICT (Immunochromatographic Test): Rapidly detects IgM antibodies against Chikungunya virus

Molecular Tests

Real-time RT-PCR: Detects and quantifies viral RNA in blood samples.
Nested RT-PCR: Detects viral RNA in blood samples with high sensitivity.

Other Tests

Viral Antigen Detection: Detects viral antigens in blood samples using techniques like ELISA or ICT Neutralization Test: Measures the ability of antibodies to neutralize the virus

Sample Collection

Blood samples (serum or plasma) are collected during the acute phase of the illness (first 5-days) Samples can also be collected during the convalescent phase (after 7 days) for serological tests.

RISK FACTORS

Individuals with certain characteristics are more susceptible to chikungunya infection and severe disease.[16] Older adults (≥65 years) are at higher risk of experiencing severe symptoms and complications, while pregnant women face an increased risk of severe disease and transmission to the fetus.[16] People with chronic medical conditions, such as diabetes, hypertension, and heart disease, are more likely to develop severe illness.[16]

Additionally, individuals with weakened immune systems, including those with HIV/AIDS, Cancer, or taking immuno-suppressive drugs, are more vulnerable to severe disease.[17] Environmental factors also play a significant role in determining the risk of chikungunya infection.[17] Living in or traveling to areas with ongoing chikungunya transmission increases the risk of infection, particularly in areas with high mosquito density and inadequate mosquito control measures.[18]

Warm and humid environments, typical of tropical and subtropical regions, facilitate mosquito breeding and virus transmission.[18] Furthermore, poor sanitation and inadequate waste management can contribute to the formation of mosquito breeding sites.[19] Behavioral factors, such as inadequate protection against mosquito bites and poor travel practices, also increase the risk of infection.[20] Failure to use mosquito repellents, wear protective clothing, or install window and door screens can leave individuals exposed to mosquito bites.[20] Traveling to areas with ongoing chikungunya transmission without taking preventive measures also heightens the risk of infection.[21] Finally, genetic predisposition and previous infection may also play a role in determining an individual's risk of severe disease.[22]

TREATMENT

Treatment for Chikungunya typically involves managing symptoms and providing supportive care.[23] Over-the-counter pain relievers like acetaminophen (Tylenol) and Ibuprofen (Advil, Motrin) can help alleviate fever and joint pain whereas in some cases, prescription medications like Tramadol (Ultram) or Codeine may be necessary for severe pain, anti-inflammatory medications like Prednisone or Corticosteroids may also be used to reduce swelling and inflammation.[23]

CONTROL PROGRAM OF CHIKUNGUNYA VIRUS

A comprehensive control program for chikungunya involves a multi-faceted approach.[10] Vector control measures are crucial, including eliminating breeding sites by removing standing water around homes, communities, and public areas.[10] Using mosquito nets and screens on windows and doors can also prevent bites.[10] Insecticides can be applied to water containers and areas where mosquitoes rest, and regular fogging and spraying can be conducted in affected areas. [20] Individuals can protect themselves by wearing protective clothing, long-sleeved shirts, and pants and applying insect repellents containing DEET (N,N-Diethyl-meta-toluamide), picaridin, or oil of lemon eucalyptus.[8] Avoiding outdoor activities during peak mosquito hours (dawn and dusk) can also reduce the risk of bites.[8] Surveillance and monitoring are also essential, involving establishing a reporting system for suspected cases, conducting regular blood tests to confirm chikungunya infection and monitoring mosquito populations to test for virus presence.[11]

CONCLUSION

Chikungunya is a mosquito-borne viral disease that has become a significant public health concern globally. Characterized by severe joint pain, fever, and swelling, Chikungunya can lead to chronic arthritis, neurological disorders, and even death. While there is no specific treatment or vaccine available, early diagnosis and supportive care can help manage symptoms and prevent complications. Prevention measures, such as mosquito control and personal protective measures, are crucial in controlling the spread of the disease. Further research is needed to develop effective treatments and vaccines, and to understand the long-term consequences of Chikungunya infection. By raising awareness and strengthening public health responses, we can mitigate the impact of Chikungunya and improve the lives of those affected.

REFERENCE

1. Muhammed Muhsin Varikkodan, Faisal Kunnathodi, Sarfuddin Azmi and Tzong-Yuan Wu. An Overview of Indian Biomedical Research on the Chikungunya Virus with Particular Reference to Its Vaccine, an Unmet Medical Need. *Journal of Vaccines and Immunization* 2023;11:1102-1106.
2. B Pastorino, J J Muyembe-Tamfum, M Bessaud, F Tock, H Tolou, J P Durand, C N Peyrefitte. Epidemic resurgence of Chikungunya virus in democratic Republic of the Congo: Identification of a new central African strain. *Journal of Medical Virology*. 2004;74:277–282.
3. Schmidt, C.Schnierle, B.S.Chikungunya Vaccine Candidates: Current Landscape and Future Prospects. *Journal of Drug Design, Development and Therapy.* 2022;*16:* 3663–3673.
4. J J Muyembe-Tamfum, C N Peyrefitte, R Yogolelo, E Mathina Basisya, D Koyange, E Pukuta, M Mashako, H Tolou, J P Durand. Epidemic of Chikungunya virus in 1999 and 200 in the Democratic Republic of the Congo. *Journal of Tropical Medicine.2003;*63:637-638.
5. Gerardo Montalvo Zurbia-Flores, Arturo Reyes-Sandoval and Young Chan Kim. Chikungunya Virus: Priority Pathogen or Passing Trend? *Journal of Vaccines and Immunization.* 2023;*11:*568-591.
6. Kibet Sergon , Charles Njuguna, Rosalia Kalani, Victor Ofula, Clayton Onyango, Limbaso S Konongoi, Sheryl Bedno, Heather Burke, Athman M Dumilla, Joseph Konde, M Kariuki Njenga, Rosemary Sang, Robert F Breiman. Seroprevalence of chikungunya virus (CHIKV) infection on Lamu Island, Kenya, October 2004. *The American Journal of Tropical Medicine and Hygiene.* 2008;78:333–337.
7. Sarika Amdekar, Deepti Parashar, Kalichamy Alagarasu. Chikungunya virus-induced arthritis: Role of host and viral factors in the pathogenesis. *Journal of Viral Immunology.* 2017;*30:*691–702.
8. Saxena, S.K. Re-emergence of the knotty chikungunya virus: Facts, fear or fiction. Journal of Future Virology. 2007;2:121-127.
9. Maria G. Teixeira, Alcina M.S. Andrade, Maria da Conceição N. Costa, Jesuína S.M. Castro, Francisca L.S. Oliveira, Cristina S.B. Goes, Maricelia Maia, Eloisa B. Santana, Bruno T.D. Nunes, and Pedro F.C. Vasconcelos. P.F. East/Central/South african genotype chikungunya virus, Brazil, 2014.*Emerging Infectious Disease.* 2015;*21:*906-907.
10. Powers A M and Logue C H. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. The Journal of General Virology. 2007;88:2363–2377.
11. Mavalankar D, Shastri P, Bandyopadhyay T, Parmar J and Ramani K.V. Increased mortality rate associated with Chikungunya epidemic, Ahmedabad, India. *Emerging Infectious Disease.* 2008;14:412–415.
12. Tatsuo Shioda, Nathalie Chazal. The Translational Research Consortia (TRC) for Chikungunya Virus in India. Current Status of Chikungunya in India. *Frontiers of Microbiology*. 2021;12:695-173.
13. Simon-Djamel Thiberville, Nanikaly Moyen, Laurence Dupuis-Maguiraga, Antoine Nougairede, Ernest A.Gould, Pierre Roques,c,d and Xavier de Lamballerie. Chikungunya virus infection of human cells and tissues. *Journal of Virology*. 2013;87(11):6318-6327.

14. Ravi Mehta, Patrick Gerardin, Carlos Alexandre Antunes de Brito, Cristiane Nascimento Soares, Maria Lucia Brito Ferreira and Tom Solomon. Neurological manifestations of chikungunya virus infection. *Journal of the Neurological Sciences*. 2018;28(3):137-141.
15. Sanae Ali Ou Alla, Bernard Combe. Arthritis after infection with Chikungunya virus. *National Library of Medicine.* 2011;25(3):337-346.
16. Staples JE, Breiman RF, Powers AM. Chikungunya fever: an epidemiological review of a re-emerging infectious disease. Clinical Infectious Disease. 2009;49(6):942-948.
17. B.M.C.Randika Wimalasiri-Yapa, Liesel Stassen, Xiaodong Huang, Louise M Hafner, Wenbiao Hu, Gregor J Devine, Laith Yakob, Cassie C Jansen, Helen M Faddy, Elvina Viennet, Francesca D Frentiu. Chikungunya virus in Asia-Pacific: a systematic review. *Emerging Microbes and Infection*. 2019;8(1):70-79.
18. Gianluca Russo, Lorenzo Subissi and Giovanni Rezza. Chikungunya fever in Africa: a systematic review. *Pathogen and Global Health*. 2020;114(3):136-144.
19. Heidi Auerswald, Camille Boussioux, Saraden In, Sokthearom Mao, Sivuth Ong, Rekol Huy, Rithea Leang, Malen Chan, Veasna Duong, Sowath Ly, Arnaud Tarantola and Philippe Dussart. Broad and long-lasting immune protection against various Chikungunya genotypes demonstrated by participants in a cross-sectional study in a Cambodian rural community. *Emerging Microbes and Infection*. 2018;7(1):13-19.
20. Brad A. Goupil and Christopher N. Mores. A Review of Chikungunya Virus-induced Arthralgia: Clinical Manifestations, Therapeutics, and Pathogenesis. *National Library of Medicines.* 2016;10:129–140.
21. Sarika Amdekar, Deepti Parashar, Kalichamy Alagarasu. Chikungunya Virus-Induced Arthritis: Role of Host and Viral Factors in the Pathogenesis. *National Library of Medicines*. 2017;30(10):691-702.
22. J. Kennedy Amaral, Peter C. Taylor, Mauro Martins Teixeira, Thomas E. "Tem" Morrison N and Robert T. Schoen. The Clinical Features, Pathogenesis and Methotrexate Therapy of Chronic Chikungunya Arthritis. *Multidisciplinary Digital Publishing Institute*. 2019;*11*(3):289-294.
23. Eika Webb,Melina Michelen ,Ishmeala Rigby ,Andrew Dagens,Dania Dahmash,Vincent Cheng,IAn evaluation of global Chikungunya clinical management guidelines: A systematic review.*E-Clinical Medicine*.December 2022;54:101-672.