

Original article

Title- Regional variation in Chikungunya viral infection prevalence in Meghalaya- A study from tertiary teaching center from North east India

Abstract

Aim: The aim of the study is to investigate the sero-prevalence of chikungunya presented within NEIGRIHMS (North Eastern Indira Gandhi Regional Institute of Health and Medical sciences), a regional institute located in Shillong, Meghalaya, India.

Study Design: This was a hospital-based study.

Place and duration of the study: The study was carried out in NEIGRIHMS covering patients within the East Khasi Hills districts of Meghalaya, India, during the months of June to November, 2023.

Methodology: Blood samples from patients were collected and were subjected to CHIKV IgM ELISA for detection of chikungunya virus infection. A total of 100 samples (46 males and 54 females; age range: 18 above) from patients with chikungunya-like symptoms commonly fever, arthralgia, myalgia and headache were recruited for the study.

Results: Out of 100 samples tested for CHIKV IgM Elisa, 10 samples came out positive.

Conclusion: An active surveillance of cases and identification of their sources can help to identify where the resources for chikungunya prevention program should be distributed within the state of Meghalaya for optimum utilization of resources and effective disease control.

Keywords: Chikungunya virus, Chikungunya infection, Chikungunya IgM antibodies, Meghalaya, Shillong, East Khasi Hills District

Abbreviations: CHIKV (Chikungunya Virus), CHIKF (Chikungunya Fever)

Introduction

Chikungunya virus (CHIKV) is an alpha virus belonging to the Togaviridae family and is transmitted by *Aedes* mosquitoes (7, 5, 6) primarily *Aedes aegypti* or *Aedes albopictus* (4). Bite from such infected mosquitoes causes chikungunya fever (CHIKF), which was officially documented on the Makonde Plateau, south-eastern Tanzania after its breakout in 1952 (3). Hence the name Chikungunya derived from the verb kungunyala, a language spoken in the area which means “to dry up or become contorted” (3) referring to the contorted or bent posture of patients who have CHIKF with severe joint pain (2). Reports of CHIKF dated as far back as 1825, and re-emergence of the disease have been reported in Africa and Asia at an irregular interval of 2-20 years (2). In 2005-2006, a first outbreak occurred in occidental countries in the Indian Ocean, including La Reunion, spreading from Eastern Africa (2, 5). The epidemic also then spread

into India causing an estimation of 1.5 million cases (2) and was the worst affected country (1). In 2013, a case of locally transmitted CHIKV was reported in French Guyana, and since then chikungunya cases have been reported in 44 countries in the Americas (1).

In India, the first major outbreak was reported in 1963 in South India and another in 1973, in Central India(9). There was a pause in the outbreak for 32 years until 2006(8, 9). It began in the coastal regions of Andhra Pradesh(8), spreading to approximately 15 other states affecting 213 districts in India(14). A total of 565.41 million population was at risk of infection and the total of CHIKF suspected cases was around 1.39 million (14). Estimation from epidemiology, demographic and geographical data suggested that around 1.38 million people were affected till December of 2006 (9). Most of the cases are from Karnataka amounting to half of the total reported cases and a quarter are from Maharashtra (9). According to the data from National Vector Borne Disease Control Programme (NVBDCP) for the year 2006, a total of 15,504 samples were screened and 1985 samples came out positive giving a positivity rate of 12.8% for chikungunya (14). The recorded estimation data lacked accuracy due to a large proportion of the people consulting private health care and hence were not recorded in the surveillance system of India. This suggested that the number of chikungunya were much more than the recorded data (14). The reported cases of CHIKF have increased to 23 states by the year 2015, 28 states in 2016 and by the year 2019 it was reported in 30 states and Union Territories. Lakshadweep and Dadra and Nagar Haveli Union Territories have not reported any cases of CHIKF till now. Highest number of reported cases was seen in the year 2016, 2017 and 2019 (3).

Chikungunya case in the Northeastern states of India was first reported in Assam in 2008, and in 2010 in Meghalaya (15). The outbreak of CHIKV in Meghalaya was reported in the Garo Tribe dominating in the West Garo Hills District of Meghalaya of which out of 64 samples 23 came out positive for IgM antibodies against the CHIKV. However, no reports of any outbreak of the virus till date. In India, both dengue and chikungunya are circulated by a common vector, hence a high probability of chikungunya and dengue circulating simultaneously (17). Also, studies show that the northeastern states are hotspots of the *Aedes* species mosquitoes (16). Therefore, in this study, a screening of chikungunya in the East Khasi district of Meghalaya is carried out during the month of June- November, 2023 to understand its prevalence in the region by recruiting patients attending the tertiary level referral teaching center situated in Northeastern region of the country i.e. Shillong.

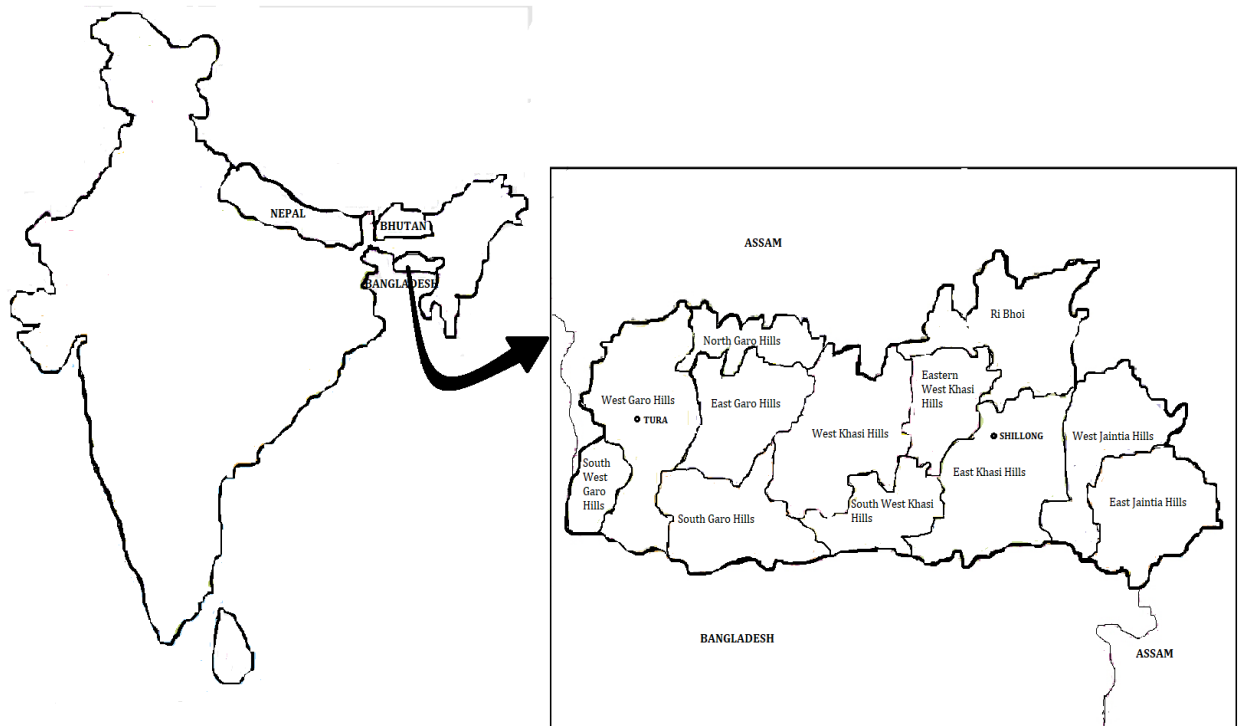


Fig 1: Map of Meghalaya. (The map is not to scale)

Clinical manifestation

Chikungunya fever (CHIKF) symptoms shares similarities with Dengue fever(12). The virus starts to replicate near the site of inoculation showing a broad spectrum of cell and tissue tropism covering the endothelial, fibroblast and brain cells (11, 7). The monocytes and lymphocytes seem to resist, however the macrophages are susceptible to infection (12). The virus then disseminates to other secondary sites which include the liver, musculoskeletal and synovium, presumably through blood (2,11). After an infection, onset of high fever and arthralgia started after an incubation period of 2 – 6 days (3). The symptoms relating to CHIKV infection are classified into two stages; the acute phase and chronic phase (3, 5). Sudden onset of fever with arthralgia are typical initial symptoms of CHIKF which can last upto 15 days and is considered as the acute phase (3, 12). The disease is associated with other symptoms like intense fatigue, arthralgia, myalgia, headache, nausea and vomiting in adults (5). After a short improvement following the acute phase, patients can be impaired by early exacerbation, inflammatory relapses, rheumatism and loss in the quality of life. This long term deterioration is mostly seen in elderly patients of 40 years and above and/ in patients with underlying diseases (5). Additional symptoms are skin maculopapular rashes (12), tenosynovitis, severe neurologic, cardiac arrest and in some instances, death. These severe clinical features are mostly seen in neonates, adults of more than 65 years old and/or patients with underlying diseases (10). Reports have shown that high rate of morbidity occurs in mother-to-infant transmission of CHIKV infection (10).

Clinical manifestations of Chikungunya infection	
Classical features	Complications
Fever	Bulbous skin lesions
Arthralgia	Fulminant hepatitis
Rashes on skin	Meningoencephalitis
Headache	Retinitis
Backpain	Uveitis
Nausea	Myocarditis
Vomiting	Nephritis
Joint Swelling	Convulsions
Myalgia	Cranial nerve palsy
Lymphadenopathy	Guillain-Barre Syndrome
Fatigue	Acute Renal failure
Restlessness	Respiratory failure
Anorexia	Meningitis
Abdominal Pain	
Diarrhea	
Leukopenia	
Lymphopenia	

Table 1: Classical and non-classical symptoms of chikungunya infection (3)

Materials and Method

Study Area and Sample collection

During the month of June to November, samples are collected from patients having symptoms similar to CHIKF disease which includes fever, arthralgia, headache, myalgia and fatigue presented within NEIGRIHMS, Shillong. The study has been approved by the ethical community IEC of NEIGRIHMS Vide No.NEIGR/IEC/M14/F16/2021 dated 26/04/2021. A total of 100 samples has been collected and were subjected to CHIKV IgM ELISA after the written consent from each patient was taken and their symptoms were recorded.

Chikungunya ELISA IgM

Serum samples separated from the 2 ml of blood collected were stored in aliquots at -80C. 1µl of each serum samples was then run for chikungunya IgM using the NIV CHIKUNGUNYA IgM Capture ELISA (National Institute of Virology, Pune, Maharashtra, India) following the manual instructions provided in the Kit.

Results

Out of the 100 samples analysed for IgM, 10 samples came out positive. All patients show similar symptoms of fever, headache, myalgia and arthralgia. The most common symptom was fever and myalgia

in patients who tested positive for CHIKV infection. 50% of the test samples are males and 50% are females.

Discussion

Northeastern states have shown to be the hotspots for Aedes mosquitoes which are vectors of chikungunya and dengue, and Meghalaya is one of them (17). It also shares borders with Bangladesh, which had a chikungunya outbreak in 2008, and soon followed by an outbreak in Tura, Meghalaya in 2010 (17). However, no outbreak has been reported in or around Tura since then (17). Moreover, during the dengue outbreak in Guwahati, Assam, in 2015, besides the dengue positive cases many dengue suspected cases came out negative. As both diseases have the same vector a study was done on the dengue negative cases. Out of 42 dengue negative samples, all came out IgM negative for CHIKV but seven samples have shown amplification for CHIKV RNA instead (16). This proves the silent existence of CHIKV which may have been concealed by dengue (16), therefore requires for an active surveillance with regard to the disease occurrence.

With available reports a recent outbreak within Meghalaya, a need for continuous active surveillance is required and with the symptoms being related to dengue, suspicions for chikungunya cases cannot be omitted. However, in this study it has shown that chikungunya has a very less rate of positive cases in East Khasi Hills (prevalence of positivity is 10%). This similar instance was also seen in a study in Sahelian region in Berke'dji (1996), where there was an absence of chikungunya cases despite the presence of Aedes mosquitoes and being a region in Africa. The reason for this could be explained due to the rate of transmission being affected by many factors, such as, the lack of availability of host in urban areas, such as monkeys, sylvatic vectors (forest dwelling mosquitoes) and low population density and movement (18). Although, the rate of transmission in this studied area can only be hypothesized due to the scarcity of researches hence, additional research is needed in this regard.

Conclusion

Absence of suitable treatment or vaccine for chikungunya and with recent study showing the prevalence of chikungunya in the state of Meghalaya (15) calls for further continuation of this study to get more evidence into accurate prevalence of chikungunya in East Khasi Hills. Also with the increase in modern transportation makes it easier for viral diseases to be transmitted from remote areas into populated urban areas. The challenges of long term sequelae post chikungunya infection can cause a huge affect on the patient's quality of life. Therefore, an active surveillance of cases and identification of their sources can help to identify where the resources for chikungunya prevention program should be distributed within the state of Meghalaya for optimum utilization of resources and effective disease control.

Acknowledgement

We would like to thank the ICMR (Indian Council of Medical Research) for funding the study. Also, we are grateful to Dr. D. Parashar, Dr. A. Tripathy and Dr. K. Alagarasu from NIV (National Institute of Virology) for their support and help in providing the Chikungunya IgM Elisa Kits to accomplish the study.

Reference

1. Co-distribution and co-infection of chikungunya and dengue viruses Luis Furuya-Kanamori^{1*}, Shaohong Liang², Gabriel Milinovich³, Ricardo J. Soares Magalhaes^{4,5}, Archie C. A. Clements¹, Wenbiao Hu³, Patricia Brasil⁶, Francesca D. Frentiu⁷, Rebecca Dunning and Laith Yakob, Furuya-Kanamori et al. *BMC Infectious Diseases* (2016) 16:84 DOI 10.1186/s12879-016-1417-2
2. Biology and pathogenesis of chikungunya virus, Olivier Schwartz and Matthew L. Albert, *NATURE REVIEWs | Microbiology VOLUME 8 | JULY 2010* doi:10.1038/nrmicro2368
3. Current Status of Chikungunya in India, The Translational Research Consortia (TRC) for Chikungunya Virus in India[‡], *Front. Microbiol.* 12:695173. doi: 10.3389/fmicb.2021.695173
4. Chikungunya virus in Asia – Pacific: a systematic review B. M. C. RandikaWimalasiri-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, *Emerging Microbes & Infections*, 8:1, 70-79, DOI: 10.1080/22221751.2018.1559708
5. Chikungunya Virus Infection Fabrice Simon & Emilie Javelle & Manuela Oliver & Isabelle Leparc-Goffart & Catherine Marimoutou, *Curr Infect Dis Rep* (2011) 13:218–228 DOI 10.1007/s11908-011-0180-1
6. Chikungunya virus infection: an overview Claudia Caglioti, Eleonora Lalle, Concetta Castilletti, Fabrizio Carletti, Maria Rosaria Capobianchi, Licia Bordi, *NEW MICROBIOLOGICA*, 36, 211-227, 2013
7. New Insights into Chikungunya Virus Infection and Pathogenesis Vasiliya Kril,^{1,*} Olivier Aïqui-Reboul-Paviet,^{2,*} Laurence Briant,² and Ali Amara¹, *Annu. Rev. Virol.* 2021. 8:327–47, <https://doi.org/10.1146/annurev-virology-091919-102021>
8. Chikungunya Infection: A Re-emerging Epidemic Binoy J. Paul .Shajit Sadanand *Rheumatol Ther* (2018) 5:317–326 <https://doi.org/10.1007/s40744-018-0121-7>
9. Chikungunya epidemic: An Indian perspective, S.P. Calantri, Rajnish Joshi, Lee W. Riley, *The national medical journal of India*, Vol. 19, No. 6, 2006
10. Reemergence of Chikungunya Virus Thomas E. Morrison, *Journal of Virology* p. 11644 –11647 October 2014 Volume 88, doi:10.1128/JVI.01432-14
11. Chikungunya virus replication in skeletal muscle cells is required for disease development Anthony J. Lentscher, ... , Thomas E. Morrison, Terence S. Dermody, *J Clin Invest.* 2020;130(3):1466-1478. <https://doi.org/10.1172/JCI129893>.

12. Chikungunya Virus David M. Vu, MDa, *, Donald Jungkind, PhD^{b,1}, Angelle Desiree LaBeaud, MD, Clin Lab Med 37 (2017) 371–382 <http://dx.doi.org/10.1016/j.cll.2017.01.008>
13. Genome-Scale Phylogenetic Analyses of Chikungunya Virus Reveal Independent Emergences of Recent Epidemics and Various Evolutionary Rates ‡ Sara M. Volk,¹ †§ Rubing Chen,¹ † Konstantin A. Tsetsarkin,¹ A. Paige Adams,¹ Tzintzuni I. Garcia,² ¶ Amadou A. Sall,³ Farooq Nasar,¹ Amy J. Schuh,¹ Edward C. Holmes,⁴ Stephen Higgs,¹ Payal D. Maharaj,⁵ Aaron C. Brault,⁵ and Scott C. Weaver¹ *, JOURNAL OF VIROLOGY, July 2010, p. 6497–6504 Vol. 84, doi:10.1128/JVI.01603-09
14. Burden of chikungunya in India: estimates of disability adjusted life years (DALY) lost in 2006 epidemic K. Krishnamoorthy, K.T. Harichandrakumar, A. Krishna Kumari & L.K. Das Vector Control Research Centre, Puducherry, India, J Vector Borne Dis 46, March 2009, pp. 26–35
15. Dutta P, Khan SA, Phukan AC, Hazarika S, Hazarika NK, Chetry S, et al. Surveillance of Chikungunya virus activity in some North-eastern states of India. Asian Pac J Trop Med 2019; 12(1): 19-25.
16. Dutta P, Khan SA, Hazarika NK, Chetry S. Molecular and phylogenetic evidence of chikungunya virus circulating in Assam, India. Indian J Med Microbiol 2017;35;389-93
17. Chikungunya outbreak in Garo Hills, Meghalaya: an epidemiological perspective Siraj Ahmed Khan, Prafulla Dutta, Rashmee Topno, Jani Borah, Purvita Chowdhury & Jagadish Mahanta, Indian J Med Res 141, May 2015, pp 591-597
18. Vectors of chikungunya virus in senegal: current data and transmission cycles mawlouthdiallo, jocelynthonnon, moumounitraore-lamizana, and didierfontenille, am. j. trop. med. hyg., 60(2), 1999, pp. 281–286