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Distribution of Chikungunya Cases in Madurai District during Outbreak

[1]Dr. Vasanthapriyan Moongilpatti Ramasami, [2]Dr.Sugumari Chandrasekaran, [3]Dr.Selva Prabhu Antonyraj

[1]Assistant professor, Institute of Microbiology, Madurai Medical College, Madurai

[2]Associate professor, Institute of Microbiology, Madurai Medical College, Madurai

[3]Research Scientist, VRDL, Institute of Microbiology, Madurai Medical College, Madurai

Corresponding Author: Dr. Vasanthapriyan Moongilpatti Ramasami**,** Assistant professor, Institute of Microbiology, Madurai Medical College, Madurai.

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Abstract

Background: Chikungunya is an acute viral fever which occurred as an epidemic form with the main symptoms of joints pain for prolonged duration. It persists as major public health problem till date.This study was done to assess the magnitude of the outbreak & to evaluate the epidemiological and virological features of Chikungunya infection in patients with acute febrile illness from several Primary health centres under Madurai HUD.

Methods: A retrospective observational study was conducted on the 75 blood samples received from suspected cases of chikungunya fever from different PHCs in Madurai are tested for IgM antibody against (CHIKV) using ELISA as evidence of recent infection in Viral Research Diagnostic Laboratory, Institute of Microbiology, Madurai Medical College from March to October, 2018. We diagnosed 13 epidemis of chikungunya during the study period.

Results: Of the 75 cases tested, 51 cases (68 %) were positive for IgM antibodies; 19 cases (25.33%) were Negative. The major symptoms were fever (100%), followed by joint pain(93.3%), headache(64%), myalgia (86.6%), and rash (29.3%) respectively. CHIKV IgM positivity was seen throughout the year, with a peak between September and October.

Conclusion: This study emphasizes the need for continuous surveillance for disease burden & to establish an effective syndromic surveillance system for early detection and timely public health intervention of future chikungunya outbreaks in resource-limited settings like VRDLs. This was high in late monsoon and winter, suggests that it continues to be a major health problem in our setup and indicates the need of appropriate strategies to reduce the severity of disease.

Introduction

Chikungunya fever is an acute febrile illness caused by an arthropod borne alphavirus,Chikungunya virus (CHIKV),which is transmitted by the bite of infected Aedes mosquitoes. Chikungunya virus was first

isolated in Tanzania by Ross and colleagues [48]. It is an arbovirus that belongs to the genus *Alphavirus* in the *Togaviridae* family. The virus has a diameter of 60–70 nm, a positive-sense, single-stranded RNA genome with 11,438 nucleotides and a phospholipid envelope with hemagglutinin protein spikes [16, 17] Two different transmission cycles exist for the CHIKV, namely the sylvatic cycle seen mainly in Africa and the urban cycle that was initially seen in Asia but is also now found in Africa.The disease presents with sudden onset of fever, joint pain, myalgia ,head ache, nausea, fatigue & rash. Most cases of chikungunya fever are self limiting and the symptoms usually resolve within 7 days, however joint pain may persist for several months or even years in some patients. Emerging and constantly evolving arthropod –borne viruses (Arboviruses) represent a significant warning to human health worldwide. Chikungunya is endemic in parts of Africa, South East Asia and the Indian sub-continent. In India, the disease was first reported and isolated in Calcutta in 1963 (Shah, et.al., 1964). Thereafter, Chikungunya Virus (CHIKV) infection reappeared in late 2005 with large outbreaks being reported from the States of Andhra Pradesh, Maharashtra, Orissa, Karnataka, Tamil Nadu, Madhya Pradesh and Gujarat (IMA 2006).

CHIKV can damage collagen and alter connective tissue metabolism in cartilage and joints to produce severe acute arthritis. Several studies have reported persistent clinical manifestations mainly arthralgia for several months after acute infection, suggesting the possibility of chronic forms of CHIKV infection (Ciampi de Andrade, et. al.,2010).

Clinical disease manifestations emerge after an incubation period that lasts an average of 4 to 12 days. The first symptom is usually a high fever, followed hours later by myalgia and generalized arthralgia and arthritis, which are often incapacitating and debilitating, the most significant feature of this disease. After a few days, fever may abate and recrudesce, giving rise to a “saddleback” fever curve. These are often associated with chills, headache, malaise, vomiting, headache and back pain. Most cases of chikungunya fever are self limiting and the symptoms usually resolve within 7 days (Mahendradas, 2009).

Joint pain is mostly polyarticular, bilateral and symmetrical. This polyarthropathy frequently involves the peripheral joints of the hand, wrist, and ankles and the larger joints such as the knee and shoulder. Disabling acute tenosynovitis is also frequently present and Periarticular swelling is frequently observed.Following initial infection, a rapid humoral response occurs with huge production of neutralizing Anti Chickungunya antibody. The immunoglobulin M (IgM) can be detected very early, usually from the third to fourth day after the onset of clinical symptoms and antibody levels are highest 3 to 5 weeks after the onset of illness (Litzba et al., 2008). Due to rapid seroconversion, Immunoglobulin G (IgG) appears only after two or three days of appearance of IgM where IgG subclass 3 is the predominant. In addition, CHIKV infection is clinically similar to other arboviral infections such as dengue virus and Zika virus which makes the diagnosis of this disease quite challenging.

The testing algorithm to diagnose CHIKV infections is based on the characteristics of CHIKV infection and the timing of specimen collection. Reverse Transcriptase Polymerase Chain reaction (RT-PCR) act as the most sensitive method for the detection of CHIKV.

The CHIKV from the East/Central/South African (ECSA) genotype was the main causative agent for this re-emergence and Aedes albopictus was identified as

the main vector in several regions. In India, the National Vector Borne Disease Control Program (NVBDCP) conducts surveillance for chikungunya in sentinel hospitals while the Integrated Disease Surveillance Program (IDSP) conducts surveillance for chikungunya as a part of surveillance for outbreak-prone diseases. Both surveillance systems report the aggregate number of cases. During 2013–2018, the Indian Council of Medical Research and the Department of Health Research (DHR) established a network of 102 Virus Research and Diagnostic Laboratories (VRDLs) in 30 states/union territories of India to strengthen laboratory capacity to provide timely diagnosis of disease outbreaks.

Recently Madurai District has confronted about 13 outbreaks on Chikungunya in 2018 where severe damages have been imposed on the social and economic lives of people. Although several minor cases have been reported in Madurai District previously in the year of 2006, this was first time when the scale is so immense where such a wide distribution occurred.There is a lack of sufficient data to properly understand the magnitude and assess the different perspectives of this disease. Hence, this study aims to evaluate the epidemiological & vorological features Chikungunya infection in patients with Acute febrile illness with ELISA as the reference method and to see whether it can be established as a reliable technique where resource facilities are poor and identify possible risk factors associated with the infection.

Materials and Methods

Place of study

This study was conducted at the laboratory facility of Viral Research Diagnostic Laboratory (VRDL), Institute of Microbiology, Madurai Medical College, Madurai.

VRDLs receive samples from district public health authorities for laboratory confirmation of disease clusters (suspected outbreaks) to provide diagnosis (Joshua, et. al., 2016). Demographic, clinical and laboratory data from all patients are entered in a web-based data entry system. As per the protocol, patients with AFI with joint swelling, rash, arthralgia& myalgia were investigated for chikungunya.

The sera samples were tested for immunoglobulin M (IgM) antibodies against CHIKV using IgM antibody capture (MAC) enzyme-linked immunosorbent assay (ELISA) developed by the National Institute of Virology (NIV), Pune (Hundekar, et. al., 2002).

Period of Study

This study was carried out in 13 different fever outbreaks between March 2018 and October 2018.

Sample Size

Totally 75 patient's blood samples were received from different areas of the Primary Health Care centres under Madurai HUD from March 2018 to October 2018 (totally 13 outbreaks) were included in the study. As such, there are no exclusion criteria.

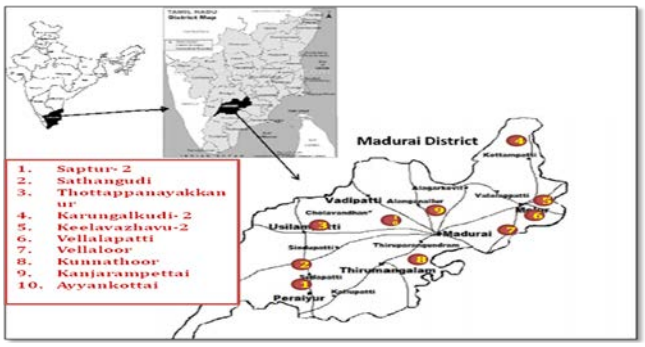
Method for Detection of IgM Antibody against Chikungunya

Blood samples were centrifuged, serums separated, and then proceeded by IgM Elisa to detect antibody. All reagents were brought to room temperature before 30 minutes of performing test. Sandwich (qualitative) ELISA technique was used for the accurate qualitative measurement of IgM class antibodies against chikungunya virus in human serum and plasma. The sensitivity and specificity for the CHIK IgM antibody capture ELISA is 95.00% and 97.22%, respectively. A 96-well plate was precoated with anti-human antibodies to bind to corresponding antibodies of the sample. Controls or test samples are added to the wells and

incubated. Following washing, the chikungunya virus antigen was added and incubated. After washing again, biotinylated chikungunya virus antibodies were added, followed by incubation. After washing for one more time, streptavidin peroxidase (SP) conjugate were added to the wells, which binds to the biotinylated chikungunya virus-specific antibodies. TMB is then catalyzed by the SP to produce a blue color product that changes to yellow after adding an acidic stop solution. The density of yellow coloration is directly proportional to the amount of chikungunya IgM present in the sample captured in the plate. The intensity of color/optical density (OD) was monitored at 450 nm. The sample was considered positive for IgM antibody if the OD of the sample exceeded OD of negative control by a factor 4.0 (sample OD ≥ negative OD × 4.0). Both positive and negative controls were used to validate the test.

Study design

Blood Samples from patients with AFI with suspected chikungunya infection from various PHC areas under Madurai District (Saptur, Sathangudi, Thottappanayakkanur, Karungalkudi, Keelavazhavu, Vellalapatti, Vellalloor, Kunnathoor, Kanjarampettai and ayyankottai) were collected and sent for testing of anti Chikungunya antibodies (IgM). For confirmation of outbreak. These villages were under block like Melur, kottampatty, Sedapatty, Usilampatty, Madurai West, Thirumangalam, Alanganallur and Madurai East).



Results

Of the 75 cases tested, 51 cases (68 %) were positive for IgM antibodies; 19 cases (25.33%) were Negative and 5 cases (6. 66% Equivocal. Out of the 51 positive cases,20 (39.21%) were Males & 31 (60.76%) were females, which shows a female predominance. Seropositivity for CHIKV IgM ranged from 3.92 % to 17.64 % in different age groups. Among the 51 positive cases, highest positivity range in Males were noticed in 5 cases (9.8%)in the age group of 31-40 years and in females,in 9 cases (17.64%) in the age group of 21 -30 years.This is shown in Table -1 & chart -1

Table 1: Age & sex wise distribution of Chikungunya positive cases

N=51

S. No.	Age Groups	Male		Female	
		Positive	%	Positive	%
1	0-10	02	3.92	00	0.00
2	11-20	03	5.88	02	3.92
3	21-30	03	5.88	09	17.64
4	31-40	05	9.80	07	13.72
5	41-50	03	5.88	07	13.72
6	51-60	02	3.92	04	7.84
7	>60	02	3.92	02	3.92
Total		20	39.21	31	60.78

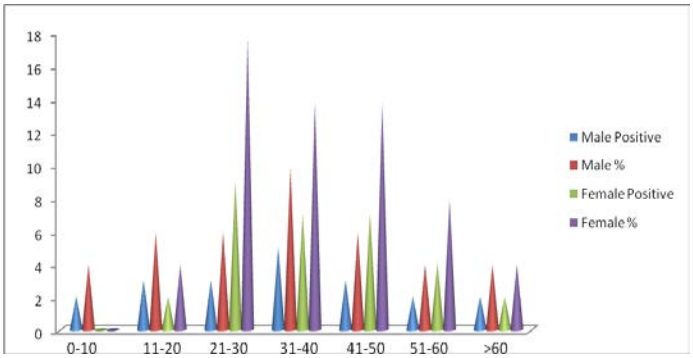


Chart -1: Age & Sex wise distribution of Chikungunya positive cases

Table 2: Signs and symptoms of Chikungunya positive

Table 2: Signs and symptoms of Chikungunya positive cases

N=75

S. No.	Symptoms	Positive case for Chikungunya	
		Number	Percentage
1	Fever	75	100
2	Arthralgia	70	93.3
3	Myalgia	65	86.6
4	Headache	48	64
5	Rash	22	29.3

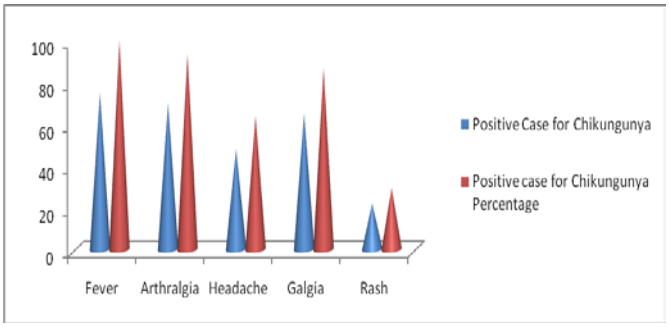


Chart - 2: Signs and symptoms of chikungunya suspected cases

Of the total 75 suspected cases of Chikungunya, all presented with fever (100%), followed by Arthralgia(93.3%,) Myalgia(86.6%,) Headache (64%) and Rash (29.3%)respectively. This is depicted in Table -2 & Chart -2.

Table -3 & Chart -3 shows that, Out of the total 75 suspected cases of Chikungunya with blockwise distribution of outbreak cases with CHIK Ig M positive antibodies were observed more in Melur Block 26 (86.6%) followed by Kottampatty 7(70%)Sedapatty,Madurai East&Madurai west 6(60%) and in Usilampatty, Thirumangalam and Alanganallur Blocks 4 (40%) respectively.

Table 3: Block wise distribution of chikungunya positive cases

N=75

Block	Tested	Positive	%
Melur	30	26	86.6
Kottampatty	10	7	70
Sedapatty	10	6	60
Usilampatty	5	2	40
Madurai West	5	3	60
Thirumangalam	5	2	40
Alanganallur	5	2	40
Madurai East	5	3	60

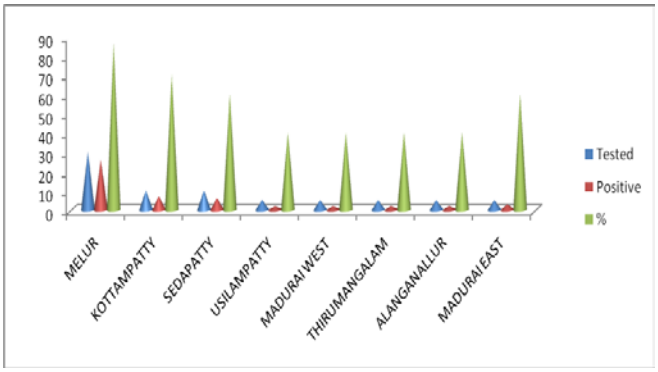


Chart- 3: Block wise distribution of outbreak cases for chikungunya

Table -4 & Chart -4 shows that out of the 75 suspected cases, PHC wise distributions for CHIKV IgM antibodies ranged from 40 % to 93.3 % respectively.

Keelavazhavu PHC (93.3 %) marked the highest number of positive cases followed by Vellaloor (80%)Karungalakudi (70%)Saptur (60%) Kalimangalam&Vellalapatty (40%)and lowest positivity observed in Thottappanayakkanur, Kanjarampettai, Sathankudi and Ayyankopttai (20%).

Table 4: PHC wise distribution of chikungunya positive cases

N=75

PHC	Tested	Positive	%
Keelavazhavu	15	14	93.3
Vellaloor	10	08	80
Karungalakudi	10	07	70
Saptur	10	06	60
Thottappanayakkanur	05	02	40
Kanjarampettai	05	02	40
Sathankudi	05	02	40
Ayyankottai	05	02	40
Kalimangalam	05	04	80
Vellalapatty	05	04	80

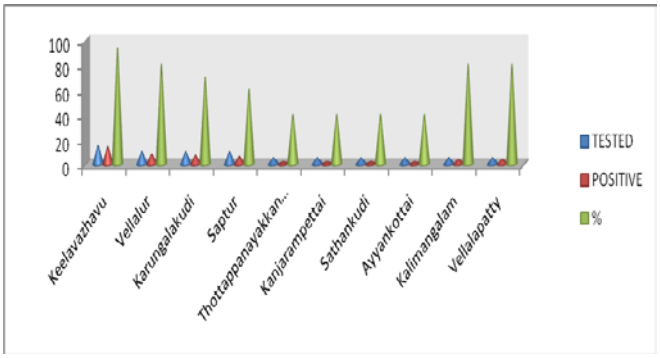


Chart- 4: PHC wise distribution of outbreak cases for chikungunya

CHIKV IgM positivity was seen throughout the year, with a peak between September and October.

Table -5 shows that, of the total 13 Outbreaks observed in the year of 2018. The maximum number of outbreaks fall between September and October 2018.

Table 5: PHC wise distribution of outbreak for 2018

PHC	Out Breaks
Keelavazhavu	July & October
Vellalur	September
Karungalakudi	September & October
Saptur	March (2)
Thottappanayakkanur	September
Kanjarampettai	June
Sathankudi	July
Ayyankottai	July
Kalimangalam	October
Vellalapatty	August

Discussion

In this study, the rate of chikungunya was very high in September and October, during late monsoon; and, again, there was an increase in March, followed by reduction up to June, increase in July, and decrease in August. The variation in the number of cases in different seasons is because of high vector density during the rainy season. Similar findings were observed in different studies as well (Brazier, et. al., 1999, Rajeswari, et. al., 2005 and ILO, 2010).

Fever and joint pain were present in all, followed by headache, body ache, joint swelling, and rash in descending order. Similar pattern were observed in study done by Mohanty et al. Chikungunya affects humans of all age groups worldwide. In this study, there was no mortality but the morbidity was high with loss of work as the population most affected belonged to the age group of >30 years. The virus is spreading to new areas in this part of the state, as there is no herd immunity to the virus. The *Aedes* mosquito is present in varying density in different regions of the state and may be a potential for the spread to other areas. In Indian setting, low socioeconomic conditions, overcrowding, and poor sanitary conditions facilitated by the presence

of the *Aedes* vector species contribute to the spread of the chikungunya virus to wider areas. Therefore, screening of chikungunya, dengue, and other arboviruses is necessary, because, although the clinical features are similar, the outcomes may vary.

The laboratory surveillance data from the national VRDL network indicated that one-fifth of the AFI patients investigated by VRDLs had chikungunya. Among the AFI patients investigated, CHIKV positivity was higher among patients ≥30 y of age and in the northern and eastern regions. CHIKV positivity was seen throughout the year, with a peak from September to December. During 2016–2018, the VRDLs diagnosed 28 CHIKV outbreaks. The IgM seropositivity to CHIKV found in the VRDL network was comparable to that from the NVBDCP. As per the NVBDCP, >150 000 suspected chikungunya cases were reported during 2015–2017, of which 26.5% were laboratory confirmed. The positivity during these 3 y was 12.1% in 2015, 41.2% in 2016 and 18.5% in 2017 (NVBDCP, 2018). The occurrence of cases across age groups indicates exposure to infected mosquitoes as well as susceptibility to infection among individuals of all age groups.

The higher CHIKV positivity from September to December observed in our analysis, overlapped with higher dengue positivity (Joshua, et. al., 2016), supports favourable environmental conditions for vector breeding during these months across different regions in India. Our analysis has certain limitations. First, medical colleges where VRDLs are located are tertiary care hospitals, serving large populations. As the precise estimates of populations served by these medical colleges were not available, we could not calculate the prevalence of infection. Instead, we calculated the proportion of positivity by using the number of patients tested as the denominator. Second, the data presented pertain to patients seeking care from selected sentinel sites, which are predominantly from urban areas and hence might not be representative of the entire country.

Conclusions

In conclusion, Chikungunya fever is self limiting; the morbidity can be very high in major outbreaks, resulting in a heavy social and economic tolls. The impact of chik outbreak in the affected areas on human health generally long lasting particularly with reference to prolonged arthralgia or joint pain,but also due to other associatedillnesses such as skin rashes etc.,

Our findings would contribute to establish an effective syndromic surveillance system for early detection and timely public health intervention of future chikungunya outbreaks in resource-limited settings like VRDLs. This was high in late monsoon and winter, suggests that it continues to be a major health problem in our setup and indicates the need of appropriate strategies to reduce the severity of disease.

Challenges for Future

Chikungunya infection is an important threat to mankind in view of the pronounced, long-lasting musculoskeletal morbidity and loss of productivity caused by it. A greater understanding of the pathogenesis and recognition of novel markers implicated in the viral persistence and progression of the disease into disabling arthritis is a realistic goal. Newer research avenues with the development of preventive strategies would go a long way to tackle this menace.

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