

Clinical profile of chikungunya fever in patients in a tertiary care centre in Maharashtra, India

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Background & objectives: In India a chikungunya fever outbreak started in December 2005 when the country experienced more than 13 lakhs of chikungunya infected cases. We undertook this study to study detailed clinical profile of chikungunya fever in both indoor and outdoor patients in a tertiary care hospital in Nagpur, Maharashtra in 2006.

Methods: Suspected cases of chikungunya fever (n=405) during the period of July to September 2006, having clinical triad of fever, arthralgia and/or rashes were included in the study. Clinical profile was studied in all the cases. Of the 405 samples collected, 166 were tested for serum CHIK IgM antibodies.

Results: Of the 166 samples tested for CHIKV IgM antibodies, 87 (52.4%) were positive (confirmed cases). Male: female ratio was 2.3:1. Fever and arthralgia were present in all cases. Rash was present in 27(31%) confirmed and 38(12%) suspected cases. Lymphadenopathy was present in 12 (13.8 %) confirmed and 4 of suspected cases. Chronic polyarthritis was seen in 22 (25.3%) confirmed and 75 (23.6%) suspected cases. Neurological manifestations were observed in 08 (9%) confirmed and 10(3.14%) suspected cases. Mortality was 7(2.2%) in 318 suspected cases and 3 (3.4%) in 87 confirmed cases.

Interpretation & conclusions: Our findings showed that about half of the serum samples for CHIKV IgM antibody tested positive from cases suspected to have chikungunya fever. Fever, joint pain and headache were major symptoms. Certain rare manifestations like lymphadenopathy, oral ulcers and encephalitis were also seen. Mortality in confirmed cases was about 3.4 per cent.

Key words CHIK IgM antibodies - chikungunya fever - epidemic - polyarthritis

Chikungunya fever outbreaks had affected many countries since January 2005. The outbreak occurred in 2006 appeared to be the more severe and one of the biggest outbreaks caused by chikungunya virus (CHIKV) in India affecting over 13 lakh people^{1,2}. This disease was first described in 1955, following an outbreak on the Makonde Plateau along the border of Tanganyika and Mozambique³.

Chikungunya virus is no stranger to the Indian subcontinent. Since its first isolation in Kolkata^{4,5} in 1963, there had been reports from different parts of India viz. Vellore⁶, Chennai⁷, Nagpur⁸, Barsi, Solapur District⁹. Since the last outbreak of chikungunya fever there had been hardly any active or passive surveillance carried out in our country suggesting disappearance of the virus from the subcontinent. However, large scale

outbreaks of fever caused by this virus in several States of India including Andhra Pradesh and Maharashtra have confirmed its re-emergence¹⁰.

Due to paucity of literature about detailed clinical profile and atypical manifestations of the CHIK fever, we carried out a study on diagnosing and analyzing various manifestations of chikungunya cases in a tertiary care hospital in Maharashtra State in 2006.

Material & Methods

In this descriptive study, a total of 405 suspected cases of chikungunya fever during the epidemic period of July to September 2006 were enrolled consecutively. These patients visited Medicine OPD (Outdoor) or admitted in Medicine wards (Indoor) at Indira Gandhi Government Medical College, Nagpur, (Maharashtra).

During these three months subjects having clinical triad of fever, arthralgia (joint pain) and rashes or presence of any two of the above three clinical features suggestive of chikungunya fever were included in the study for screening⁵.

Case definition¹¹:

Suspected case - An acute illness characterized by sudden onset of fever with one or many of the following symptoms: joint pain, headache, backache, photophobia, arthralgia, rashes, *etc.*

Probable case - Above features and positive serology when single serum sample was taken either in acute onset phase or during the convalescence.

Confirmed case - A confirmation was done by one of the following methods:

(i) Four-fold haemagglutination inhibitor (HI) antibody difference in paired sera; (ii) Detection of IgM antibodies against chikungunya virus (CHIKV IgM); (iii) Virus isolation from serum/body fluid; and (iv) Detection of chikungunya virus nucleic acid in sera by RT-PCR.

Detailed history was taken and clinical examination was carried out. After obtaining informed consent blood (8-10 ml) was withdrawn. Routine investigations (total leucocytes count, differential leucocytes count, platelets count, and haemoparasites in peripheral smear, liver function test) were done and detection of CHIKV IgM antibodies in serum by ELISA method was carried out in all subjects. Special investigation like Widal test, ASO titre, throat swab, blood culture, dengue specific IgM antibodies by IgM capture ELISA using DEN antigen,

leptospira antibodies by dry dot method using leptospira antigen were carried out, if and when required. These tests were done in our Microbiology Department. None of the suspected cases was positive for the above tests. For detection of CHIK virus IgM antibodies by ELISA serum samples were sent to National Institute of Virology (NIV), Pune.

Of the 405 cases, only 166 serum samples could be processed for CHIK IgM antibodies. This could be due to hundreds of blood samples reaching at NIV, Pune, during this period, so a few were randomly selected. Of the 166 tested, 87 were reported as IgM CHIK antibodies positive (confirmed cases) and the remaining 318 (suspected cases) were analyzed separately for detailed clinical profile. This included looking for rash (not only blanching), lymphadenopathy, number and type of joints affected, range of movements, oral cavity examination, bleeding tendency, detailed nervous system examination, cardiovascular, respiratory and abdominal examination, *etc.*

Results

There were 405 suspected chikungunya fever cases inclusive of 87 seropositive confirmed cases and 318 suspected cases. Maximum cases were seen in month of August 2006, (83.2%) (Table I).

In the confirmed chikungunya cases (n=87), (mean age \pm SD 26 \pm 11.7 yr range 13 to 70 yr, 60 per cent were in the age group of 20-30 yr and this age group was affected more than others. Male to female ratio was 2.3:1 (61males and 26 females). Fever with joint pain and headache were predominant symptoms while rash, oral ulcers and arthritis (joint pain and swelling) were prominent findings on clinical examination (Table II).

Rashes were generalized, erythematous, nonpruritic and maculopapular. Aphthous ulcers were present on oral mucosa and tongue. Persistent large and small joint arthritis was observed in 22 (25.28%) confirmed patients. Lymph nodes were enlarged in 12 (13.7%) and were tender with soft in consistency. Neurological manifestations were seen in 8 cases (9.2 %), encephalitis in 6(6.9%) and transverse myelitis in 2(2.2%). Six cases were labelled as encephalitis after excluding bacterial meningitis and metabolic causes. CSF analysis in these cases revealed a few lymphocytes. CSF was also sent for virology study at NIV, Pune. Computed tomography (CT) could be done in five cases of encephalitis of whom three did not show any abnormality, two had diffuse cerebral oedema.

Table I. Reported period of suspected chikungunya cases

Month(2006)	Outdoor cases	Indoor cases	Total (%)
July	05	03	08(2)
August	232	105	337(83.2)
September	33	27	60(14.8)
Total (%)	270(66.66)	135 (33.33)	405 (100)

Table II. Clinical profile of chikungunya cases (n=405)

Symptoms	No. of confirmed (n=87) cases (%)	No. of suspected (n=318) cases (%)
Fever	87 (100)	318 (100)
Joint pain	87 (100)	318 (100)
Headache	48 (55.17)	179 (56)
Rash	27 (31)	38 (12)
Oral ulcer	09 (10.34)	31 (10)
Lymph node enlargement	12 (13.7)	04 (1.25)
Altered consciousness	06 (6.8)	05 (1.5)
Bleeding tendencies	01 (1.1)	01 (0.3)
<i>Signs</i>		
Chronic polyarthritis	22 (25.28)	75 (23.5)
Rash (Maculopapular)	27 (31.03)	38 (12)
Cervical lymphadenopathy	08 (9.19)	04 (1.25)
Generalized lymphadenopathy	04 (4.5)	01 (0.3)
Oral ulcer /gingivitis	09 (10.34)	31 (10)
Encephalitis	06 (6.9)	05 (1.5)
Transverse myelitis	02 (2.2)	03 (0.7)
AIDP (GB syndrome)	Nil	02 (0.4)
Haemorrhagic manifestation	01 (1.1)	01 (0.3)

One case showed haemorrhagic manifestation in the form of upper gastrointestinal (GI) bleeding, cutaneous petechiae and coagulation abnormality. In these patients dengue specific IgM antibodies were not detected.

Twenty nine (33.3%) of the 87 cases required hospitalization while the remaining 58 (66.6%) were treated on OPD basis. Duration of hospital stay ranged from 2 to 15 days (04±2.01days).

Haematological investigations revealed lymphocytosis in 50 per cent cases. Total leukocytes count did not show significant abnormality. Thrombocytopenia was seen in 16(18.39%) cases. Platelet count was in the range of 35,000 -1, 00,000/ μ l in these cases. Radiological screening of joints did not reveal any significant abnormality in 22 chronic polyarthritis cases.

Mortality occurred in three (3.4%) confirmed cases. Two cases were of encephalitis and one had haemorrhagic manifestations.

Clinical profile of 318 suspected cases of chikungunya fever was similar to those of confirmed cases. (Table II) Only one patient had bleeding manifestations, platelet count in this case was 35,000/ mm^3 . Seven (2.2%) of the 318 suspected cases died; six had neurological manifestation and one haemorrhagic manifestation.

A 90 days follow up was done in 22 confirmed cases having persistent polyarthritis. These cases were on different drugs like ibuprofen, paracetamol, diclofenac, chloroquine, hydroxychloroquin and steroids. Only half of these cases showed improvement in the form of subsidence of joint pain, swelling and restoration of normal range of movement. Mean (\pm SD) duration required for improvement was 41.81±8.73 days. Response to any particular drug was not assessed.

Discussion

Amongst a total of 13,64,135 suspected chikungunya fever cases reported from various States; 2, 63,268 (19.29%) were from Maharashtra (until 26-10-2006)^{1,2}. Overall, 14465 samples were sent to NIV, Pune or National Institute of Communicable Diseases, (NICD), New Delhi and 1674 (11.5%) were confirmed. Of the 5040 samples sent from Maharashtra, 679 (13.5%) were confirmed.

In the present study sero-positivity was 52.4 per cent, 87 were IgM antibody positive out of 166 tested samples. More than 63 per cent cases were \leq 30 years of age. A serosurvey conducted at Calcutta (now Kolkata)¹⁰ a decade ago revealed that only 4.37 per cent of the serum samples were positive for chikungunya antibodies with highest seropositivity rate in age group of 51-55 yr and none detected in younger population. These findings probably suggest that there is indeed a lack of herd immunity to chikungunya virus. This lack of herd immunity in younger population probably account for affection of younger patients (\leq 30 yr) than elderly ($>$ 50 yr) patients (12%) in our study.

In the present study maximum cases were reported in the month of August. Duration of hospital stay ranged from 2 to 15 days. No similar data are available to compare these results. The main clinical features in the present study were lymphadenopathy and oral ulcers which have been rarely reported earlier in literature.

Chronic polyarthritis was observed in about one fourth of confirmed and suspected cases. Brighton reported in chronic joint symptoms 12 per cent of patients with Chikungunya virus infection, and 50

per cent patients improved with chloroquin phosphate treatment¹².

Neurological manifestations are not commonly observed in patients with chikungunya fever, but in the present study 9 per cent cases presented with encephalitis and transverse myelitis.

No State or central government has officially declared any deaths caused by chikungunya except for Gujarat¹³, where 11(4.8%) deaths out of 225 laboratory confirmed cases of the virus had been reported. Although the Kerala State government reported 74 deaths, the central government team investigated 56 of these and concluded that they were not caused by chikungunya virus¹³. Reunion Island of Indian Ocean reported 2,66,000 cases and 237 confirmed deaths with cases fatality rate 1/1000, which included cases of nervous system involvement and hepatitis. In the present study mortality was 3.5 per cent and was observed only in cases with encephalitis and haemorrhagic manifestation. CT scan head showed diffuse cerebral oedema in two cases. Postmortem examination was done in one suspected case which showed brain oedema. CHIK virus could be isolated from CSF of one confirmed encephalitis case but not from serum. IgM antibody against CHIKV was absent in serum as well as CSF. In another case virus could be isolated from serum but not from CSF. PCR and IgM antibody were negative both in serum and CSF. Of the above two cases one died and another recovered; this will help us in studying and understanding in more details about the neuro-trophism and more virulence of chikungunya virus strain.

In conclusion, 52.4 per cent seropositivity for CHIK IgM antibodies was found in the present study. Younger patients were affected more than elderly. Rare manifestations of chikungunya in present study were lymphadenopathy, oral ulcers as well as the neurological manifestations like encephalitis and transverse myelitis. Our study had certain limitations. Only 166 out of 405 serum samples were processed for CHIK IgM antibodies at NIV, Pune. These could be under-reporting also as those who came prior to our study were not included in the official reporting that started later. Blood counts were not repeated. Paired second serum samples in convalescent phase were not sent and tested for IgM antibody. Yergolkar *et al*¹⁴ reported that 9 cases turned positive for IgM CHIKV antibodies, which were negative during acute phase Follow up could be done only in 22 cases with chronic polyarthritis up to 3 months only.

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