Original Article

Emergence of Chikungunya infection in North India

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ABSTRACT

Background: Since re-emergence of chikungunya virus (CHIKV) infection in Indian subcontinent in 2005, it has become a major public health threat. Because of paucity of literature from north India, we undertook this study to determine incidence of Chikungunya infection and to assess clinical spectrum of disease.

Methods: 248 clinically suspected cases of CHIKV were enrolled. IgM ELISA for CHIKV was done on all samples. RT- PCR for CHIKV was performed on 53 selected samples.

Result: Thirty samples were positive for CHIKV IgM Ab of total 248 suspected cases. Of 53 samples tested by RT-PCR, 17 were found to be positive. Majority of the confirmed cases were in age group 21-40 yrs. Male: female ratio was 1.38:1. The most common clinical features were fever with joint pain and rash. Apthous ulcers were seen in 36% and arthritis was seen in 25% of the confirmed cases. Lymph nodes were enlarged in 16% and hemorrhagic manifestations were seen in 15.9% of the positive cases. Neurological involvement was present in 7 of the CHIKV infected cases and was more common in young children. Case fatality rate amongst CHIKV infected was 4.5% (2/248, both children).

Conclusion: CHIKV IgM positivity of 12% was seen in the present study. Largest proportion of confirmed cases was in the age group 21-40 years. Neurological manifestations were present in 7 of CHIKV confirmed cases, five being children. Mortality in confirmed cases was 4.5%. The increased severity of illnesss & high case fatality rate among children demands for a more detailed understanding of the neurotropism & needs to be analysed in detail.

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Introduction

Chikungunya (CHIKV) fever is a re-emerging viral disease characterized by abrupt onset of fever, skin rash and incapacitating arthralgia. [1] Chikungunya virus (CHIKV) is a RNA virus belonging to genus Alphavirus and family Togaviridae. Chikungunya fever outbreaks have been affecting many countries since January 2005. The outbreak which occurred in 2006 appeared to be more severe and one of the biggest outbreaks caused by CHIKV in India affecting over 13 lakh people.[2][3] This disease was first described in 1955, following an outbreak on the Makonde Plateau along the border of Tanganyika and Mozambique.[4]

Chikungunya virus is no stranger to the Indian subcontinent. Since its first isolation in Kolkata in 1963, [5][6] Recently CHIKV resurfaced in India affecting several South Indian states. [7][8] The outbreak started in 2005 from the coastal regions of Andhra Pradesh and Karnataka. With more than 1.3 million people estimated to be affected CHIKV prevailed across 150 districts of 8 states in India. [9] Despite the number estimated, the actual disease burden was thought to be much higher due to potential underestimation from lack of accurate reporting.[10]

Due to paucity of literature about incidence, clinical profile, atypical manifestations and complications of the Chikungunya from Northern India we carried out a study on diagnosing and analyzing various manifestations of Chikungunya cases at KGMU & SGPGIMS, two main tertiary care hospitals in Lucknow, Uttar Pradesh State from September 2010- August 2011.

Materials And Methods

In this prospective study, the study population comprised of all suspected cases (as per NICD, New Delhi) which included patients with an acute illness characterized by sudden onset of fever with one or more of the following symptoms: joint pain, headache, backache photophobia, arthralgia, rash visiting out/inpatient department of Paediatrics, Medicine and Rheumatology at our institute during the period of September 2010-August 2011.

Detailed history was taken and clinical examination was carried out. After obtaining informed consent, blood (3-5 ml) was collected in plain serum vials. Routine investigations (total leucocytes count, differential leucocytes count, platelets count and haemoparasites in peripheral smear) were done. Confirmation of cases was carried out by detection of CHIKV IgM antibodies in serum using IgM Antibody capture ELISA Kit (NIV, Pune, India). Reverse Transcriptase PCR was also performed on 53 selected samples as per Hasebe *et al*(2002). Chikungunya strain TND/SGPGI/2007/01 from Department of Microbiology, SGPGIMS, Lucknow served as the positive control.

Special investigations like IgM ELISA for Dengue (IVD Research Inc. Quality Diagnostics, USA) IgM ELISA for JE (Xcyton Diagnostics, Bangalore, India), smears and Optimal test (Diamed, USA) for malarial parasite, Widal test (In- house) and Typhidot test (SD Biodiagnostics, Korea) for typhoid fever were carried out as requested by the concerning clinician.

Statistical Analysis: Data were entered in an excel file and analyzed using Stata 9.2 (College Station Tx, USA). Clinical and epidemiological features were compared between Chikungunya positives and negatives using bivariate analysis. $p<0.05$ was taken as significant.

Result

A total of 248 patients presented with clinical suspicion of Chikungunya from September 2010 to August 2011. IgM ELISA (NIV, Pune) for Chikungunya was done on all the 248 serum samples of which 30 were IgM positive. RT-PCR was done on 53 selected samples (45 IgM negative and 8 IgM positive) of which 17 were positive. Three of these were IgM positive as well & so a total of 44 cases were considered as Chikungunya infected.

Majority of Chikungunya cases (suspected as well as positive) occurred in the months of September-December (71.8%) (Table 1). Largest proportion of suspects was in the age group 21-40 years (Fig 1). Amongst Chikungunya confirmed cases, majority (40%) hailed to the age group 21-40 years. Male: female ratio was 1.38:1 in CHIKV confirmed cases and majority of the positive cases (61.3%) were from urban areas, maximum (47.7%) being reported from Lucknow district.

The most common clinical features seen in CHIKV infected patients were fever with joint pain and rash. (Table2) Rashes were generalized, erythematous and maculopapular. Aphthous ulcers present on oral mucosa and tongue were seen in 36% of CHIKV confirmed cases. Arthritis mainly involving joints of lower limbs was seen in 25% of the confirmed cases. Lymph nodes were enlarged in 16% and hemorrhagic manifestations were seen in 15.9% of the positive cases. Neurological involvement with encephalitis and seizures was present in 7 of the CHIKV infected cases. CSF analysis in these cases revealed predominantly lymphocytes. Proportion of neurological involvement was more common in young children as of these 7 cases, five were children. On bivariate analysis, involvement of elbow, wrist and hip joint, rash, conjunctival congestion and photophobia were found to have significant association with CHIKV infection positivity as shown in Table 2.

Hematological investigations revealed lymphocytosis in 52% of confirmed cases. Total leukocyte count did not show any significant abnormality. Thrombocytopenia was

seen in 7(16%) cases. Platelet count was in the range of 25,000 -80000/µl in these cases.

Case fatality rate amongst CHIKV infected was found to be 4.5% (2/44), which was slightly higher as compared to Chikungunya negative patients. Both the cases belonged to paediatric age group were 3 & 7 years of age respectively. They had neurological manifestations comprising of encephalitis and seizures & were CHIKV RT-PCR positive. They were tested for other possible etiologies including J.E., Dengue and Malaria and turned out to be negative for them.

All the 44 CHIKV infected cases were tested for DENV by IgM ELISA. Out of total 44 confirmed Chikungunya cases 16 (36.4%) turned out to be positive for Dengue IgM. JE IgM was done in 20 of the 44 CHIKV infected cases and 4 (20%) were positive. Smear & Optimal test for malaria was done in 41 cases and 3 (7.3%) were positive for *Plasmodium falciparum*.

Table 1: Month wise Distribution of clinically suspected and positive cases of Chikugunya.

Month & Year	Clinically suspected cases (n=248)	Positive cases (n=44)	% positivity
September 2010	1	1	100
October 2010	90	28	31
November 2010	50	8	16
December 2010	37	4	10.8
January 2011	10	0	0
February 2011	9	0	0
March 2011	2	0	0
April 2011	4	0	0
May 2011	5	0	0
June 2011	14	1	7.1
July 2011	12	1	8.3
August 2011	14	1	7.1
Total	**248**	**44**	

Table 2: Comparison of clinical and demographic features at initial presentation of Positive and Negative cases (n=248).

Variable	Negative (n=204)		Positive (n=44)		OR (95% CI)	p-value
	N	Mean±SD or n (%)	N	Mean±SD or n (%)		
History						
Seasonal variability (Sep-Nov vs Dec-August)	204	138:66	44	41:3	1.241 (1.129-1.364)	0.001
Sex ratio: Female:Male	204	73:131	44	31/13	1.050 (0.934-1.179)	0.430
Fever	204	204 (100)	44	44 (100)	1.039 (0.917-1.177)	0.562
Joint Pain/Arthralgia	197	175 (88.8)	41	39 (95.1)	1.121 (0.978-1.285)	0.224
Joint swelling	202	28 (13.9)	44	11 (25.0)	1.171 (0.953-1.438)	0.067
Headache	197	183 (92.9)	41	35 (85.4)	0.834 (0.662-1.117)	0.114
Rash	204	85 (41.7)	44	25 (56.8)	1.116 (0.988-1.260)	0.046
Lymphadenopathy	204	24 (11.8)	44	7 (15.9)	1.071 (0.878-1.308)	0.451
Aphthous ulcers	204	48 (23.5)	44	16 (36.5)	1.130 (0.969-1.319)	0.078
Pruritis	204	19 (9.3)	44	8 (18.2)	1.190 (0.925-1.530)	0.087

Variable	Negative (n=204)		Positive (n=44)		OR (95% CI)	p-value
	N	Mean±SD or n (%)	N	Mean±SD or n (%)		
Conjunctival congestion	204	56 (27.5)	44	21 (47.7)	1.190 (1.025-1.381)	0.008
Photophobia	202	13 (6.4)	43	7 (16.3)	1.292 (0.932-1.791)	0.032
Haemorrhagic manifestation	204	35 (17.2)	44	7 (15.9)	0.984 (0.848-1.143)	0.841
Altered sensorium	184	58 (31.5)	41	10 (24.4)	0.941 (0.830-1.067)	0.369
Seizures	188	22 (11.7)	42	7 (16.7)	1.089 (0.878-1.350)	0.381
Encephalitis	188	18 (9.6)	42	7 (16.7)	1.152 (0.895-1.482)	0.182
JOINTS INVOLVED						
Elbow	170	42 (24.7)	40	22 (55.0)	1.336 (1.108-1.611)	<0.001
Knee	170	165 (97.1)	40	37 (92.5)	0.765 (0.466-1.314)	0.175
Shoulder	170	15 (8.8)	40	3 (7.5)	0.969 (0.779-1.205)	0.788
Wrist	170	20 (11.8)	40	19 (47.5)	1.711 (1.253-2.335)	<0.001
Ankle	170	110 (64.7)	40	28 (70)	1.045 (0.915-1.194)	0.526
Hip	170	35 (20.6)	40	2 (5)	0.825 (0.739-0.921)	0.020
Metacarpophalangeal	170	2 (1.2)	40	2 (5)	1.631 (0.611-4.355)	0.111

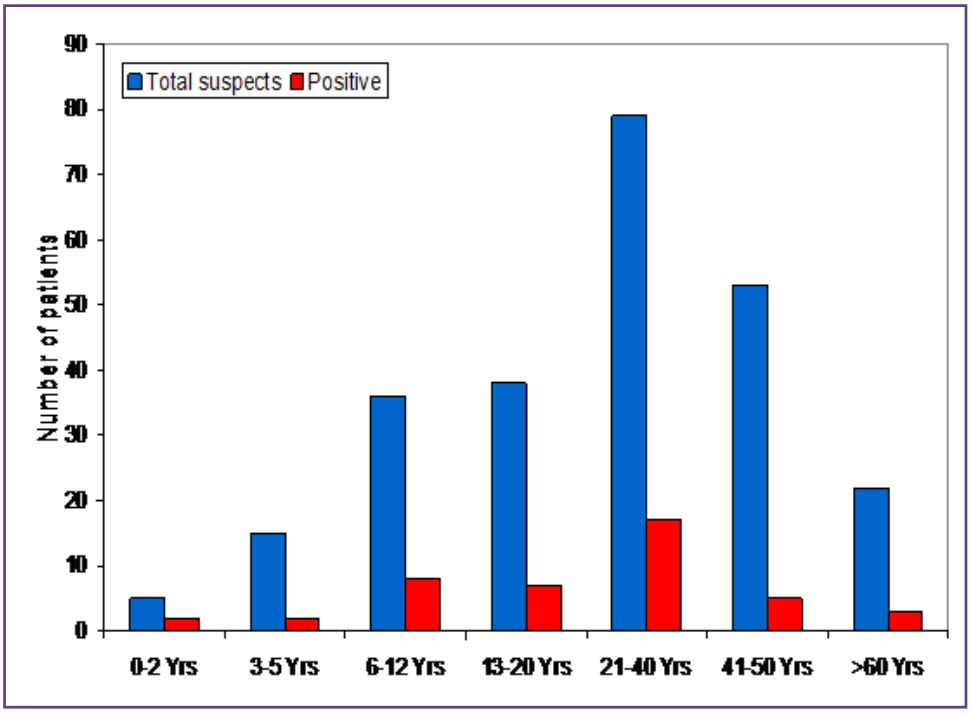

Fig:1 Age wise Distribution of clinically suspected and positive cases of Chikungunya.

Discussion

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, Kerela, Tamilnadu, and Maharashtra have confirmed its re-emergence. [11][13] [14] At present, Chikungunya has become an important health concern in India. For treatment and prevention, a detailed understanding of epidemiology and pathogenesis is required. Furthermore, it is important to have the information regarding the prevalence rate of chikungunya infection and course of the disease.

In the present study, Chikungunya IgM positivity was found to be 12%. 17 of the 53 tested samples were positive by RT-PCR. . Largest proportion of suspects and confirmed cases were in the age group of 21-40 years. Movement of people outdoors during daytime when the activity of mosquito vector is at its peak, lesser personal protection (towards mosquitoes) and individual's different immune response to disease are some of the speculative reasons for increased CHIKV positivity seen in this age group.[15]

In the present study majority of Chikungunya suspected and positive cases occurred in the months of September-December (71.8%) which can be explained by the high vector density in the post monsoon period. Majority of the positive cases (61.3%) were from urban areas. Most of the previous outbreaks in India were also found to be confined mainly to urban areas and large cities. This can be attributed to *A aegypti* being the dominant CHIKV vector in India which has a strong predilection for urban and semi-urban environments.

The main clinical features in the present study were fever with joint pain, rash and apthous ulcers. Lymphadenopathy and hemorrhagic manifestation were also seen in 16% of the cases. In our study neurological involvement with encephalitis and seizures was present in 7 of CHIKV infected cases, of which 5 were children. Also the severity of infection in CHIKV infected children was quite high, terminating in death in 2 of the positive cases. Our study strongly supports CHIKV to be an important cause of neurological disorders in children and that clinicians should be aware of the fact that CHIKV may be a cause of CNS infections in children.

No State or central government has officially declared any deaths caused by chikungunya except for Gujarat, 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 virus. [16] In the present study, case fatality rate amongst CHIKV infected was found to be 4.5% (2/44), which is slightly higher as compared to Chikungunya negative patients. Both the cases had neurological involvement and were 3 &7 years of age. The high case fatality rate among children is a serious and unusual finding and demands for a more detailed understanding of the neurotropism and virulence of CHIKV.

In our study, 36.4% of the CHIKV positive patients tested positive for Dengue IgM. This can be attributed to either coinfection or dual infection. In Asia, the CHIKV-affected areas overlap with DENV-epidemic areas and provide opportunities for mosquitoes to become coinfected with both viruses resulting in significant coinfection.

Conclusion

CHIKV IgM positivity of 12% was seen in the present study. 17 of the 53 samples tested positive by RT-PCR. Largest proportions of confirmed cases were in the age group 21-40 years. Neurological manifestations were present in 7 of CHIKV confirmed cases, five being children. Mortality in confirmed cases was 4.5%. The increased severity of illness & high case fatality rate among children demands for a more detailed understanding of the neurotropism & needs to be analyzed in detail.

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Competing Interests

None Declared

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