

42 Clinical Profile of Chikungunya Fever

Abstract: Chikungunya is a rare form of viral fever caused by genus alpha virus in the family Togaviridae and transmitted to humans by the bite of *Aedes aegypti* mosquito. The present prospective study is undertaken with the aim of the clinical manifestations, course, complications and outcome of Chikungunya cases in Haroti region of Rajasthan state during the recent epidemic in India.

Method

This prospective study has been conducted in hospitalized and outdoor patients from August 2006 to January 2007. Hundred cases with positive Chik IgM rapid card test in the age group of 4 months to 84 years, comprising of 74 males and 26 females are included in the study group out of large number of clinically suspected cases with typical triad of fever, joint pain and rash. Cases are studied in detail and followed up for improvement and any permanent damage or death.

Observations

Detailed symptoms and signs observed are:

Fever (102°-103°F) for 4-5 days with other constitutional symptoms and joint pain involving knee, ankle, wrist, elbow, small joints of hands and feet on 1st or 2nd day of fever in all the cases. In dermatological symptoms and signs, we observed pruritus (86%), facial erythema (82%), bilateral lymphedema (65%), maculopapular rash (22%), aphthous like ulcers (11%) and lymphadenopathy (3%). Conjunctival injection (15%), hematemesis/melena (4%), epistaxis (3%) and hematuria (3%) are the bleeding manifestations. Neurological symptoms and signs are noted in 27% of cases. They are in the form of altered level of consciousness (in 26 cases) [Confusion, drowsiness, delirium, psychosis], seizures (in 8 cases), motor paresis with diminished reflexes (in 6 cases), involuntary movements (in 4 cases), total blindness due to retrobulbar neuritis (in 2 cases), and coma (in 1 case). CSF examination of these cases shows increased cells (in 10 cases), raised protein (in 21 cases) whereas sugar is normal in all cases. CT scan brain is normal in 24 cases and abnormal in 2 cases [ring enhancing lesion (in 1 case) and multiple small hemorrhages with diffuse cerebral edema (in 1 case)].

In laboratory investigations, we observed anemia (67%), leukocytosis (15%), thrombocytopenia (31%), raised ESR (83%), positive CRP (87%), altered renal (58%) and liver functions (74%), microalbuminuria (66%), dyselectrolytemia (58%), malaria parasite (8%), dengue IgG (2%). Widal test and RA factor negative and Chik IgM antibody positive in all cases. Abnormal X-ray chest (3%) [Consolidation (2%), pleural effusion (1%)], USG abdomen shows hepatosplenomegaly (11%), pleural effusion (1%) and renal medical disease (3%).

In the final outcome, 94% cases improved completely, 2% cases had total blindness due to retro bulbar neuritis and 4% cases expired.

Conclusion

Fever and joint pain are the main presenting symptoms during this epidemic. Joint pains, maculopapular rash, bilateral lymph edema and absence of frank hemorrhage/shock are the main distinguishing features of Chikungunya fever from dengue fever. Increased morbidity is due to (a) electrolyte imbalance, (b) secondary infections, (c) neurological complications and increased mortality is observed in elderly person with associated systemic illnesses such as diabetes, hypertension and chronic renal failure.

INTRODUCTION

Chikungunya is a viral fever caused by RNA alpha virus in the family Togaviridae that is transmitted by the bite of infected *Aedes aegypti* mosquito. The name is derived from the Makonde word meaning “that which bends up” in reference to the stooped posture developed because of the arthritic symptoms of the disease. Chikungunya fever affects all age groups and both sexes are equally affected. The incubation period ranges from 3-12 days (usually 3-7 days). In susceptible population, Chikungunya fever can have attack rates as high as 40 to 85 percent.¹ CHIK-V is geographically distributed in Africa, India, and South-East Asia. In Africa, the virus is maintained through a sylvatic transmission cycle between wild primates and mosquitoes such as *Aedes luteocephalus*, *A. furcifer*, or *A. taylor*.² In Asia, CHIK-V is transmitted from human to human mainly by *A. aegypti* and to a lesser extent by *A. albopictus* (Tiger mosquito).

The disease was first described by Marion Robinson and WHR Lumsden.³ In 1955, following an outbreak on the Makonde Plateau, along the border between Tanganyika and Mozambique in 1952. The first documented Asian outbreak was in Bangkok and Thailand in 1958. Chikungunya virus is not a stranger agent to the Indian subcontinent. Since its first isolation in Calcutta in 1963, there have been several reports of Chikungunya virus infection in different parts of India.⁴ CHIK-V has emerged in the islands of the southwestern Indian Ocean at the end of 2004. The most affected island is Reunion (total population: 770,000) with an estimated 244,000 cases (16 April 2006). In Reunion Island, this alpha virus has already infected about one-third of the human population. Large-scale outbreaks of fever caused by chikungunya virus infection in several parts of Southern India have confirmed the re-emergence of this virus.⁵ It has been estimated that over 1,80,000 cases have occurred in India since December 2005. Andhra Pradesh (AP) was the first state to report this disease in December 2005 and was one of the worst affected states (over 80,000-suspected cases). Tamil Nadu reportedly had the large number (77575) of cases in July 2006. Several districts of Karnataka state such as Gulbarga, Tumkur, Bidar, Raichur, and Bellary, Chitradurga, Davanagere, Kolar and Bijapur districts have also recorded large number of fever cases. Over 2000 cases of Chikungunya fever have also been reported from Malegaon town in Nasik district of Maharashtra state (India) between February-March 2006. Chikungunya is not considered to be fatal, however, 200 deaths in 2005-2006, have been associated with Chikungunya on Reunion island and a widespread outbreak in Southern India (especially in Tamil Nadu, Karnataka and Andhra Pradesh).

The precise reasons for the re-emergence of Chikungunya in the Indian subcontinent as well as the other small countries in the southern Indian Ocean are an enigma. Although, it is well recognized that re-emergence of viral infections are due to a variety of social, environmental, behavioral and biological changes, which of these contributed to the re-emergence of Chikungunya virus would be interesting to unravel.⁶

Clinical Features

Most often Chikungunya is a self-limiting febrile illness. The classical triad of fever in the range of 101°F- 103°F, arthralgia or arthritis affecting multiple joints and petechial or maculopapular rash usually involving the limbs and trunk are the characteristics symptoms of the disease. Other constitutional symptoms of chikungunya are headache, body ache, myalgia, anorexia, lethargy, photophobia and conjunctival injection. Symptoms are generally self-limiting and last 1-10 days. However, arthralgia may persist for months or years. In some patients, minor hemorrhagic signs such as epistaxis or gingivorrhagia have also been described.⁷

MATERIAL AND METHOD

The study is conducted in clinically suspected cases of Chikungunya who presented with an acute febrile illness characterized by high fever, crippling arthralgia/arthritis and a maculo-

popular rash. The study cases are taken from the medical outdoor and indoor of MBS hospital, Medical College Kota and private nursing homes of Kota city. These hospitals mainly drain the patient from various parts of Hadoti region of Rajasthan namely Kota, Baran, Bundi, Jhalawar. Clinically suspected cases are subjected to Chikungunya IgM antibody card test.⁸ Cases with positive card test are included in the study group and cases with negative card test are excluded.

Chikungunya IgM antibody positive cases are subjected to detailed history, clinical examination, routine investigations and other supportive lab tests. SGOT, CRP, total platelets count done in all cases. EEG, CT scan head, CSF examination is done in patients showing neurological symptoms and signs. Cases are also investigated for other febrile illness such as malaria, dengue and typhoid fever. Seriously, ill patients are admitted in various hospitals of Kota city and followed up in wards. Patients with mild form of disease are examined and followed up in outdoor.

Chikungunya IgM Card test (from CTK Biotech): It is the onsite Chikungunya IgM rapid test that is a lateral flow chromatographic immunoassay for the qualitative detection of IgM anti-Chikungunya virus "Chik-V" in the human serum or plasma. It is a screening test. The onsite Chikungunya IgM rapid card test is an IgM capture immunoassay, utilizing recombinant antigen derived from its structural protein. It detects IgM anti Chikungunya in patient's serum or plasma within 10 minutes. There are few limitations of this card test:

1. Failure to follow the procedure closely may give inaccurate result.
2. A negative result indicates either absence or low titer of IgM antibodies but does not preclude the possibility of exposure to Chikungunya infection.
3. The results obtained with this test should be interpreted in conjunction with other diagnostic procedures and clinical findings.

RESULTS

Hundred cases in the age group (4 months-84 years) are studied during this Chikungunya epidemic (August 2006-January 2007) in the Haroti region (Kota, Baran, Bundi and Jhalawar) of Rajasthan state. Patients who complained of fever, joint pains and skin eruption, are investigated for Chikungunya IgM antibody and those showed positive Chikungunya IgM antibody test, are included in the study group. Cases are taken from OPDs as well as indoors. The study group is composed of 74 males and 26 females. Detailed signs and symptoms observed in the cases are as follow:

Fever and other constitutional symptoms: In the majority of the cases, the onset of fever is abrupt and associated with chills and joint pains. Fever is moderate (100-103°F) for first 4-5 days, there after; became mild (99-100°F) for next 3-4 days. Two cases remained febrile with temperature of >103°F for more than 7 days All the cases have associated headache, body ache, lethargy, insomnia and anorexia with fever. Duration and range of temperature is shown in Table 1.

Musculoskeletal symptoms/signs: The most striking complaint with fever is joint pains, which is sudden in onset, moderate to severe in severity and has affected more than one joint at a time. The joints involved in order of severity and preference are knee, ankle, wrist, small joints of hand and feet and elbow. Because of severe pains, the most of the cases are confined to bed on 1st or 2nd day of fever and 10 cases developed characteristic stooped flexed posture. Sixty-five cases have joint swelling around knee and ankle. Various musculoskeletal symptoms and signs are shown in Table 2. Predominance of affected joints is shown in Table 3, Dermatological manifestations in Table 4 and Bleeding manifestations in Table 5.

Neurological symptoms/signs: Occurrence of neurological symptoms and signs in Chikungunya cases are observed early in the course of disease on 2nd or 3rd day of fever. Various neurological symptoms and signs are shown in Table 6. Final outcomes of the study cases are shown in Table 7.

Laboratory investigations: All the cases are investigated in detail for complete blood counts, clotting time, bleeding time, Hb, ESR, blood sugar, CRP, electrolytes, urine complete, MP, widal, renal function tests, liver function test, Chik-IgM card test, dengue IgM and IgG antibody test, ultrasound of abdomen and pleural space, X-ray chest PA view, ECG, CT scan head, EEG, CSF analysis and HLA-B27 in 02 cases. Various laboratory parameters are shown in Table 8.

Sixty-seven cases have hemoglobin <12 gm%, four cases showed thrombocytopenia (<50,000 platelets), ESR is raised in 83 cases, CRP is positive in 87 cases. They are positive for Chikungunya IgM antibody. Eight cases are positive for malaria parasite, 02 are positive for dengue IgG. All cases are negative for Widal test, RA factor. Hyponatremia is found in 58 cases and hypokalemia in 19 cases. One of the case has severe hypokalemia (< 1.9 mEq/L). Blood urea is raised in 38 cases (> 45mg/dl) and s. creatinine is raised in 20 cases (> 1.5 mg/dl). Urine examination shows pus cell (3%), blood/RBCs (6%) and microalbuminuria (66%). X-ray chest PA view of 02 cases showed consolidation, in 01 case it showed minimal right sided pleural effusion and 03 cases have prominent bronchovascular markings. Ultrasonography of abdomen shows mild hepatosplenomegaly in 11 cases, right sided pleural effusion in 01 case and early renal medical disease in 03 cases. CT scan of head is done in 26 cases those have altered level consciousness. It is normal in 24 cases. CT scan head of two cases have shown following abnormality—Multiple small hemorrhages with diffuse cerebral edema in one case and ring-enhancing lesion in left basal ganglia region in other case. ECG and EEG are normal. MRI and EMGNC were not done.

DISCUSSION

Alpha viruses are known to give rise to a spectrum of diseases in humans ranging from silent asymptomatic infections, undifferentiated febrile illness to devastating encephalitis.⁹ Chikungunya virus, belonging to same genus is causing current epidemic with spectrum of diseases ranging from a self-limiting febrile illness to crippling acute and lingering arthritis and other complications.

Popular and readily diagnosable mosquito born diseases such as malaria and dengue fever are reportable diseases for which free tests are available in the government institutions, so that their magnitude can be assessed. However, present mosquito born disease “Chikungunya fever” is not a reportable disease and timely unavailability of the tests for confirmation of the diagnosis underestimated the affected number of population but this is definitely true that the disease in southern states and in our state was more rampant than malaria and dengue fever during the “Chikungunya season.” Chikungunya disease, which was not even known and read by many doctors and medical personnel, suddenly became popular in the community in affected states of India. Multiple cases in the same family are so common that it is doubtful whether there is any single affected family where it left off without affecting more than one member. The prototypic clinical picture in more than one/whole family members is a triad of fever, joint pain and rash. Exclusion of other common causes of arthritis such as rheumatic, rheumatoid, viral and acute bacterial arthritis and supportive lab tests strongly support the diagnosis of Chikungunya fever in the study cases. In present study, the diagnosis is confirmed by positive chik IgM card test.⁸ The cost of card test is a major limiting factor and so could not be employed for screening the whole affected population. Rapid card tests are the useful assay techniques for detection of IgM antibodies against any infectious agent without any additional requirement of instrumentation. Virus isolation, polymerase chain reaction (PCR) and ELISA are the confirmatory tests, but have their own limitations to perform at point of care and are not cost effective commercially.

The onset of disease is characteristically sudden and sharp, to the degree that the patients frequently report the hour of becoming aware of illness in the present study. Fever and joint pain are the main presenting symptoms during this epidemic. Fever is moderate (100-103°F) for first 4-5 days, there after became mild (99-100°F) for next 3-4 days (Table 1). This pattern of fever is also supported by the studies carried out during an epidemic of a febrile illness in Calcutta 1963 by

Parvi KM et al.¹⁰ All the cases have associated headache, bodyache, lethargy, insomnia and anorexia. Severity and duration of the fever observed in the study cases is slightly different as seen in the cases of dengue fever in which high-grade fever persists for more than 5-7 days. Constitutional symptoms such as headache, myalgia, cough, rhinitis and anorexia are more predominant in Chikungunya fever.

Because of severe pains, the most of the cases are confined to bed on 1st or 2nd day of fever and 10% cases developed characteristic stooped flexed posture. This observation is supported by a study of clinical impression of Chikungunya fever in Vellore (1964), conducted by De Ranitz CM et al.¹¹ Sixty-five (65%) cases have joint swelling around knee and ankle. On follow-up, 5% cases showed mild arthralgia at 6 month. Severe arthritis with periodic reoccurrence of arthralgia for the period of as long as six months has been reported. Severity, character, duration and associated joint swelling are the characteristic features of Chikungunya, which are not so common in dengue fever.

Macules/maculopapular rash, pruritus, bilateral lymphedema, and facial erythema/pigmentation are the main dermatological symptoms and signs in Chikungunya cases (Table 4). Rash appeared on 3rd-4th day of illness. It was most often macular type and spread over face, trunk, arms and legs. Most of the affected cases complained of itching. Dermatological manifestations observed in a recent outbreak of Chikungunya fever in Southern India are— maculopapular rash, nasal blotchy erythema, freckle-like pigmentation over centrofacial area, hyperpigmentation in photo distributed areas, bilateral/unilateral lymphoedema, multiple aphthous-like ulcers over scrotum and axilla.

Arbo viruses are known to cause viral encephalitis in many epidemics in the past. Chatterjee et al⁹ observed neurological complications in Calcutta (1963) in the form of LMN paraparesis, slurred speech and encephalitis. They did not perform CSF examination. Neurological complications were encountered during a clinical and pathological study on Chikungunya fever in Madras city in 1964, in the form of external ophthalmoplegia, polyneuropathy and transient slurring of speech (by Thiruvengadam et al).¹² In 15 cases (out of 2424 seropositive), meningoencephalitis has been reported in Chikungunya outbreak in Reunion island from March 2005- January 2006.¹³ In our study, 27 cases have shown the affection of CNS at various levels in the form of encephalitis (in 20 cases), encephalomyelitis (in 04 cases), optic neuritis (in 02 cases) and hypokalemic paralysis (in 01 case).

Laboratory Investigations

All the cases are positive for Chik-IgM antibody. Mild anemia, thrombocytopenia, raised ESR, positive CRP and mildly deranged renal and liver functions are noted in the study cases. All cases are negative for widal and RA factor, malaria parasite seen in 8 cases and dengue IgM/IgG positive in 2 cases. Urine examination shows microalbuminuria. A clinicopathological study on Chikungunya fever in Madras city in 1964 conducted by Thiruvengadam et al¹² and they found leukopenia (12%), leukocytosis (49%), thrombocytopenia (6%) and raised ESR >25 mm in 1 hour (40%).

No vaccine or specific antiviral treatment for Chikungunya fever is available. All the cases are treated symptomatically -rest, oral (ORS) or intravenous fluids, and non-steroidal anti-inflammatory drugs (ibuprofen, naproxen, acetaminophen, or paracetamol) which relieve the symptoms of fever and aching. Aspirin and steroids are avoided during the acute stages of the illness as to decrease the risk of gastrointestinal bleeding. One case with severe hypokalemia is treated with injection KCL (80 mEq) infusion in 5% dextrose drip. Serious cases those required ventilator support and monitoring are managed in ICU. Infected persons are advised to protect themselves from further mosquito exposure (staying indoors and/or under a mosquito net during the first few days of illness) so that they cannot contribute to the transmission cycle.

The causes of increased morbidity in Chikungunya fever are severe dehydration, electrolyte imbalance, loss of glycemic control and articular involvement.¹ Recovery is the rule except for about 3-5% incidence of prolonged arthritis. In our study, cases the neurological complications lead to prolonged hospitalization and secondary complications in form of electrolytes imbalance (55%), secondary infection (69%), bedsores (4%), urinary tract infection (3%), altered renal parameters (58%) and aspiration pneumonia (2%). On the follow-up 5%, cases are found to be suffering from mild to moderate arthritis at 6 months of period.

Ninety four cases improved and discharged with mild to moderate joint pain, one case did not improve and left the hospital against medical advise with paraplegia and expired, two cases had blindness due to retrobulbar optic neuritis and four cases died (Table 7). No case perse died of electrolyte imbalance or altered renal parameters as they are mildly deranged and corrected accordingly. Old persons with associated systemic illness like diabetes, hypertension, renal disease are more often succumbed to disease because of secondary infections and complications. In the study of Rao AR,¹⁴ the mortality rate was 0.42% and it was highest in the infants under 1 year with 2.8% and in the old over 50 years with 1.6%.

CONCLUSION

1. Chikungunya epidemic in the Haroti region of Rajasthan state (from July 2006 – January 2007) presented with fever and joint pain, which leads to characteristic stooped posture. Other associated symptoms and signs are myalgia, maculopapular rash, bilateral lymphedema, leukopenia and thrombocytopenia.
2. Regarding to age and sex there is slightly greater preponderance of males (2.8 M: 1 F) in older age (48%) group.
3. Duration of fever is 5-7 days.
4. It has affected more than one joint simultaneously and has greater preference to the larger joints of the body. Knee and ankle joints were predominantly affected. The affected joints show the signs of arthritis in 65% cases.
5. Maculopapular rash, generalized pruritus, bilateral lymphedema and facial erythema were the main dermatological features.
6. There is no frank hemorrhage in spite of severe thrombocytopenia in four cases.
7. Increased morbidity is due to (a) electrolyte imbalance, (b) secondary infections, (c) neurological complications.
8. Increased mortality is observed in elderly person with associated systemic illnesses such as diabetes, hypertension and chronic renal failure.

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MULTIPLE CHOICE QUESTIONS

- 1. Chikungunya disease was first described by?**
 - A. Robinson
 - B. Lumsden
 - C. De Ranitz CM
 - D. A and B
- 2. Alpha virus causing Chikungunya disease is:**
 - A. α RNA
 - B. ds DNA
 - C. ss DNA
 - D. None of above
- 3. Chikungunya name is derived from the 'Makonde' word that means:**
 - A. Bends up
 - B. Stands up
 - C. Gets up
 - D. None of above
- 4. Vector of Chikungunya fever is.**
 - A. Culex mosquito
 - B. Anopheles mosquito
 - C. Mansonia mosquito
 - D. Aedes mosquito
- 5. Treatment of Chikungunya fever is:**
 - A. Antiviral drugs
 - B. Antibiotics
 - C. NSAIDs
 - D. Iron and folic acid
- 6. Typical triad of Chikungunya disease is, *except*:**
 - A. Fever, joint pain and rash
 - B. Joint pain, bleeding and jaundice
 - C. Rash, bleeding and shock
 - D. Pain abdomen, joint pain and rash
- 7. Incubation period of Chikungunya fever is:**
 - A. 3-12 days
 - B. 15-20 days
 - C. 21-25 days
 - D. 26-30 days
- 8. First outbreak of Chikungunya fever in India was reported in:**
 - A. 1963-64
 - B. 1971-72
 - C. 1999-2000
 - D. 2005-06
- 9. Chikungunya disease was first described in.**
 - A. 1952
 - B. 1955
 - C. 1958
 - D. 1963
- 10. Increased morbidity in Chikungunya fever cases is due to:**
 - A. Electrolyte imbalance
 - B. Secondary infections
 - C. Neurological complications
 - D. All of above