CHAPTER

27

Chikungunya - An Overview

M. Ganu, A. S. Ganu

Introduction

Chikungunya fever, a disease caused by chikungunya virus, was almost a forgotten disease until recently; when it reemerged in Indian ocean islands in 2005-2006. Within no time it acquired gigantic proportions affecting few million people in Asian countries, mainly India and Southeast Asian countries. Previously characterised as a self limiting disease, it appeared in more aggressive form during this epidemic. Most of the affected countries being favourite tourist destinations, there was a threat of spread of the disease globally.

The disease was responsible for severe morbidity during acute stage and caused systemic involvement including neurological complications. It also had long term impact on musculoskeletal system causing crippling arthritis in a few. Deaths were reported from several areas of the country causing panic among masses.

There were many factors responsible for rapid spread of the disease during this epidemic in India. These included paucity of knowledge about the natural history of the disease, environmental conditions favoring rapid spread of the vector, changed viral genome making it more aggressive and its introduction in immunologically naive population. In this scenario, early control of the epidemic was a challenge for the health care system. Lack of adequate facilities for continuous serveillance and unavailability of laboratory facilities for early diagnosis were major hurdles. Concurrent occurrence of other similar looking diseases like dengue fever made the diagnosis difficult. Non availability of vaccine for prevention and specific drugs for treatment compounded the problem.

At the field level, affection of the breadearner for family changed family economics. Explosive nature of disease with involvement of multiple(at times all) family members made nursing care difficult at home. Nonavailability of labor in affected areas during harvesting season had its impact on rural economy. Poultry industry was worst hit due to rumors of spread of the disease through consumption of infected chiken.

Epidemiology

Chikungunya is a specifically tropical disease[1,2] geographically restricted to Africa and Asia. The word chikungunya means bent up posture and is derived from Makonde language.[3] Chikungunya fever occurs in sporadic forms and large epidemics.[4] Epidemics of episodic fever, rash and polyarthritis resembling chikungunya fever have been recorded from India and elsewhere, as early as 1824,[5] however first virus isolation was done from man and mosquitoes during

Table 1 : Chikungunya epidemics by country , year and virus strains

Africa	
Tanzania	1952-53 (TA53- Ross-East African)
South Africa	1956;1975-77 (SA76-2123 East African)
Congo	1958 ;1999-2000
Zimbabwe	1959
Uganda	1958, 1968
Zambia	1962
Senegal	1966 (SE 66 PM2951-West African), 1982 (SE 37997-West African), 1996-97
Nigeria	1964, (NI 64 IBH 35-West African), 1969;1974
Angola	1970-71
Asia and Indian ocean islands	
Thailand	1958,; 1962 (TH 62 15561-Asian) ; 1995 (TH95 CO39295- West African), 1996-97
India	1963-64(IN63 Gibbs-Asian), 1973(IN73 PO731460-Asian); 2006(IN06-various-East African
Cambodia	1963
Vietnam	1963
Philippines	1968;1985-86 (PH85 H12483-Asian)
Sri Lanka	1965
Indonesia	1985 (ID85 RSU1-Asian); 2001-03
Malaysia	1998(Asian); 2006 (Asian)
Comoros islands	2005 (East African)
Maritius, Reunion islands	2005-06 (RE06 OPY1-East African)

* Adapted from--- Kalantri et al[7]

the epidemic that occurred in Makonde platue in Tanzania in 1952.[3,6] Between 1960-1982, outbreaks of chikungunya fever were reported from eastern, south eastern and western Africa and from Asia.

African epidemics occurred in people dwelling in the vicinity of forests through epizootic transmission cycles and were restricted to smaller geographic areas. In contrast,Asian epidemics occurred in people in rural and semiurban areas affecting large number of people.[7]

The first outbreak of chikungunya in Asia was reported from Thailand (1958), followed by various epidemics in different Asian countries including Malaysia (1999) and French Reunion islands in 2005.[8,9]

The first Indian outbreak occurred in 1964 in south India (Vellore, Chennai, Pondichery)[10,11] and was followed by epidemics in central India at Nagpur (1965) and Barsi (1973).[12,13]

Epidemiological studies reveal a distint cyclic pattern of chikungunya fever epidemics[5] in affected areas with interepidemic period of 7-8 years (which may extend upto 20 years). As per this characteristic epidemiological profile, chikungunya appeared in Indonesia in 1999 and reemerged in 2005-2006, in various Indian ocean islands (Comoros, Mauritius, Reunion islands, Sychelles)and in many South East Asian countries including India, after a gap of more than 20 years.[5]

Till Oct. 2006, according to Directorate General of Health Services, Ministry of Health and Family Welfare, Govt of India, chikungunya is reported from 213 districts from 15 states all over India, affecting about 1392027 persons.[14] This almost certainly is a gross underestimation, since govt health facilities were overwhelmed during the epidemic due to sheer number of patients and majority of the patients seeked medical help from private medical practitioners (qualified as well as unqualified). Ongoing chikungunya fever outbreaks have been reported by World Health Organisation till Oct 2006, in the following states of India: Andhra Pradesh, Andaman and Nikobar island, Tamilnadu, Karnataka, Gujrat, Madhya pradesh, and Kerala.[5]

A unit of the Ministry of Healthcare and Nutrition in Srilanka.[15] reported laboratory confirmed cases in various districts. Chikungunya fever outbreaks on the Indian Ocean islands of Mayotte, Mauritius, Reunion islands, and Sychelles that began in March 2005 are now on the wane.[15]

Chikungunya Fever Situation in the Country during 2006 (Prov.)

Sl. No.	State	No. of districts affected	Total fever cases/Suspected Chikungunya fever cases	No. of samples sent to NIV/ NICD	No. of confirmed cases	No. of deaths
1	Andhra Pradesh	23	77535	1224	248	0
2	Karnataka	27	762026	5000	298	0
3	Maharashtra	34	268333	5421	786	0
4	Tamil Nadu*	35	64802	648	116	0
5	Madhya Pradesh	21	60132	892	106	0
6	Gujarat	25	76012	1155	225	0
7	Kerala	14	70731	235	43	0
8	A&Nicobar	2	4469	0	0	0
9	GNCT of Delhi	12	560	560	67	0
10	Rajasthan	1	102	44	24	0
11	Pondicherry	1	542	52	9	0
12	Goa	2	287	75	2	0
13	Orissa	13	6461	171	34	0
14	West Bengal	1	-	21	21	0
15	Lakshadweep	2	35	6	6	0
	Total	**213**	**1392027**	**15504**	**1985**	**0**

* Out of total 40 Administrative districts.

Adapted from National Vector Borne Disease Control Programme, Directorate General of HealthServices , Ministry of Health and Family Welfare, Govt of India. , 8/23/2007 (14)

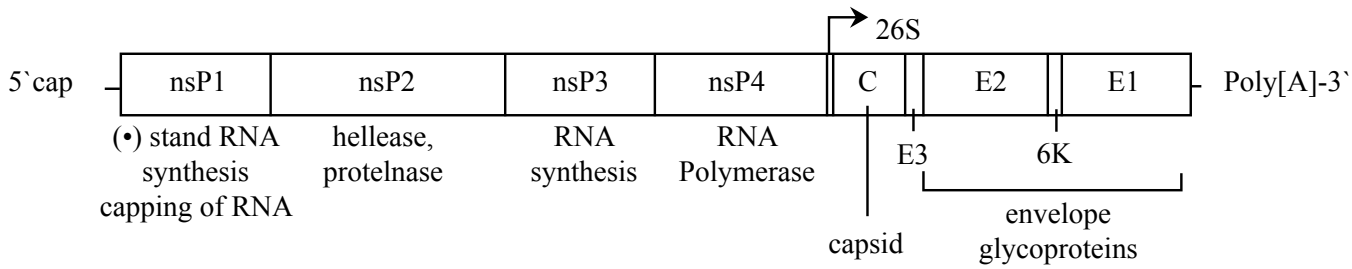
Vector

Chikungunya is transmitted through infected Aedes mosquito including Aedes albopictus and Aedes aegypti species and Ae. furcifer tylorie.[16,17] Aedes Albopictus (asian tiger mosquito) is considred to be the vector in Indian ocean islands however Ae. Egypti is the main vector in India.[18] Effective transmission of the virus depends on susceptibility of the vector, its breeding and biting habits and its availability in abundance in environment. Ae. aegypti is an efficient vector[19] because of its peculiar features like preference for human blood for feeding and daytime biting habits. Moreover, it is capable of biting several people in a short period of time for one blood meal and the bite is almost painless. It breeds in clean stagnant water i.e. household containers like tins, tyres earthenware pots, plastic containers, buckets, and cement tanks.[20]

Knowledge of mosquito dispersal is critical for understanding ways of pathogen dissemination. It helps to plan strategies for prevention and control for vector borne diseases. Studies have shown that Ae.aegypti disperse relatively short distances making it unlikely to spread the disease over large geographical areas.[21] It is thus obvious that movement of humans rather than mosquitoes is responsible for spread of the virus over a large area.

Susceptibility of mosquitoes and their ability to transmit the infection decides endemicity of the virus in a given area. Studies of susceptibility patterns of various strains of Aedes Aegypti and A. Albopictus show that regardless of the geographical location of the mosquito, infection rates were consistently higher in strains of Ae. Albopictus than Ae. Aegypti, making it a more competent vector for chikungunya virus.[22]

Figure 1 : Organization of the *Alfavirus* genome. Gene products and associated functions are indicated. Adapted from Khan et al[30]



Because chik fever epidemics are sustained through human – mosquito - human transmission, the epidemic cycle is similar to dengue and urban yellow fever.[23, 24]

Transmission Cycles

Major determinant of outbreak dynamics is the ecological cycle of the virus and its vector. Transmission cycles of different geographical genotypes of viruses are different.[25] Maintenance of sylvatic cycle involves wild primates and forest dwelling Ae. Aegypti mosquitoes, akin to the epidemiological cycle of yellow fever. It is characterised by circulation periodicity during which disease is transmitted to hosts and silent intervals lasting for about three years during which virus is maintained in primates.[26] In Asian countries, chikungunya virus transmission is characterised by the absence of an animal reservoir, and direct human to human transmission through peridomestic mosquitoes. This resembles cycle of Dengue fever and has potential for major epidemics.[24]

Other modes of transmission include vertical transmission of the virus in mosquitoes by gregarine parasites.[27] which has a role in transmission especially during interepidemic period. Low level human to human transmission is known in chikungunya. Due to resemblance of symptoms to dengue fever the diagnosis may be missed in interepidemic period. This may be responsible for a resurgence of chikungunya.[28]

Aedes albopictus, originally indigenous to south east Asia, had spread recently to many parts of the world, apparently through carriage of dormant eggs along with transportation of tyres.[29] This being a competent vector for various arboviruses including chikungunya, has alarmed health authorities for possible spread of the disease across the world. . High viral loads in patients returning from indian ocean islands to countries where Ae albopictus is prevalent might be a source of epidemic in their native countries.[24]

Virus

Chikungunya virus is a member of genus Alfa virus and family Togaviridae.[16,30] The virus is found in tropical areas.[1] mainly restricted to Asia and Africa. Two distinct lineages of chikungunya virus could be traced by doing the genetic sequencing of chikungunya virus. One contained all isolates from western Africa and second comprising of southern and east African strains.[25,31] Structurally, the virus has polyadenylation site, flanked by 5'and 3' sequences. It encodes 9 genes, consisting of coding sequences for non structural polyproteins (precursors of nsP1 - nsP4 proteins) and also structural polyproteins (precursor of C, E1-3, and 6K proteins).[30,32] Viral replication occurs within the cytoplasm and virions mature by budding through plasma membrane and virus encoded surface glycoproteins E1 and E2 are encorporated in the virus.

E1 protein correlates with the serological response in human hosts and modulates penetration of the virus in the mosquito species.[32,33,34] E1 and E2 glycoproteins are targets of numerous serological reactions and tests (neutralisation and hemagglutination inhibition).[32]

In the recent Reunion island outbreak, viral genetic analysis showed that the outbreak began with strains related with east African strains of virus, which subsequently developed into several distinct variants.[34,25]

In India, scientific studies confirmed that the outbreaks of febrile polyarthritis which occurred in 2006 were due to chikungunya virus of central/ east African genotype.[18] Phylogenetic analysis based on partial sequences of NS4 & E1 genes showed that all earlier isolates (1963-1973) were Asian genotype whereas current 2006 and Yavat 2000 isolates were African genotype and it is speculated that introduction of the current genotype in India might have occurred more than 5 years before the current outbreak started.[35]

Members of the genus alfa virus typically maintain their natural transmission cycle through an arthropod vector and susceptible hosts. Virus vector interactions may be highly specific, limiting the distribution of the virus.[32]

Reemergence of Chikungunya– Causes

Chik virus, known to circulate in Indian subcontinent remained silent for years. Why it has reemerged so aggressively and after such a long gap is still an enigma. Some of the possible explanations are as follows:

Ecoclimatic conditions with dry weather and infrequent replenishment of domestic water supply favoured breeding of mosquitoes and transmission of chik virus.[36] RNA viruses have a unique ability to expand their host range rapidly.[24] Virus has acquired the capacity to infect new strains of vector mosquito like A. albopictus, facilitating its transmission.Viruses usually require cholesterol to infect their human as well as mosquito host cells. It is speculated that the mutation (226 of E1) that had occurred in the virus, has allowed it to thrive in cholesterol lacking mosquito cells, increasing its infectivity.[34]

Increased tourism facilitating widespread dispersal of infected mosquitoes.[37,31] and virus evolution and its introduction to a population lacking herd immunity.[38,24] are some of the other possible contributing factors for its reemergence in south east Asian countries. However in some countries, outbreak might have occurred from endemic infection.[28]

Pathogenesis and Pathology

Chikungunya Virus enters and replicates in the midgut epithelium of mosquito, which has taken a blood meal from the viremic host.[39] Mosquito remains infective all throughout its life. Humans are infected by the bite of the infected mosquito resulting in deposition of virus in sub cutaneous and possibly cutaneous tissue. After inoculation virus reaches regional lymph nodes. Viremia starts 3-7 days later.[40] The level of viremia closely parallels the fever curve. Fever subsides as viremia decreases.

Virus multiplies in tissue macrophages and not in circulating blood cells like lymphocytes/ monocytes of the host. These infected macrophages are responsible for infection of the tissues affected by the disease i.e. muscle and joints. In addition they also infect "adherent" cells like endothelial cells, epithelial cells, fibroblasts etc. Virus identifies precursor muscle cells i.e. satellite cells, which are very permissive to the virus. Their role as a reservoir for the virus and recurrence of muscle pain is under study.[40,63]

Role of immune response in reducing infection[39] is suggested by rising titers of HI and neutralising antibodies as fever subsides and viremia decreases.

Extravasation of RBCs from superficial capillaries and lymphocytic perivascular cuffing is seen on histopathological study of maculopapular rash. Joint fluid is inflammatory in nature and contains viral antigens but no infectious virus.[39]

Clinical Manifestations

All age groups & both the sexes are equally affected by chikungunya fever. Attack rate in susceptible

population may be as high as 40-85%.[17] Incubation period ranges from 2-12 days. Silent CHIKV infections(infection without illness)are known but its frequency of occrrence is not known. Disease confers life long immunity.[16]

Case Definition[41]

As per guidelines from government health authorites, issued during epidemic, suspect case of chik is one who presents with acute onset high grade fever of less than 7 days duration associated with headache arthralgias and myalgias, with or without rash. Probable case is defined as one coming from high vector density area or area with confirm case and having clinical features of suspect case. Those who have positive viral isolation test, serological test for IgM antibodies or four fold rise in IgG in paired sera are categorised as confirm cases.

Disease may present in two stages,[42] an initial severe eruptive polyarthritis followed by disabling peripheral rheumatism that can persist for months

Onset is usually abrupt. Patients experience flu like[43] symptoms. Fever and incapacitating arthritis aptly described as "Akadya" in local Marathi language, are the most important symptoms of the disease seen in almost all patients. Disease starts with sudden onset high grade fever with chills. Fever usually subsides within 3-5 days but resurgence after few days may occur causing a typical biphasic or saddle back pattern.[17,44]

3-5 days later, maculopapular rash,[45] widespread exanthema with intervening patches of healthy skin, sometimes displaying diffuse, congestive and edematous features may appear on the trunk and extremities. It may have itchy character[17,45,46] typically resembling monkey scratching its body and at this stage disease is described as "Makadya" in local Marathi language. Rarely peeling of skin may occur. Thus "Akadya" is followed few days later by "Makdya" in some cases.

Other dermatological features that are observed during outbreaks in southern india[47] are nasal blotchy erythema, freckle like pigmentation over centro facial area, flagellate pigmentation on face and extremities, lichenoid eruption and hyperpigmentation in photodistributed areas, multiple aphthous like ulcers over scrotum crural areas and axilla and uni or bilateral lymphedema in acral distribution.

Multiple ecchymotic spots (in children) vesiculobullous lesions (in infants), subungual hemorrhages, photourticaria, acral urticaria and scaling with dyschromic patches have also been described.[46]

General manifestations like fatiguability, weakness, loss of appetite, backache, bodyache, restlessness, giddiness and hypotension, puffy face, edema feet[45,48] lmphadenopathy[17,45] are usually present. This may be accompanied by pharyngitis, gingivitis, oral ulcerations.

Arthropathy is a predominant feature of chikungunya fever.[42] In acute phase it may present as arthralgias only or arthritis. Onset is acute or explosive affecting the joints within minutes. Some patients can exactly pinpoint the timing of onset of arthritis.[45] Joint involvement is polyarticular and symmetrical and occasionally migratory.[4,44] Joints are tender, swollen and with presence of morning stiffness. Both large and small joints of hands and feet are involved including MCPS , PIPS, MTPS, rarely DIP, knees ,ankles shoulder, and wrists.[42] Occasionally only small joint involvement or monoarticular[45] involvement is seen.

Other components of the musculoskeletal system may get involved presenting as tenosynovitis,[45,42] bursitis, soft tissue pain over arms, thighs and feet and occasionally tenderness over shin of tibia. Arthritis is usually severe enough to immobilise the patient.Pain on movement is worse in morning, improved by mild exercise,and exacerbated by strenuous exercise.[44] Most patients usually recover from arthritis within 2-3 weeks however prolonged arthralgias lasting beyond 4 months are seen in 12-

13%.[16,45,49,51] and destructive arthropathy[50] can occur in a few.

Severe and unusual forms of arthritis, previously not described in literature have been observed in the recent epidemic.

Female sex, preexisting arthropathy and advanced age are the risk factors for prolonged arthralgias.[45] Severity of the disease and duration are less in younger patients and pregnant women.[47] Prolonged arthralgias may occur as continuation of arthralgias after acute attack (i.e. persistent arthralgias). However in a significant no. of patients, arthralgias recover completely within 3-4 wks only to recur after a gap of 6-9 months (relapse arthritis). Disease involves both peripheral joints & axial skeleton without sacroiliac joint involvement & may be accompanied by tenosynovitis and bursitis.

Presentation patterns seen in prolonged arthralgias are as follows:

1. Symmetric polyarthritis involving large and small joints of hands and feet with morning stiffness, mimicking Rheumatoid arthritis clinically and with or without DIP joint involvement.
2. Inflammatory backache with symmetric polyarthritis without sacroiliac involvement.
3. RS3PE like picture, with edema of hands and feet, commonly seen with relapse arthritis.

Relapse arthritis usually is more severe and disabling causing significant morbidity in contrast to those having persistent prolonged arthralgias which present as a relatively milder disease.

CHIK in younger patients have a slightly different clinical picture with lesser severity and duration[47] with relatively mild arthralgias and infrequent appearance of rash.[44]

In contrast to earlier descriptions of the disease, available through historical review, disease presented with multiple systemic involvement during 2006 epidemic.

Ophthalmic symptoms include retroorbital pain, conjunctival congestion and photophobia.[47,44] Ocular involvement is in the form of conjunctivitis, minor bleeding in eyes granulomatous and nongranulomatous anterior uveitis, retinitis with retinal changes consistent with viral retinitis. Ac iridocyclitis and nodular episcleritis[52] optic neuritis, retrobulbar neuritis, and dendritic lesions have also been described.[53] Visual prognosis is generally good with most patients recovering good vision.[53,52]

GI involvement[45,54] is in the form of mild diarrhea, gastritis and rarely pancreatitis,[45] fulminant hepatitis.[9,17]

Kidney involvement may be seen as asymptomatic urinary abnormalities, Ac. glomerulonephritis occasionally leading to ac. renal failure.[45]

CNS involvement may be marked by appearance of ac. confusional state, convulsions, meningoencephalitis[45,51,55] (causing significant morbidity and rarely mortality also.) Cerebellar ataxia, peripheral neuropathy, autonomic neuropathy (presenting as retention of urine, severe postural hypotension) and proximal muscle weakness is seen.[45,48] Areflexic quadriplegia responding to methylprednisolone was reported from patients of Andaman, Nicobar islands.[56]

Hemorrhagic manifestations are relatively rare.[17,54] Mild hemorrhagic symptoms like positive torniquet test , epistaxis, bleeding gum and patechial rash are sometimes seen.

Peripheral vascular disorder[42,45] vasculitis involving small and medium sized vessels presenting as non healing ulcer, gangrene of the toes and fingers, and rarely myocardial infarction may occur.

Dengue and Chikungunya

Many clinical features of chikungunya are indistinguishable from dengue[57] highlighting the importance of high index of clinical suspicion. Unlike dengue however; hemorrhagic manifestations are rare and shock is never seen in chikungunya.[15] Simultaneous occurrence of both the diseases is known.[20,31] Serology of dengue may be confirmatory.

Impact of the disease

Chikungunya fever, which was considered to be a self limiting, non fatal disease, appeared in a more aggressive form with multiple system involvement[45] and significant morbidity, during 2006 epidemic. Deaths have been reported from French reunion islands, India and Srilanka.[47,54] Chronic chikungunya arthropathy may be crippling.

Chikungunya in Special Situations

Chikungunya in pregnant patients occurs with less severity and shorter duration.[47] Maternal –fetal transmission of chikungunya can occur[58,59,60] but most newborns are asymptomatic. Meningoencephalitis, intravascular coagulation, intracerebral hemorrhage due to thrombocytopenia is described in a few.

Transplacental transfer of antibodies to CHIK V in infant circulation may protect them from illness upto 9 months,[59] explaining the mild severity of the disease in infants. This also may guide about optimal time for vaccination, should the vaccine be available in future.

Diagnosis and Laboratory Features

In absence of widespread availability of diagnostic tests for chikungunya, diagnosis is essentially clinical. Epidemiology of diseases caused by alfa viruses is highly specific and gives a clue to the diagnosis. It should be suspected in all patients with febrile polyarthritis with recent history of travel to areas with CHIK V transmission.

During epidemics the diagnosis is obvious .Other alfaviral infections like Mayaro, O'Nyong nyong, Ross River, Sindbis virus may cause similar illness[39] but are not so common in India. In addition, prodrome of Hepatitis B, Juvenile Rheumatoid arthritis, Parvovirus infection, Rubella, and Dengue need to be differentiated by doing appropriate tests.

Laboratory features of chikungunya fever are non specific in acute phase and include normal hemoglobin levels, mild leukopenia, lymphopenia[45,54] normal platelet count or mild thrombocytopenia, raised ESR, elevation of trans aminases and hypocalcemia.[54] Urinary abnormalities like albuminuria, microscopic hematuria may be noticed.

Specific diagnosis of chikungunya fever can be obtained by viral isolation, molecular methods, and serological tests depending on the timing of appearance of symptoms. Since the patient of chikungunya fever is viremic for the first 72 hours, virus isolation[39] and culture, which is the gold standard for diagnosis, is done in early phase of the disease. It is expensive, time consuming and needs specialised laboratory.

Molecular methods like RT –PCR amplification technique described by Pfeffer et al provides genus specific detection of the virus.[61] Real time RT-PCR is fast and 10 times more sensitive than conventional block based RT-PCR and could detect as low as 20 copies of RNA transcript[62] and is suitable for surveillence.

RT loop mediated isothermal amplification(RT-LAMP) assay is a valuable tool for rapid real time detection as well as quantification of CHIK V in acute phase serum samples without requiring any sophisticated equipment and has potential usefulness for clinical diagnosis and surveillence of CHIKV in the developing countries.[64]

Decline in viremia parallels rapid rise in Hemagglutination inhibition(HI) and Neutralising(N) antibodies. Antibody assays are quite specific[61] but seroconversion occurs only after 4-5 days. Serological tests include detection of anti chik Ig M antibodies (HI, CF, N antibody), by IgM capture ELISA. IgM antibody response is fast and subtype specific. H I antibodies[50] develop as viremia is cleared and is paralleled by Neutralising antibody production. Complement fixation antibodies are positive by third week and slowly decrease over subsequent year. Also four fold rise in antibody titers of IgG antibodies in paired sera with acute and convalescent phase samples spaced two weeks apart is confirmatory but retrospectively diagnostic.

Investigations of prolonged arthralgias reveal raised ESR, raised CRP, negative or low titers R-Factor[50] and negative antiCCP antibody[45] which may help differentiate from Rheumatoid Arthritis.

Prevention

Since no effective vaccine or drugs are available for treatment, prevention is most important and can be achieved by early identification of outbreaks and vector control underscoring the need for continuous surveillence.

Multifaceted approach with community based vector control programmes are necessary and should include following measures.

1. Source reduction achieved through measures like spraying dwellings with residual action insecticides, biological control, use of larvicidals, and getting rid of mosquito breeding sites by emptying standing water in containers, tyres and flower pots etc. Studies have proved their efficacy in reducing burden of other vector borne diseases like Dengue and Malaria.[65] The appeal by Govt. Health authorities of Maharashtra to observe "weekly dry day" by emptying all water containers had good response from public and contributed in reducing the vector density.
2. Reduction in man-virus contact through personal protection measures to prevent mosquito bite by wearing long sleeved clothes and pants by using insect repellant on exposed skin. Use of secure window screens and doors to keep mosquitoes out are also useful measures. Further spread of the disease can be halted by limiting chikungunya fever patient's exposure to mosquito bite.
3. Legislative measures for junk disposal, and building appropriate water tanks in buildings for storage of water.[41]

Treatment

No vaccine or specific antiviral treatment is available. Symptomatic treatment with rest, fluids analgesics (acetaminophen) and antiinflammatory agents like ibuprofen, naproxen[7,9,15] may relieve symptoms in acute phase. Aspirin should be avoided.[16,47] Prolonged arthralgias may need treatment with, rest, mild exercises (range of motion exercises) which may be helpful in relieving pain and morning stiffness.[45] Excessive exercises may worsen the symptoms. Chloroquine phosphate 250 mg/day is helpful in managing prolonged arthralgias.[66] It offers symptomatic relief and also may act as antiviral agent to combat chikungunya virus.[47] Patients with persistent prolonged arthralgias respond better to chloroquine, which may be required upto 3-6 months.

Patients presenting with marked chronic synovitis or RS3PE syndrome like picture do not show adequate response to chloroquine alone. Short course of low dose steroids along with sulfasalazine maybe helpful in these cases.

Steroids are not indicated for treatment of acute chikungunya arthritis, however few reports of their use for complications of the disease are available. Low dose short term steroids for peripheral vascular disorder,[42] autonomic neuropathy,[45] chronic arthritis and methyl prednisolone[56] for areflexic quadriparesis, have been tried, however data is insufficient and further study is warranted.

No specific antiviral treatment is currently available. Studies on cytokine analysis of these patients may provide the rationale for use of interferons for treatment.[67] Experimental studies on antiviral compounds like human recombinant interferon alfa, iota carrageenan, glycyrrhizin, 6-azauridin, ribavirin have shown their effectivity in vitro. [68] IFN alfa2b and ribavirin have synergistic antiviral effects and need to be studied further.

Reports on development of CHIK vaccine are available,[69] but it is still in experimental stage.

References

1. Pialoux G, Gauzere BA, Jaureguiberry S, Straubel M, Chikungunya an epidemic arbovirosis, *Lancet Infect Dis*, 2007 May; 7(5):319-27

2. Vanlandingham DL, Hong C, Klingler K, Tsetsarkin K, McElroy KL, Powers AM et al Differential infectivities of Onyong nyong and chikungunya virus isolates in Anopheles Gambiae and Ae egypti mosquitoes, *Am J Trop Med Hyg*, 2005 May;72(5):616-

3. Lumsden WHR, An epidemic of arbovirus in southern province, Tanganyika territory, in1952-53; II.General description and epidemiology. *Trans. R. Soc. trop. Med.* Hyg1955;49;33-57

4. Chikungunya fever –patient UK, available on http://www.patient.co.uk/showdoc/40025279, accessed on 8/23/2007

5. Chikungunya fever information sheet, WORLD HEALTH ORGANISATION , Southeast Asia Regional office available on http.//www.searo.who.int/en/Section 10/Section 2246.htm , accessed on 8/23/2007

6. Robinson MC, An epidemic of virus disease in southern province, Tanganyika territoty, in 1952-53;I .clinical features. *Trans R Soc ofTrop Med and Hyg* 1955;49:28-32

7. Kalantri SP, Joshi R, Riley LW ,Chikungunya epidemic :an Indian perspective, Natl Med J India 2006; 19(6): 315-324

8. Kamath S, Das AK, Parikh FS. Chikungunya.*JAPI*; 2006; 54:725-6

9. Mohan A. Chikungunya fever:clinical manifestations and management. *Indian J Med Res* 2006; 124:471-4

10. Jadhav M, Namboodripad M , Carman RH ,Carey DE, Myers RM. Chikungunya disease in infants and children in Vellore: A report of clinical and haematological features of virologically proved cases. *Indian J Med Res* 1965;53:764-76

11. Thiruvengadam KV, Kalyansundaram V, Rajgopal J. Clinical and pathological studies on chikungunya fever in Madras city. *Indian J Med Res*1965; 53:764 – 44

12. Rodrigues FM, Patankar MR, BanerjeeK, et al. Etiology of the 1965 epidemic of febrile illness in Nagpur city, Maharashtra State, India. *Bull World Health Organ* 1972;46:173-9

13. Padbidri V S, Ganeshwar T T. Epidemiological investigations of chikungunya epidemic in Barsi, Maharashtra state, India. *J Hyg Epidemiol Microbiol Immunol* 1979; 23:445-51

14. National Vector Borne Disease Control Programme, Directorate general of health services, ministry of health &family welfare Govt of India, available on http.//www.nvbdcp.gov.in/Chikun-cases.html, accessed on 8/23/2007

15. CDC : travellers health, Update: outbreak notice-Chikungunya fever in Srilanka, India and Indian ocean islands available on http.//wwwn.cdc.gov/travel/content ChikungunyaIndia.aspx, accessed on 8/19/2007

16. CDC: Chikungunya fever fact sheet . available on http:///www.cdc.gov/ncidod/dvbid/chikungunya/chikvfact.htm, accessed on 8/19/2007 V17 Sam IC, AbuBakar S. Chikungunya virus infection, Available on http://www.mma.org.my/info/2_chikungunya_06.htm, accessed on 8/29/2007.

18. Yergolkar P. Tandale BV, ArankalleVA, SathePS, SudeepAB, Gandhe SS et al. Chikungunya outbreaks caused by African genotype, India. Emerg infect dis 2006, Oct. available from http://www.cdc.gov/ncidod/EID/vol12no10/06-0529.htm.

19. Wilder-Smith A, Schwartz E. Dengue in travellers. *N Engl J Med* 2005;353:924-32.

20. Sharma RS, Entomological studies during outbreak of chikungunya in Marathwada region of Maharashtra(India). *Indian J for practising doctor*; 3(5):(2006-11-2006-12)

21. Harrington LC,Scott TW, Lerdthusnee K, Colem an RC, Costero A, Clark GG et al. Dispersal of the dengue vector Aedes egypti within and between rural communities. *Am J Trop Med Hyg.* 2005 Feb:72(2):209-20.

22. Turell MJ, Beaman JR, Tmmariello RF. Susceptibility of selected strains of Aedes aegypti and Aedes albopictus(Diptera;Culicidae) to chikungunya virus. *J Med Entomol,* 1992 Jan; 29(1): 49-53.

23. CDC -MMWR Morb Mortal Wkly Rep. 2006 Sep 29; 55(38):1040-2.

24. Parola P, De Lamballerie X, Jourdan J, Rovery C, Villant V, Minodier P et al. Novel chikungunya virus varient in travellers returning from Indian ocean islands. *Emerg I nfect Dis,* 2006, Oct; 12(10):1493-9.

25. Powers Am, Brault AC, Tesh RB, Weaver SC. Reemergence of chikunguya and O" nyong nyong viruses:evidence of distinct geographical lineages and distant evolutionary relationships. *J Gen Virol,* 2000;81:471-479.

26. Diallo M, ThonnonJ , Trore -Lamizana M , Fontenille D. Vectors of chikungunya virus in Senegal: current dat and transmission cycles. *Am J Trop Med Hyg* 1999, Feb; 60(2): 281-6.

27. Moury DT, Singh DK, Yadav P, Gokhale MD,Barde PV, Narayan NB et al. Role of gregarin parasite Ascogregarina culicis(Apicomplexa:Lecudinidae)in the maintenance of chikungunya virus in vector mosquito. *J Eukaryot microbiol* 2003; 50(5):379-82 (ISSN: 1066-5234).

28. Abu Bakar S,Sam IC, Wong PF, MatRahim N , HooiRoslanN Reemergence of endemic chikungunya Malaysia. Emerg Inf Dis[serial on internet]2007 Jan[Jan2007], available on http.//www.cdc.gov/ncidod/EID/13/1/147.htm, accessed on 8/25/2007

29. Grantz NG.Critical review of the vector status of Aedes albopictus. *Med Vet Entomol* 2004 Sept; 18(3):215-27.

30. Khan AH, Moitra K, Parquet M MC, Hasebe F, Mathenge EG, Igarashi A. Complete nucleotide sequence of chikungunya virus and evidence for an internal polyadenylation site. *J Gen Virol.* 2002; 83(Pt 12):3075-84 (ISSN:0022-1317).

31. Ravi V. Reemergence of chikungunya virus in India. *Indian J med Microbiol* 2006;24(2):83- 4.

32. Powers AM, Brault AC, ShirakoY, Strauss EG, Kang W, Strauss JH et al. Evolutionary relationship and systematics of alfa viruses. *J of Virol* 2001 Nov; VOL75(21):10118-10131.

33. Simizu B, Yamamoto K , HAashimoto K , Ogata T, Structural proteins of chikungunya virus, *J Virol;*1984 July; 51(1):254-258

34. Schuffenecker I, Iteman I, Michault A, Murri S, Fraungeul L, Vaney MC et al. Genome microevolution of chikungunya

viruses causing Indian ocean outbreak. PLOS MED. 2006 Jul;3(7):e263. Epub 2006 May 23.

35. Arankalle VA, Shrivastava S, Cherian S, Gunjikar RS, Walimbe A, Jadhav SM et al. Genetic divergence of chikungunya virus in India (1963-2006) with special reference to the 2005-2006 explosive epidemic. *J Gen Virol* 2007; 88: 1967-1976 .

36. Chretien JP, Anyamba A, Bedno SA, Breiman RF, Sang R, Sergon K, et al. Drought associated chikungunya emergence along coastal East Africa. *Am. J. Trop. Med Hyg* 2007; 76(3):405-7(ISSN0002-9637)

37. Lam SK, Chua KB, Hooi PS, Rahimah MA, Kumari S, Tharmaratnam M et al. Chikungunya infection –An emerging disease in Malaysia. *Southeast Asian J Trop Med Public health* 2001 Sep; 32(3):447-51.

38. Mourya DT, Mishra AC. Chikungunya fever. *Lancet* 2006; 368:186-7.

39. Markoff L. Alfaviruses in Principles and practice of infectious diseases, Vol II, 6th edn,Editors Mandell, Douglas and Benette, Elsevier Churchill Livingstone. pp1913-1920

40. Broom AK, Smith DW, Hall RA, Johansen CA, Mackenzie JS. Arbovirus infections. Mansons Tropical Diseases, 21st edn 2003. Editors Cook G Zumla A, Saunders Elsevier science, Pp725-764.

41. National Vector Borne Disease ControlProgrmme, Circular from Deputy Director, Health services, (malaria & Filariasis) Pune, Circular no. DDHS/VBD/ FEVEROUTBREAK/ Technical-1/n no/189/10166-295/06, date22/04/2006

42. Simon F, Parola P, Grandadam M, Fourcade S, Oliver M, Brouqui P et al. Chikungunya infection : an emerging rheumatism among travellers returned from Indian Ocean islands. Report of 47 cases. *Medicine*(Baltimore) 2007 May; 86(3):123-37.

43. Taubitz W, Cramer J P, Kapaun A,Pfeffer M, Drosten C, Dobler G et al . Chikungunya fever in travellers : Clinical presentation and course. *Clin Infect Dis*. 2007 Jul 1;45(1): el - 4. Epub 2007 May 23.

44. LamSK, Chua KB. Alfaviruses. Available on http;//www. vadscorner.com/alfaviruses. html, accessed on 8/23/2007.

45. Ganu MA,Ganu AS. Chikungunya –A field experience. Paper presented at 1st National conference of infectious diseases, 2007 Feb, Mumbai.

46. Talarmin F, Staikowsky F, Schoenlaub P, Risbourg A, Nicolas X, Zangoli A et al. Skin and mucosal manifestations of chikungunya virus infection in adults in Reunion islands. *Med Trop*(Mars). 2007 Apr;67(2):167-73

47. Chikungunya – from wikipedia the free encyclopedia, retrieved from http;//en.wikipedia.org/wiki/Chikungunya accessed on 8/19/2007

48. Subbalaxmi MVS, Srinivasan VR, Prasad AK, Shetty M, Laxmi V. Clinical profile of Chikungunya fever at Nizam's Institute of Medical Sciences . Paper presented at 1st National Conference of Infectious Diseases 2007 Feb. Mumbai.

49. CDC Update -chikungunya fever diagnosed among international travellers-- United states 2006. MMWR *Morb Mortal Wkly Rep*. 2007 Mar30; 56(12):276-7.

50. Naides SJ. Viral arthritis ,in Oxford T B of Rheumatology, 3rd edn 2004, Editors Isenberg DA, Maddison PJ et al. Oxford university press, pp620-628.

51. Bodemman P,Genton B. Chikungunya :an epidemic in real time. *Lancet* 2006;368:258.

52. Mahendradas P, Ranganna S K, Shetty R, Balu R, Narayan K M, Babu R B et al. Ocular manifestations associated with chikungunya. Ophthalmology 2007Jul 11; [epub ahead of print], accessed on 8/23/2007

53. Lalitha P, Rathinam S , Banushree K , Maheshkumar S, Vijaykumar R, Sathe P. Ocular involvement associated with an epidemic outbreak of chikungunya virus infection. Am. J Ophthalmol 2007Aug 8; Epub ahead of print], accessed on 8/23/2007

54. Borghenini G, Paubeau P, Staikowski F, Lory M, Le Moullec N, et al Outbreak of chikungunya on Reunion islands; Early clinical and laboratory features in 157 adult patients. Clin Infect Dis 2007; 44(11); 1401-7, (ISSN 1537-6591).

55. Euroserveillance 2006;11(2):060202, available at http:// www.euroserveillance.org/ew/2006/060202.asp, accessed on 8/27/2007

56. Manimunda SP, Singh SS, Sugunan AP,Singh O, Roy S, Shriram AN et al. Chikungunya fever, Andaman and Nikobar islands ,India.Emerg Inf Dis [serial on the internet]2007Aug Dis.Vol13(8). available from http://www.cdc.gov/EID/ content/13/8/1259.htm, accessed on 8/23/2007

57. Thaikruea L, Charearnsook O, Reanphumkarnkit S, Dissomboon P et al. Chikungunya in Thailand : A reemerging disease? *Southeast Asian J Trop Med Public Health* !997 Jun;2892):359-64.

58. Robillard PY,Boumahni B, Gerardin P, Michault A, Fourmaintraux A, et al. Vertical maternal fetal transmission of the chikungunya virus. Ten cases among 84 pregnant women, Presse. Med.2006;35(5 pt 1):785-8(ISSN;0755-4982)

59. Watanaveeradej V, Timothi PE, Simasanthien S, Kerdapanich A, Polprasert N, Aree C et al .Transplacental chikungunya antibody kinetics, Thailand. Infect Dis[serial on internet]2006 Nov[Nov 2006], available from http.// www.cdc.gov/ncidod/EID/vol12no11/05-1560.htm, accessed on8/23/2007.

60. Touret Y, Randrianaivo H, Michault A, Schuffenecker I, Kauffmann E, Lenglet Y et al .Early maternal-fetal transmission of the chikungunya virus.*Presse Med* .2006Nov;35(11pt1): 1656-8.

61. Wang E, Paessler S, Aguilar PV, Carrara AS, Ni H, Greene IP et al Reverse transcription- PCR-Enzyme linked immunosorbent assay for rapid detection and differentiation of alfa virus infections. *J Clin Microbiol* 2000 Nov, pp4000-4008.

62. Edwards CJ, Welsch SR, Chamberlain J, Hewson R, Tolly H, Cane PA, Lloyd G. Molecular diagnosis and analysis of chikungunya virus. *J Clin Virol*. 2007 Aug; 39(4):271-5.Epub 2007 Jul12.

63. Chikungunya: virus target cells identified. Institute Pasteur. Available at http://www.pasteur.fr/actu/presse/07chik_cibles_E.htm. accessed on 8/29/2007

64. Parida MM, Santhosh SR, Dash Pk, Tripathi Nk, Laxmi V, Mamidi N.et al. *J.Clin Microbiol* 2007 feb;45(2):351-7

65. Singh N , Shukla MM, Mishra Ak, Singh MP, Paliwal JC, Dash AP. Malaria control using indoor residual spraying and larvivorous fish:a case study in Baitul, Central India. *Trop Med Int Health* 2006 Oct;11(10):1512-20.

66. Brighton SW. Chloroquine phosphate treatment of chronic chikungunya arthritis: an open pilot study. South Afr Med J. 1984; 66:217-18.

67. Lee N, Wong CK, Lam WY, Wong A, Lim W, Lam CWK et al. Chikungunya fever, Hongkong[letter]. Emerg. Inf. [Serial on internet] 2006 Nov; available on http://www.cdc.gov/ncidod/EID/vol12no11/06-0574-htm.accessed on 8/29/2007

68. Briolant S, Garin D,Scarramozzino N, Jouan A, Crance JM. In vitro inhibition of Chikungunya and semliki forest viruses replication by antiviral compounds: synergisticeffect of interferon -alfa and ribavarin combination. *Antiviral research*, 2004:61(2):111-7, (ISSN:0166-3542)

69. Edelman R, Tacket CO, Wasserman SS,Bodyson SA et al. Phase II safety and immunogenicity study of live vaccine TSI-GSD-218. Am J Trop Med Hyg 2000 Jun. Available onhttp://www.promedmail.org/pls/pm/pm?an=20060219.0544. accessed on 8/27/2007