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# STUDY OF CLINICAL SPECTRUM OF CHIKUNGUNYA OF RECENT OUTBREAK 2010 IN WESTERN RAJASTHAN AND THEIR 2YR FOLLOW UP

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## ABSTRACT

**Background**: Chikungunya virus is a member of the Alphavirus genus of the family Togaviridae. The Alpha viruses consist of 30 species of arthropod borne viruses, which are further sub grouped into seven serocomplexes. O'nyong-nyong virus (ONN) is considered to be closely related to CHIK. The percentage identities of non-structural and structural polyproteins between CHIK and ONN were 85% compared with 42-70% between CHIK and other alpha viruses.

**AIM**: To find out a clinical and laboratory profile during recent outbreak of Chikungunya during September 2010 in Bikaner (North-Western Rajasthan) and they were followed for 2 years to know about their complications.

**Results**: In our study highly significant relation was found between age, number of joints partially recovered, CRP positivity, raised ESR and persistent arthralgia. In our study CRP was positive in 17(8.5%) patients in 41-60yr age group,15(7.5%) patients in 20-40 yr age group and 9(4.5%) patients in >60yr age group. In our study we find that mean ESR progressively increased with duration; the mean ESR was 48.6mm at onset of disease, 55.81mm at one year and 64.15mm at 2year.In our study all the patients were tested for Rheumatoid factor, among them 5(2.5%) patients found positive for RF. These all 5 patients had persistent arthralgia and 82 patients having persistent arthralgia were tested for anti CCP antibody, among them 17(20.73%) patients found positive.

**Conclusion**: Our findings draw attention to the importance of assessing management issues such as strategies for supportive treatment of CHIK illness in further studies. Finally, these studies should be designed in order to estimate the magnitude of chronic rheumatic illness directly attributable to CHIKV infection and its potential effect on quality of life over a prolonged period.

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**Key Words :** CHIK, Polyproteins, O'nyong-nyong Virus, Serocomplexes

## INTRODUCTION

Chikungunya fever, a disease caused by chikungunya virus, was almost a forgotten disease until recently; when it reemerged in Indian Ocean islands in 2005-06. It is spread by mosquito bites from the Aedes aegypti mosquito. The name is derived from the Makonde word meaning "that which bends up" in reference to the stooped posture developed as a result of the arthritic

symptoms of the disease. The disease was first described by Robinson[1] in 1955, following an outbreak on the Makonde Plateu, along the border between Tanganyika and Mozambique in 1952. Chikungunya is closely related to O'nyong'nyong virus.

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The disease is self-limiting without much of complications. But few severe and fatal cases have been reported mainly in infants and children. particularly in a form associated with high grade fever, seizures, and with neurological deficits suggestive of encephalitis[2].

CHIK virus may cause myopericarditis[3], sudden sensorineural hearing loss[4], acute flaccid paralysis[5], bilateral retinitis[6] encephalomyeloradi-culitis[2,7], cutaneous ulceration[8]. It was considered as a risk factor for endemic Burkifs lymphoma in Malawi.

Children and young adults generally have mild transitory pains, whereas the arthritic symptoms[9] are more severe and persistent in older individuals. Recovery sometimes taking 2-3 years in 12-14% of patients.

Residual symptoms[10] ranged from mild discomfort and stiffness to persistent pain with effusions or synovial thickening but no destructive changes or muscular atrophy.
Radiographs of patients mainly show soft tissue swelling but small erosions were noted in a metacarpophalangeal joint of a patient.

When an Aedes mosquito bites an infected host it gets infected for life. The virus multiplies in midget of the mosquito, disseminate and involve its salivary glands. When such mosquitoes bite another host he gets the infection. Viral replication, takes place in lymphoid & myeloid cells stimulating an immune reaction[11]. Not much is known or studied in detail about the pathogenesis of the disease process. It is also hypothesized that it causes a transient bone marrow suppression and also platelet dysfunction.

## MATERIAL AND METHODS

Present study was conducted among 200 patients attending the OPD and indoor from department of medicine. This study was carried to find out clinical and laboratory profile of recent outbreak of Chikungunya during Sept-Dec in Department of Medicine, S.P. Medical College and A.G. Hospital, Bikaner (North-Western Rajasthan), and their 2 year follow up.

**Selection of Patients:** Patients were selected on the basis of IgM antibody positive against chikungunya virus for this study. After explaining the detail and moto of this study, informed consent was taken. The fever was defined on clinical ground.

**Techniques:** Each selected patients were subjected to detail history and complete physical examination. History regarding age, sex, socioeconomic status, personal history of any disease, history of smoking, alcohol, use of drugs for any aliments, occupational history, dietary history. Height and weight were measured with patient in light clothing and without shoes. Weight was

measured with a traditional spring balance which was kept on horizontal surface the zero was duly checked.

**Method:** The onsite chikungunya IgM rapid test[12] is a lateral flow chromatographic immunoassay based on the principles of the IgM capture assay. The test cassette consists of (1) a burgundy colored conjugated pad containing Chik antigen conjugated with colloid gold (CHIC conjugates) and rabbit IgG gold conjugated, (2) a nitrocellulose membrane strip containing a test band (T band) and a control band (C band). The T band is pre coated with anti-human M antibody and the C band is pre-coated with goat
anti-rabbit IgG.

**Positive:** When an adequate volume of test specimen is dispensed into the sample well of the cassette the specimen migrates by capillary action across the cassette. The IgM antibody to CHIK, if present in the specimen will bind to the Chik conjugates. The immuno-complex is then captured on the membrane by the pre-coated IgM antibody, forming a burgundy colored T band, indicating a Chik IgM positive test result.
**Negative:** Absence of the T band suggests a negative result. The test contains an internal control (C band) which should exhibit a burgundy colored band of the immuno-complex of goat anti rabbit IgG/rabbit IgG gold conjugate regardless of the color development on the T band. Otherwise, the test result is invalid and the specimen must be retested with another device.

## RESULTS AND DISCUSSION

**Table 1 Distribution of cases according to C-reactive Protein in relation to age group**

| Age Group | C-Reactive Protein | | | | Total | |
|---|---|---|---|---|---|---|
| | Present | | Absent | | | |
| | No. | % | No. | % | No. | % |
| ≤20 | 0 | - | 18 | 9.0 | 18 | 9.0 |
| 21-40 | 15 | 7.5 | 65 | 32.5 | 80 | 40.0 |
| 41-60 | 17 | 8.5 | 49 | 24.5 | 66 | 33.0 |
| >60 | 9 | 4.5 | 27 | 13.5 | 36 | 18.0 |
| Total | 41 | 20.5 | 159 | 79.5 | 200 | 100 |
| $\chi^2$ | 6.359 | | | | | |
| p | 0.095 | | | | | |

**Table 2 Distribution of cases according to ESR in relation to age group**

| Age Group | ESR Group | | | | Total | |
|---|---|---|---|---|---|---|
| | ≤ 20 | | >20 | | | |
| | No. | % | No. | % | No. | % |
| ≤20 | 10 | 5.0 | 8 | 4.0 | 18 | 9.0 |
| 21-40 | 25 | 12.5 | 55 | 27.5 | 80 | 40.0 |
| 41-60 | 3 | 1.5 | 63 | 31.5 | 66 | 33.0 |
| >60 | 0 | - | 36 | 18.0 | 36 | 18.0 |
| Total | 41 | 20.5 | 159 | 79.5 | 200 | 100 |
| $\chi^2$ | 40.834 | | | | | |
| p | <0.001 | | | | | |

**Table 3 Distribution of cases according to Rheumatoid Factor in relation to age group**

| Age Group | Rheumatoid Factor | | | | Total | |
|---|---|---|---|---|---|---|
| | Present | | Absent | | | |
| | No. | % | No. | % | No. | % |
| ≤20 | 0 | - | 18 | 9.0 | 18 | 9.0 |
| 21-40 | 2 | 1.0 | 78 | 39.0 | 80 | 40.0 |
| 41-60 | 3 | 1.5 | 63 | 31.5 | 66 | 33.0 |
| >60 | 0 | - | 36 | 18.0 | 36 | 18.0 |
| Total | 5 | 2.5 | 195 | 97.5 | 200 | 100 |
| $\chi^2$ | 2.517 | | | | | |
| p | 0.472 | | | | | |

**Table 4 Distribution of cases according to Anti CCP in relation to age group**

| Age Group | Anti CCP (n=82) | | | | Total | |
|---|---|---|---|---|---|---|
| | Present | | Absent | | | |
| | No. | % | No. | % | No. | % |
| ≤20 | 0 | - | 0 | - | 0 | - |
| 21-40 | 5 | 6.1 | 32 | 39.0 | 37 | 45.1 |
| 41-60 | 8 | 9.8 | 17 | 20.7 | 25 | 30.5 |
| >60 | 4 | 4.9 | 16 | 19.5 | 36 | 24.4 |
| Total | 17 | 20.8 | 65 | 79.2 | 82 | 100 |
| $\chi^2$ | 131.23 | | | | | |
| p | <0.001 | | | | | |

In our study patients those had persistent arthralgia on two year follow up mimicked rheumatological disorder like RA in 35(42.7%), OA in 20(24.3%), SSA in 4 patients (4.9%), LB in 8 patients (9.8%) and non specific aches and pains in 15(18.3%) patients. The entity of post-chikungunya chronic arthritis is not well defined. Whether there is such a separate entity or a viral trigger producing Rheumatoid arthritis (RA) in a genetically susceptible individual is not known. Combe et al reported 21 cases of RA following Chikungunya infection[1]. Few previous studies have addressed the long-term clinical outcome of CHIKV illness. In a small case series of 28 residents of Pretoria with confirmed CHIKV infection, Fourie and Morrison[13] reported that 73% of the subjects experienced severe arthralgia in the acute phase of the illness whereas 18% reported longstanding rheumatic symptoms as long as 20 months after infection. A similar study is performed in South Africa in 1980 by Brighton et al[14], in which several patients were questioned only by telephone, 94(87.9%) of 107 patients were free of symptoms 3-5 years after acute infection. The discordance between this study and our study can be easily explained .In the study by Brighton et al[15].patients were assessed later than they were in our study and almost one half of the patients were <17 years; it is known that arthralgia has a milder course in children.

In addition, a recent study conducted on Reunion Island in the setting of a hospital-based recruitment had evaluated at month 18, 88 of 202(44%) CHIKV infected patients who fulfill the inclusion criteria[16]. Among these, 56 patients (63.6%) reported persistent arthralgia, with 29 (51.8% of the 56) ascertaining a history of arthralgia before CHIKV illness.

Considering the size of affected population in India this amounts to a huge number. In our study, the disease affected all age groups and both sexes. Slight female preponderance (1.44:1) might

be due to more susceptibility of females to immunological insult. Past and family history revealed onset of disease as acute febrile polyarthritis, affection of multiple family members during acute phase consistent with biting habits of Aedes aegypti mosquito[17] and recovery in most within few weeks. Appearance of chronic polyarthritis might be due to development of immunological phenomena after CHIK infection. Chronic disease affected all components of musculoskeletal system including joints, synovium, tendons and bursae. Soft tissue pain present may be attributable to myofasciitis. Fatiguability and prolonged morning stiffness denote inflammatory nature of arthritis. Disease affected small and large joints of hands and feet in rheumatoid arthritis (RA) like distribution including MCPs, PIPs, wrists, elbows, shoulder, knee, ankles and MTPs. However in contrast to RA, DIP joints were also affected. None had affection of TM or sternoclavicular joint. Affection of spine and SI joints was noted in the patients studied. All the patients had symptoms of moderate to severe degree to start with.

Musculoskeletal disorders are common features of CHIK fever. Diffuse joint and muscular pains are usual in the acute phase of the infection, with a resolution of symptoms in most cases in a few days or weeks. Persistent polyarthralgia and arthritis have been reported in 10 to 20% of patients at 20 to 36 months[13].

Clinical features of RA with joint destruction and rheumatoid factor positivity have been described in a limited number of cases after CHIK fever[13,18].

In our study highly significant relation was found between age, number of joints partially recovered, CRP positivity, raised ESR and persistent arthralgia. In our study CRP was positive in 17(8.5%) patients in 41-60yr age group,15(7.5%) patients in 20-40 yr age group and 9(4.5%) patients in >60yr age group. In our study we find that mean ESR progressively increased with duration; the mean ESR was 48.6mm at onset of disease, 55.81mm at one year and 64.15mm at 2year.In our study all the patients were tested for Rheumatoid factor, among them 5(2.5%) patients found positive for RF. These all 5 patients had persistent arthralgia and 82 patients having persistent arthralgia were tested for anti CCP antibody, among them 17(20.73%) patients found positive.

## CONCLUSION

The results of this study highlight the fact that, following the CHIKV outbreak in 2010 in Bikaner (western Rajasthan) a substantial proportion of persistent and disabling residual rheumatic symptoms could be identified for at least 2 year after infection onset, especially in middle age group. Our findings also draw attention to the importance of assessing management issues such as strategies for supportive treatment of CHIK illness in further studies. Finally, these studies should be designed in order to estimate the magnitude of chronic rheumatic illness directly attributable to CHIKV infection and its potential effect on quality of life over a prolonged period.

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