

## Research Article

# Vitamin D deficiency may exacerbate or prolong arthritis in Chikungunya fever

Rao V. N. Bhavana<sup>1\*</sup>, Raman V. S. Bhavana<sup>2</sup>, Narmada Vatti<sup>3</sup>, Prabhakar Rao V. Dirisana<sup>1</sup>

<sup>1</sup>Department of Medicine, Queen's NRI Hospital, Visakhapatnam, Andhra Pradesh, India

<sup>2</sup>Department of Neurosurgery, King George Hospital, Visakhapatnam, Andhra Pradesh, India

<sup>3</sup>Department of E.N.T, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India

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### \*Correspondence:

Dr. Rao V. N. Bhavana,

E-mail: bhavanavnrao@gmail.com

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### ABSTRACT

**Background:** Chikungunya is a self-limiting acute febrile illness with acute arthritis. It is carried by *Aedes aegypti* and *Aedes albopictus*. The disease mainly affected Africa and Asia, though sporadic cases occurred in the other regions of the world. Background: During an outbreak of this illness in India in 2015 we observed that a portion of the patients were suffering from prolonged arthritis. While investigating for the cause of prolonged arthritis we found that most of them were deficient in Vitamin D. Hence we carried up this study of Vitamin D deficiency in Chikungunya patients.

**Methods:** All the probable cases of Chikungunya that attended our hospital between 20th July 2015 to 30th January 2016 were registered for study. Their symptoms and clinical signs were analyzed. All were investigated for hematological abnormalities and excluded for dengue fever by serological testing. Those who were hospitalized with severe arthritis were tested for vitamin D deficiency on the day of admission and those who had arthritis beyond a month on 30th day. Those who had a vitamin D deficiency were treated with supplementation and followed up for another three months.

**Results:** Symptoms were analyzed and charted. Tenderness of the skin of the legs just above the ankle was found in 38% of patients which was not documented in the earlier study. 86% of patients had elevated C-reactive protein average being 21 mg/l. 90% Of patients admitted to the hospital had Vitamin D deficiency and 62% of patients who had arthritis beyond one month had Vitamin D levels less than 20 ng/ml. Correction of vitamin D deficiency alleviated their pain early.

**Conclusions:** Testing for Vitamin D deficiency in all the patients of Chikungunya admitted to the hospital and those suffering from joint pains beyond one month and treating with Vitamin D supplementation, may be prudent to alleviate the suffering of Chikungunya.

**Keywords:** Chikungunya fever, Vitamin D deficiency, Prolonged arthritis, C-reactive protein, Ankle oedema, Facial pigmentation

### INTRODUCTION

Chikungunya viral fever is caused by an *arbovirus* (an RNA virus) of family *Togaviridae* and genus *Alphavirus*. It is transmitted by *Aedes* mosquitoes. Though *Aedes aegypti* is the common vector, *Aedes albopictus* has been implicated in rural outbreaks. The first outbreak of the

disease was noted in Tanzania. The name derived from the local language, meaning "it bends up" as the patient attains a peculiar posture due to pain and stiffness. This disease is mainly found in Africa and Asia including India. Cases occur in epidemics in the background of sporadic cases. In 2007, the outbreak has extended up to Italy. The incubation period is 2 to 4 days from the day of

mosquito bite. Viraemia persists up to 5 days from clinical onset of the disease. Common presenting features are fever, polyarthralgia of abrupt onset and may be associated with headache and backache. Children may develop a maculopapular rash. Fever may recur after an afebrile period. Small joints are commonly involved and may also have early morning stiffness.

Arthritis may persist for longer periods. Stomatitis, oral ulcers, hyper pigmentation, exfoliative dermatitis, gastrointestinal symptoms may occur. Meningeal syndromes, including encephalopathy have been reported. Diagnosis is by serology in the presence of appropriate clinical features. Immunoglobulin M (IgM) anti-Chikungunya antibodies may be detected as early as 5 days and may persist for months. Immunoglobulin G (IgG) antibodies appear in two weeks' time and persist for years. Viral cultures and molecular techniques are important research tools. Chikungunya virus RNA can be detected by PCR during first five days of illness.

Treatment of Chikungunya is symptomatic with analgesics and antipyretics. Antiviral agents are not found to be effective in treating human infection. Prevention is by minimizing exposure to mosquitos either by avoiding mosquito bite or preventing the mosquito biting the infected person so that transmission can be curtailed.

During an outbreak of this fever in 2015 it was observed by the authors that some were asymptomatic within a month's time while some were suffering from prolonged arthritis. While searching for other causes of chronic arthritis, it was found that most of them were suffering from vitamin D deficiency and they became better after supplementation of vitamin D. Very few reports were found in literature regarding vitamin D deficiency in chronic arthritis in Chikungunya viral disease, hence this study was taken up.<sup>1</sup>

## METHODS

Visakhapatnam is a metropolitan city in India with a population of 2,500,000, surrounded by many rural populations. The population involved in the study is both urban and rural. The study period was from 20th July 2015 to 30th Jan 2016. All the cases with acute onset of fever and polyarthritits not explained by other medical conditions were taken for registration. WHO defines a probable case as 'patient meeting the clinical and epidemiological criteria' for Chikungunya.

All the cases need not be tested for confirmation as immunological test may not be positive in the acute phase and management doesn't differ between probable case and confirmed cases.<sup>2</sup> In this study 200 probable cases were registered and they were followed up on day 1, day 15 and day 30. All the cases registered were excluded for Dengue fever by serological testing. Chikungunya serology was not tested as the cost is prohibitive and it may not give accurate information in acute illness. Those

people who were admitted with severe symptoms were tested for vitamin D on the day of admission. Those having arthritis symptoms beyond 30 days were tested for Vitamin D, uric acid and rheumatoid factor. Total 25-hydroxyvitamin D was estimated in plasma using the Electro-chemiluminescence immunoassay (ECLIA) using Cobas-e analyser.

88 patients (44%) were found to have low Vitamin D in their blood. They were supplemented with vitamin D 60,000 units per week orally for 8 weeks and followed up for another three months at monthly interval. Complete blood count, erythrocyte sedimentation rate (ESR), blood sugar, liver function tests, serum creatinine, C - reactive protein (CRP) and urine examination were done.

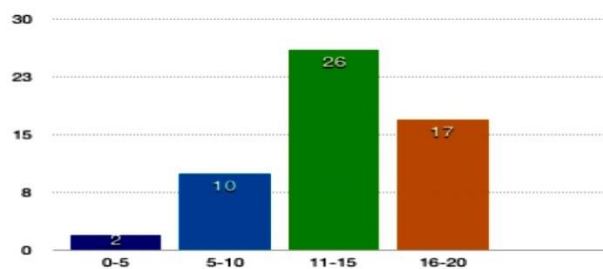
## RESULTS

Symptoms, signs and investigation reports of all Vitamin D deficient patients (n=88) were analyzed. Males and females were equally affected, youngest was 9 years old and the oldest was 81 years with an average age of 43. Children were not registered in particular, because the author was not treating the Paediatric cases. The longest duration of febrile illness recorded was 20 days and shortest duration was 1 day. In a maximum number of patients fever lasted for 5 days.



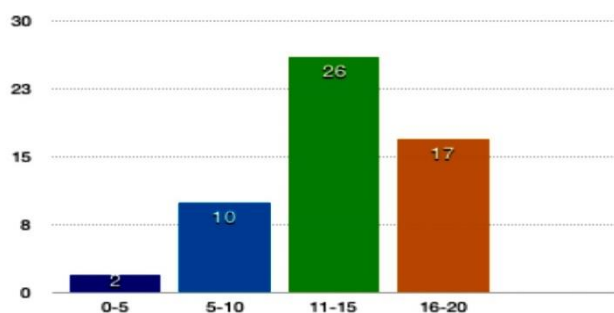
**Figure 1: Facial pigmentation.**

All the patients had polyarthritits and none presented with mono arthritits. Among the other symptoms 42% had back pain, 20% had a headache, 20% had gastrointestinal symptoms, 12% had oral ulcers, 5% had rash, and 5% had lymphadenopathy. One patient developed significant facial pigmentation (Figure 1).



**Figure 2: Elevated C-reactive protein.**

37% had ankle edema and interestingly 38% patients had tenderness of the skin of the legs just above ankle, which is classical clinical feature not documented in earlier literature. One patient developed Guillain Barre syndrome but none had encephalopathy or encephalitis. 20% of patients had a past history of Chikungunya, 19% were diabetic, 21% hypertensive, 2% asthmatics and 2% had chronic kidney disease.



**Figure 3: Low vitamin -D in patients with prolonged arthritis.**

Laboratory results were analyzed, 37% had hemoglobin less than 12 g/dL (Range 8.8 to 16.4 g/dL), 72% patients had Packed cell volume (PCV) less than 35% and interestingly 12% of patients had PCV less than 35% in spite of normal hemoglobin. Total white cell count (WBC) ranged from 3,200 to 13,700 ( $\times 10^3$  cells/mm<sup>3</sup>) with an average of 7,200 ( $\times 10^3$  cells/mm<sup>3</sup>). 6% of patients had WBC less than 4000 ( $\times 10^3$  cells/ $\mu$ L).

A small number of patients (6.6%) had a low platelet count, minimum recorded was 117,000 (cells/mm<sup>3</sup>). ESR ranged from 9 to 80 and 81% had elevated ESR. CRP was elevated in 86% of the patients, average being 21 mg/L. Uric acid is elevated in 6% of patients and none had a positive rheumatoid factor. 62% of the patients had vitamin D levels less than 20 ng/ml (Figure 2). 90% of the patients admitted to the hospital with severe symptoms had low Vitamin D (Figure 3). Duration of hospital stay was 3 to 5 days. None of them required ventilator support and no fatalities were recorded.

## DISCUSSION

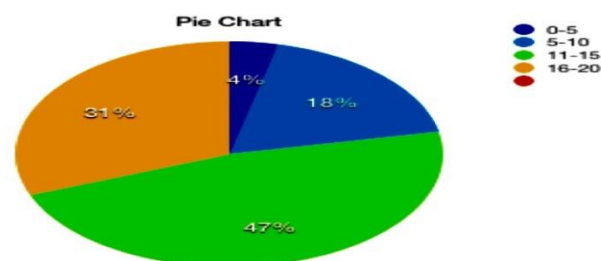
Following an acute illness of Chikungunya some patients may suffer from prolonged symptoms including arthritis.<sup>3,4</sup> In this study, 88 patients (44%) among the 200 registered Chikungunya cases had prolonged arthritis beyond 30 days. Fever was a common symptom and all patients had polyarthralgia. Back ache, headache and gastrointestinal symptoms were other symptoms reported. Duration of symptoms lasted from 1 to 20 days.

These findings are consistent with other studies, albeit gastrointestinal (20% versus 47%) and skin rash (10% versus 40%) were recorded less than that of the reports from other studies.<sup>5</sup> Interestingly diagnostic symptom of edema feet (37%) and sign of tenderness of leg above the

ankle joint (38%) was recorded. Patient winces if point a finger at the skin of leg above the ankle joint. This was not reported in the earlier literature. Persistent arthritis with local edema was reported up to 63% patients in the literature.<sup>6</sup> None had ocular manifestation in contrast to 9% involvement of in an earlier study.<sup>7</sup>

One case of Guillain Barre syndrome was recorded, whereas the literature search revealed a report of 4 cases in a retrospective study.<sup>8</sup> Pigmentation over the nose disfiguring the individual was noted in one patient whereas 4 cases of nasal necrosis were reported earlier (Figure 1).<sup>9</sup> Neither use of mechanical ventilation or fatality was reported in our study in contrast to increased death rates in previous reports.<sup>10</sup>

Among laboratory reports 12% patients had a lower PCV in spite of normal hemoglobin. Elevated C-reactive protein was a consistent lab abnormality that was found in 86% of the patients (Figure 2). Similar elevated C-reactive protein was found in earlier series.<sup>11</sup> 20% of our patients had suffered from Chikungunya in the past. 11 patients were hospitalized with severe symptoms and 10 of them significantly deficient in Vitamin D (Figure 4), suggesting that Vitamin D deficiency may exacerbate arthritis in Chikungunya sufferers.



**Figure 4: Low vitamin -D in patients admitted to hospital with severe arthritis.**

62% of patients who had arthritis at the end of the 30 day had low vitamin D. Their joint symptoms improved with correction of vitamin d deficiency. it may be hypothesized that vitamin d deficiency may prolong the arthritic symptoms in Chikungunya victims and supplementation may result in early improvement in symptoms. It may be argued that most of the Indians are deficient in vitamin D though authentic epidemiological data is not available. But none of our patient had symptoms related to bones before onset present illness.

## CONCLUSION

Chikungunya is an acute and short illness of fever and arthritis. Arthritis may have a prolonged course, if the subject is deficient in vitamin D. Symptoms may incapacitate the patient requiring hospitalization if the deficiency is severe. It is a burden to the to the patient and health care providers. Simple measure of correction of this deficiency may alleviate the suffering early. It may

be futile to check for Vitamin D deficiency in Chikungunya sufferers if they have prolonged arthritis or severe arthritis requiring hospitalization.

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