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**Dr. Shilpi Agrawal**  
Assistant Professor, Department  
of Organon of Medicine &  
Homoeopathic Philosophy,  
Ahmedabad Homoeopathic  
Medical College, Bopal Ghuma  
Road, Ghuma, Ahmedabad,  
Gujarat, India

**Dr. Gaurav Bhatt**  
Professor, Department of  
Physiology, Ahmedabad  
Homoeopathic Medical College,  
Bopal Ghuma Road, Ghuma,  
Ahmedabad, Gujarat, India

**Dr. Hima Adhvaryu**  
Assistant Professor, Department  
of Homoeopathic Materia  
Medica, Ahmedabad  
Homoeopathic Medical College,  
Bopal Ghuma Road, Ghuma,  
Ahmedabad, Gujarat, India

**Dr. Gauri Sharma**  
Associate Professor, Department  
of Organon of Medicine &  
Homoeopathic Philosophy,  
Ahmedabad Homoeopathic  
Medical College, Bopal Ghuma  
Road, Ghuma, Ahmedabad,  
Gujarat, India

**Dr. Krunal Dabhi**  
Assistant Professor, Department  
of Repertory, Ahmedabad  
Homoeopathic Medical College,  
Bopal Ghuma Road, Ghuma,  
Ahmedabad, Gujarat, India

**Dr. Jagruti Patel**  
Assistant Professor, Department  
of Forensic Medicine &  
Toxicology, Ahmedabad  
Homoeopathic Medical College,  
Bopal Ghuma Road, Ghuma,  
Ahmedabad, Gujarat, India

**Corresponding Author:**

**Dr. Shilpi Agrawal**  
Assistant Professor, Department  
of Organon of Medicine &  
Homoeopathic Philosophy,  
Ahmedabad Homoeopathic  
Medical College, Bopal Ghuma  
Road, Ghuma, Ahmedabad,  
Gujarat, India

## A study to ascertain the utility of *Gaultheria procumbens* mother tincture in management of post chikungunya arthropathy

**Dr. Shilpi Agrawal, Dr. Gaurav Bhatt, Dr. Hima Adhvaryu, Dr. Gauri Sharma, Dr. Krunal Dabhi and Dr. Jagruti Patel**

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### Abstract

To observe the utility of *Gaultheria procumbens* Mother tincture in management of Post Chikungunya Arthropathy. Post chikungunya arthropathy, a prospective experimental study was conducted at Sainath Hospital attached to Ahmedabad Homoeopathic Medical College, 50 patients were enrolled based on the predefined inclusion criteria which were observed for a period of one month. Results were evaluated on the basis of symptomatic relief, where marked improvement was seen in majority of the cases, confirming the utility of *Gaultheria procumbens* Mother tincture in management of Post chikungunya arthropathy.

**Keywords:** Chikungunya, arthropathy, polyarthritis, oedema, immobility, *Gaultheria*, mother tincture

### 1. Introduction

The largest epidemic ever recorded for chikungunya, a disease caused by infection with the chikungunya virus (CHIKV), began in Africa in 2004 and spread to >100 countries on four continents. The epidemic caused >10 million cases of often debilitating rheumatic disease, classically involving rapid onset of fever and polyarthralgia, often with polyarthritis. The clinical diagnosis of chikungunya is often complicated by infections with dengue or Zika virus. For many individuals with chikungunya, the disease is benign and self-limiting; however, some patients have a complex spectrum of atypical and severe manifestations. Many patients also experience a chronic phase of the disease, primarily involving arthralgia (which can be protracted (>1 year)), and a number of sequelae are also recognized. CHIKV-induced arthropathy arises from infection of multiple cell types in the joint and the infiltration of mainly mononuclear cells. Innate responses (primarily involving type I interferon responses and natural killer cells) and cognate responses (primarily involving CD4 T helper 1 cells), alongside activation of macrophages and monocytes, mediate CHIKV-induced arthritic immunopathology.

The acute phase may be further subdivided into viraemic (5–10 days) and sub-acute post-viraemic (6–21 days) phases.<sup>12</sup> The viraemic phase is characterised by sudden onset of high-grade fever (often >39 °C), severe polyarthralgia/polyarthritis, myalgias, conjunctivitis and exanthema.

The exanthema can present as diffuse or focal skin rash. Many patients also develop pruritus, vesicles, purpura and skin hyperesthesia. In the sub-acute phase, fever settles but articular symptoms and fatigue persist. Polyarthritis is usually symmetrical and involves small and large joints. Tenosynovitis and bursitis can also occur which are usually very painful.

The prevalence of chronic joint pain in a cohort study from Latin America is reported to be approximately 25% after a median follow-up of 20 months. The prevalence of chronic arthritis after acute CHIKV infection has been reported at approximately 14%.<sup>10</sup> Factors such as an age of more than 45 years, high viral load (>109/mL) during the acute phase and severe immunologic response in post-viraemic phase are predictors of development of chronic symptoms.

The chronic phase of the disease may follow a pattern similar to rheumatoid arthritis, peripheral spondyloarthritis, undifferentiated arthritis and fibromyalgia. The ankles, knees, hips, wrists, elbows and metacarpo-phalangeal joints are mainly involved. A recent epidemiologic study from Colombia has found that about 25% of patients remained symptomatic with joint pain after 20 months follow-up.

Chikungunya virus infection has emerged as global pandemic for last two decades<sup>[1, 2]</sup>. CHIK-V infection presents as fever-arthralgia-rash syndrome<sup>[1]</sup>. Its predominant action is on musculoskeletal system, similar to the symptoms of polyarthritis and autoimmune inflammatory arthritis<sup>[1, 2]</sup>.

CHIK-V is a member of *Togaviridae* family, responsible for arboviral infection in tropical areas<sup>[1-3]</sup>. Spread of infection is through mosquito(vector) female *Aedes aegypti* and *Aedes albopictus* for tropical and temperate countries respectively. *Culex* and *Anopheles stephensi* supports transmission of CHIK-V<sup>[1-3]</sup>.

CHIK-V was first isolated in 1953 in Tanzania, but first ever documented major outbreak was in 2004-2011, which affected about 6.5 million people<sup>[3]</sup>.

Recent epidemiology studies show CHIK-V is poly systemic disorder, involving more of musculoskeletal, neurological and gastro-intestinal system. The virus secretes toxins and its residue tends to attack the cartilages and lead to inflammation in the joints. Results could be excruciating pain and frozen joints<sup>[3]</sup>.

## 2. Literature Review

Chikungunya infection can be divided into an acute phase (<3 months) and chronic phase (>3 months)<sup>[3]</sup>.

The acute phase is further subdivided into viraemic (5–10 days) and sub-acute post-viraemic (6–21 days) phases. The viraemic phase is characterised by sudden onset of high-grade fever (often >39°C), severe polyarthralgia/polyarthritis, myalgias, conjunctivitis and exanthema. Many patients also develop pruritus, vesicles, purpura and skin hyperesthesia.

In the sub-acute phase, fever settles but articular symptoms and fatigue persist. Polyarthritis is usually symmetrical and involves small and large joints. Tenosynovitis and bursitis can also occur which are usually very painful. Patients who have co-morbidities (osteoarthritis, heart failure, respiratory disease, renal disease and diabetes) are likely to develop more severe manifestations of acute infection. Acute CHIKV infection may aggravate underlying rheumatic diseases. Studies show CHIKV infection cause relapses of autoimmune arthritis<sup>[1, 2, 6]</sup>.

The reported prevalence of CHIKV arthritis patients progressing to a chronic stage (>3 months) ranges from 4.1–78.6%<sup>[1, 2]</sup>.

The prevalence of chronic joint pain in a cohort study from Latin America is reported to be approximately 25% after a median follow-up of 20 months. The prevalence of chronic arthritis after acute CHIKV infection has been reported at approximately 14%.<sup>10</sup> Factors such as an age of more than 45 years, high viral load (>109/mL) during the acute phase and severe immunologic response in post-viraemic phase are predictors of development of chronic symptoms<sup>[5-7]</sup>.

The chronic phase of the disease follow a pattern similar to rheumatoid arthritis, peripheral spondyloarthritis, undifferentiated arthritis and fibromyalgia. The ankles, knees, hips, wrists, elbows and metacarpo-phalangeal joints are mainly involved. A recent epidemiologic study from Colombia has found that about 25% of patients remained symptomatic with joint pain after 20 months follow-up. Similar findings were reported in a meta-analysis of studies of post-CHIKV infection; chronic inflammatory rheumatism (CIR) was present in 25% of cases and chronic arthritis in 14% of cases.<sup>11</sup> In a study from the island of Martinique in

the Caribbean, 128 patients (all had positive serologic findings and medical histories consistent with diagnosis of CHIKV arthritis); about 21% of patients progressed to seronegative rheumatoid arthritis in 1 year. In the same study, 37% of patients had flare of underlying degenerative arthritis, 35% had relapse of previous clinically inactive spondyloarthritis and 7% patients had fibromyalgia<sup>[1, 2, 6]</sup>.

Chikungunya virus arthritis is an acute severe polyarthritis following upon the bite of infected mosquitoes in endemic areas. With rapid air transport an increasing number of tourists are being exposed to potential infection. Whether tourists returning home in the incubation viraemic stage can infect local mosquito populations in their home countries is unknown. Most cases recover from the severe joint pains within several weeks but up to 12% retain some residual joint symptoms for years. A case report is given of probable Chikungunya arthritis progressing to joint destruction before ultimately subsiding after 15 years leaving a sequela of destroyed metatarsal heads and late osteoarthritic changes in the ankles<sup>[5-7]</sup>

Chikungunya virus infection causes arthralgia and arthritis in the acute phase of the disease but, in more than half of the cases, musculoskeletal manifestations can be prolonged over time and, in some cases, become chronic. Although polyarthralgia is the most frequent chronic manifestation, forms with polyarthritis, tenosynovitis and enthesopathy are also common<sup>[5-7]</sup>

About 20% of patients with chronic CHIKV infection may have chronic pain with neuropathic features including paraesthesia, tingling, numbness and itching.<sup>16</sup> A study of pregnant women conducted on the island of Réunion during 2005–2006 epidemic showed that the mother to child (vertical) transmission rate was 50% when CHIKV infection occurred in the intra-partum (2 days either side of delivery) period. Delivery by caesarean section did not prevent the transmission of virus, the babies were born healthy, however they developed fever, weakness and thrombocytopenia between 3–7 days<sup>[1, 2, 5-7]</sup>

Immunological response In the acute phase of CHIKV infection, intense viremia is associated with activation of host type I interferon and interleukin (IL)-6. Other pro-inflammatory cytokines, chemokines, and soluble factors (IL-4, IL-7, macrophage migration inhibition factor (MIF), CCL2, CCL4, CXCL10 etc.) are also activated.

This strong immune response leads to the clearing of the virus by macrophages, cluster of differentiation (CD)8+ T and natural killer (NK) cells within 7–10 days of acute infection and virus levels become undetectable.<sup>7,14</sup> For this reason, after first week of infection, diagnosis using CHIKV polymerase chain reaction (PCR) is discouraged.

Immunological studies have shown decreased viral clearance due to immune dysregulation in the elderly and in patients with co-morbidities such as type 2 diabetes, chronic kidney disease and chronic heart diseases, explaining the occurrence of more intense infection in these patients.<sup>4,5,6,7</sup>

Chikungunya virus arthritis is an acute severe polyarthritis following upon the bite of infected mosquitoes in endemic areas. With rapid air transport an increasing number of tourists are being exposed to potential infection.

Chronic infection is associated with high levels of monocyte chemoattractant protein (MCP-1), macrophage inflammatory protein (MIP-1), IL-6 and IL-12 with CD4+ T cells playing a major role in ongoing inflammatory arthritis. Persistence of CHIKV ribonucleic acid in perivascular

synovial macrophages has been linked to high immunoglobulin M (IgM) response and chronic arthritis symptoms. However, the exact immunological basis for ongoing persistent inflammation causing musculoskeletal symptoms is still not clear [1, 2, 4, 6, 7]

### 3. Methodology

**3.1 Project site:** Sainath hospital affiliated with Ahmedabad homoeopathic medical college, Ahmedabad.

**3.2 Study type:** prospective, experimental

**3.3 Study type:** Prospective, Experimental

**3.4 Study duration:** 1 month

### 3.5 Sampling

**3.5.1 Method:** Purposive Sampling

**3.5.2 Number of Samples:** 50 Cases

### 3.5.3 Inclusion criteria

- All patients of arthropathy having history of chikungunya.
- Patients with post chikungunya arthropathy but not taking any other form of treatment.
- Patients included irrespective of age, sex, and socioeconomic status
- Patients regular with their medication and follow up. All subjects who were registered for the study had given their consent in written.

### 3.5.4 Exclusion criteria

- Immunocompromised Patients.
- Patients with fever but not documented chikungunya fever.
- Patients with pre-existing other form of arthropathy or arthritis.
- History of chronic co morbid condition leading to similar arthropathy.

**4. Data collection:** Data of patients was collected according to instructions of case taking given in aphorisms 83-104 in Organon of Medicine.

## 5. Description of investigational product

### 5.1 *Gaultheria procumbens* Mother Tincture

### 5.2 Botanical Name- American Wintergreen

**5.3 Description:** An evergreen, small, low growing shrub. Flowers are pendulous. Fruit is red and looks like berry, but is actually a capsule surrounded by fleshy calyx.

**6. Study design:** Prospective, experimental study to see the utility of *Gaultheria* mother tincture in Post chikungunya arthropathy, which was prescribed to 50 patients and observed for one month. Assessment criteria for post chikungunya arthropathy has been done on the improvement in the following complaints.

- Arthralgia
- Oedema
- Joint stiffness
- Joint immobility

## 7. Treatment of subject

**7.1 Medicine:** *Gaultheria procumbens* mother tincture from authentic pharmacy prepared according to Homoeopathic Pharmacopeia of India.

**7.2 Dosage and repetition:** 10 drops twice a day, in half cup of water

**7.3 Follow up:** On weekly basis for period of one month.

## 8. Assessment of efficacy

Final assessment will be carried out by the changes observed at the end of one month of the treatment regimen in the following groups:

- Marked Improvement,
- Moderate Improvement
- No Improvement

## 9. Results

**Table 1:** Socio-demographic parameters affecting post chikungunya arthropathy

Demographic Range Age	No. of cases
20-30 years	4
31-40 years	6
41-50 years	12
51-60 years	28

**Table 2:** Socio-demographic parameters affecting post chikungunya arthropathy

Gender	No. of cases
Males	22
Females	28

**Table 3:** Distribution according to Preponderance of Symptoms

	Symptomatic Preponderance In Cases Treated With <i>Gaultheria procumbens</i>	Symptoms present in no. of cases	Symptoms relieved in no. of cases
1.	Arthralgia	50	42
2.	Oedema	5	2
3.	Joint stiffness	43	38
4.	Joint immobility	21	10

**Table 3:** Result outcome

Result Outcome	No. of cases
Marked improvement	38
Moderate improvement	10
No improvement	2

## 10. Medication prescribed

For the study, 50 patients were administered homoeopathic medicine *Gaultheria procumbens* Q on the basis of its effectiveness in cases of post chikungunya arthropathy. (Arthralgia, swelling, stiffness, immobility)

### 11. Adverse Effects

No adverse events have been reported after the administration of the Medicine. The subjects were examined throughout the study to evaluate any adverse effects after consumption of homoeopathic medicine.

Discussion: Homoeopathy has produced lot of successful results in post chikungunya arthropathy without any side effects. In study out of the 50 cases treated and observed that cases showed positive result in arthralgia (96%), swelling (88%), mobility (68.1%), stiffness (60%) with the use of the remedy *Gaultheria procumbens* Q

### 12. Contraindications

There is no contraindication for *Gaultheria procumbens*, in this study, pregnant and lactating females were not included.

### 13. Discussion

Homoeopathy has produced successful results in post chikungunya arthropathy without any side effects. In study, 50 cases were treated and it was observed that cases showed positive result in arthralgia (84%), oedema (4%), immobility (20%), stiffness (76%) with the use of the remedy *Gaultheria procumbens* mother tincture.

In our study, out of 50 patients, 28 were in the age group of 50-60 years. A significant positive correlation between age and incidence was found. In 50 cases enrolled, female patients were more in number accounting to 56% and males were 44%. It is observed that out of 50 cases, 48 cases showed improvement, where marked improvement was seen in 38 cases and moderate in 10 cases, and no relief was seen in 2 cases.

There is currently no vaccine or drugs against the virus. Cases of death from chikungunya are very rare, homoeopathy can be helpful in giving symptomatic relief.

### 14. Conclusion

The success in achieving the significant results in majority of cases is due to the effect of *Gaultheria procumbens* in the post chikungunya arthropathy which helps to draw significant conclusion.

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