

**CONTRIBUTION OF HOST FACTORS TOWARDS ARBOVIRAL INFECTIONS IN EASTERN INDIA AND
EFFECT OF CURCUMIN AGAINST ARBOVIRAL INDUCED ARTHRITIS**

Abstract

Arboviral infections caused by various arthropod-borne viruses viz. dengue (DENV) and chikungunya (CHIKV) have emerged as one of the most serious emerging threats to global health, leading to high mortality and morbidity. Both DENV and CHIKV are transmitted by same vector *Aedes aegypti* in India. Dengue endemic areas of India overlap with regions having chikungunya infection, leading to DENV-CHIKV co-infection. CHIKV mono-infection and DENV-CHIKV co-infection among symptomatic Eastern Indian patients was determined by RT-PCR, anti-CHIKV/DENV IgM and dengue-NS1 ELISA. 26.05% (167/641) CHIKV mono-infection and 19.96% (128/641) DENV-CHIKV co-infection was detected among suspected febrile patients presenting WHO-recommended symptoms. 40-60% of CHIKV-infected patients develop chronic inflammatory rheumatism and musculo-skeletal disease known as post-chikungunya chronic arthritis (PCA). This study revealed serum-levels of arthritic biomarkers viz. C-reactive protein (CRP), cartilage oligomeric matrix protein (COMP), anti-cyclic citrullinated peptide (anti-CCP) antibody, interleukin-2 receptor (IL-2R) significantly increased among PCA patients. Also, patients with IL-2R-rs743777-GA, G-allele and COMP-rs144778694-GA genotypes were susceptible to chikungunya infection. COMP-rs144778694-GA genotype was susceptible towards development of arthralgia. Upon DENV-CHIKV co-infection, Toll-like receptors (TLR) and CRP triggers innate immunity activation resulting in elevated cytokines leading to a plethora of defensive mechanisms. Thus, this study identified patients with certain single nucleotide polymorphisms (SNPs) of TLR3,7,8 and CRP were susceptible to co-infection. Moreover, probable role of specific genotypes of TLR7,8 and CRP SNPs towards imparting high dengue/chikungunya viral load during competitive viral replication among co-infected patients were identified. Till date, no FDA-approved analgesic drug is available for treatment of CHIKV-induced arthritis. Hence, in this study analgesic and prophylactic effect of curcumin, among CHIKV-induced arthralgic mice was explored. Curcumin treatment significantly alleviated CHIKV-induced arthritic pain by improving pain-threshold, locomotory behavior and reduced feet swelling of CHIKV-induced arthralgic mice. Also, decreased proteoglycan loss and cartilage erosion with lower arthritic scores were observed after curcumin treatment. Compared to infected mice, 1-2-fold increased intensity of type II collagen in knee articular regions was observed among curcumin-treated mice by immunohistochemical staining. Thus, the entire study imparted valuable inputs regarding contribution of host factors towards arboviral infections in eastern India and analgesic and prophylactic effect of curcumin against arboviral induced arthritis.

Siddhartha Sengupta
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Anusri Tripathi
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Dr. Anusri Tripathi, Ph.D.
Assistant Professor (Molecular Biology)
Department of Biotechnology and
Medical Biotechnology
School of Tropical Medicine, Koinata
Koinata - 751005, Odisha, India-75