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Chikungunya outbreaks in India: A prospective study comparing neutralization, sequelae and molecular epidemiology during two outbreaks in 2010 and 2016

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Chikungunya fever (CHIKF) is a major public health concern in India. In 2005, the etiologic agent, chikungunya virus (CHIKV) was reintroduced into the Indian subcontinent after a gap of 32 years and thereafter, occurred as outbreaks in several parts of the country. We recruited 588 patients in the acute phase of CHIKF during outbreaks in 2010 and 2016 from a tertiary-care-hospital in New Delhi, India and collected their blood along with their clinical information. Their arthralgic status was documented after 12 weeks post onset of fever. We evaluated IgM/IgG CHIKV-binding antibodies and their neutralizing capacity for all sera. We sequenced whole genomes of 22 CHIKV strains, analyzed them for mutations and correlated these with patient sequelae status. We performed infections of murine models using representative strains from both the outbreaks to evaluate differences in their pathogenesis. Our detailed screening and analysis revealed that patients afflicted during the 2016 outbreak developed earlier IgM and neutralizing antibodies that were negatively correlated with CHIKF sequelae as compared to 2010 patients. Mutation analysis and in vivo pathogenesis studies of the viral isolates revealed differences in virulence based on their genetic makeup. Our study provides insights into CHIKF progression in the Indian subcontinent during outbreaks in an endemic setting with respect to host response as well as viral pathogenesis. Importantly, we provide information on the development of neutralizing antibodies and sequence variation in clinical isolates that correlate with human sequelae.

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