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An outbreak of chikungunya in Jamshedpur, Jharkhand in 2011

Sir,

Increase in number of fever cases with joint pains, rashes as common symptoms and respiratory, gastrointestinal symptoms and mortality among a few cases[1,2] were reported during July- August 2011 by the district health authorities in Jamshedpur (Latitude: 22°48′N, Longitude: 86°11′E), East Singhbhoom district, Jharkhand. This is a major industrial centre of East India with population of 11,04,713 (Census of India 2001)[3]. About 30,000 people were reported with fever (on an average daily 500 patients) and visited the outpatient departments of various hospitals in the city[4]. Tata Main Hospital in Jamshedpur, Jharkhand sent 10 blood samples from hospitalized patients suspected to have viral fever to National Institute of Virology (NIV), Pune on July 25, 2011. In the third week of July, district health authorities also sent serum samples from 10 patients with viral fever to National Center for Disease Control, New Delhi and anti-chikungunya virus (CHIKV) immunoglobulin M (IgM) antibodies were detected in three cases (District Surveillance Officer, Jamshedpur, personal communication). Serum samples from another 10 viral fever cases were also sent to School of Tropical Medicine, Kolkata, and anti-CHIKV IgM antibodies were detected in three cases and anti-dengue virus (DENV) IgM antibodies were detected in two cases suggesting co-circulation. Mortality reported in two fever cases admitted in the hospitals in the city created a panic situation among the citizens, of Jamshedpur[2,4]. Therefore, NIV, Pune, attempted to investigate the viral fever cases reported from August 2-9, 2011, to establish the aetiology and to suggest the preventive and control measures.

A suspected case was defined as a person with acute history of fever with any one or more of the following symptoms: joint pain, rash, headache, myalgia, photophobia and arthralgia. A subset of suspected cases (n=220) visiting the outpatient department, and/or admitted in tertiary care hospitals (Tata Main Hospital, Mahatma Gandhi Memorial Medical College Hospital and TELCO Hospital) in the city were examined and blood samples (2-3 ml) were collected for diagnosis. Blood samples were also collected from line-listed suspected cases (n=78) by district health authorities from three localities in Jamshedpur *i.e.* Somaya Zopadi Ghageri South (n=29), Gulti Zopadi Ghageri North (n=18), and Refugee Colony Mango (n=31).

Clinical samples (n=220) [blood from fever cases and cerebrospinal fluid (CSF) [referred by Tata Main Hospital (n=5) from patients presented with fever and neurological involvement] were aseptically collected and transported on ice to National Institute of Virology, Pune. Detection of anti-CHIKV IgM antibodies (n=220) and anti-DENV IgM antibodies (n=220) was carried out by enzyme linked immuno sorbant assay[5,6]. Blood samples (n=92) collected in early post onset day (duration <7 days) were screened for the presence of CHIKV and DENV by real time polymerase chain reaction (RT-PCR)[7].

Intracranial inoculation of suckling mice with suspected clinical specimen for initial isolation and amplification of arboviruses is a classical procedure used worldwide[8]. Therefore, in this study infant (24-48 h old) Swiss albino mice were used for virus isolation. Methods for extraction, amplification and sequencing of viral RNA have been described previously[9,10]. Partial gene sequences of non-structural protein 1 (NS1) of CHIKV were used for phylogenetic analysis. Phylogenetic analysis was performed using the freeware[11] MEGA 5. Best fit model for nucleotide substitution was selected from 24 models available in MEGA 5 based on minimum Akaike Information Criterion value[12]. Tamura Nei + I model of nucleotide substitution, obtained in the model test, was used for

constructing phylogenetic tree based on maximum likelihood method. Reliability of the phylogenetic tree was estimated using bootstrap values run for 1000 iterations. In the Reunion Island most CHIKV isolated from patients presented an amino-acid substitution in the E1 glycoprotein, from an alanine (E1-226A) to a valine (E1-226V)[13]. This mutation has selective advantage in *Aedes albopictus*[13]. Therefore, it was thought desirable to investigate the presence of the E1-A226V change in these isolates. The same samples were screened for A226V mutation from E1 region by RT-PCR followed by sequencing[9].

A total of 13,228 suspected cases were reported by public health authorities at Jamshedpur (District Surveillance Officer, personal communication). Among the 220 suspected cases investigated, 99 were male and 51 per cent were in the age group of 20-39 yr and 89 required hospitalization. Duration of hospitalization ranged between 1 and 14 days (median 4 days). Common clinical feature observed among suspected cases were fever (100%), joint pain (83.2%), rash (52.6%), headache (34.5%), myalgia (33.6%), retro-orbital pain (21%), nausea (20%) and vomiting (20%), diarrhoea (19%), itching (3.2%), oral ulcers (2.3%), cough (1.8%) and sore throat (0.9%). Neurological manifestations included altered sensorium (4.5%), unconsciousness (4.1%) and convulsions (4.1%). Rash was non pruritic, maculopapular and erythematous in character and started appearing 1-3 days after the initial symptom (fever/joint pain) and distributed on face,

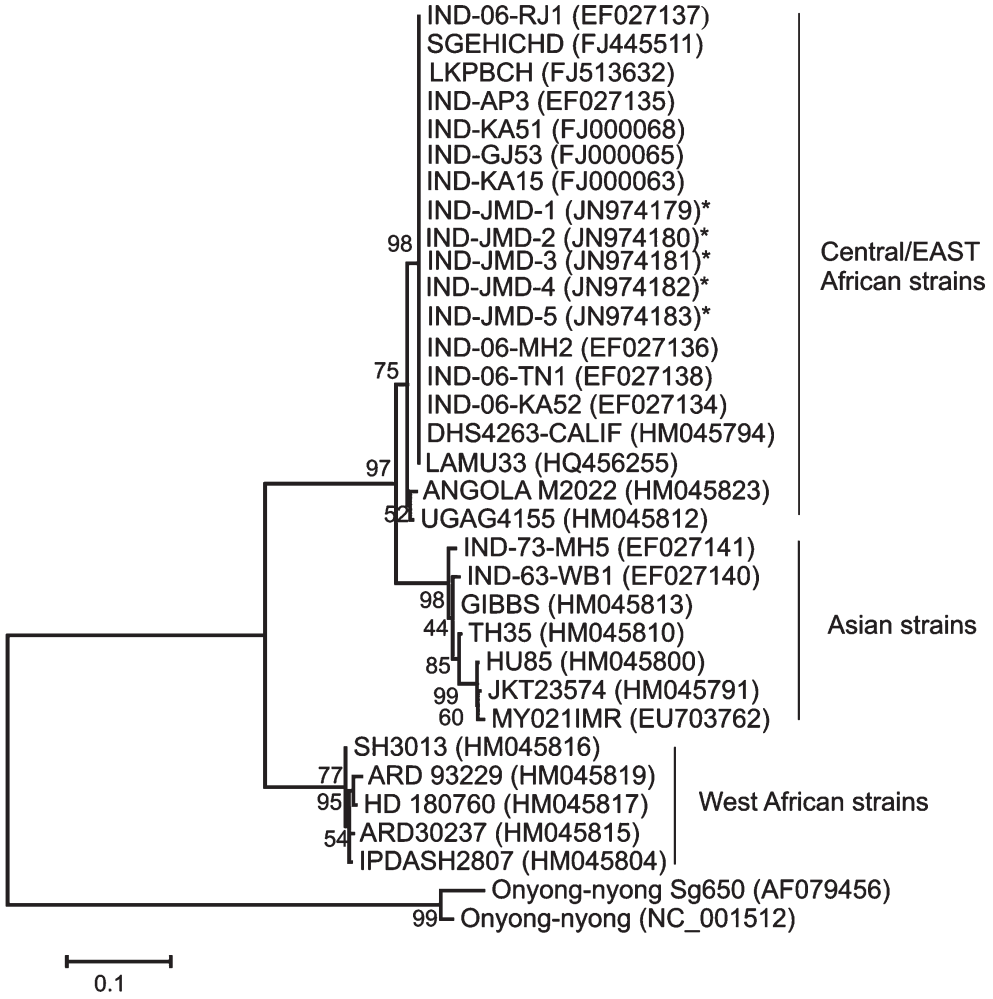

Fig. Phylogenetic relationships of chikungunya virus isolates from the 2011 Jamshetpur outbreak, India. The maximum likely hood tree was constructed using nucleic acid sequences of the ns1 gene (1160-1700 bp), with O'nyong nyong virus as an out-group virus. *Denotes the strains of present study (Accession Numbers JN974179, JN974180, JN974181, JN974182 and JN974183). The scale represents genetic distance.

limbs and trunk of the body. Pre- and post-auricular lymphadenopathy was also noted among four patients.

Clinical samples collected from 220 suspected cases included 220 serum samples, 2 convalescent serum samples and 5 cerebrospinal fluids samples. Anti-CHIKV IgM antibodies were detected in 61.4 per cent (135/220), viral RNA in 45.6 per cent (42/92 *i.e.*, the only available early POD samples) cases [serum collected during early post onset days (duration <7 days)] and both anti-CHIK IgM antibodies and CHIKV RNA detected in two cases. Anti-CHIKV IgM antibodies in serum and CSF sample were also detected in a 45 days old male suspect case presented with febrile convulsions. Anti-DENV IgM antibodies were not detected in any suspected cases, however, two serum samples were indeterminate for anti DENV IgM antibodies. Dengue viral RNA was not detected in any samples (n=92). Thus chikungunya infection was confirmed in 81.4 per cent (179/220) suspected cases. Laboratory findings in chikungunya cases were as follows; total leukocyte count (n=59), less then 4000/ ul was in two cases; platelet count (n=52), less then 1,50,000/ul in 29 cases; serum creatinine (n=37) more then 1.5 mg/dl in four cases; blood urea (n=37) more than 40 mg per cent in eight cases; serum glutamic oxaloacetic transaminase (n=25) more then 40 U/l in 15 cases; serum glutamic pyruvic transaminase (n=35) more than 40 U/l in 19 cases. Malarial parasite was not detected any of the suspected cases.

Mortality was reported in three laboratory confirmed chikungunya cases which presented with co-morbidity; a 45 yr old female with hypertension, a 60 yr old male with ischaemic heart disease and a 68 yr old male with diabetes mellitus. These three patients died due to multi organ failure. Febrile convulsions among children were also reported in two chikungunya positive cases.

CHIKV was isolated from 14 of 20 randomly selected from RTPCR positive serum samples collected (early POD) during the outbreak from suspected chikungunya cases and were RT-PCR positive for CHIKV. Sequencing based on ns1 region revealed homology with the African genotype. A226V mutation from E1 region was not observed in five isolates investigated. For phylogenetic analysis, ns1 sequences were obtained for five chikungunya cases. A phylogenetic tree was constructed based on partial ns1 region of 540 bp, over nucleotide positions 1161 to 1700, numbered according to the CHIKV prototype S27. The five isolates from the current Jamshedpur outbreak matched with recent Central/East African isolates from 2005 to 2008, sharing 98-99 per cent nucleotide identity (Figure). Sequencing of E1 gene of these five chikungunya isolates reveled that there is no amino-acid substitution in the E1 glycoprotein, from an alanine (E1-226A) to a valine (E1-226V).

Earlier, during May-September 1954, fever cases with increase in hospital admissions were also reported in Jamshedpur[14]. However, no conclusive aetiology was established[15]. The presence of CHIKV antibodies in human serum was also reported in 1964 from Jamshedpur[16]. Important preventive and control measures suggested to district health authorities include increasing awareness among people about how to avoid mosquito bites and strengthening vector surveillance for *Aedes* mosquito together with biological, chemical and environmental control measures against mosquitoes. Important observation noted in this outbreak was mortality associated with chikungunya infection in three suspected cases. Mortality due to severe chikungunya infection has been previously reported from Ahmedabad[17,18] and Pune[17,19].

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