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Chandipura Virus Recognized among AES for the First Time in Bihar, India

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A B S T R A C T

The epidemic outbreak of Acute Encephalitis Syndrome (AES) was continuing specially from 2014 onwards and taking toll of pediatric age group distributed in different blocks of Gaya district of Bihar, India. In an extensive survey during outbreak (2016), a case of high fever history was diagnosed having Chandipura virus out of 24 acute fever cases admitted at Anugrah Narayan Memorial Magadh Medical College and Hospital (ANMMMCH) Gaya. Off which nine cases were from Gaya district. The age group of affected cases was 1-15 years. Male were affected more than females (M:F::55.5:44.4). Records of death were found five. Patients were suffering from acute-onset of fever with change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and often with new onset of seizures. All were diagnosed as equivocal JE by IgM ELISA except one. It was the first case report from Bihar, India. The treatment was only based on sign and symptoms. AES is a seasonal and major health problem of Bihar coming every year. This study has disclosed one of the reasons of AES in Bihar.

Introduction

Chandipura virus (CHPV) is a vesiculo virus of the Rhabdoviridae family. It was for the first time reported in 1965 in Chandipur village in the Nagpur region of India from two adults with a febrile illness during an outbreak caused by dengue and chikungunya viruses (Bhatt *et al.*, 1967). Time to time several outbreaks of CHPV encephalitis has been reported from India. These have been characterized by rapid onset of fever, involvement of the central nervous system and a high case-fatality rate (Rao *et al.*, 2003; Chanda *et al.*, 2005). Most studies from India in outbreak and surveillance settings between 1975 and 1999 indicated that Japanese encephalitis virus (JEV) was the most common virus in acute encephalitis syndrome (AES), but studies after 2000 have shown a predominance of CHPV and Enterovirus (Joshi *et al.*, 2012). AES is defined as the acute-onset of fever with change in mental status (including symptoms such as confusion,

disorientation, coma, or inability to talk) and often with new onset of seizures in a person of any age at any time of the year (Solomon *et al.,* 2008). JE has been considered as leading cause of AES in India (Gendelman and Persidsky, 2005; Das, 2005). It is a major health problem in Asia region. AES includes illness caused by many infectious as well as non infectious causes considered as viral encephalitis (Jmor *et al.,* 2008). The main etiological agent is Japanese encephalitis virus (JEV), a positive sense single stranded zoonotic flavivirus transmitted by *Culex* spp. mosquitoes (Geevarghese *et al.,* 2004) between wild/domestic birds and pigs; where birds act as reservoir host and pig act as amplifying host (Reuben and Gajanana, 1997). It is a leading cause of viral encephalitis in Asia with 30,000-50,000 clinical cases reported annually. Man is the accidental host and dead end for the transmission of the disease (Diagana *et al.,* 2007). The first major Outbreak of JE occurred in 1973 in Bankura & Burdwan districts of West Bengal. The first clinical case of JE was observed in 1955 at Vellore in India. The sources of virus may be different causing almost similar symptoms. In1976, wide spread outbreaks were reported from Andhra Pradesh, Assam, Karnataka, Tamil Nadu, Uttar Pradesh and West Bengal. Hence, all JE cases are being reported under Acute Encephalitis Syndrome (AES) after the outbreak of JE in Gorakhpur and Basti divisions in Eastern Uttar Pradesh during 2005 (WHO, 2010). It is a disease of major public health importance. The highly affected states include Andhra Pradesh, Assam, Bihar, Goa, Karnataka, Manipur, Tamil Nadu, Uttar Pradesh and West Bengal. Outbreaks of JE usually coincide with monsoons and post-monsoon period when the vector density is high (Ministry of Health and Family Welfare, 2009). Early management of the viral disease is essential, because there is no specific treatment. High vaccine coverage along with active surveillance is essential. The ultimate objective is to prevent the disease occurrence by early diagnosis, implementation of effective control measures and high vaccine coverage with onset of the disease during the particular season of the year.

Materials and Methods

The patient record was collected from Anugrah Narayan Memorial Magadh Medical College and Hospital (ANMMCH) Gaya, Govt. of Bihar. Blood and cerebro spinal fluid (CSF) samples were tested for AES including JE IgM (ELISA), Leptospira (RDT IgM & IgG), Chikungunyia (ELISA IgM), HSV 1&2 (ELISA), JEV (PCR) Scrub typhus (ELISA IgM) West Nile Virus (PCR), Chandipura virus (PCR) following antigen-capture ELISA method described by Chadha *et al.,* (2005) and PCR with the method of (Rao *et al.,* 2003). All affected households were screened by a door-to-door visit and recorded the cases and deaths. The information on topography of the affected area, demography, differential diagnosis and other relevant informations were collected using standard questionnaire. Sand flies were collected using flash light and aspirator during dusk from resting indoor walls and Centre for Disease Control (CDC) light traps (miniature incandescent light trap, model 1012; J. W. Hock Co., Gainesville, FL, U. S. A.) installing over night from the affected villages like Singha par in Neemachak Bathani block, chakand, etc. The diagnosis and treatment data of the patient was under taken at treating hospitals.

Ethics statement

The study was conducted in accordance with the current version of the Declaration of Helsinki and the Indian Council of Medical Research (ICMR) ethical guideline of the biomedical research on human participants (2006). Informed written consent was taken from adult participants and parents/local

guardians of the children involved in the study. The photographs of patients, households, and field conditions were taken with the consent of the person concerned. The collection of data was made on different aspects of the study like clinical, epidemiological and entomological in rural Bihar, India, following the Government guidelines.

Results and Discussion

Gaya is stretched in between 24.72130N and 84.8568^{0}E (Figure 1). During the outbreak period of the disease in June 2016 the average minimum temperature was 27^{0}C (23^{0}C-30^{0}C), average maximum temperature was 39^{0}C (36^{0}C-44^{0}C), average relative humidity was 61% (34%-97%) and average precipitation was 2 mm. This was the hottest month of the year 2016. This mysterious viral outbreak occurred in June 2016 at Gaya district with high attack rate in Bihar, India. An epidemic investigation was carried out to explore the possible causative factors by visiting the affected areas.

Fig.1 Location of Gaya district in Bihar and Chandipura viral disease in Gaya in Neemchak bathani block

The first AES outbreak investigation was conducted in Eastern India in 1973 (Chatterjee, 1974; Chatterjee and Banerjee, 1975). During the first epidemic of Chandipura virus at in tribal population of Odisha in 2009, sudden death of 10 children occurred (Dwibedi *et al.,* 2015). The first epidemic of AES appeared in 2011 in North Bihar. Only one or two cases were found in each affected village. A total of 85 cases were reported, out of which 55 cases were from KDKM hospital and 30 cases from Department of Pediatrics of SKMCH Muzaffarpur till June and July 2011 during the survey period. Out of these 81% of the cases were from Muzaffarpur and rest were from adjacent districts like Sitamarhi, Sheohar and East Champaran. The disease was presumed as a viral out break/ AES due to short duration of severe illness and senselessness resulting in death. The first case was admitted at KDKM hospital on 11the June 2011 (Dinesh *et al.,* 2013). There was record of 26 deaths (31%). The case fatality rate was found 20% in Gorakhpur at India (Singh *et al.,* 2013) and 25% from 2004-2009 epidemic in Vietnam (Paireau *et al.,* 2012) and North India (Bouchama, 1995). The median age of the patients was found to be 5 years ranging between 3 months to 10 years, belonging to weaker socio- economic section of the society mainly schedule caste populations. However in the outbreak at Gorakhpur, India 93.69% cases were below age group of 15 years (Singh *et al.,* 2013). The sex ratio was found to be 1.2:1 male to female. It was 1.45:1 in Gorakhpur of Uttar Pradesh. In this study the nine cases of AES appeared in nine different blocks individually.One case of Chandipura viral disease was found in Singha par village of Neemachak Bathani block (Figure 1). The affected age group was found between 1-15 having male (55.5%) and feamle (44.4%). Out of which, six to 10 years of age group was found highly affected with JE equivocal viruses. All patients belong to low socio-economic group. The trend of the disease progression was found increasing and 1.2:1 in Vietnam (Paireau *et al.,* 2012*)* gradually and reaching to the peak on 6^{th} day started declining gradually reaching to the baseline on 14 day coinciding with rainfall. Almost all cases had similar clinical presentation such as high fever, headache, coughing, sneezing, running nose, chills, diarrhea, vomiting, rash, sudden convulsion, and loss of consciousness but not stiff neck, Kernig's sign or Brudzinski's sign. In the case of severity of the patient, the symptom included change of personality, paralysis, back pain, sleepiness that progressed to coma or death in Muzaffarpur out break during 2011(Dinesh *et al.,*2013). Before the onset of disease, patients had no history of any illness or sickness. Based on the clinical presentation and hematological reports a provisional diagnosis of Encephalopathy was made and the differential diagnosis like viral meningitis, tuberculosis meningitis, heat stroke, malaria, bacterial meningitis, etc. needed to be explored. Paracetamol injections and cold sponging was also done for control of fever. Outbreak of acute encephalitis was found in children coinciding with hottest season before rain. Harvesting (May- July) reported in Bac Giang Province in north Vietnam from late 1090s. Environmental, agronomic and climatic factors were also found associated with the disease outbreak (Paireau *et al.,* 2012). The exposure for viral infection cannot be ignored due to the sudden change of body temperature frequent movement of children from house to orchard and vice versa. Heat stroke due to $>40.6^{0}$C temperatures affects central nervous system dysfunction (Boucham, 1995). Raised body temperature and CNS dysfunction are common to both classic and external (Moseley, 1997). Sandflies were also collected from the affected village. The resting density of sandfly (*Phlebotomus argentipes*) was found

5 per man hour and overnight cdc collection was found 11 per trap per night. Sandflies were tested for Chandipura Virus by RT-PCR but none was found positive. Similar result was found in Odisha Chandipura out break in 2009 (Dwibedi *et al.,* 2015). There was no vector control measure in that area prior to out break. Vector control major is essential for prevention of the disease outbreak in future.

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