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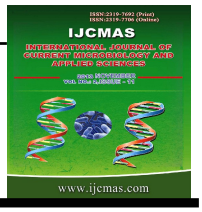


**Original Research Article**

# Possible factors causing Acute Encephalitis Syndrome outbreak in Bihar, India

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**Keywords**

AES; epidemic; brain fever; litchi season; heat stroke.

**A B S T R A C T**

The first epidemic outbreak of Acute Encephalites Syndrome appeared in North Bihar districts during 2011 particularly among poorest community in the pediatric age group. Patient Data were collected from Shri Krishna Medical College and Hospital, Muzaffarpur and Krishnadevi Deviprasad Kejariwal Maternity under KDK Matri Sadan Trust at Muzaffarpur. The topography of the affected villages was studied using standard questionnaire. The disease appeared in pediatric age group (median 5 years between 3 months to 10 years) coinciding with the litchi (*Litchi chinensis*) fruit season. A total of 85 cases appeared in Muzaffarpur and a few in two districts namely Sitamarhi, Sheohar and East Champaran with 31% death from June-July, 2011. The symptomatic treatments were given to the patients due to lack of diagnosis. Heat stroke was suspected as major possible factor

## Introduction

Acute encephalitis syndrome (AES) is be 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 (excluding simple febrile convulsion) in a person of any age at any time of the year (Solomon *et al.*,2008). It is a major health problem in Asia. AES includes illness caused by many infectious as well as non infectious causes and most are considered as viral encephalitis (Jmor *et al.*,2008). JE has been considered as leading cause of AES in India (Gendelman and Persidsky, 2005; Das, 2005). 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). Man is the accidental host and dead end for the transmission of the disease (Diagana *et al.*,2007; Scherer

*et al.*,). It is a leading cause of viral encephalitis in Asia with 30,000-50,000 clinical cases reported annually. The first clinical case of JE was observed in 1955 at Vellore in India (Namachiviyam and Umayal ). The first major Outbreak of JE occurred in 1973 in Bankura & Burdwan districts of West Bengal. In1976, wide spread outbreaks were reported from Andhra Pradesh, Assam, Karnataka, Tamil Nadu, Uttar Pradesh and West Bengal. The sources of virus may be different causing almost similar symptoms. 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 because of its epidemic potential and high case fatality rate. 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 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, high vaccine coverage with strong and active surveillance system(Vandana *et al.*,2008).

This mysterious viral outbreak occurred in June 2011 at Muzarffarpur district with high attack rate and comparatively with low attack rate in other adjacent districts like Sitamarhi, Sheohar and East Champaran of Bihar, India. An epidemic investigation was carried out to explore the possible causative factors for sudden onset of the disease during the particular season of the year.

## Materials and Methods

The latitude and longitude of the highly affected area i.e. Muzaffarpur, India is $26^0$7'0"N/$85^0$24'0"E situated at the elevation of 170' and stretched in an area of 13122.56 sq. km. (Fig-1). The season was very hot i.e. peak summer having meteorological data of temperature; Max. (38.2°C -27.4°C), Min. (30°C -23.2°C), Relative Humidity; Max. (97-66%), Min. (97-59%) and Precipitation (0-47.6 mm) coinciding with the setting in of rainy season providing congenial environmental conditions for this AES outbreak.

The patient record was collected from (i) Shri Krishna Medical College and Hospital (SKMCH), Govt. of Bihar and (ii) Krishnadevi Deviprasad Kejariwal Maternity (KDKM) under KDK Matri Sadan Trust at Muzaffarpur. The information on topography of the affected area, demography, differential diagnosis and other relevant informations were collected using standard questionnaire. Mosquitoes and sand flies were collected using flash light and mouth aspirator after dusk from indoor and outdoor habitats using Centre for Disease Control (CDC) light traps (miniature incandescent light trap, model 1012; J. W. Hock Co., Gainesville, FL, U. S. A.) from the villages Mithansarai of, Musahri PHC and Manikpur, Harpur, Purenia, Mahdaiya, Chakjamal, Madhubani of highly affected Minapur PHC of Muzaffarpur district. The diagnosis and treatment data of the patient was 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

The first AES outbreak investigation was conducted in Eastern India in 1973(Chatterjee, 1974; Chatterjee and Banerjee, 1975). However, 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. 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) (Fig-2). The sex ratio was found to be 1.2:1 male to female. It was 1.45:1 in Gorakhpur of Uttar Pradesh[15] and 1.2:1 in Vietnam (Paireau *et al.*,2012). The trend of the disease progression was found increasing gradually and reaching to the peak on 6$^{th}$ day started declining gradually reaching to the baseline on 14$^{th}$ day (Fig-3) conciding with rainfall (Fig-4).

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. 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. Serum and Cerebro Spinal Fluid (CSF) was taken from all the patients by anti cubital vein puncture and lumber puncture respectively. Electrolyte estimation (Sodium, Potassium, Calcium, etc.) were estimated and corrected. The CSF was normal and the serological tests did not confirm Japanese B Encephalitis. Brain tissue was taken from two dead patients after taking written informed consent from the parents and the results were inconclusive.

**Figure.1** Map of Bihar showing location of affected districts


**Figure.2** Age distribution of the patients

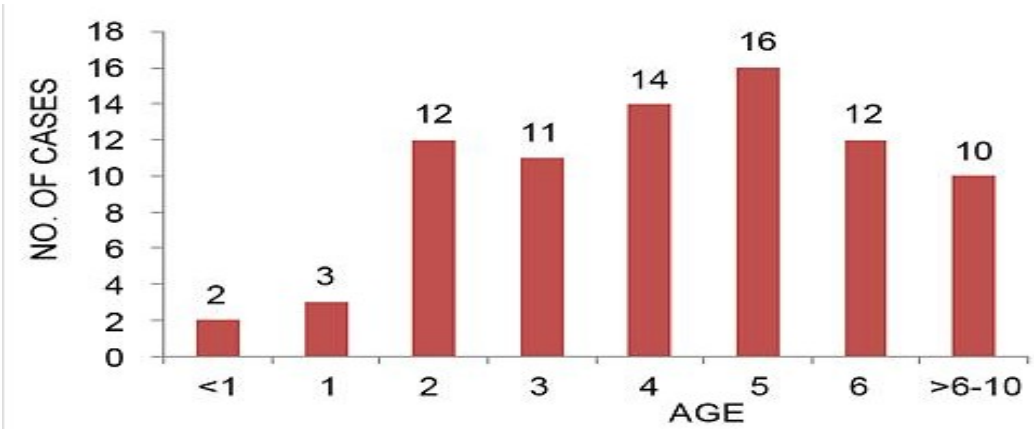


**Figure.3** Daywise progression of the disease

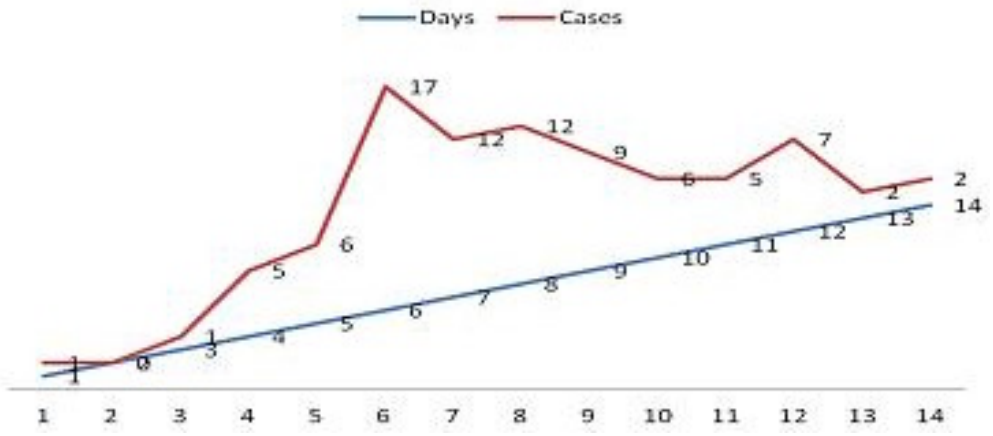

**Figure.4** The effect of temperature (Max), Relative humidity (max.) and rain fall on the incidence of the disease.

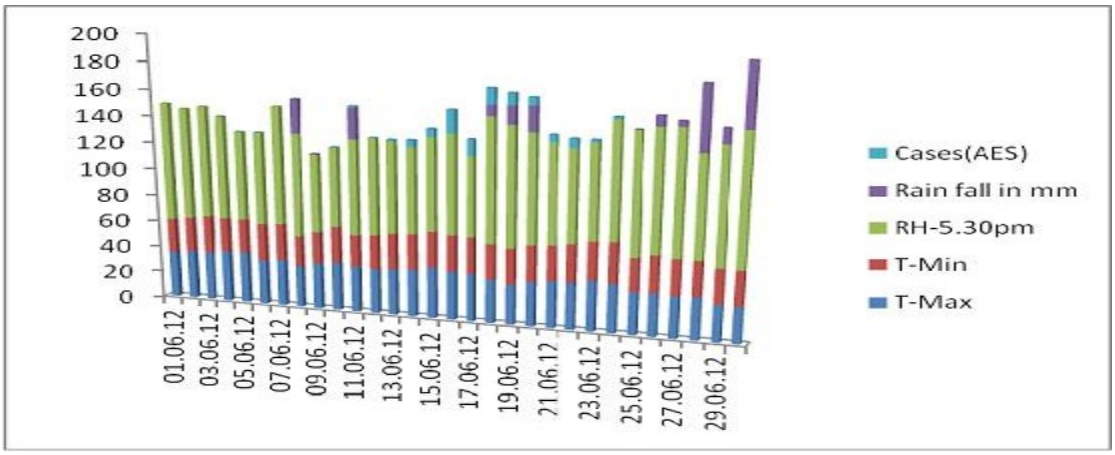


**Figure. 5** Relationship of production of litchi (in tonnes) with incident cases

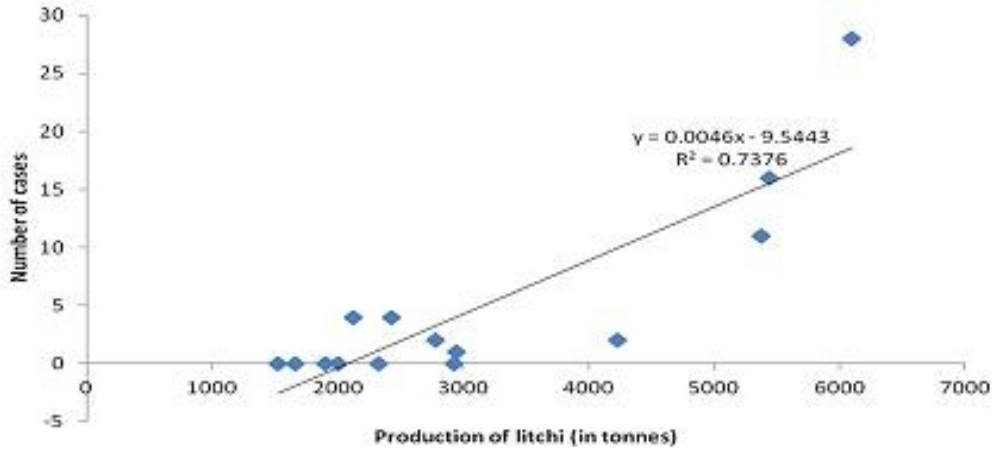


**Figure.6** Large No. of bats hanging/sitting on tree

In general all the patients were treated with anti-edema measures like 20% mannitol/glycerol, IV fluids (hyper/isotonic) etc. Acyclovir was given in two patients who were Herpes Simplex Virus type-I (HSV-I) positive by ELISA in the dose of 30mg/kg in three divided doses. Computerized Tomography/ Magnetic Resonance Imaging also revealed exudates in the frontal/temporo-parietal regions of the brain suggestive of HSV-I encaphalitis. Phenytoin sodium was given for convulsions intravenously in a loading dose of 20 mg/kg in Normal Saline (0.9%) followed by a dose of 6-8 mg/kg in divided doses. Paracetamol injections and cold sponging was also done for control of fever. Both established causes of such cerebral fever were scrutinized.

This incidence coincides with large scale production of litchi, a very famous seasonal fruit grown in part of the state with a high demand of export worldwide. The incident cases with that of quantum of production of litchi is depicting a strong relationship ($R^2$ = 0.7376, r (correlation coefficient) = 0.86) coinciding with season also (Fig-5).

The high quantum of production of litchi fruit might not be directly acting as a causative factor, but some other ecological, environmental and behavioral factors might have some indirect effect that could be acting as causative factors for high incidence of disease among the populations residing by the orchard. Outbreak of acute encephalitis in children coinciding with litchi harvesting (May-July) reported in Bac Giang Province in north Vietnam from late 1090's. 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). Hence, this may be one of the reasons for severity of the disease. Their source of drinking water was hand pump. People generally rest in shadow of the litchi orchards in the day time.

Bats were found in large number resting on trees (Fig-6). Most of these fruits might have been rotten due to some kind of infection through saliva of birds, bats or lizards or decaying due to bacteria. It was reported by the parents of affected patients in course of investigation that some children had eaten fallen fruits in the orchard few days before illness. The possibility of transmission of pathogen through this rout cannot be ignored. Nipah virus (NiV) is transmitted by bats causing encephalitis or respiratory disease to human population. The first outbreak of NiV was reported in Malaysia and subsequently eight out breaks have been reported from India and Bangladesh since 2001. This virus is transmitted from human to human also. There, it was suggested to make efforts to prevent transmission focused on decreasing bat access to date palm sap and reducing family members and friend's exposure to infected patients saliva ) Luby *et al.,*2009).

However, among the affected children some of them were in age of <1 year who can't eat fruits. Hence, there could be possibility of getting infection through different transmission mechanism other

than oral routes in this group of children. One of the possible reasons might be due to mosquitoes or bed-bug bite in addition to complete carelessness on sanitation and hygiene. These conditions could cause highly conducive and favorable conditions for the growth of bacterial or fungal infections.

Mosquitoes comprising *Culex tritenorhynchus, Cx. quinquefasciatus, Cx. gelidus, Mansonia uniformis, Anopheles subpictus, Armigeres subalbatu* and *Aedes aegypti* along with sand flies comprising *Phlebotomus argentipes, P. papatasi and Sergentomyia sp* were collected from indoor and outdoor situations resting on vegetation and bushes around cattle shed and pig stays during dusk and identified using standard keys for mosquitoes (Reuben *et al.,*1994) and sand flies(Lewis, 1978). These were collected in different villages of the affected blocks of Muzaffarpur in 2011 other than study villages of which 11 species of mosquitoes were identified. Antigen capture ELISA was carried out to detect the JE antigen in the pools were found negative for JEV and dengue (Samuel *et al.,*2013). The man to man transmission of the disease was presumed, based upon the analysis of time and place distribution of AES cases in Gorakhpur district (Singh *et al.,*2013). This epidemic might be due to health related illness because of global warming (Mehta *et al.,*2003). Invasive methods to search out the responsible factors associated with this epidemic need to be explored to find out the real causative agent and their effective control measures.

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