Original Article

Out break of coma epidemic in children in Muzaffarpur, Bihar — Mystery or missed diagnosis

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In the month of June 2005 and June 2011, there was an outbreak of fever with convulsion and coma [Acute Encephalopathy Syndrome (AES)] occurred in children in Muzaffarpur district of Bihar. About 500 children were affected and more than 200 died. The outbreak of acute encephalopathy syndrome among children were investigated to confirm the etiology and describe clinico-epidemiological feature. A retrospective study involving 50 patients of AES admitted to S K Medical College, Muzaffarpur in June 2005 and June 2011 was carried out. These patients presented with a rectal temperature of >40°C and central nervous system disturbance. The patient were treated with standard regimen of management of acute encephalopathy syndrome and sponging in ICU. The main presenting feature were fever (100%), convulsion (100%), unconsciousness (100%), decebrate rigidity (50%), tachycardia (80%), tachypnea (80%) and no splenomegaly. Serum and CSF were tested for IgM antibodies and RT-PCR against Chandipura virus (CHPV), Japanese encephalitis virus (JE) and Nipah virus. A total of 50 AES cases were recorded in children <12 years of age. Case fatality ratio was 60%. Male to female ratio was 1:1.5. There was no evidence of any infective etiology. All patient were negative of IgM and PCR of CHPV, JE and Nipah virus. As heat hyperpyrexia is a diagnosis of exclusion, It include such as drug withdrawal syndrome, neuroleptic malignant syndrome, septicemia, cerebral malaria, CNS infection, thyroid storm, drug toxicity (anticholinergic). So the outbreak of acute encephalopathy syndrome may be due to heat hyperpyrexia.

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Key words **: Classical heat stroke, clinicopathological aspect, potentially fatal, rapid cooling.**

In the month of June 2011, most of parts of Muzaffarpur district (Bihar) and few neighbouring district witnessed a large outbreak of mysterious illness that killed more than 50 children over a span of 15 days[1]. About 35 patients were admitted in SK Medical college Muzaffarpur with death toll about 18[1]. This type of disease occur every year in this area in May-June depending upon environmental temperature and humidity. In the history of Muzaffarpur the most severe epidemic occur in 1995 and 2005 when more than 500 and 100 death occur respectively. This outbreak occurs when environmental temperature approachs 38°C-44°C and remain sustained for 3 to 4 days. This outbreak is 100% associated with high environmental temperature and humidity.

- **Heat stroke is presented as acute encephalitis syndrome and is a multi system disorder**
- **Heat stroke is the diagnosis of exclusion.**
- **Its incidence is increasing with increasing global warming.**
- **It is inherently preventable, fatality warranting a high index of clinical suspicion in appropriate setting. Treatment of heat stroke should be prompt as the incidence of severe complication is related to degree of hyperpyrexia and duration of exposure to hyperpyrexia and shock.**
- **Public perception of hazards of heat stroke is often poor and underplayed by public media and even the medical community.**
- **The recurrence of such an epidemic is likely to be avoided only with aggressive implementation of a community-wide disaster plan. This emphasizes the need for education at all level of medical care in conjunction with an aggressive prehospital prevention and rescue plan when faced with this type of environmental catastrophe.**

Material and Method

Study area- the study area in India is located between 26° and 26.07°N and 85° and 85/.45°E. The cases were reported from different block of Muzaffarpur like Meenapur, Kanti, Bochahan, Aurai, Gayaghat and Musshari and also from and joining district like Sithamadhi and sheohar. This region lies at an altitude of approximately 60 metre above mean sea level. The population is mostly rural. Average annual rain fall is 11.87 cm. The climatic condition in May – June is extremely hot and humid the temperature ranges from 28°C to 40-44°C and humidity may goes upto 100%.

Patients and clinical specimens- a case was defined as a hospitalized cases (in June 2005 and in June 2011), age 2 to 12 years, with acute onsets of fever with central ner-

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vous system involvement (convulsion, unconsciousness, decerebrate rigidity and coma) and negative test for malaria, tuberculosis and other common bacterial causes. Outbreak investigations was initiated immediately after cerebrospinal fluid (CSF) and blood samples were sent to National Institute of virology Pune, by Directorate of Health Services, Bihar. Predesigned proforma was used to collect information from the cases. Clinical investigations included recording history, clinical findings and result of routine laboratory investigations, review of hospital records and collection of CSF and/or blood from patients. Acute CSF and/or serum specimen were tested for anti-JEV, anti-CHPV and anti-Nipah IgM antibodies using enzyme-linked immunosorbent assay (ELISA). Detection of RNA of these viruses was done by RT-PCR in acute serum sample and CSF according to the method described earlier.

Observation

Discription of this disease outbreak in Muzaffarpur.

Presenting Feature :

- All patients were between 2 to 12 years of age.
- Patient present with sudden attack of convulsion, followed by coma, decebrate rigidity, opistonous posture, cerebellar dysfunction, dystonia and death.
- Death comes within 36 hours of hospitalization.
- More alarmingly some patient died within 5 to 10 hours of attack of convulsion.

Examination

- All patients (100%) have fever >104°F.
- 80% patients presents with hot, dry skin and absence of sweating.
- All patients (100%) comes with status either in the form of persistence of convulsion for more than 30 minutes or a series of convulsion occur without regaining consciousness.
- All (100%) patients were comatose.
- 50% patients have decebrate rigidity.
- 40% patients have irregular respiration.
- 30% patients have absent dolls eye reflex.
- Some patients have heart rate greater than 120 to 140.
- No any patients have splenomegly.
- Some patients show sign of dehydration.
- Blood pressures were low and normal.
- 30% patients have oculogyric crisis.
- 50% patients have no response planter reflex.
- 50% patients have absent tendon reflex.
- 50% patients have flaccidity.
- No any patients have sign of meningeal irritation.

Investigation

Hematological — (80%), patients had leucocytosis (13000-17000/cu mm) with neutropilia (75-80%).

Biochemical Investigation — Hyponatremia (90%), Hypokalemia (5%), mild raised SGPT (50-100IU/L)(30%), mild raised blood urea (40-50mg/dl)(40%) and normal creatinine. Smear for malarial parasites were negative. ECG showed non-specific ST changes and tachyarrhythemia. Lumber puncture and CSF examination done within 24 hours of admission. The CSF was 100% normal but under raised pressure. CSF and serum was sent to national institute of virology Pune for detection of three virus-chandipura, Nipah and JE, but all are negative by Elisa for IgG and IgM and by PCR. Plasma enzyme (CPK, AST) done in 25 cases all are under normal. Coagulation screen was not done because no patient has bleeding tendency

Difference Between Encephalitis and the Current Illness :

On the basic of history, clinical examination and laboratory finding these patient seem to be not suffering from encephalitis. There is major epidemological, clinical and lab finding difference between current illness and encephalitis.

(A) Epidemological Diffrence

- Japanese Encephalitis (JE) occurs mostly in monsoon and post monsoon months (July to Sept), but this disease occur in May – June[2]
- The vector of JE culex mosquito which breeds in flooded rice field, marshes and standing water and field. So JE occur in rainy season which is favorable time for reproduction of cluex mosquito[3], but this disease occur in may – June, in that time there is high environmental temperature which may reach up to 38°C to 42°C. At that temperature the mosquito do not survive, so there is no chances of JE outbreak in this season of high temperature.
- JE mostly occur where pigs are found in residential area because pig is the amplifier host of this virus but this illness is not related to pig residing area. Countries that do not rear pig like Pakistan had JE only very rarely[4].
- During epidemic of JE the adult population may also be suffered but this disease occurs Almost Exclusively in children of age group 2 to 15 years. Not single cases of adult were found.
- The outbreak of JE usually not occur each year in same area, but this illness occur each year in this area in May-June when environmental temperature approaches 38°C to 42°C

- In JE, the sibling almost never affected but in this illness sibling affected mostly.

(B) Clinical Diffrence :

- A typical case of JE present with (i) prodromal stage (1 to 3 days) of fever, headache, nausea, diarrhea, vomiting and myalgia.
- Encephalitis stage (3 to 4 days) : There is CNS manifestation of convulsion, coma, focal neurological sign and death[5].
- Convalescence stage - There is defervescene of fever and neurological improvement. But this illness present with convulsion followed by neurological sign and death. There is No Any Prodromal symptom at all.
- In JE some patient may have sign of meningeal irritation like neck rigidity, brudzinski sign, kerning sign but in this illness no any patient have sign of meningeal irritation.
- The frequency of seizure in different study of JE varies from 30% to 80% but in this illness frequency of seizure is 100%[6].
- In JE, progress to deep coma occur slowly but in this illness it is very fast (1 to 2 hours).
- The mortality rate of JE is reported to 20 to 50% , but this illness mortality rate is more than 60%[7,8].
- In patients of JE, about 33% to 50% have neurological sequeale after survival of 1 year but this illness there is 10-14% neurological sequelae after survival[9,10,11].
- Duration of illness in JE, is days to weeks but in this illness hours to days.

Laboratory Finding Diffrence :

- The CSF- in JE there is mild pleocytosis (initially polymorph nuclear but in a few days predominantly lymphocyte) and mild elevation of protein with normal glucose but in this illness the CSF picture was Absolutely Normal[11].
- In JE there is normal serum level of Na+ but in this illness about 90% of patient's shows hyponatremia[11].
- In JE there is no change of liver enzyme (SGPT) but in this illness some patient sows increase in SGPT.
- In JE there is normal level of blood urea but in this illness, some patients sows increases in blood urea.
- In this disease there in dramatic response to rapid cooling of body, good response within 4 hours to iv mannitol and easily controllable seizure with one dose of diazepam and phenytoin.

Fig 1 shows the various average temperature and humidity in 2005 and 2011. In the year 2005 there was double epidemic of heat stroke occurs, as there is double rise of temperature, first in 10-20 june and second in 25-29 June.

In 2005 majority (70, 70%) of cases occurred between 12 to 18 June and (30, 30%) between 24 to 28 June. In 2011 majority (22, 73.3%) of cases occurred between 14 to 23 June

Fig 2 shows how this outbreak is related to high temperature and humidity. This figure shows the average temperature, average humidity and number of cases from 2005 to 2011. This clearly indicate the outbreak is 100% associated with high temperature and humidity ie No High Temperature No Outbreak.

Discussion

The above feature of disease suggesting the outbreak is due to heat stroke. The epidemiology and demography clearly suggested that this outbreak is related to high temperature and humidity. The affected children were from low socioeconomic area. They were from village with overcrowding housing condition and poor ventilation. The Muzaffarpur is a zone of high temperature and humidity in May- June (when outbreak occurs).

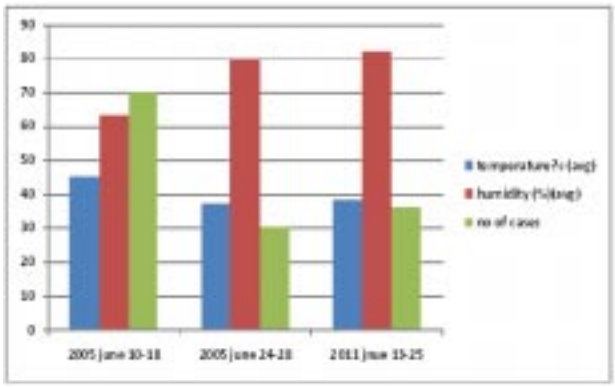

Fig 1 — The no of cases in the graph shows admitted patients in the S K Medical college only. The Actual cases are much more

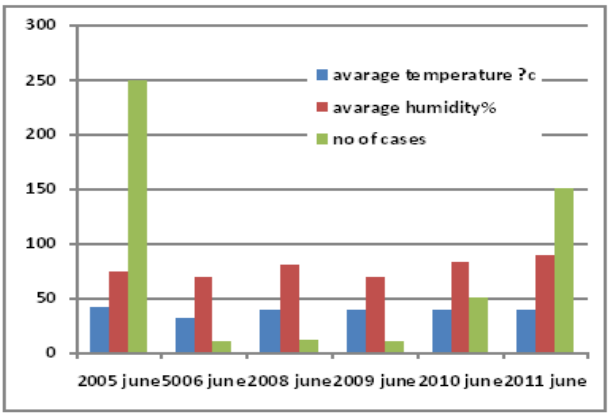

Fig 2 — Weather recorded from-www.undergroundweather.com and number of cases from S K Medical college record room and various news paper of that day

Heat hyperpyrexia was first documented in 24BC by the Romans, but was not demonstrated to result in multi-organ dysfunction until 1946[12]. People of the extreme of age are predisposed to classical heat hyperpyerxia—children due to immature thermoregulatory system, lower rate of sweating and poor acclimatization[13]. Heat wave continues to be a serious problem for the homeless and the very poor in India. The consequence of heat waves have been appalling, both in the West as well the East, both in tropical and temperate regions of the world. In India HS occurs frequently in areas of northern and western India. Over 1000 lives were lost in Andhra Pradesh (AP) when the temperature touches 122°F in 2002 and over 1600 in the whole of the India. Yet the public perception of the hazards of high environmental temperature is often poor and played by public media and even the medical community.

Heat stroke (HS) is life thretning medical emergency – defined clinically as core temperature >40°C accompanied by central nervous system dysfunction[14]. It is an important treatable form of Multiple Organ Dysfunction Syndrome (MODS) resulting from thermo-regulatory failure coupled with a exaggerated acute phase response and possibly altered expression of heat shock protein[15]. Despite the advances in last fifty years, mortality due to HS continues to be as high as 10 to 50 %[16].

There are two form of heat strokes – classical heat stroke occurs during period of high environmental temperature and humidity as in summer heat waves. It usually affects infants or invalid children who are dependent on adults for water and for moving to cooler or shaded surroundings[17]. Classical HS occurs in epidemic form following a rapid rise in environmental temperature. The very young and elderly are particularly susceptible[18,19].

The final report of 2011 outbreak has submitted by Directorate General of Health Services (Emergency Medical Relief) in September with reg no D540/11/-EMR, Nirman Bhavan, New Delhi dated 12th September 2011. They conclude that 'clinico-epidemiological and environmental evidence support the diagnosis of Acute Encephalitis Syndrome which has significient mortality, affecting predominantly rural population with poor sanitation'. However it is unlikely to be Japanese Encephalitis, West Nile, cerebral malaria, NIPAH virus or chandipura virus

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