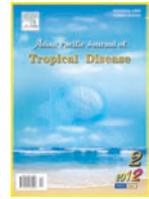




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## Leptospirosis presenting as acute encephalitis syndrome (AES) in Assam, India

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### ABSTRACT

**Objective:** To establish leptospirosis as a new aetiology of the patients presenting acute encephalitis syndrome (AES). **Methods:** Japanese encephalitis, West Nile, Dengue and Chikungunya negative samples were tested by IgM capture ELISA for leptospira specific IgM. For further confirmation, the IgM positive samples were subjected to Microscopic agglutination test (MAT). The clinical details and laboratory findings of the positive patients were recorded. **Results:** We report 8 cases of leptospirosis presenting as AES, proven on IgM capture ELISA and confirmed by MAT. Fever (100%) and altered sensorium (62.5%) were two most common symptoms. Low haemoglobin ( $7.5 \pm 2.8$  g/dL, elevated blood urea ( $79.16 \pm 46.43$  mg/dL, serum creatinine ( $1.5 \pm 1.2$  mg/dL, SGOT ( $66.5 \pm 14.84$ ) U/L and SGPT ( $70.5 \pm 4.9$ ) U/L were observed in positive patients. **Conclusions:** This is the maiden study reporting leptospirosis as a new aetiology of the patients presenting AES. Establishing aetiology is very important for a successful therapy at least in treatable conditions like leptospirosis.

## 1. Introduction

Acute encephalitis syndrome (AES) is caused by a wide range of viruses and bacterial<sup>[1]</sup>. Japanese encephalitis (JE) is considered as a main viral aetiology of patients with AES in Assam<sup>[2]</sup>. In the year 2006, West Nile (WN) virus emerged as another cause of encephalitis in this part of the country<sup>[3]</sup>. In the year 2008–2010, we investigated 550 patients with AES admitted to nine Government and private hospitals representing 14 districts of Assam. Two hundred and fifty nine patients were identified as positive for JE virus<sup>[4]</sup> and 56 patients for WN virus. Recent infection of Dengue (28 cases) and Chikungunya (10 cases) have also been reported for the first time in this region<sup>[5]</sup>. But the etiologic agents in a large number of cases still remain unidentified.

Leptospirosis is a zoonosis which in its milder form resembles any other viral illness and in its severe form needs to be differentiated from other common infection in tropical regions of India like viral encephalitis, scrub

typhus, dengue, malaria, viral hepatitis, and Hantavirus infection. Leptospira is a thin spiral organism  $0.1 \text{ mm} \times 6 - 20 \text{ mm}$ , with tightly set coils, and it is characterized by very active motility, by rotating (“spinning”) and bending. Usually one or both ends of this single-cell organism are bent or hooked, but straight forms also occur that rotate and travel more slowly than hooked forms. Because of their narrow diameter, the leptospire are best visualized by dark-field illumination or phase contrast microscopy. It affects both humans and animals and it is emerging as an important public health problem in India and other developing countries<sup>[6]</sup>. The clinical spectrum can range from an asymptomatic, subclinical infection to a fatal hepatorenal syndrome<sup>[7]</sup>. The severity of the infection depends on the age and general health of the patient, plus the serovar (strain) of bacteria involved and the number of bacteria that entered the patient’s body. Leptospira is also associated with neurological manifestations<sup>[8]</sup>. Most cases of human leptospirosis worldwide have been attributed to rodents. Human leptospiral infection is primarily resulted from direct or indirect exposure to the urine of infected animals. The confirmed cases of leptospirosis for the first time in Assam were reported in patients with pyrexia of unknown origin in the year 2008<sup>[9]</sup>. We have focused here

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on the detection of leptospira in AES patients from Assam, India.

## 2. Materials and methods

JE, WN, Dengue and Chikungunya negative 197 cases of serum samples were tested by MAC ELISA for leptospira specific IgM at the Regional Medical Research Centre, ICMR, NE region, Dibrugarh, Assam, India. For further confirmation by Microscopic agglutination test (MAT), the IgM positive samples were sent to Regional Medical Research Centre, Andaman and Nicobar Islands, India which is the National Leptospirosis Reference Centre. MAT was performed on the sera using nine live leptospiral strains as antigens. The strains belonged to the serogroups Australis, Bankinang, Ballum, Canicola, Icterohaemorrhagiae, Grippotyphosa, Hebdomadis, Hardjo, Pomona and Pyrogenes. The symptoms of the patients with laboratory test results including total leukocyte count, haemoglobin estimation, blood urea and major biochemical estimations have been reported. The study was approved by the Institutional Ethical Committee of Regional Medical Research Centre, ICMR, Dibrugarh, Assam, India. Written informed consent was obtained from the patient or guardian.

## 3. Results

Out of 197 samples tested, 8 cases were found positive for serum anti leptospira IgM antibody by ELISA. Three of 8 positive sera tested by MAT were positive for anti leptospira antibody. Out of 3 patients Icterohaemorrhagiae and Canicola was seen in 1 each. The remaining 1 patient's MAT showed titers against Icterohaemorrhagiae (1:640), Australis (1:320), Grippotyphosa (1:80) and Pomona (1:80). The age of the patients ranged between 10–70 years and the median age was 37 years. Six of the 8 patients (75%) were males. Seven of eight patients belonged to rural background and depended on agriculture for their livelihood.

**Table 1**

Clinical features of patients with leptospirosis in Assam, India, n(%).

Clinical findings	Frequency
Fever	8 (100)
Altered sensorium	5 (62.5)
Headache	4 (50.0)
Nausea	4 (50.0)
Vomiting	3 (37.5)
Diarrhoea	3 (37.5)
Neck rigidity	2 (25.0)
Seizure	2 (25.0)
Decreased micturation	2 (25.0)
Hypertension	1 (12.5)
Abdominal pain	1 (12.5)
Anorexia	1 (12.5)
Unconsciousness	1 (12.5)

Prevalence of various symptoms is summarized in table 1. Fever was the most common symptom in all the patients. Of the 8 patients, 5 (62.5%) had altered sensorium. Follow up of all the patients were done and 3 patients (37.5%) died after discharged from the hospital.

Mean haemoglobin level was found to be low in 50% patients ( $7.5 \pm 2.8$ ) g/dL. Leukocytosis was observed in 37.5% patients  $13800 \pm 4365$  cells/mm<sup>3</sup> with leptospirosis. Six (75%) patients showed evidence of hyperbilirubinemia. The mean concentration of serum bilirubin was ( $3.1 \pm 1.5$ ) mg/dL. Renal dysfunction was observed in 2 (25%) patients. Elevated blood urea ( $79.16 \pm 46.43$ ) mg % and serum creatinine ( $1.5 \pm 1.2$ ) mg /dL were found in 3 and 4 patients respectively. Liver function tests revealed elevated SGOT ( $66.5 \pm 14.84$ ) u/L in 4 patients and elevated SGPT ( $70.5 \pm 4.9$ ) u/L in 2 patients.

## 4. Discussion

The present study reveals leptospira as an aetiology of AES in Assam, India. The clinicians were not aware of the possible presence of leptospirosis in this region and thus they diagnosed the cases as AES. As such, it becomes difficult to detect actual numbers of leptospira cases. Moreover, most the cases of leptospirosis present as a mild flu like illness<sup>[10]</sup>. If the patient is not treated for the severe form within 2–3 days after the onset of illness, it may progress in severity and sometimes be fatal. Lack of awareness among local people and treating clinicians, similar clinical manifestation with the other viral and bacterial aetiology and lack of appropriate laboratory diagnostic facilities are the other reasons for under-reporting of this disease.

Clinical presentation of the patients showed that fever was the most common symptom as recorded in other studies<sup>[11, 12]</sup>. Involvement of nervous system was also observed exhibiting altered sensorium in most of the cases which is in conformity with previous findings<sup>[8]</sup>. All the dead patients had a history of altered sensorium in the present study. Previous studies also reported that altered sensorium was associated with an increased risk for mortality in leptospirosis infection<sup>[8, 13]</sup>. It is essential to make the physicians of this region aware about these uncommon manifestations of leptospirosis, especially the neurological deficits. As effective and specific treatment is available, early diagnosis of leptospirosis is mandatory to reduce mortality of the patients. The beginning of early pertinent antimicrobial therapy within 4 – 5 days after the onset of illness and proper supportive therapy and use of dialysis to treat renal failure have reduced the leptospirosis-related mortality.

Evidence of renal and hepatic dysfunction in the present study is in conformity with the other studies<sup>[11,14]</sup>. An elevated serum creatinine level which is recorded in the present study appears to be one of the best diagnostic

signs and this is rather uncommon for most of the differential diagnoses (influenza-like illness, viral hepatitis, gastroenteritis, or meningitis) as reflected in an earlier study<sup>[11,15]</sup>. A combined effort of clinical expertise and awareness along with the confirmatory laboratory back up in all the hospitals can dramatically increase the recognition of patients with leptospirosis and facilitate their treatment as well<sup>[16,17]</sup>. It is important to investigate the factors associated with the transmission of leptospirosis to human for effective and sustained prevention and control programs<sup>[18–21]</sup>. Our findings underscore the need for greater awareness. So, information, education and communication activities should be carried out by targeting the high-risk rural populations and educating them about the zoonotic disease which would make prevention programs more effective<sup>[2,22]</sup>.

### Conflict of interest statement

We declare that we have no conflict of interest.

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