Dwindling incidence of Japanese encephalitis and rising scrub typhus encephalitis: A new scenario to consider in Uttar Pradesh

Akash Kumar Pandey[1], Shambhavi[2], Akhilesh Kumar Verma[1]

From [1]Consultant, Department of Paediatrics, District Hospital, Deoria, Uttar Pradesh, [2]Assistant Professor, Department of Pediatrics, Patliputra Medical College and Hospital Dhanbad, Jharkhand, India

Correspondence to: Dr. Shambhavi, Department of Pediatrics, Patliputra Medical College and Hospital Dhanbad, Jharkhand, India. E-mail: 21me.shambhavi@gmail.com

Received - 19 February 2020 Initial Review - 28 February 2020 Accepted - 04 April 2020

ABSTRACT

Background: Acute encephalitis syndrome (AES) is a major public health problem**,** which is caused by several agents, among which viral causes predominate. Japanese encephalitis (JE) has remained a major cause of AES in Uttar Pradesh. **Aim:** This study aims to identify the current status of JE in a public sector hospital of UP. **Materials and Methods:** A retrospective study was conducted in a tertiary hospital of Eastern UP. A total of 63 patients presenting with AES over a period of 1 year were included in our study. General characteristics and clinical features were noted. Routine investigations were done, and cerebrospinal fluid and serum samples were sent for malaria, JE, scrub typhus (ST), dengue chikungunya, and leptospira. **Results:** About 46% of cases had a history of 2 days of illness before presentation. About 46% of cases were vaccinated for JE. Diagnosis could not be established in 50.7% of cases. About 38.0% of patients had ST encephalitis. JE was not detected in any patient. **Conclusion:** The study illustrates how vaccination can change the dynamics of an epidemic. And also, we were able to identify the upcoming threat. Azithromycin needs to be included in the empirical treatment of AES in the area.

Key words: *Acute encephalitis syndrome, Japanese encephalitis, Scrub typhus encephalitis*

Acute encephalitis syndrome (AES) has emerged as a major public health problem in recent times. It is defined as an acute onset of fever with change in mental status and/or new onset of seizures, excluding simple febrile seizures in a person of any age [1]. The worldwide incidence is 3.5–7.4/100,000 population [2]. AES has varied etiology; viral causes being the most common, but bacteria, parasite, fungi, and toxins are also implicated. The prognosis is also variable, and it may range from healthy survivors, to survivors with sequelae such as paralysis, seizure disorder, and intellectual disability to fatality. In India, 70% of the disease burden is carried by the state of Uttar Pradesh [3]. Japanese encephalitis (JE) has been considered to be the major and consistent cause of AES in UP, accounting for 10–15% of cases [3]. It was first discovered in Japan in the 1920s. JE is a major public health challenge as it has a high epidemic potential, high case fatality, and neuropsychiatric sequelae among survivors. We did a retrospective study to identify the current status of JE in public sector hospital located in eastern part of UP.

MATERIALS AND METHODS

This was a retrospective study done in the pediatric intensive care unit at the district hospital of eastern part of UP from January 1 to December 31, 2019. The children with AES were included in the study. AES was defined as acute onset of fever at any time of year and a change in mental status (symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures). The cases with different final diagnosis (bacterial meningitis, brain abscess, tubercular meningitis, neurocysticercosis, and seizure disorder) were excluded from the study.

Data regarding demographics, clinical features, JE vaccination status, duration of hospital stay, need for ventilation, complications, referral, sequelae, and residual neurological disability and outcome were collected on a predesigned abstraction form.

Investigations carried out were complete blood picture, rapid diagnostic test, peripheral smear for malaria parasite, and kidney and liver function tests. Acute-phase IgM antibodies were detected in both cerebrospinal fluid (CSF) and serum for JE. Acute-phase IgM antibodies were detected in serum for scrub typhus (ST). Contrast-enhanced computed tomography scan of the head was done as per clinical indication. CSF and serum were collected within 48 h of admission with proper aseptic precautions from all patients. CSF was transported on ice and stored at −20°C until processed. In both CSF and serum, IgM antibodies for JE were estimated by capture enzyme-linked immunosorbent assay (ELISA) as per the manufacturer's instructions (National Institute of Virology, Pune). In serum IgM, antibody for ST was estimated by IgM capture ELISA (ELISA kits by InBios International Inc., Seattle, WA, USA). Samples were considered positive when the optical density was above the cutoff specified by the manufacturer. Standard rapid diagnostic kits based on immune chromatographic lateral flow technology were used for the detection of antibodies against dengue, leptospira, and chikungunya.

RESULTS

The total number of patients included in our study was 63. Out of these, 35 (55.5%) were male and 28 (44.4%) were female. A total of 54 (85%) cases were from rural background. There were 29 cases (46%) who received JE vaccine (Table 1). The maximum patients were admitted in the months of July (21) followed by September (16) and August (12). We were unable to identify the etiology in 32 (50.7%) patients; 2 (3.1%) patients were diagnosed as leptospirosis, 5 (7.9%) had dengue encephalitis, while remaining 24 (38%) patients had developed encephalitis due to ST. JE etiology could not be established in any case.

DISCUSSION

JE is caused by JE virus (JEV), which is an arthropod-borne flavivirus, found in many countries of Asia, Western Pacific, and Northern Australia. Around 24 countries from Southeast Asia and Western Pacific regions are endemic for this disease and more than 3 billion people are at risks of infection [4]. Although symptomatic cases occur in 1 out of 250 patients, JE remains a major threat with case fatality rate up to 30% among the cases [5,6]. The infection causes a spectrum of clinical illness that begins with flu-like symptoms, neck stiffness, disorientation, coma, seizures, spastic paralysis, and eventually death. Those who survive suffer from severe neuropsychiatric sequelae that necessitate lifelong support causing considerable socioeconomic burden.

Table 1: Baseline characteristics of patients and final etiology

BASIC characteristics	Number of patients
Male	35
Female	28
Urban patients	9
Rural patients	54
Vaccinated for JE	29
Duration of illness before presentation	
2 days or less	29
3–6 days	19
More than 6 days	15
Presenting complaints	
Fever	55
Seizure	50
Vomiting	54
Altered sensorium	53
Neck rigidity	21
Established diagnosis	
Scrub encephalitis	24
Dengue encephalitis	5
Leptospirosis	2
Unknown	32

JE: Japanese encephalitis

In India, JE is a leading pediatric health issue. Since 1955, several epidemics have been reported from many areas. The first documented evidence of JEV in India was obtained through the studies conducted in 1952 [7]. The most affected states comprise Andhra Pradesh, Assam, Bihar, Haryana, Karnataka, Kerala, Maharashtra, Manipur, Tamil Nadu, Orissa, UP, and West Bengal [4]. UP has been under constant surveillance for JEV activity since 1978 [8]. A major epidemic of viral encephalitis was reported in UP in Gorakhpur district in 2005 when a total of around 6000 patients were reported, of which 1500 persons succumbed to the disease [9]. The impact of this virus in this area until recently underlines the importance of this study.

JE outbreaks coincide with monsoons and post-monsoon period due to a marked increase in vector density. However, in endemic areas, sporadic cases may occur throughout the year. In India states such as Karnataka and Andhra Pradesh experience two epidemics every year, first from April to July that is quite severe while the second from September to December being milder similar to the rest of India.

Beyond our expectations, in our study, none of the patients of AES had JE. Vaccination measures by the government could be the reason behind it. In 2006, the Government of India launched a JE vaccination campaign for children from 1 to 15 years of age. This included immunization with single dose of live-attenuated JE vaccine (SA–14-14-2) in 11 highly endemic districts of four states (Assam, Karnataka, UP, and West Bengal). Gradually in a phased manner, multiple other districts were included [10]. In our study, 46% of patients were vaccinated for JE. The live-attenuated vaccine provided by the government has a documented efficacy of about 85–95%. Seropositivity rates are known to increase significantly beyond 10–15 years of age in endemic areas [11].

Studies focusing on AES patients in this state have documented that cases with unknown etiology accounted for 61% of cases in 2007, 41.6% in 2011–2012, and 59% in 2013–2014 [3,12]. In the present study, we were unable to find the exact etiology in 50.7% of patients; although, we could not rule out Herpes simplex encephalitis due to financial constraints. Investigations which were conducted in 2014 and 2015 in Gorakhpur region, indicated the possibility of ST [13,14]. A case–control study revealed higher odds of IgM antibodies against *Orientia tsutsugamushi*, in AES patients compared with healthy controls, further suggesting the role of ST in the etiology of AES [15].

ST is a zoonotic disease, which presents with fever, headache, inoculation eschar, and lymphadenopathy. Pneumonia, myocarditis, azotemia, shock, gastrointestinal bleed, and meningoencephalitis are known complications. Not many studies are available in this area focusing on its incidence. A study done in 2016 in Gorakhpur region identified ST as a cause of encephalitis in 65.4% of patients. Our study reveals ST encephalitis in 38% of patients. A study done in Tamil Nadu in AES cases in 2014 recognized it in 30% of cases [16].

We were unable to identify characteristic eschar of ST in any patient. Various studies reported its presence in 20–86% of cases [17]. Precipitation and temperature are two important determinants of vector density that decides the disease burden. At cooler temperatures, virus transmission rate gets reduced. The ST outbreak starts after the monsoon and rainy season with the peak incidence in July followed by September [18]. Our patient density of AES was highest during the same months. After vaccination in 2006, there was a decline reported in the positive cases of JE in UP. However, about 10–15% of the total AES cases were annually reported indicating that the virus is the consistent cause of outbreaks in the eastern region of the state, as reported by Saxena *et al*. [19]. JEV accounted for <10% of AES cases, while the etiology of the remaining cases remained largely unknown. Murhekar *et al*. in their study observed that about one-fifth of the patients with acute febrile illness were due to ST [20].

Doxycycline is the drug of choice in ST, but injectable azithromycin is also a good alternative, which is a good option in encephalitic patients who cannot take oral doxycycline [17]. Further studies are required to identify the etiology of about a third of AES cases that test negative for ST, JEV, or dengue. This study had a few limitations. We were unable to rule out HSV encephalitis due to financial reasons. The sample size was small. Appropriate conclusion cannot be drawn unless more studies are done from this area. We cannot explain such reduced incidence of JE, when only 46% of patients were vaccinated.

CONCLUSION

Our study shows that ST encephalitis is a major cause of AES; hence, empirical use of azithromycin should be considered in AES cases till the final etiology is identified.

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Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Pandey AK, Shambhavi, Verma AK. Dwindling incidence of Japanese encephalitis and rising scrub typhus encephalitis: A new scenario to consider in Uttar Pradesh. Indian J Child Health. 2020; 7(4):156-158.

Doi: 10.32677/IJCH.2020.v07.i04.005