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Original Research Article

Epidemiology and Etiological Study of Adult Acute Encephalitis Syndrome in the Rural Setup of Purwanchal, India

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Abstract

Background: Acute encephalitis syndrome (AES), known as *Chamki Bukhar*a, is a major public health problem, claiming hundreds of lives yearly. AES has various etiologies and causes, making it difficult for clinicians to manage. The current study is conducted to describe the incidence, manifestations, etiology, and prognosticators of morbidity and mortality.

Aims and Objectives: To evaluate the Epidemiology and Etiology of Adult Acute Encephalitis Syndrome in the rural setup of Purwanchal (eastern UP), India.

Materials and Methods: This study enrolled 300 patients for AESs to study viral etiologic causative agents and their epidemiology. Cerebrospinal fluid (CSF) samples of the AESs were tested for IgM antibodies using Commercial enzyme immunoassays were used to test for Japanese encephalitis virus (JEV), dengue virus (DV), herpes simplex virus (HSV), measles virus (MV), mumps virus, varicella zoster virus (VZV), and enterovirus.

Results: Of the 300 subjects, 50% have confirmed AES; the main etiologies were JEV (20%) is the most common, followed by DV (10%) and HSV (7%). Co-positivity with more than one virus was observed in 22 (7%) patients out of 150 confirmed cases.

Conclusion: JEV infection resulted in the most significant mortality, whereas HSV infection resulted in the greatest residual neuropsychiatric disability. The main AES-causing agents are JEV and DV, in Central India, mainly during monsoon season.

Keywords: Encephalitis, Cerebrospinal Fluid, Neuropsychiatric Disability.

Introduction

Acute encephalitis syndrome (AES) is characterized by the sudden appearance of a fever, a change in mental status (including signs like confusion, disorientation, coma, or speech impediment), and new seizures (excluding simple febrile seizures) in a person of any age at any time of the year. [1]

The Government of India introduced the Japanese encephalitis virus (JEV) vaccine in areas severely affected by the outbreak in 2005, resulting in 5737 cases and 1344 fatalities. The National Vector Borne Disease Control Programme (NVBDCP) also started sentinel surveillance for acute encephalitis syndrome. [2]

At this time, JEV is known to be the main etiology of AES globally. Every year in ASIA 68000 cases of JVE are reported with an estimated mortalities of 1360 to 24000. People with acute encephalitis syndrome

can die in up to 30% of cases, and 30–50% of patients can have long-term neurological or mental health problems. These estimates are only for JEV and don't consider the burden and death rate of acute encephalitis syndrome caused by other causes. [3]

Since 2005, there has been no noticeable decline in the overall incidence of acute encephalitis syndrome in India. Between 10,867 and 13,672 cases were reported to the NVBDCP annually between 2014 and 2017. [4]

Only 14–18% of cases of acute encephalitis syndrome that have been reported are associated with JEV infection, and the cause of the majority of these cases in India is still a mystery. [2]

Sporadic cases are more likely to have multiple causes than epidemics, so testing for multiple pathogens is necessary to monitor them. Despite advances in virology, identifying these agents is still expensive and limited to a few reference laboratories. Regular hospital-based epidemiological studies are needed to identify AES agents. This knowledge allows for etiologic agent prevention.

Materials and Methods

The current study was conducted in eastern UP, which is known for JVE outbreaks; study data were obtained from samples collected at a viral diagnostic laboratory in the hospital area.

After getting consent from patients and approval from the Ethics Committee, we enrolled the patients with a clinical diagnosis of AES in the study over 2 years, from January 2021 to December 2022.

Inclusion criteria used as cases of probable AES as a patient with an acute onset of fever at any time of the year and at least one of the presentations of altered sensorium, disorientation, confusion, coma, inability to talk, new seizures excluding the febrile seizures. Exclusion criteria include patients with a history of head injury, poisoning, or hypertension.

A detailed history of demography, including the address and signs and symptoms, including seizures, headache, rashes, trauma, vomiting, arthralgia, and breathlessness, were obtained. Laboratory testing includes using ELISA kits for the Cerebrospinal fluid (CSF) test for anti-JEV IgM and anti-DV IgM antibodies. The presence of IgM antibodies against HSV 1 and 2, MV, mumps virus, and VZV were tested using ELISA kits. The cutoff values and criteria for labeling a sample positive if panbio units>11 and negative if panbio units < 9).

As per national guidelines, a virus was considered the etiologic agent of AES if IgM antibodies specific to that particular virus/viral genome were detected in the CSF sample.

As part of this study, we collected the standardized clinical, demographic, and laboratory data stored in Microsoft Excel. Descriptive analysis to identify the frequencies and percentages of various causative agents was done using the statistical software IBM SPSS.

Result

Out of the total (300) enrolled patients, 150(50%) were confirmed diagnosed with AES. Distribution of causative agents shows JEV (20%) is the most common, followed by DV (10%), HSV (7%), MV (4%), mumps virus (6%), and VZV (3%).

Immunoglobulin M (IgM) positivity for more than one virus was observed in 15 (10%) patients, 7 (5%) of whom were co-infected by JEV and DV, three were with HSV and mumps virus, and there were by measles and mumps viruses (Table 1).

Table 1: Distribution as per causative agent

Causative Agent	Count (150)	Percentage
JVE	30	20%
DV	15	10%
HSV	10	7%
MV	6	4%
Mumps Virus	9	6%
VZV	4	3%

Mortality and residual neuro-psychiatric disability were significantly higher among patients with established AES etiology, 11% and 9%, respectively, which is more than in patients with unknown etiology, i.e., 6% and 3%, respectively. A mortality rate of 30% was recorded among the patients who tested positive for JEV, followed by DV (20%) and 11% by Mumps virus.

The mean age of patients was 14 years (min 7 years – max 70 years); males were 60% females were 40%.

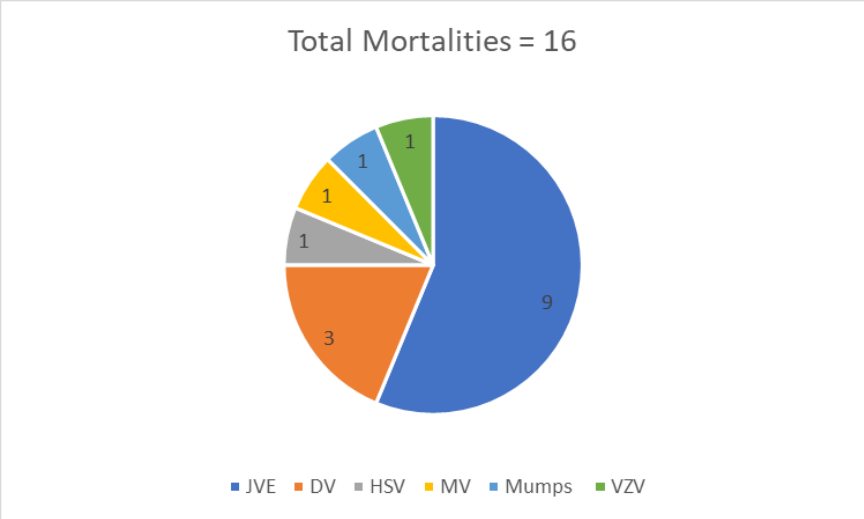

Figure 1: Distribution as per mortality in the different causative agents

Age distribution of AES patients shows the mean age was 14 years (min 7 years – max 70 years); gender-wise, 180 (60%) were male, and 120 (40%) were females.

The majority of the AES cases with etiologies of DV and JEV were recorded in the rainy season, i.e., between July and October, while this correlation with the season is not significant for other etiologies.

Discussion

Patients with AES may have a cause that is not viral, viral, or unknown. These subtypes presented clinically different symptoms. Cases not caused by viruses presented with higher CSF protein concentrations, longer fevers, and stiffer necks before exhibiting altered sensorium. Before neurological deterioration occurs, tuberculous and cryptococcal meningitis typically move slowly through their stages. [1] Meningeal inflammation was suspected in patients with a viral cause for their condition because they exhibited symptoms such as a stiff neck and pleocytosis in their CSF. Patients with viral or unknown causes of their illness had comparable clinical and survival outcomes. [2] Patients with known viral encephalitis may have had higher viral loads and more meningeal inflammation, whereas patients whose causes of encephalitis were unknown may have had lower viral loads. Due to the myriad

etiology and various causative agents, AES became challenging to diagnose and manage, and we attempted to describe and document the etiologies and outcomes of AES. [5]

In the present study, out of 300 enrolled patients, 150(50%) confirmed AES etiologies. A similar study by Singh et al. [6] reported confirmed AES in 70.2% of the patients (n = 198), and Roy D B et al., [7] 2022 found only 36% of the patients have confirmed etiologies for AES.

In this study distribution of causative agents shows that JEV (20%) is the most common, followed by DV (10%), HSV (7%), MV (4%), mumps virus (6%), and VZV (3%) which is comparable to the results of the study by Tandale BV et al (2022) [8] where viral causes distribution was JEV (58, 20.9%), HSV (22, 7.9%), DV (15, 5.4%) and CHPV (3, 1.1%). JEV confirmation was significantly higher in enrolled cases than in referred patients (10.2%) ($p < 0.05$). In another study by Srivastava N et al. (2022) [9], the identified etiologies of AES were Japanese encephalitis virus (5–20%), enterovirus (0.1–33%), Orientia tsutsugamushi (45–60%) and other viral (0.2–4.2%), bacterial (0–5%) and Rickettsial (0.5–2%) causes.

In this study, IgM positivity for more than one virus was found in 15 (10%) patients, 7 (5%) of whom were co-infected by JEV and DV, 3 (2%) were with HSV and mumps virus, and there were by measles and mumps viruses. This finding follows the study by Singh KP et al. (2014) [10], where out of 1410 patients whose sera tested for anti-DV and anti-JEV antibodies and found 129 (9.14%) were co-positive for both.

Similarly, antigens of measles and mumps viruses are well known to have cross-reactivity, rendering it challenging to differentiate co-infections from cross-reactivity based on only IgM-positivity.

Mortality and residual neuro-psychiatric disability were significantly higher among patients with established AES etiology, i.e., 11% and 7%, respectively, than the group with unknown etiology, i.e., 5% and 3%, respectively. Our findings agree with the National Vector Borne Disease Control Programme (NVBDCP) [4], which reported that in 2019 alone, 14995 AES cases and 710 deaths were reported from 21 Indian states, with a case fatality rate near 5%. (NHP)

Kakoti G et al. (2020) [11], in a similar study, reported that the fatality rate among hospitalized AES cases was very high (27.6%). The age-specific CFR was highest in children below 1 year of age, and males were more fatal. Children with GCS <8 and the presence of meningeal irritation had a significantly high fatality rate.

A mortality rate of 30% was recorded among the patients who tested positive for JEV, followed by DV (20%) and 11% by Mumps virus. This observation supports the WHO Position Paper (2006) [12] findings, which reported globally that JEV infection has a 20–30% case fatality rate and 30–50% residual neurological or psychiatric disability in survivors. A similar study by Parul Jain et al. (2014) [13] reported that out of the 1,578 enrolled patients, JEV was the most commonly recorded (16.2%), followed by DV (10.8%), HSV (9.3%), MV (8.9%), mumps virus (8.7%), VZV (4.4%), and enterovirus (0%). Co-positivity with more than 1 virus was observed in 12 patients. [14]

The mean age of patients was 14 years (min 7 years – max 70 years); males were 60% females were 40%. Most DV and JEV incidents were seen during and after the monsoon period, i.e., between July and October. This observation supports other studies by Parul Jain et al. (2014) [13] and Kakoti G et al. (2020) [11], who strongly liked the AES outbreak with seasonality.

Conclusion

In eastern India, AES is significantly linked to morbidity and mortality across all age groups. Despite advanced diagnostic testing, the diagnosis of this condition is

still challenging because of its diverse etiologies. The primary factor responsible for a significant amount of mortality is discovered to be JVE. During the monsoon season, there is a sporadic increase in AES cases. In conclusion, early detection, targeted treatment, and knowledge of the range of etiologies in a given area will reduce morbidity and mortality.

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