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A Clinical Study on Viral Encephalitis Patients-A Hospital Based Study

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ABSTRACT:
Introduction: *Viral encephalitis refers to a diffuse inflammatory process affecting the brain. Most common causes are the arboviruses that spreads through the bite of infected mosquito mainly belonging to Culex, Aedes and Anopheles groups.* ***Materials and methods:*** *In this cross sectional hospital based study, 242 patients meeting the case definition of acute encephalitis syndrome were included. A detailed neurological evaluation was done in all the patients. Serological studies were performed on both CSF and serum for JE*
Results: *The pre-dominant age group was 40-49 yrs with male predominance. Fever and altered sensorium were present in all patients. Other manifestations were headache (27.27%), seizure (13.22%) and movement disorders (13%). Serological studies were positive for JE in 95 cases (39.26%).*
Conclusion: *The clinical features of viral encephalitis include fever, altered sensorium, headache , seizures, behavioural and motor abnormality.*
Key words: *Viral Encephalitis, Japanese Encephalitis (J.E), Fever, Seizure*

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I. INTRODUCTION:

Acute Encephalitis Syndrome (AES) is defined as acute onset of fever and change in mental status (including signs and symptoms such as confusion, disorientation, delirium or coma) and/or new-onset of seizures (excluding simple febrile seizures) in a person of any age at any time of the year.[1] For decades, JE has been considered to be the leading cause of AES in Asia[2,3] with over 50,000 cases and 10,000 deaths reported each year.[4] The history of AES in India has paralleled that of JE, with the virus first being reported from Southern India (Vellore, Tamil Nadu) in 1955.[5] Various subsequent studies confirmed that most cases of AES in India are due to JE, which has been considered as the only major cause of AES in India.[6]The Northeast India is endemic for Viral Encephalitis, especially in the upper part of Assam. During the epidemics of viral encephalitis in 2005 and 2006 high mortality of 30—50% was recorded.

II. METHODOLOGY:

Case Definition
AES(acute encephalitis syndrome): Fever or recent history of fever with change in mental status (including confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures). Other early clinical findings could include an increase in irritability, somnolence or abnormal behaviour greater than that seen with usual febrile illness.
AES of Suspected Viral Aetiology: was defined by fulfilling the definition for AES (above) and having a discharge diagnosis of suspected viral encephalitis or meningo-encephalitis, supported by a CSF cell count < 1000 cells/mm3 with a lymphocyte predominance and no positive identification of non-viral pathogens (e.g. bacteria or parasites) in the CSF or blood.

Confirmed JE: A suspected case which is shown to have IgM antibodies (= 40 units) specific to JE virus in a single (CSF and/or serum) sample (or a rise in titres among paired samples) as detected by IgM-capture ELISA .
Non-JE: A suspected viral case which is shown to have an absence of IgM antibodies specific to JE virus based on a negative test for a single sample collected after the ninth day of illness or no change in titres in paired samples collected at least seven days apart.

JE Status Unknown: A suspected viral case which was either not tested for anti-JE IgM antibodies or had samples tested that were collected too early during illness to confidently rule out AES of Unknown Viral Aetiology: ***A suspected viral case which was not confirmed as JE;*** this group included both of the categories described above, i.e. Non-JE, and JE Status unknown.

AES of Non-viral Aetiology*:* was defined by fulfilling the definition for AES (above) and either;

(a) having a documented discharge diagnosis of suspected bacterial meningitis or meningo-encephalitis, supported by a CSF cell count > 1000 cells/mm3 or a pleocytosis with a polymorph predominance and a raised CSF protein (> 0.45 g/L) or

(b) having a positive identification of non-viral pathogen in CSF or blood of this prospective observational study was to study the clinical spectrum of viral encephalitis in a tertiary care hospital in Upper Assam, India for a duration of one year.

A total of 322 patients were selected for the study who attended the Department of Medicine of Tertiary care Hospital in Assam, meeting the case definition of Acute Encephalitis Syndrome (AES).

After fulfilling inclusion and exclusion criteria, 242 patients were finally taken up for the study as 80 patients were excluded. Data was collected in a predesigned proforma. The patients or next of kin were fully informed about the study and their prior informed consent was taken.

INCLUSION CRITERIA:

All cases meeting the case definition and:

(1) Age > 12 years of both sexes;
(2) CSF picture suggestive of viral encephalitis.

EXCLUSION CRITERIA:

(1) Non-viral causes of AES like cerebral malaria, CNS tuberculosis, scrub typhus etc
(2) Known neurological disease;
(3) Presence of co-morbidities like seizure disorders, hepatic and other metabolic encephalopathies

A detailed neurological evaluation was carried out in all the patients. The level of consciousness was assessed by Glasgow coma scale. Presence of seizures, behavioral abnormality, focal weakness, wasting and deep tendon reflexes were examined in all the patients. Sensations of pinprick,(pain sensation) joint position and vibration sense were tested in those who could cooperate. Extrapyramidal signs such as rigidity, dystonia, dyskinesia, tremor, and other movement disorders were noted. Cerebrospinal fluid was examined in all patients for protein, glucose, cells, bacteria, and fungi.

Serological studies: Serological studies have has been done on CSF and/or sera to diagnose JEV. Immunoglobulin M (IgM) antibody capture ELISA for JE was done for all CSF and serum samples using IgM ELISA kits manufactured by National Institute of Virology, Pune, India. Outcome was defined at the time of discharge as Recovered Completely, Partial Recovery (recovered with neurological sequelae), and Death. Neurological sequelae were defined by the presence of one or more of the following at discharge; impaired consciousness, weakness (monoparesis, hemiparesis, and quadriparesis), focal or generalized abnormal limb tone (hypertonia and hypotonia), focal or generalized abnormal limb reflexes (hyperreflexia and hyporeflexia), diagnosis of new onset or recurrent seizures, or new or recurrent extra pyramidal movement disorders.[1,7,3]

STATISTICAL ANALYSIS :

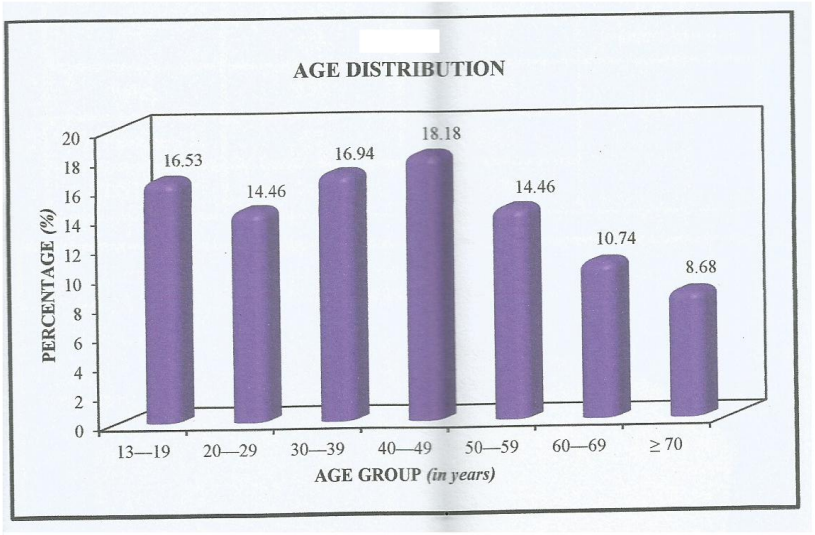
Statistical analysis was performed with the SPSS version 20 and Microsoft Excel. Calculation was done using Chi Square Test and Fischer's Exact Test. P value <0.05 was considered to be significant.

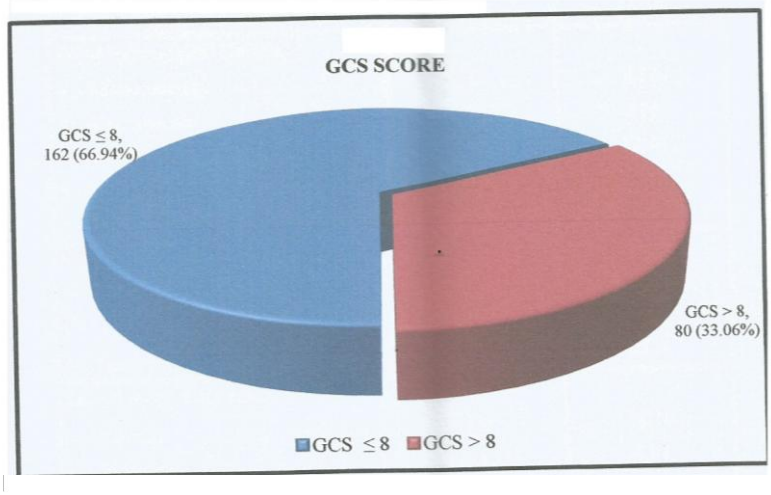
III. RESULTS AND OBSERVATIONS :

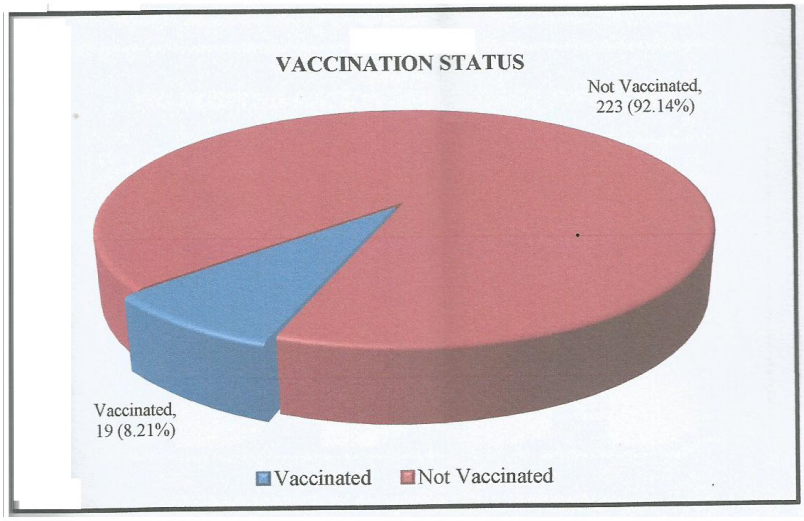
In our study, Male to female ratio was 1.78:1, with 44 (18.18%) case in the age group of 40-49 years followed by 13-19 years (16.53%) 30-39 years (16.94%), 20-29 years (14.46), 50-59 years (14.46%), 60-69 years (10.74%) and = 70 years (8.68%). Out of 242 patients, 19 (8.21%) were vaccinated against JE. 87(35.95%) cases were brought to the hospital on 3rd-4th day after onset of symptoms followed by 5th-6th day (31.40%), 1st-2nd day (25.62%) and 7 th day(7.02%). Glasgow Coma Scale was assessed in all the patients. 66.94% patients had GCS score less than or equal to 8 and 33.06% had GCS score > 8. Outcome was compared between the two groups. In JE patients GCS Score was = 8 in 73 patients and > 8 in 22 patients, it was statistically significant ($p<0.05$).

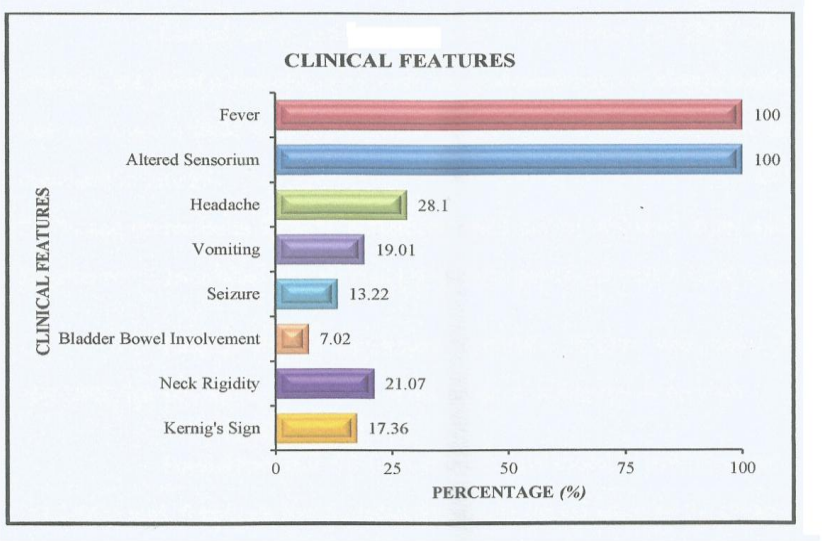
Out of 242 patients, only 19 (8.21%) were vaccinated against JE. All of the 242 patients showed lymphocytic predominance in CSF.

The mean CSF protein was 65.36 (range 23-400) mg/dl. The sugar level had a range of 8-108 mg/dl with mean value 14.35. CSF was negative for bacteria and fungi both by direct staining and culture. Serum and/or CSF were tested for IgM against JE Virus. Out of 242 patients 95 (39.26%) were JE Positive . Out of 242 patients, Complete Recovery was seen in 79 (32.64%), Partial Recovery in 103 (42.56%) and Death in 60 (24.79%). In JE group Complete recovery, Partial Recovery and Death were noted in 33.68%, 41.05% and 25.26 % cases.









IV. DISCUSSION :

Though AES was previously thought to be a disease of mainly paediatric age group[1,7,] we have found that a high percentage of adults are affected by this disease similar to other recent reports[1,7,8]. Our study showed 39.26% serologically confirmed JE cases. Different types of viral encephalitis can have similar clinical presentation, and hence clinically they can not be differentiated.

Beig et al., 2010 in their study among eighty-seven children from Uttar Pradesh observed that the most common aetiology of viral encephalitis was Enterovirus [10] (42.1%), followed by Measles(21.1%), Varicella Zoster Virus (15.8%), Herpes Simplex Virus (10.5%), and Mumps (10.5%). Japanese encephalitis virus was not found in this study.[14] In another study by Joshi R et al., 2013 out of a total of 152 viral encephalitis patients, viral aetiology was confirmed in 31 cases: [11] (11.2%) Entero virus; 8 (5.2%) Flavi virus; 3 (1.9%) Varicella Zoster; 1 (0.6%) Herpes virus; and 2 (1.3%) Mixed Aetiology); the aetiology remained Unknown in remaining [1,2] (79.6%) cases. Advances in molecular diagnostics, viral culture and isolation, as well as use of an extended panel of tests for potential etiological agents should be of priority in this part of the country for identification of alternative etiologies. The emergence of non-JEV etiologies in outbreaks and surveillance studies directly has an impact preventive measures for AES.

The majority of the patients belonged to non-vaccinated group. Till now there is paucity of other studies showing effect of vaccination on occurrence of AES. This finding, though preliminary, emphasizes the effect of vaccination on the incidence of AES and JE. In the current study, children and young adults from vaccine covered districts were also found to be positive for JE; this could be attributed to low vaccination coverage in the corresponding districts, or changes in the genotype of the circulating strains. A higher percentage of JE-positive patients was recorded from under-vaccinated districts. In this study we have seen fever and altered sensorium were present in 100% of the cases. Headache, vomiting and neck rigidity were present in 27.27%, 19.01% and 21.07% of cases respectively. We found that amongst important clinical features, JE patients have significantly more depressed sensorium as compared to the non JE group. Joshi R et al., 2013[11] has reported fever and altered sensorium in all cases, and neck stiffness in 47% patients. In another study performed by Thapa LJ et al., 2013 fever was present in 96.5%, unconsciousness in 51.8%, and headache in 48.2%.[12] Among various movement disorders, tremor was noted in 15 (6.20%) patients mainly at the time of discharge or during follow up visits. Parkinsonian features may be prominent in adults while both dystonia and parkinsonian features are equally common in children[13]. In one study movement disorders were reported in 10.5% of patients with JE which included head nodding, coarse tremor, choreoathetosis, dystonia and parkinsonian features.[14] In another study movement disorders seen in JE included monotonous speech in 7 patients, masked facies in 11 cases, tremor in 7 cases choreoathetosis in 7 patients and parkinsonian features in 8 patients.[15]

The majority of our patients came to hospital after 3 to 5 days of onset of the illness, suggesting that most of the primary care centres did not think it fit to treat these cases emphasizing the importance of continued updation of primary care physicians in our part of the country.

About 30% of patients admitted to hospital with Japanese encephalitis died, and around half of the survivors have severe neurological sequelae. In this present study 24.79% patients died during acute phase of illness. Complete recovery was seen in 32.64% and partial recovery in 42.56%. In a similar study by Joshi R et al., 2013 death was noted in 36% patients.[11]The reasons for low mortality in our study could be probably

attributable to advanced patient care (as the study was conducted in a tertiary care hospital), immunological status and referral bias.

Vector control programmes and JE vaccination remain important strategies. In addition, we need to move from JE surveillance to surveillance for the entire spectrum of AES, so that evidence-based public health actions can be planned and carried out, including greater vaccination coverage even in the middle aged and elderly population in our JE endemic region.

V. CONCLUSION:

The majority of the patients belonged to non-vaccinated group. Till now there is paucity of other study showing effect of vaccination on occurrence of AES. This finding, though preliminary, emphasizes the effect of vaccination on the incidence of AES and JE. In the current study, children and young adults from vaccine covered districts were also found to be positive for JE; changes in the genotype of the circulating strains may be an attributing factor. A higher percentage of JE-positive patients was recorded from under-vaccinated districts. In this study we have seen that fever and altered sensorium were present in 100% of the cases. Headache, vomiting and neck rigidity were present in 27.27%, 19.01% and 21.07% of cases respectively. We found that amongst important clinical features, JE patients have significantly more depressed sensorium as compared to the non JE group. Joshi R et al., 2013 has reported fever and altered sensorium in all cases, and neck stiffness in 47% patients. In another study performed by Thapa LJ et al., 2013 fever was present in 96.5%, unconsciousness in 51.8%, and headache in 48.2%. Among various movement disorders, tremor was noted in 15 (6.20%) patients mainly at the time of discharge or during follow up visits. Parkinsonian features were prominent in adults while both dystonia and parkinsonian features are equally common in children. In one study movement disorders were reported in 10.5% of patients with JE which included head nodding, coarse tremor, choreoathetosis, dystonia and parkinsonian features. In another study movement disorders seen in JE included monotonous speech in 7 patients, masked facies in 11 cases, tremor in 7 cases choreoathetosis in 7 patients and parkinsonian features in 8 patients.

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