

Research Article**Clinical Profile and Outcome of Japanese Encephalitis & Non- Japanese Encephalitis adults Admitted with Acute Encephalitis Syndrome: A comparative prospective cohort study****Dr. Rakesh Kumar**

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Abstract: Acute encephalitis syndrome (AES) is a major health problem in north eastern Uttar Pradesh as it affects thousands of patients & heavy morbidity and mortality leading to death of several hundreds and even greater number as disabled. This study was undertaken to assess the viral JE & Non JE and epidemiology of acute encephalitis in adults in Northern Uttar Pradesh. Between August 2009 to October 2010 in the Department of Medicine, Nehru hospital, attached to the B.R.D. Medical College, Gorakhpur, a total of 200 patients with history of fever with altered mental state of short duration patients included. Study showed that mean age of Non JE was 31.28 yrs and 41.5 yrs in JE cases and most common cause of AES was acute viral (Non JE) encephalitis (57.5%). Dominant clinical presentation in both group were fever and altered sensorium and meningeal irritation sign were frequently observed in half of patients. Extra pyremidal sign disorder was statistically predominant in JE patients. Abnormalities in liver and renal functions were noted while Aspiration pneumonitis (17%) was the most common secondary complication. Neurological sequelae like Cognitive impairment in JE and psychosis in Non-JE cases while 13.79% in JE and 10.43% in Non JE had died in hospital. In conclusion AES is still a major cause of AES in adults in this part of India. These significant research findings seek the attentions of the global community to combat the hazard of this arboviral encephalitis in saving the life of adults.

Keywords: AES, Japanese encephalitis, Non- Japanese encephalitis, clinical feature, Neurological sequelae.

INTRODUCTION

Acute viral encephalitis is often an unusual manifestation of common viral infections and most commonly affects children and young adults; it can lead to considerable morbidity and mortality. The incidence of viral encephalitis is 3.5—7.4 per 100,000 persons per year 2 Herpes simplex encephalitis (HSE) is the most common cause of sporadic encephalitis in western countries. Japanese encephalitis (JE), occurring in Japan, United States, southeast Asia, China and India, is the most common viral encephalitis, affecting around 50,000 people per year.[1-3] . However, in developing countries where encephalitis is problem, annual incidence of Viral Encephalitis is most likely underestimated. A very small number of studies of viral encephalitis have emanated from India territory, although it can be considered the epicentre of many emerging or re-emerging viral encephalitis diseases in India.

Acute encephalitis syndrome is a major health problem in north eastern Uttar Pradesh since 1978 as it affects thousands of patients presenting as epidemic mostly in the post monsoon period with heavy morbidity and mortality leading to death of several

hundreds and even greater number as disabled. [4-7] In last 3 years, a total of 8160 cases were reported as Acute Encephalitis Syndrome (2194 in 2008, 2663 in 2009 and 3303 in 2010), out of which 968 were due to JE. The disease affects persons mainly from 7 districts under Gorakhpur and Basti division namely Gorakhpur, Basti, Deoria, Maharajganj, Santkabeer Nagar, Siddharth Nagar and Kushinagar [8-11] Various agencies have been working to study the epidemiology, clinical feature and outcome of AES. Massive efforts as well have been made for the Virology Centre at Gorakhpur has claimed the isolation of EV - 86, EV - 76, and Coxsackie B-5 viruses in some AES patients [12] Japanese B encephalitis virus (JEV) is an emerging pathogen in North India and has entrenched itself firmly in the Northern parts of Uttar Pradesh. This study was undertaken to assess the viral JE & Non JE and epidemiology of acute encephalitis in adults in Northern Uttar Pradesh. These included clinical signs and symptoms, radiological and cytological findings, seasonal variation, and other demographic variables. No such study has been conducted in this region because most of studies were focused on children.

MATERIALS & METHODS:

A total of 200 patients with acute encephalitis syndrome (AES) formed the study material. These were hospitalized patients in the Department of Medicine, Nehru hospital, attached to the B.R.D. Medical College, Gorakhpur. The study period was from August 2009 to October 2010. During this period, the total hospital admissions were 42565 and total AES patients were 4922. Thus AES constituted 1165% of total hospital admissions. Among the total AES patients, 1103 (22.40%) were admitted in the Medicine department and 3819 (77.60%) in the Pediatric department. All the 200 patients were subjected to detailed clinical examination and investigations. Detailed history was recorded and detailed clinical examination was done in all the patients who presented with fever with altered mental state of short duration. Investigations done included: Haemoglobin, total leucocyte count, differential leukocyte count, renal function tests, liver function tests and rapid diagnostic test for malaria parasite, chest radiography and electrocardiogram. Samples for blood cultures, IgM ELISA for Japanese encephalitis virus in serum and urine cultures were collected and any clinically obvious site of sepsis was investigated. Lumbar puncture was carried out in all the patients at admission, and cerebrospinal fluid (CSF) was analyzed for cytology,

protein levels, glucose to blood glucose ratio, gram stain, and culture sensitivity for microbes. All patients underwent non-contrast- and contrast-enhanced computed tomography (CT) of the brain. This was followed by a magnetic resonance imaging (MRI) scan of the brain using contrast, if required.

Statistical test of significance

We applied Z score as test of significance. In statistics, a result is called statistically significant if it is unlikely to have occurred by chance. A statistically significant difference simply means there is statistical evidence that there is difference; it does not mean that the difference is large, important, or significant in the common meaning of the world.

RESULTS

A total of 109 cases (54.5%) belonged to less than 30 yrs of age, suggesting that the disease has higher incidence in younger population. Overall Male: Female ratio was 1.32: 1. The age of presentation of the cases in Non JE was less than in JE, both in males and females and was statistically significant as is evident by the Z value. The mean age of presentation in Non JE cases was 31.28 yrs, while it was 41.5 yrs for JE. Male: Female ratio in Non JE cases was 1.25: 1, while it was 1.52: 1 in JE. (Fig-1).

Table 1: Age & sex wise distribution of JE & Non-JE cases (Fig. showing no { %})

| Age group (in years) | No. of JE cases (%) | | | No. of Non-JE cases | | |
|----------------------|---------------------|-----------|-----------|---------------------|--------------|---------------|
| | Male | Female | Total | Male | Female | Total |
| <20 | 3 (5.1) | 6 (10.3) | 9 (15.1) | 18 (15.6) | 21 (18.2) | 39 (33.9) |
| 21-30 | 5 (8.6) | 6 (10.3) | 11 (18.9) | 15 (13.0) | 16 (13.9) | 31 (26.9) |
| 31-40 | 7 (12) | 3 (5.1) | 10 (17.2) | 11 (9.56) | 5 (4.34) | 16 (13.9) |
| 41-50 | 9 (15) | 1 (1.7) | 10 (17.2) | 10 (8.69) | 7 (6.08) | 17 (14.7) |
| 51-60 | 6 (10) | 2 (3.4) | 8 (13.7) | 6 (5.2) | 2 (1.7) | 8 (6.9) |
| >60 | 5 (8.6) | 5 (8.6) | 10 (17.2) | 4 (3.4) | 0 (0) | 4 (3.4) |
| Total | 35 (60) | 23 (39.6) | 58 (100) | 64 (55.6) | 51 (44.3) | 115 (100) |
| | | | | Z=3.0 | Z=2.4 | Z=3.94 |

Although, the cases of Non-JE were seen throughout the year but peaked incidence were seen in

the month of September (42.61%) and October (31.30%) (Fig 2)

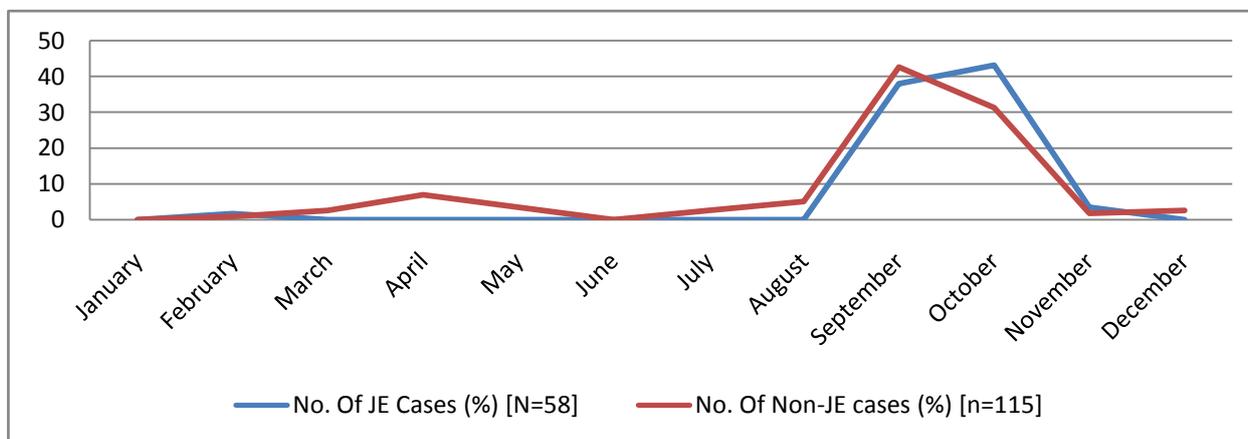


Fig 1: Comparability of Month wise distribution of JE & Non-JE Cases

The most common cause of Acute Encephalitis was acute viral encephalitis (Non JE) responsible for 57.5% cases followed by acute viral encephalitis (JE) in 29% while 8.5% cases were acute bacterial meningitis & 5% were cerebral malaria (Fig 1).

COMPARISON OF CLINICAL FEATURES OF JE AND NON JE CASES

The most common presenting symptoms were fever and altered sensorium followed by headache cases

in both groups. Seizures were present in 46.55% of JE cases and more than half Non JE cases. Symptoms like Abdominal pain, loose stools & breathlessness were more common in Non JE cases and statistically significant. Temperature ≥ 100 F was predominant feature in both groups followed by tachypnea (24.13%) in JE and (27.82%) in Non JE. Icterus and edema in Non JE were the prominent features of Non JE; among those predominance of icterus was statistically significant (Table- 3).

Table 3: Clinical & General Examination finding

| SYMPTOM | NO. OF JE CASES (N=58) | NO. OF NON-JE CASES (N=115) | Z VALUE |
|------------------------------------|------------------------|-----------------------------|---------|
| FEVER | 58 (100) | 115 (100) | 0 |
| HEADACHE | 52 (89.65) | 103(89.56) | 0.018 |
| VOMITING | 32 (55.17) | 71(61.74) | 0.83 |
| ALTERED SENSORIUM | 58(100) | 115(100) | 0 |
| SEIZURES | 27(46.55) | 58(50.43) | 0.482 |
| PARALYSIS | 1(1.72) | 1(0.87) | 0.496 |
| BREATHLESSNESS | 2(3.44) | 17(14.78) | 2.22* |
| ABDOMINAL PAIN | 3(5.17) | 26(22.60) | 2.898* |
| LOOSE STOOL | 0(0) | 23(20) | 3.657* |
| SWELLING OF BODY | 1(1.72) | 9(7.82) | 1.23 |
| COUGH | 2(3.44) | 4(3.47) | 0.01 |
| GENERAL EXAMINATION FINDING | | | |
| TEMPRATURE (≥ 100 F) | 36(62.06) | 69(60) | 0.263 |
| TACHYCARDIA | 11(18.96) | 22(19.13) | 0.026 |
| BRADYCARDIA | 3(5.17) | 1(0.87) | 1.77 |
| TACHYPNEA | 14(24.13) | 32(17.82) | 0.518 |
| PALLOR | 8(13.79) | 18(15.65) | 0.323 |
| PERIPHERAL CIRCULATORY FAILURE | 1(1.72) | 1(0.87) | 0.496 |
| ICTERUS | 0(0) | 9(7.82) | 2.188* |
| EDEMA | 1(1.72) | 9(7.82) | 1.623 |
| LYMPHADENOPATHY | 0(0) | 0(0) | 0 |
| CYANOSIS | 1(1.72) | 2(1.73) | 0.071 |
| CLUBBING | 1(1.72) | 1(0.87) | 0.496 |

* Statistical significant (p<0.05)

At the time of admission Glas Gow Coma Scale (GCS) was found to be between 7—10 in half of cases in both groups (JE-53.44% & Non-JE -51.30%) (Fig 2).

The commonest CNS finding was plantar extensor [62.6% in Non JE and 68.96% in JE], meningeal irritation [65.51% in JE and 50.53% in Non

JE]. Cerebellar signs, brisk DTR, hypertonia and hemiparesis were statistically predominant in JE cases. Hepatomegaly and ascitis were more common in Non JE cases and Respiratory failure was more common in JE cases. Raised JVP, muffled heart sounds, gallop rhythm and murmur were all more common in Non JE cases. Nevertheless none of the findings had statistically significant difference(Table -4).

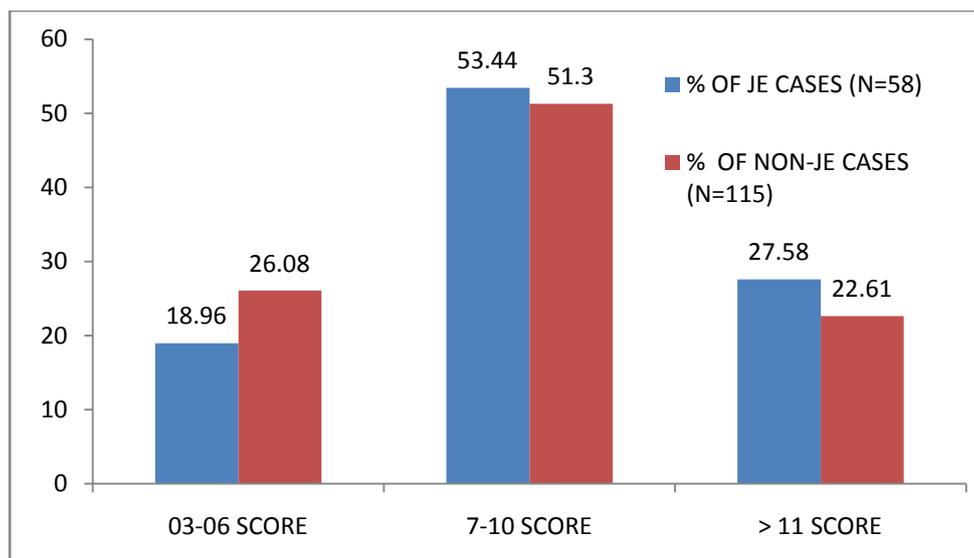


Fig 2: Glasgow Coma Scale (Fig. Showing %)

Table-4: CNS and Systemic Examination JE & Non-JE cases

| CNS examination finding | No. OF JE CASES (N=58) | No. OF NON-JE CASES (N=115) | Z value |
|---------------------------------------|------------------------|-----------------------------|---------|
| Signs of meningeal irritation | 38(65.51) | 58(50.43) | 1.884 |
| Cranial nerve palsies | 3(5.17) | 4(3.47) | 0.533 |
| Pupil (dilated & sluggish reacting) | 5 (8.62) | 16(13.91) | 1.006 |
| Fundus (Papilledema) | 8 (13.69) | 12(10.43) | 0.652 |
| Hypertonia | 6(10.34) | 3(2.60) | 2.163* |
| Hypotonia | 2 (3.44) | 3(2.60) | 0.311 |
| Hemi paresis | 2(3.44) | 0(0) | 2.002* |
| Brisk DTR | 14(24.13) | 13(11.30) | 2.195* |
| Diminished DTR | 2(3.44) | 5(4.34) | 0.283 |
| Planter extensor | 40(68.96) | 72(62.60) | 0.826 |
| Cerebellar sign | 8(13.79) | 1(0.87) | 3.613* |
| Extra pyramidal signs | 6(10.34) | 4(3.47) | 1.826 |
| Systemic finding of AES Cases | | | |
| Abdominal examination | | | |
| Hepatomegaly | 3 (5.17) | 15 (13.04) | 1.600 |
| Splenomegaly | 1 (1.72) | 2 (1.73) | 0.007 |
| Hepato spenomegaly | 1 (1.72) | 2 (1.73) | 0.007 |
| Ascitis | 0 (0) | 5 (4.34) | 1.611 |
| Respiratory system examination | | | |
| Bronchial breath sound | 0 (0) | 2 (1.73) | 1.010 |
| Adventitious sound (crepts/rhonchi) | 10 (17.24) | 20 17.39() | 0.008 |
| Respiratory failure | 5 (8.62) | 6 (5.21) | 0.866 |
| CVS Examination | | | |
| Raised JVP | 0 (0) | 6 (5.21) | 1.770 |
| Muffled heart sounds | 0 (0) | 2 (1.73) | 1.010 |
| Gallop rhythm | 0 (0) | 2 (1.73) | 1.010 |
| Murmur | 0 (0) | 2 (1.73) | 1.010 |

* Statistical significant (p<0.05)

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Table-5: Investigation reports of JE & Non-JE cases

| Haemoglobin (gm/dl) | No. of JE cases (%) (N=58) | No. of Non-JE cases (%) (N=115) |
|-----------------------------------|----------------------------|---------------------------------|
| <9 | 5 (8.62) | 15 (13.03) |
| 9-12 | 35 (60.34) | 55 (47.82) |
| >12 | 18 (31.03) | 45 (39.13) |
| TLC (cells/mm³) | | |
| ≤4000-12000 | 44 (75.86) | 88 (76.52) |
| >12000 | 14 (24.14) | 27 (23.48) |
| SGPT (U/L) | | |
| ≤40 | 40 (68.96) | 52 (45.28) |
| ≥40 | 18 (31.04) | 63 (54.78) |
| Serum creatinine (mg/dl) | | |
| ≤1.5 | 51(87.93) | 100 (86.95) |
| ≥1.5 | 7 (12.07) | 15 (13.05) |
| CSF Analysis | | |
| TLC (cells/mm³) | | |
| ≤6-100 | 49 (84.47) | 104 (90.44) |
| >100 | 9 (15.52) | 11 (9.56) |
| DLC | | |
| Lymphocytic dominance | 10 (17.24) | 27 (23.47) |
| Polymorphic dominance | 48 (82.76) | 88 (76.53) |
| Protein (mg/dl) | | |
| <40 | 16 (27.59) | 34 (29.56) |
| 40-100 | 33 (56.90) | 65 (56.52) |
| >100 | 9 (15.52) | 16 (13.92) |
| Sugar (mg/dl) | | |
| ≤40 | 5(8.62) | 8 (6.95) |
| ≥40 | 53 (91.38) | 107 (93.05) |
| CT Scan Head finding | | |
| Meningeal enhancement | 3 (5.17) | 7(6.08) |
| Cortical hypodensities | 4 (6.89) | 2 (1.73) |
| Hydrocephalus | 1 (1.72) | 2 (1.73) |
| Inflammatory granuloma | 1 (1.72) | 1 (0.87) |

COMPARISON OF JE AND NON JE CASES ON THE BASIS OF INVESTIGATION

There was no statistical significant difference between two groups in investigation report of Hemoglobin, Total Leucocyte count & Serum Creatinine, however statistical predominance [z= 2.955] of raised SGPT was found in Non JE cases. CSF pleocytosis, Raised protein & Polymorphic dominance

were found in almost similar in both groups. There was no significant difference in CSF findings of TLC, DLC, protein, sugar and gram's staining reports. The most common CT scan finding in JE cases was cortical hypo densities (6.89%), while in non JE it was meningeal enhancement (6.08%). But there was no significant difference in CT scan findings between two groups (Table 5).

Table 6: Outcome measures of JE T non-JE cases

| Outcome | No. of JE cases (%) (N=58) | No. of Non-JE cases (%) (N=115) | No. of JE cases (%) (N=58) |
|------------------------------------|----------------------------|---------------------------------|----------------------------|
| Fully recovery | 40 (68.96) | 86 (74.78) | 0.812 |
| Partial recovery (sequelae) | 8 (13.79) | 13 (11.30) | 0.473 |
| Cognitive impairment | 6 (10.34) | 5 (4.34) | 1.526 |
| Psychosis | 2 (3.44) | 7 (6.08) | 0.737 |
| Extra-pyramidal symptom | 2 (3.44) | 2 (1.73) | 0.706 |
| Cerebellar ataxia | 0 (0) | 1 (0.87) | 0.712 |
| Hemi paresis | 2 (3.44) | 0 (0) | 2.002* |
| Cranial nerve palsy | 0 (0) | 3 (2.61) | 1.24 |
| LAMA | 2 (3.44) | 4 (3.48) | 0.010 |
| Death | 8 (13.44) | 12 (10.43) | 0.652 |

* Statistical significant (p<0.05)

Full recovery was achieved in 68.96% JE and 74.78% Non JE cases while case fatality was 13.79% in JE and 10.43% in Non JE cases. Partial recovery i.e. sequelae was seen in about one tenth cases in both group and most common sequelae was cognitive impairment found in JE (13.79%) and psychosis (6%) in Non JE. The only significant difference in outcome was predominance of hemi paresis in JE cases (Table-6).

DISCUSSION

This study was a hospital based prospective study of the patients with acute encephalopathy syndrome admitted in the Department of Medicine, Nehru hospital, attached to the B.R.D. Medical College, Gorakhpur from August 2009 to October 2010. The aimed of study to compared the JE & Non-JE patients with the etiology and to correlate the clinical & outcome profile of the adult patients. Our study shows some important observations among JE & Non-JE patients. The most common cause of AES was acute viral (Non JE) encephalitis (57.5%). It was followed by acute viral Japanese encephalitis seen in 29% of patients.

In present study, almost all age groups suffered from acute encephalopathy syndrome but half of them suffered population was younger age group. The mean age of JE group was 41.5 yrs while it was 31.28 yrs in Non JE group. The study shown male predominance cases which might be due to the fact that skin amenable to mosquito bites is higher in men as compared to women or can be attributed to the male dominated social system where a sick male gets preferential medical attention in India. A previous study, Panagaria *et al.*; have shown a similar features of male predominance in HSV encephalitis [3].

The most dominant clinical presentation observed in JE & Non-JE patients were fever and altered sensorium followed by headache, vomiting and seizures. Similar manifestation was also illustrious in previous studies [13, 14]. The main presenting symptoms which were statistically significant and can be used to differentiate JE from Non JE were the predominance of abdominal pain, loose stools and breathlessness in Non- JE patients. Signs of meningeal irritation were frequently observed in more than half of the study patients in both groups of present study were also recorded in other studies [15, 16]. In finding of general examination of JE & Non-JE patients was pyrexia, followed by tachypnea, tachycardia and pallor. The statistically significant difference between JE and Non JE groups was the presence of icterus in Non JE. The most common CNS examination finding in AES patients was plantar extensor followed by signs of meningeal irritation, brisk DTR and papilledema (11.5%). Extra pyremidal sign disorders were statistically predominant in JE patients which are consistent with previous studies. [17-18, 20]

On general physical examination of JE & Non-JE patients, hepatomegaly, ascitis, hepatosplenomegaly, respiratory & cardiovascular system involvement was major feature in both groups. There was no significant statistical difference observed in systemic examination between JE and Non JE patients while these feature were dominant in Non-JE group in Bhatt C G. *et al.*; study. [18]

In routine blood investigation showed derangement of Liver & Renal function but without any significant difference in both groups, however statistical predominance of raised SGPT was found in Non JE cases which might be due to injurious impact on liver structure or functions by Non-JE infections as compare to JE infection. Abnormalities in liver and renal functions in JE and non-JE patients were noted in our study. Some of earlier studies have shown deranged liver functions and renal functions in patients with JE. [19-20]

Elevated cell count (>100 cell/mm³) in CSF was noted in 15% in JE cases while 10% in Non-JE cases with polymorph predominance and elevated CSF protein level (>40mg/dL) was recorded in 73% in JE cases while 70% in Non-JE cases of study cases but these groups not shown any significant difference. However, Avabratha *et al.*; study showed elevated cell count in 45.06% and protein in 74.67% study patients [14, 20].

The most common CT scan finding in JE & Non-JE patients was meningeal enhancement seen in 6%, followed by cortical hypodensities and hydrocephalus without any significant difference between both groups which was same as previous study [21].

In present study, Aspiration pneumonitis (17%) was the most common secondary complication in followed by respiratory failure (13%) during hospitalization which same in both groups. In our study, 10.34% JE patients and 6.08% in Non JE had neurological sequelae at the time of discharge, while 13.79% in JE and 10.43% in Non JE had died in hospital. Neurological sequelae like Cognitive impairment in JE and psychosis in Non-JE cases the common observation. Similar association was also noted in other different studies [14, 20-25]. This may be mentioned here that our observation is only from a small number of patients who died in hospital and it is an ongoing study. In future with more number of patients we may be able to shed some more light on mortality and its association with meningeal signs.

CONCLUSION

Acute viral encephalitis is still a major cause of AES in adults in this part of India. These significant research findings seek the attentions of the global

community to combat the hazard of this arboviral encephalitis in saving the life of adults. A mass vaccination may be carried out in adults for the prevention of JE. The most common illness among AES patients observed in our study was Non JE cases, which requires a clear elucidation with regards to aetiology, (clinical picture) treatment and prevention. Multisystem involvement in these patients requires special attention. A surveillance system for such infection should be developed which should monitor the trends of such infection and further studies should be conducted to ascertain the clinical profile and epidemiological course of the disease, so that standard protocols can be developed and such patients are managed effectively.

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