Original research article

International Journal of Medical Science and Education | pISSN- 2348 4438 | eISSN-2349- 3208

PATTERN OF INFECTIONS IN ADULT PATIENTS PRESENTING AS ACUTE ENCEPHALITIS SYNDROME (AES)

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Received: 29/09/2014 ***Revised: 22/12/2014*** ***Accepted:28/12/2014***

ABSTRACT:

Objectives: Encephalitis is an acute inflammatory process that affects brain parenchyma, presents as a diffuse and / or a focal neuropsychological dysfunction and is almost always accompanied by inflammation of adjacent meningitis which is most commonly caused by viral infection. Acute viral encephalitis is the most common cause of acute encephalitis syndrome (AES). The study was regarding the pattern of infections in patients presenting as acute encephalitis syndrome in adults and to note any change in the pattern of infection particularly with reference to enterovirus infection.

Material and Methods: A total of 200 patients with AES which were hospitalized patients in the Department of Medicine, Nehru hospital, attached to the B.R.D. Medical College, Gorakhpur during August 2009 to October 2010 and were followed during hospitalization. All were subjected to detail clinical examined and investigated along with viral diagnostic studies on cerebrospinal fluid (CSF) samples to determine the aetiology of AES.

Results: Non JE responsible for 57.5% cases while common presenting symptoms were fever and altered sensoriurn & mean GCS at the time of admission were 8.95 in AES cases. In AES cases full recovery seen in 72.5% and common sequelae was cognitive impairment while the case fatality rate was 13%.

Conclusion: Our results demonstrate that for this highly fatal condition a hospital-based monitoring system with periodic diagnostic testing is feasible and can provide information useful for clinicians as well as public health planners

Key Words: acute encephalitis syndrome**,** viral infection, enterovirus infection, cerebrospinal fluid.

INTRODUCTION

Encephalitis is an acute inflammatory process that affects brain parenchyma, presents as a diffuse and/or a focal neuropsychological dysfunction and almost always accompanied by inflammation of adjacent meningitis. The disease is most commonly caused by viral infection. It can also be caused by bacterial and protozoal infection. Acute viral encephalitis is the most common

cause of acute encephalitis syndrome (AES). Children and young adults are usually the most frequently affected groups. **(1-3, 5)** 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. Arbo-viruses are the most common cause of episodic encephalitis with reported incidence same to that of HSV. Japanese encephalitis (JE), occurring in Japan, Southeast Asia, China and India, affecting around 50,000 people per year. **(3-5)**

Northeastern Uttar Pradesh has been experiencing regular epidemics of encephalitis since 1978. **(4-7)** 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. In last 3 years, a total of 8160 cases were reported as AES (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. **(6, 8-10)** 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.**(11)**

The study was aimed to study the pattern of AES among the adults. An attempt was made to study the differences in the various demographic, hospitalization, clinical features, secondary complications and outcome among the AES cases.

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 11.56% of total hospital admissions. Among the total AES patients, 1103 (22.40%) were admitted in the Medicine department and 3819 (77.60%) in the Paediatric department. All the 200 patients were subjected to detailed history, clinical examination and investigations were done in all the cases who presented with fever with altered mental state of short duration. Following investigations were included: Haernoglobin, total leucocyte count, differential leucocvte count, platelet count, general blood picture, random blood sugar, renal function tests, liver function tests, serum electrolytes, Widal test 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

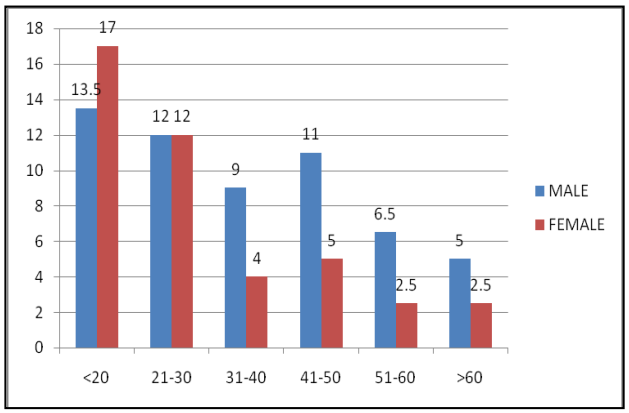
We applied Z score as test of significance. In statistics, a result is called statistically significant if it is unlikely to have occurred by chance. A statistically significant difference simply means there is statistical evidence that there is difference; it does not mean that the difference is large,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

RESULTS

Demography and hospital stay

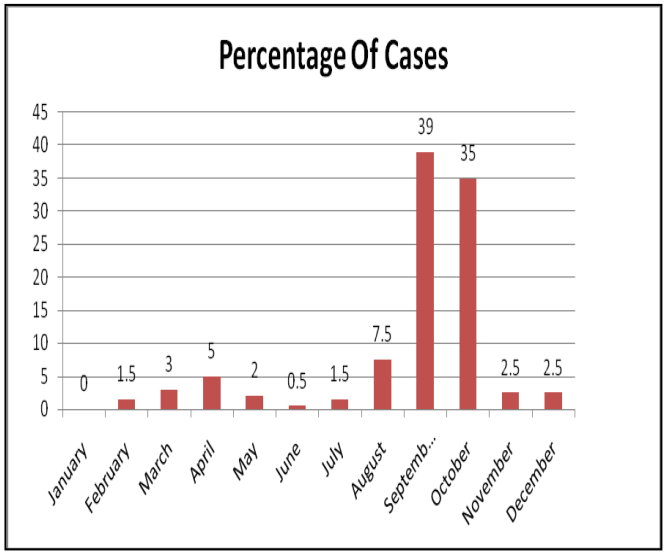
A total of 109 cases (54.5%) belonged to less than 30 yrs of age, suggesting that the disease has higher incidence in younger population. Male: Female ratio was 1.32: 1. (Fig.1)

Figure 1: showing age & sex wise percentage distribution of AES cases



Although, the cases were seen throughout the year but the incidence was peaked in the month of September (39%) and in the month of October 70 (35%), suggesting the seasonal occurrence of the disease. **(Fig. 2)**

Figure 2: Showing Month Wise Percentage Distribution of AES Cases



The most common presenting symptoms were fever and altered sensoriurn in 100% cases, followed by headache in 180 (90%) and vomiting in 127 (63.5%). Seizures were present in 94 (47%) cases. Pyrexia was predominant feature in 127 cases (63.5%), followed by tachypnea in 56 (28%), tachycardia in 41 (20.5%) and pallor in 33 (16.5%). **(Table — 1 & 2)**

Figure 3: showing duration of stay in hospital of AES cases (figure showing percentage)

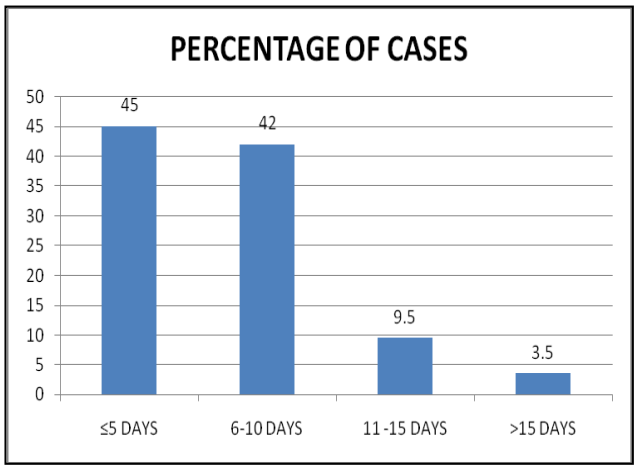


Table 1: General and Systemic Examination of AES cases

General Examination Finding of AES Cases	No. of cases (%)
Temperature (≥ 100^0 F)	127 (63.5)
Tachycardia	41 (20.5)
Bradycardia	5 (2.5)
Tachypnea	56 (28)
Pallor	33 (16.5)
Peripheral circular failure	8 (4)
Icterus	16 (8)
Edema	16 (8)
Lymphadenopathy	4 (2)
Cyanosis	6 (3)
Clubbing	4 (2)
Systemic finding of AES Cases	
Abdominal examination	
Hepatomegaly	24 (12)
Splenomegaly	7 (3.5)
Hepatospenomegaly	8 (4)
Ascitis	8 (4)
Respiratory system examination	
Bronchial breath sound	8 (4)
Adventitious sound (crepts/rhonchi)	36 18()
Respiratory failure	13 (6.5)
CVS Examination	
Raised JVP	8 (4)
Muffled heart sounds	4 (2)
Gallop rhythm	4 (2)
Murmur	2 (1)

Hepatomegaly was the most common finding on abdominal examination found in 24 cases (12%), followed by hepatosplenomegaly and ascitis in 8 each (4%). Adventitious sounds (crepts/rhonchi) were present in 36 cases (18%), followed by respiratory failure in 13 (6.5%). **(Table - 2)**

At the time of admission GCS was between 7—10 in 108 cases (54%). The GCS between 3—6 and >10 was found in 46 cases each (23%). The mean GCS at the time of admission was 8.95.

Table 2: Clinical Symptoms & Secondary complication during hospital admission in AES cases

Symptoms	No. of cases (%)
Fever	200 (100)
Headache	180 (90)
Vomiting	127 (63.5)
Alter sensorium	200 (100)
Seizure	94 (47)
Paralysis	4 (2)
Breathlessness	23 (11.5)
Abdominal pain	35 (17.5)
Loose stools	25 (12.5)
Swelling of body	15 (7.5)
Cough	6 (3)
Secondary complications during hospitalization	
Aspiration pneumonia	34 (17)
Respiratory failure	13 (6.5)
Psychosis	10 (5)
Peripheral circulatory failure	4 (2)
Sepsis	4 (2)
UGI bleeding	4 (2)
Bed sore	4 (2)
Hemiparesis	2 (1)
Pericardial effusion	2 (1)
Drug reaction	2 (1)

3. INVESTIGATION OF THE AES CASES

The haemoglobin of the cases was between 9—12 gm/dl in majority {108 cases (54%)}, followed by >12 in 69 (34.5%). The mean haemoglobin of the cases was 11.13 gm/dl. SGPT was raised in 48% and Serum creatinine was raised in 15.5% cases.

Table 3: Haematological, Biochemical & CSF investigation of AES cases

Haemoglobin (gm/dl)	**No. of cases (%)**		**No. of cases (%)**
<6	3 (1.5)	**TLC (cells/mm^3)**	
6-9	20 (10)	**<4000**	2 (1)
9-12	108 (54)	**4000-12000**	149 (74.5)
>12	69 (34.5)	**>12000**	49 (24.5)
SGPT (U/L)		**Serum creatitine (mg/dl)**	
≤40	**≤1.5**	169 (84.5)	
≥40	**≥1.5**	31 (15.5)	
CSF Analysis		**Protein (mg/dl)**	
TLC (cells/mm^3)		**<40**	58 (29)
≤5	6 (3)	**40-100**	100 (50)
6-100	157 (78.5)	**>100**	42 (21)
>100	37 (18.5)	**Sugar (mg/dl)**	
DLC		**≤40**	27 (13.5)
Lymphocytic dominance	46 (23)	**≥40**	173 (86.5)
Polymorphic dominance	154 (77)	**Gram staining**	
IgM status in cases with JE		**Gram positive cocci**	7 (3.5)
IgM for JE +ve in CSF	29 (14.5)	**Gram negative cocci**	0 (0)
IgM for JE +ve in Serum	46 (23)	**Gram positive bacilli**	0 (0)
IgM for JE +ve in CSF & Serum	18 (9)		
IgM for JE +ve in either CSF or Serum	58 (29)		

The CSF pleocytosis was seen in 97% cases and protein level between 40—100 mg/dl was present. CSF examination suggested that the majority of the cases were of acute viral encephalitis. The 1gM for JE positivity was more in serum {46 cases (23%)}, than CSF {29 cases (14.5%)}. In 50% and more than 100 in only 21% cases while Sugar was decreased in only 13.5% cases. Gram +ve cocci were found in only 3.5% only. The Positivity either in serum or CSF was

found in 58 (29%) cases and therefore, these 58 cases were labeled as confirmed cases with Japanese Encephalitis. **(Table 3)**

The most common CT scan finding was meningeal enhancement seen in 12 cases (6%), followed by cortical hypodensities in 6 (3%), hydrocephalus in 4 (2%) and 1% showed inflammatory granuloma.

4. COMPLICATIONS DURING HOSPITALIZATION AND OUTCOME

Aspiration pneumonitis was the most common secondary complication during hospitalization present in 34 cases (17%), followed by respiratory failure in 26 (13%) and psychosis in 10 (5%). **(Table 2)** The most common outcome of the AES cases was full recovery seen in 145 cases (72.5%). Partial recovery i.e sequelae were seen in 21 cases (10.5%). The most common sequelae was cognitive impairment seen in 11 cases (5.5%), followed by psychosis in 9 (4.5%) and extrapyramidal symptoms in 4 (2%). Of all AES cases, 26 (13%) cases were expired. Therefore the case fatality rate of AES was 13%.

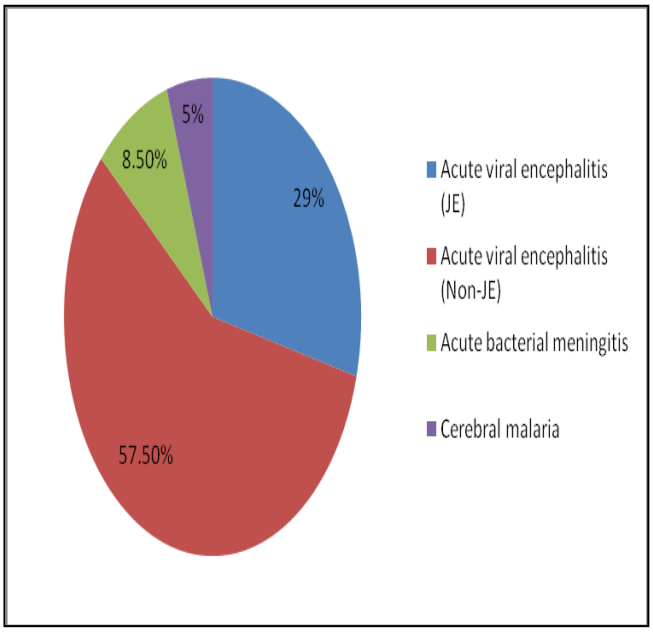
Thirteen cases (50%) expired within 3 days of admission and 8 (30.77%) expired between 4—7 days of admission. The most common cause of AES was acute viral encephalitis (Non JE) responsible for 115 cases (57.5%), followed by acute viral encephalitis (JE) in 58 (29%). Acute bacterial meningitis and cerebral malaria were responsible for 17 (8.5%) and 10 (5%) cases respectively.

Table 4: Age & sex wise distribution of JE & Non-JE cases (Fig. showing no {%})

Age group (in years)	JE			Non-JE		
	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	The age of presentation of the cases in Non JE (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**

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. **(Table — 4)**

Figure 4: Etiology of AES cases



DISCUSSION:

North eastern Uttar Pradesh (U.P.) draws national and international attention due to continuing epidemic of acute viral encephalitis and its changing picture temporally. Several epidemics of AES recurring since 1978 **(4-7),** have drawn massive public and political attention, but despite all the efforts, the epidemics are regularly occurring with heavy mortality and morbidity. The most severe epidemic so far has been of 2005 **(6),** with lot of hue and cry in the public.

Maximum number of the patients with AES belongs to pediatric age group and most studies have been done in these patients. In our hospital adult patients account for the approximately 25% of AES, but they have not been studied. This is the first study where adult patients with AES have been studied. A total of 54.5% of cases belonged to less than 30 yrs of age, suggesting the disease has higher incidence in younger population which was same (36 % in 1-15 Years) in study report of Jain P et al **(49-51)**. Younger patients were more affected probably because of lack of cumulative immunity due to natural infection. A male predominance was noted in our study which was same as previous study, the reason of this is not clear, but probably social customs of male preference is responsible for this discrepancy or might be due to the fact that skin acquiescent to mosquito bites is higher in men as compared to women in India.

The incidence peaked to 39% in the month of September and 35% in the month of October, suggesting the seasonal occurrence of the disease. The peak incidence of the disease was from August to October i.e. post monsoon period. The incidence of arboviral and enterovirus infections as well as malaria increases in this period due to coincidence increase population density of mosquito vector. However, variation in temperature pattern has been also considered a possible explanation; rise in temperature in summer season also corresponds to increase number of patients with encephalitis. **(12-19, 23-24)**

The most common presenting symptoms were fever and altered sensorium in 100% cases,

followed by headache in 90%, vomiting in 63.5% and Seizure in 47% in our study. It is postulated that alteration in sensorium, seizure, vomiting in a patient with CNS infection indicates an element of parenchymal involvement. **(50, 51)** This can explain the altered mental state in patients with meningoencephalitis. In AES, primary parenchymal involvement may be responsible for encephalopathy. In some extend, high intracranial pressure may contribute to distorted mental status. The postulated behind for altered mental status in meningitis to be the spillage of inflammatory cells to the adjoining brain parenchyma and the resultant parenchymal involvement. **(51)** In SAE, inflammatory cytokines and metabolic changes may play a vital role in the pathogenesis of encephalopathy, rather than direct parenchymal involvement. Pyrexia was the predominant feature, followed by tachypnea and tachycardia. At the time of admission GCS was between 7—10 in about fifty percent cases. The mean GCS at the time of admission was 8.95 which were same in analysis of Joshi et al. study & other studies **(20-22, 45).** The deranged liver and renal functions may be due to multi-organ involvement due to enteroviruses (**24-28)** and plasmodium falciparurn infection which were almost equivalent of other studies. **(11, 44)** The CSF pleocytosis was seen in 97% of cases, but in majority of them the TLC was between 6—100 (78.5%). In maximum patients the protein was either between 40—100 mg/dl (50%) or normal (29%). Sugar in CSF was decreased in only 13.5% and Gm +ve cocci were found in only 3.5%. The CSF examination suggested that the majority of the cases were of acute viral encephalitis **(44, 49).**

The IgM for JE positivity was more in serum (23%), than CSF (14.5%). Positivity either in serum or CSF was found in 29% cases and therefore, these 29% cases were labeled as confirmed cases with Japanese Encephalitis which was same as in other studies **(10-12)**. The most common sequels were cognitive impairment, followed by psychosis and extra-pyramidal symptoms**.** Full recovery was noted in 72.5% of cases and Partial recovery was observed in 10.5%. This was similar as previous studies Jain at al & other studies **(36-39, 43-44, 49).** A mortality rate 13% were observed in present study similar to previous studies which was 15-40%. **(39, 45, 49)**

Fifty percent patient died within 3 days of admission and 30.77% cases expired between 4—7 days of admission. It was interesting to note that majority of the deaths occurred in the first 3 days of admission with aspiration pneumonitis as the most common secondary complication and faulty transportation can be held responsible for this mortality. In previous studies also during the course of the disease, majority of patients who succumb to illness die within first three to four days. Patients who recover fully in seven to ten days show good outcome and go home within ten days. Children of JE not recovering within ten days have higher chances of developing neurological deficits, brain damage and have pool- outcome **(45-49).** The most common cause of AES was acute viral (Non JE) encephalitis (57.5%). It was followed by acute viral Japanese encephalitis in 29%. This clearly shows that our efforts to control AES have to be in a different direction than controlling only Japanese encephalitis. This calls for the separate epidemiologic studies to find out the exact

etiological agent for the Non JE AES and thus planning the preventive measures. **(37-38, 40-44)**

CONCLUSION

To conclude, the etiology panorama of acute encephalitis syndrome varies with time & geographical location. Non- JEV followed by JE still remains the chief causative agents of AES, although ongoing epidemiological surveillance is essential for establishing preventive strategies. While viral diagnostics are resource intensive, we can include standard protocols for identification of AES and basic CSF based diagnostics into routine clinical care and periodic diagnostic testing can provide valuable etiologic and epidemiologic information. In India, an Integrated Disease Surveillance Program (IDSP) has been developed and implemented by the government, but it needs to be strengthened. **(52, 53)**
Limitation: Sample size was small so result cannot be generalized to general population as data was collected from a single hospital of the city.

Acknowledgement: The author is grateful to all the participants for giving their cooperation and valuable time.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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