

Hospital Outcomes in AES cases from Eastern India

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Abstract

Acute Encephalitic Syndrome (AES) is defined as acute onset fever of less than 7 days duration with altered sensorium and/or seizure. 104 consecutive patients of AES presenting to the Department of Medicine, North Bengal Medical College were studied to evaluate hospital outcomes and factors contributing to mortality and morbidity.

This study showed a male dominance of 65.38%. Aetiological diagnosis was reached in all cases with JE (72%), HSV Encephalitis (HSVE) (11.5%), Scrub Typhus Encephalitis (STE) (9.6%), Dengue Encephalitis (2.88%), Cerebral Malaria (1.8%), Bacterial Meningitis (0.9%) and sepsis (0.9%). We documented 25 deaths (24%) during the course of hospitalisation, with an aetiological breakup of JE 22 (29.3%), HSVE 2 (16.6%) and STE 1 (10%). Higher mortality was observed in patients GCS < 7 (47.6%) and seizure at presentation (38.8%). Among survivors, residual neuro-deficit was predominantly seen in JE patients, with 39.6% motor deficit, 17% sensory deficit, 20.7% autonomic deficit and 43% cognitive deficit.

Conclusion: GCS < 7 at presentation and seizures were found to be independent poor prognostic markers in patients of AES. Neurological sequelae in the form of cognitive, motor, sensory and autonomic deficits were common among AES patients, particularly in JE.

Introduction

Acute Encephalitis is defined as 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)¹. The incidence of AES in India is 0.42/1,00,000 population per annum (1978 - 2011)². The most common causative viral agents are Herpes Simplex (HSV1), Japanese Encephalitis, Dengue, Enteroviruses, Measles, Epstein-Barr virus (EBV), Tickborne Encephalitis (TBE), Human Herpesvirus 6 (HHV-6) and West Nile virus. Scrub Typhus, Cerebral malaria, acute pyogenic meningitis and non-infectious causes of encephalopathy need to be excluded while considering AES³. In West Bengal, the disease remains endemic (especially JE) in Bankura, Burdwan, and Howrah districts⁴. A study by Bandyopadhyay *et al* showed an incidence of 22.76% in 2011. In 1973, a JE outbreak was first recorded in the districts of Burdwan and Bankura in West Bengal, where 700 cases and 300 deaths were reported⁵⁻⁹. Japanese encephalitis virus (JEV), a mosquito-borne flavivirus, is the most common vaccine-preventable cause of encephalitis in Asia¹¹⁻¹⁵. Japanese encephalitis (JE) occurs throughout most of Asia and parts of the Western Pacific^{11,13}. Among an estimated 35,000 - 50,000 annual cases, approximately 20% - 30% of patients die, and 30% - 50% of survivors have neurologic or psychiatric sequelae^{14,15}.

Viral encephalitis can present with low or mild severity and recover spontaneously or much more aggressively with a poor prognosis and severe neurological sequelae in survivors. The prodromal signs and symptoms are those of a classic viral infection: fever and headache, possibly accompanied by nausea or vomiting¹⁶. After a few days, symptoms of CNS involvement become manifest with altered mental status, considerable irritability and agitation, personality changes; seizures (focal or generalised) may occur, sometimes accompanied by focal neurological signs. Patients may then become lethargic or comatose; death eventually ensues. Stiff-neck is a sign of meningeal involvement and heralds a poor prognosis¹⁶.

Aims and objectives

The study was conducted from May 2018 to April 2019 on patients presenting with AES to the Department of Medicine of North Bengal Medical College, Darjeeling, West Bengal. All patients fulfilling inclusion criteria, after informed consent, were included in the study. The study was carried-out with an objective to evaluate the outcome of disease and factors contributing to clinical outcomes.

Material and methods

This was an observational, cross-sectional study done over a

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period of one year. Patients with a clinical diagnosis of AES admitted at Department of Medicine, North Bengal Medical College, Darjeeling were enrolled consecutively in the study from May 2018 to April 2019. A case of AES was clinically defined as a constellation of symptoms comprising of acute onset fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures)¹ in a person of > 12 years of age.

Inclusion criteria

- Patients > 12 years, with
- Diagnosis of AES (as defined by acute onset alteration of sensorium with fever of recent onset, i.e., 1 week or less duration).

Exclusion criteria

- Fever of more than 1 week duration.
- Patients having Metabolic Encephalopathy, Cerebrovascular Accidents, ICSOL, Trauma, Hypoxia.
- Next of kin not providing consent for study and those who left against medical advice.

Parameters to be studied

- Aetiology of AES cases.
- Hospital outcomes (died or survived).
- Residual neurodeficit at discharge.
- Clinical factors influencing the mortality.

We evaluated all patients with a detailed history, with special attention to recent onset of altered sensorium and/or seizures. Clinical examination also focused on neurological assessment and residual neuro-deficit at the time of discharge from hospital. The lab evaluation included complete haemogram, blood sugar, LFT, urea, creatinine, malaria and Dengue antigens, Scrub typhus IgM, blood culture, serum serology for JE and Typhi-dot IgM. These were supplemented with CSF analysis for cytology, biochemistry and CSF for JE Mac Elisa and RT PCR for HSV. Neuroimaging in the form of MRI brain was advised for all patients. Ethical approval for the study was obtained from the Institutional Ethical Committee and written informed consent was taken from the next of kin.

Data analysis

Data was entered in Excel Microsoft Software to prepare Master table and is presented in various tables, charts and diagrams. The data was then analysed using SPSS statistical software V 12.2.

Results

Among 104 patients of AES enrolled for this study, males dominated the clinical picture with 68 out of 104 patients (65.38%).

An aetiological diagnosis was reached in all cases. 75 cases (72%) were caused by Japanese Encephalitis. The next most common causes were Herpes Simplex Encephalitis (12 cases; 11.5%) followed by Scrub Typhus (10 cases; 9.6%). Dengue Encephalitis was also found in 3 cases (2.88%).

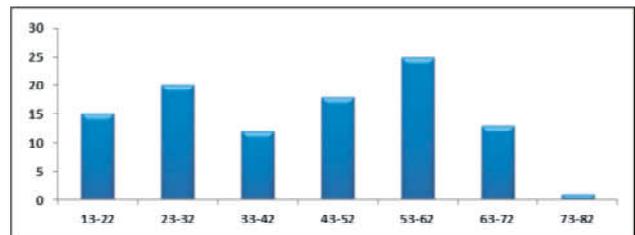


Fig. 1: Age distribution of study population.

Two cases initially diagnosed to have AES were found to have Cerebral Malaria and one case each was due to Sepsis and Acute Pyogenic Meningitis.

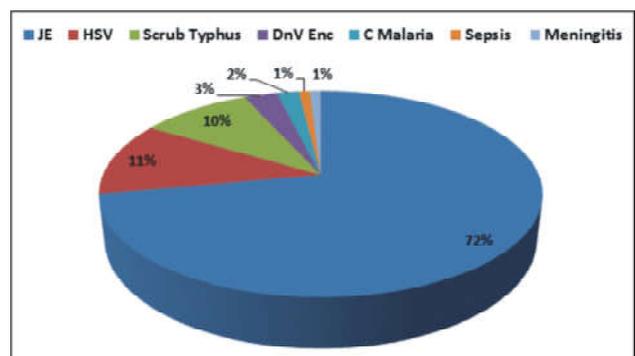


Fig. 2: Aetiology of AES in the study population.

The majority of patients (54.81%) were > 40 yrs of age as depicted above figure. Mean age of patients was 43.60 ± 17.23 years (Fig. 1).

Table I: Gender and Rural: Urban ratio, as per aetiology.

	Total (n=104)	JE (n=75)	HSV Enc (n=12)	Cer Mal (n=2)	Scr Typ (n=10)	Bact Men (n=1)	Sepsis/ MODS (n=2)	Dengue (n=3)
Male:Female	1.9:1	1.8:1	2:1	1:1	3:2	0:1	1:0	2:1
Rural:Urban	1.8:1	2.5:1	1:1	1:1	1:1	1:0	0:1	0:3

The JE cases were mostly from the rural areas whereas the Rural: Urban distribution was equal in cases of Scrub Typhus and HSV Encephalitis. All three cases of Dengue

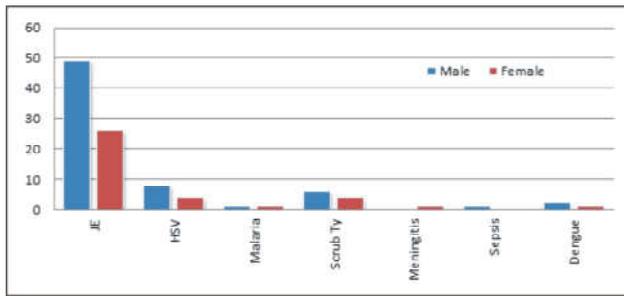


Fig. 3: M: F ratio as per aetiology of AES.

Encephalitis were residents of urban areas. Male: Female ratio was found to be highest in HSV and Dengue encephalitis followed by JE and Scrub Typhus (Table I; Fig. 3).

Table II: Mortality outcome with respect to aetiology.

	Total (n=104)	JE (n=75)	HSV Enc (n=12)	Cer Mal (n=2)	Scr Typ (n=10)	Bact Men (n=1)	Sepsis (n=1)	Dengue (n=3)
Survived	79	53	10	2	9	1	1	3
Mortality (%)	25 (24%)	22 (29.3%)	2 (16.6%)	0	1 (10%)	0	0	0

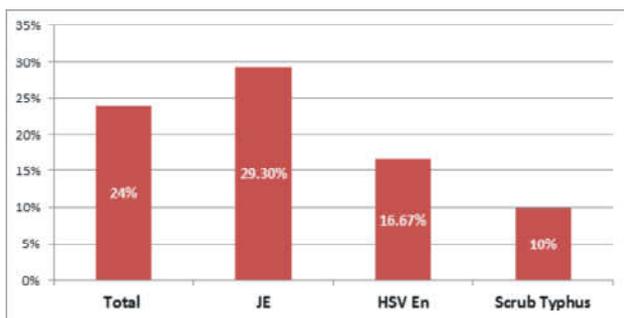


Fig. 4: Mortality in relation to aetiology.

Total 25 patients died, resulting in overall mortality rate of 24%, of which highest mortality was observed in JE (29.33%) followed by HSV encephalitis (16.67%) and Scrub typhus (10%) (Table II, Fig. 5).

During the study, it was noted that lower GCS at presentation carried poor prognosis in terms of survival. In the study group, 42 patients presented with a GCS of < 7 with a mortality of 47.6%. Those who had a GCS of more than 7 had a mortality of 8%. (p - Value < 0.0001, RR: 5.9 with 95% of Confidence Interval: 2.4 - 14.5) (Table III).

Table III: Correlation of mortality with GCS on presentation.

GCS	Died	Survived	p value*
GCS < 7 (n = 42)	20 (47.6%)	22 (52.4%)	< 0.0001 (RR = 5.9)

GCS > 7 (n = 62)	5 (8%)	57 (92%)
Total (n = 104)	25 (24%)	79 (76%)

*Pearson chi square test.

In our study, 54 patients had a presentation with seizures, mostly GTCS. 21 out of these 54 patients (38.8%) died whereas, among the rest 50 patients, who did not have any seizures, only 4 died (8%). So, presence of seizures had a significant positive correlation with mortality (p - value < 0.0002, RR - 2.01, with a 95% of confidence interval 1.47 to 2.74) (Table IV, Fig. 6).

Table IV: Correlation of Seizure with mortality.

	Death	Survived	p value*
Seizures (n = 54)	21 (38.8%)	33 (61.2%)	< 0.0002 (RR 2.01)

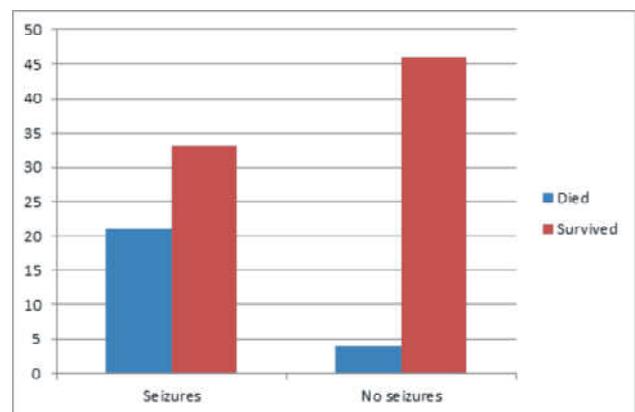


Fig. 5: Relation of mortality in respect to seizure occurrence.

No seizures (n = 50)	4 (8%)	46 (92%)
Total (n = 104)	25 (24%)	79 (76%)

*Pearson chi square test.

Table V: Residual neurological sequelae among survivors.

	Neurological sequelae				
	Motor	Sensory	Autonomic	Cranial nerve	Cognitive Deficit
JE (n = 75)	21 (39.6%)	9 (17%)	11 (20.7%)	2 (3.7%)	30 (56.6%)
HSV Enc (n = 12)	1 (10%)	0	0	0	3 (30%)
Cerebral Malaria (n = 2)	0	0	0	0	0
Scrub typhus (n = 10)	0	0	0	0	1 (11%)
Bacterial meningitis (n = 1)	0	0	0	0	0
Sepsis (n = 1)	0	0	0	0	0
Dengue (n = 3)	0	0	0	0	0

27.8 % of survivors had some motor deficit at the time of

discharge from hospital, like monoparesis, hemi paresis, motor aphasia and dystonia mostly in the JE group (39.6% of survivors). 9 patients (17% of survivors) of JE had sensory abnormalities in the form of paraesthesias, tingling and numbness of the affected paretic limb. Two patients had residual facial deviation and 11 patients of JE (20.7% of survived) had some or other sort of residual autonomic abnormality such as loss of bowel and bladder control, blood pressure and heart rate variability. 34 (43%) patients had a cognitive deficit on discharge (MMSE < 25) in our study (Table V).

Discussion

104 consecutive AES patients presenting to the Department of Medicine, North Bengal Medical College, Darjeeling were enrolled during a period of one year, of which mean age was 43 years (Range 13 - 75 years) with a male: female ratio of 1.85: 1. Karmakar *et al* showed a male: female ratio of 1.71:1¹⁷. The male predominance might be due to the occupational exposure, as majority of them work in fields.

Aetiological diagnosis was reached in all 104 patients with a viral aetiology in 86.5% cases. Among the viral causes, JE was found to be the most common (72% of all cases) followed by HSV -1 encephalitis (11.5% of all cases) and Dengue Encephalitis (2.88% of all cases). Jain *et al* found JE as the most common cause of AES in her series of 4,092 patients of AES, followed by Dengue Encephalitis, Enteroviruses and HSV¹⁸. Karmakar *et al* found that only 8.7% tested positive for JE¹⁷. In another epidemic outbreak studied by Saxena *et al*, 55.3% patients tested positive for JE¹⁹. JE is emerging as the most common cause of AES in India. In recent times, after 2012, AES cases in India have shifted towards the JE aetiology. Based on reports, the Indian states of Uttar Pradesh (UP), Bihar, Assam, West Bengal, and Tamil Nadu were identified as JE endemic zones²⁰. Also, huge population migration with availability of potential breeding sites for mosquitoes and local pig rearing at homes could be the dominating cause.

In our study, there was a positive correlation between GCS at presentation and mortality rate with a GCS of < 7 having a mortality of 47.6%. On the contrary, a GCS of > 7 had a mortality of 8%. (p value < 0.0001, RR - 5.9 with 95% confidence interval - 2.4 - 14.5). Rayamajhi *et al*²¹ showed that a lower a GCS was associated with poor outcome. Farzana *et al*²² showed a relatively poor outcome when the GCS was < 6.

Patients who presented with seizures, had a worse outcome (mortality 38.8%) in our study, with a positive correlation between poor outcome and seizures. the (p value < 0.0002, RR - 2.0, with a 95% of confidence interval - 1.4 to 2.7). Michael A Hansen *et al* also reported positive correlation

between seizure and mortality (p value < 0.01)²³. A similar observation on outcome of AES patients was reported by Takeshi Hatachi *et al* with 9,386 patients for 8 years where he opined that presence of epilepsy was a predictor of poor outcome²⁴.

Residual neuro-deficit was common among the survivor patients in the form of motor deficit (27.8%), sensory deficit (17%) and autonomic disturbance (20.7%). 34 (43%) patients had a cognitive deficit on discharge. Similar observation was reported by Rayamajhi *et al*²¹, showing, 25% of all viral AES cases and 38% of JE cases had residual neurological sequelae.

Conclusion

Among adult patients with AES, JE was the most common cause, followed by HSV-1 encephalitis and Scrub typhus, in this region of the country. GCS at presentation and seizures were found to be independent poor prognostic markers. Residual neuro-deficits in the form of motor/sensory/autonomic were common sequelae, particularly in cases of JE. Residual cognitive impairment was not uncommonly seen.

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