e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 217-225

Original Research Article

Clinical and Radiological Predictors of Outcome in Acute Encephalitic Syndrome: An Observational Prospective Study at a Tertiary Care Hospital in North East India

Mishra C [1], Mahanta A[2], Das M[3], Medhi G [4], Bhuyan D[5]

[1,2,3]Department of Neurology, Gauhati Medical College & Hospital, Guwahati, India
[4]Department of Paediatrics, Gauhati Medical College & Hospital, Guwahati, India
[5]Department of Radiology, Dhubri Medical College & Hospital, Dhubri, India

Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 26-04-2024
Corresponding Author: Dr. Mishra C
Conflict of interest: Nil

Abstract:

Background & Aims: Acute Encephalitis Syndrome (AES) is a major public health issue among children in India causing high mortality and morbidity. We aim to evaluate the clinical and radiological profile of AES patients and find the predictors of poor outcome.

Methods: We conducted a Prospective observational study among children with AES between 1-12 years of age admitted at a tertiary care center from April 2021 to March 2023 (2 years). Clinical features, biochemical tests, CSF analysis and radiological features were studied and analyzed to evaluate the predictors of poor outcome.

Results: A total of 170 pediatric cases (male: female, 1.6:1) of AES were enrolled during the study period. Infective etiology could be confirmed in 50 cases (29.5%), out of which JE was the most common (19.4%) cause. All patients admitted in our study were having fever and altered sensorium at admission. Seizure activity was present in most (94.1%) cases. In both CT and MRI brains, the thalamus followed by the cortex was the most commonly involved areas. Poor outcome (Modified Rankin Scale, MRS ≥ 3) at discharge was observed in 39% of cases. In univariate analysis, prolonged fever and altered sensorium, multiple seizures, abnormal respiration, low GCS, focal neurological deficits, meningeal signs, abnormal neuroimaging, and prolonged hospital stay were found to be significantly (p value< 0.05) associated with poor outcome. In multivariate analysis, low GCS at admission, meningeal signs and prolonged hospital stay came out to be independent predictors of outcome.

Conclusion: Low GCS, meningeal signs, and prolonged hospital stay are predictors of poor outcomes in AES.

Keywords: Japanese Encephalitis; Acute Encephalitis Syndrome; Neuroimaging.

Introduction

Acute encephalitis syndrome (AES) is defined as the acute onset of fever and a change in mental status (including signs and symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures) in a person of any age at any time of year (WHO case definition) [1]. Over 50,000 children present every year to different hospitals with clinical features suggestive of acute brain infection or AES, in Asia, with over 30% of these patients dying or suffering from significant neurological problems following their acute illness [1]. Most AES cases are considered to be due to viral encephalitis [2] although; the etiology of AES remains unknown in 68%–75% of the patients [3]. It is more common in boys and in the age group of 5 to 15 years and rare in less than 1 year of age [4]. The North-Eastern region of India, particularly the state of Assam, has been experiencing epidemics of viral encephalitis with a peak in the month of July every year [5]. Fever, altered sensorium, seizures, headache, and vomiting are the most common presenting symptoms noted in AES [6,7]. In non-fatal cases, AES may often lead to severe permanent physical, cognitive, emotional, behavioural and social difficulties in selected individuals [8]. About 20-30% of AES cases are fatal, and 30–50% result in permanent neuropsychiatric sequelae [9,10]. Most of the flaviviruses have been shown to affect subcortical gray matter such as thalamus, basal ganglia, substantia nigra and cerebellum [11,12]. MRI is considered more sensitive than CT scan in the diagnosis of pediatric encephalitis [3,14]. Basal ganglia/thalamic involvement suggest Japanese encephalitis [15]. Studies on the radiological changes in other flavivirus encephalitis like St Louis encephalitis, Murray Valley encephalitis and

tickborne encephalitis revealed non- specific changes on CT scan or MRI [11]. Identifying the etiological agent in AES cases presents a challenge to effective prevention and management [16]. Due to the high morbidity and mortality of acute encephalitis syndrome, a better understanding of the condition is the need of an hour. Careful examination of clinical and radiological parameters is expected to facilitate targeted management and prognostication of AES cases.

Materials and Methods

Ours was a hospital-based prospective observational study of pediatric patients hailing from the North-Eastern part of India who were admitted to the pediatric and neurology department of Guwahati Medical College, Guwahati with a presentation of Acute Encephalitis Syndrome (AES). This is a tertiary-level care hospital and provides health care services to Assam and neighboring states like Meghalaya. Most patients are referred to this apex institute from the periphery for better supportive care and treatment.

Inclusion Criteria

- Patients presenting with Acute Encephalitis Syndrome (AES) according to WHO case definition.
- Age 1-12 years.

Exclusion Criteria

- Patients whose parents/guardians did not give consent to be a part of the study.
- Age below 1 year or above 12 years.

Study Procedure: Detail history taking, Clinical examination, Routine blood investigations, CSF study, and Radiological studies (CT/MRI) were done. Serum serology for JEV, Dengue, Malarial antigen, and Scrub typhus were done. CSF study included IgM ELISA for JEV and PCR study for HSV.

Outcome of the Patient: The outcome at discharge was described according to the mRS (modified Rankin Scale) of the patient at discharge. Good outcome was taken as mRS score of <3 and poor outcome as mRS ≥3. The outcome was also grouped into those with: full recovery, discharge with sequelae and death during hospitalization

Study Duration: Patients were enrolled from April 2021 to March 2022.

Data were analyzed after obtaining approval from the Institutional Ethics Committee (IEC) of Gauhati Medical College and Hospital, Guwahati (Reference No MC/190/2007/Pt-11/Dec-18/11).

Statistical Analysis: Data from the case record proforma was entered into Microsoft Excel spreadsheet version 2021 and analyzed using IBM-SPSS version 26. P-value < 0.05 will be considered significant for all statistical comparisons. Multivariate analysis was done for the parameters found significant in univariate analysis.

Results

A total of 170 cases fulfilling the inclusion criteria of Acute Encephalitis Syndrome (AES) according to the WHO case definition were enrolled during the study period. Males were 62.4% with male: female ratio of 1.6:1. Highest percentage of children was in the age group 6-9 years (31.8%). 76% of cases were from rural backgrounds (table 1). Infective etiology could be confirmed in 50 cases (29.5%), out of which JE was the most common (19.4%) causative agent identified.

In 122 cases (70.5%) etiology remained unidentified (table1). All patients in our study were having fever and altered sensorium at admission. Seizure activity was present in most (94.1%) cases with a single episode of seizure in 54.7% and multiple episodes (≥2) in 39.4% cases. Focal neurological deficit at admission was present in 28.8% cases of which limb weakness was the most common (25.9%) deficit (Table 1). The majority of cases occurred during the monsoon and post-monsoon part of the year (May-September) with a peak in July.

All patients underwent routine hematological and biochemical tests. Lumbar puncture and CSF study could be done in 150 (88.2%) patients (Table 2). CT scan brain was done in all cases whereas MRI could be done in 40 cases only. MRI was more sensitive in detecting brain lesions. In both CT and MRI brain, the thalami were the most commonly involved areas followed cortex (table 3, Fig. 1a,1b). 60.4% of our AES cases recovered completely and 19.6% cases were discharged with sequelae. 34 (20%) cases in our study expired during hospital stay (Fig. 2). The motor deficit was the most common sequelae of AES at the time of discharge (42%). Seizure was observed in 26 % followed by speech abnormality and abnormal movement in 20 % and 16% of cases (Fig. 3,4).

We evaluated clinical, biochemical, CSF study, and radiological features affecting the outcome in AES patients. In univariate analysis, prolonged fever and altered sensorium, multiple seizures, abnormal respiration, low GCS, focal neurological deficits, meningeal signs, abnormal neuroimaging (both in CT and MRI), and prolonged hospital stay were found to be significantly (p value< 0.05) associated with poor outcomes in AES (table 4). Significant predictors of outcome in univariate analysis (excluding abnormal MRI due to low number of patients) were analysed by multivariate analysis in which low GCS at admission, meningeal signs, and prolonged hospital stay came out to be independent predictors of outcome (table 4).

Table 1: Demographic profile, Etiology, and Clinical features of AES.

	Number (n=170)	Percentage (%)
Age		
1--3	35	20.6%
>3-6	41	24.1%
>6-9	54	31.8%
>9-12	40	23.5%
Gender		
Male	106	62.4%
Female	64	37.6%
Place of Residence		
Rural	130	76.5%
Urban	40	23.5%
Causative Agent		
Japanese Encephalitis (JE)	33	19.4%
Scrub Typhus	6	3.5%
Malaria	3	1.8%
Dengue	2	1.2%
Herpes Simplex Virus (HSV)	2	1.2%
SARS-COV-2 (COVID-19)	2	12.5%
Tuberculosis	1	0.6%
Bacterial (Pneumococci)	1	0.6%
Organism Unidentified	120	70.5%
Clinical Parameters		
Fever	170	100.0%
Altered Sensorium	170	100.0%
Single Episode Of Seizure	93	54.7%
Multiple Seizure	67	39.4%
Vomiting	60	35.3%
Headache	50	29.4%
Shock	50	29.4%
Irritability	45	26.5%
Abnormal Respiration	42	24.7%
Abnormal Tone	66	38.8%
Motor Weakness	44	25.9%
CN Palsy	30	17.6%
Involuntary Movement	29	17.1%
Meningeal Signs	58	34.1%
GCS		
GCS >8	134	78.8%
GCS ≤8	36	21.2%

Table 2: Blood and CSF parameters in AES

Blood Parameters		
Leucocytosis	76	44.7%
Anemia	45	26.5%
Thrombocytopenia	17	10.0%
Hypoglycemia	24	14.1%
Hyponatremia	48	28.2%
Hypernatremia	10	5.9%
Hypokalemia	14	8.2%
Hyperkalemia	5	2.9%
Elevated Transaminase	46	27.1%
CSF Parameters (n=150)		
Leococytosis	64	42.7%
Increased Protein	87	58.0%
Decreased Sugar	28	18.7%
Gram Stain Positive	1	0.7%

CBNAAT Positive	1	0.7%
JE IgM ELISA Positive	30	20.0%
HSV PCR Positive	2	1.3%

Table 3: Radiological findings in AES

CT Brain Parameters (n=170)		
Normal	153	90.0%
Abnormal	17	10.0%
Thalamus	9	52.9%
Basal Ganglia	2	11.8%
Midbrain	2	11.8%
Pons	1	5.9%
Cortex	6	35.3%
Meningeal Enhancement	2	11.8%
Subcortical White Matter Lesion	4	23.5%
MRI Brain parameters(n=40)		
Normal	16	40.0%
Abnormal	24	60.0%
Thalamus	12	50.0%
Basal Ganglia	7	29.2%
Midbrain	7	29.2%
Pons	4	16.7%
Cortex	11	45.8%
Meningeal Enhancement	4	16.7%
Subcortical White Matter Lesion	6	25.0%

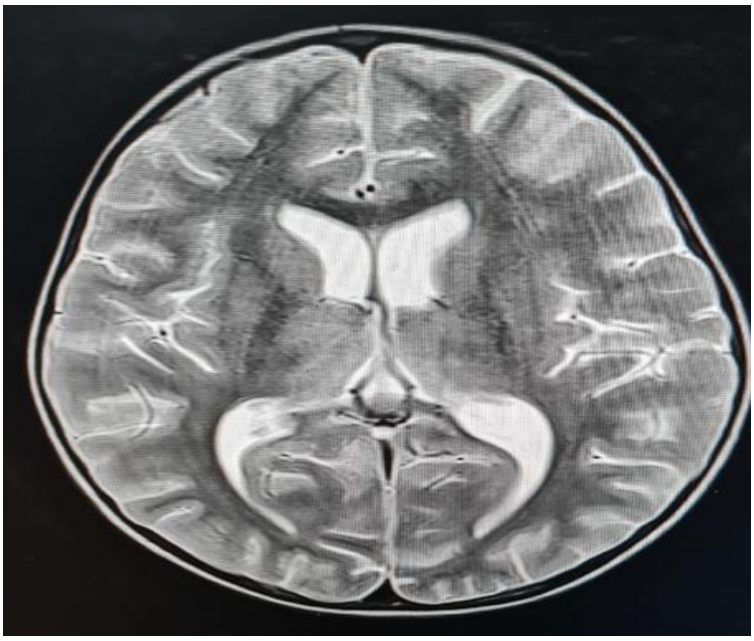

Figure 1a: MRI brain showing bilateral thalamic T2 hyperintensity in a child with JE

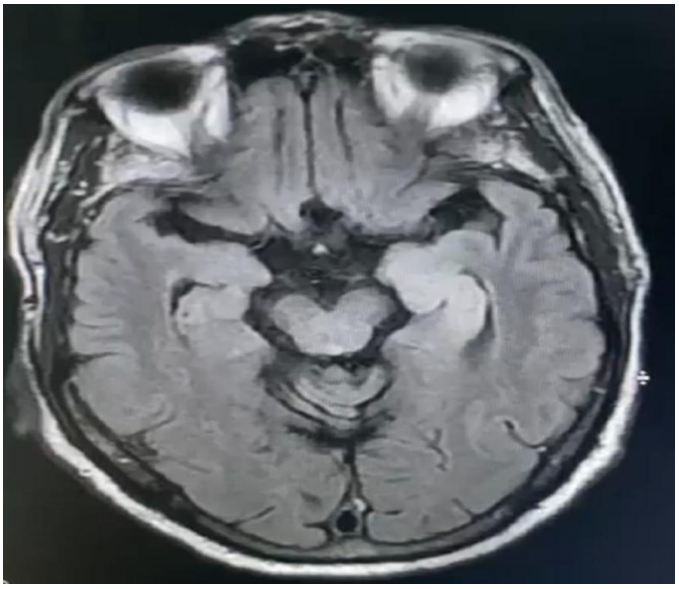

Figure 1b: MRI Brain showing Left medial temporal lobe flair hyperintensity in a pateint of HSE

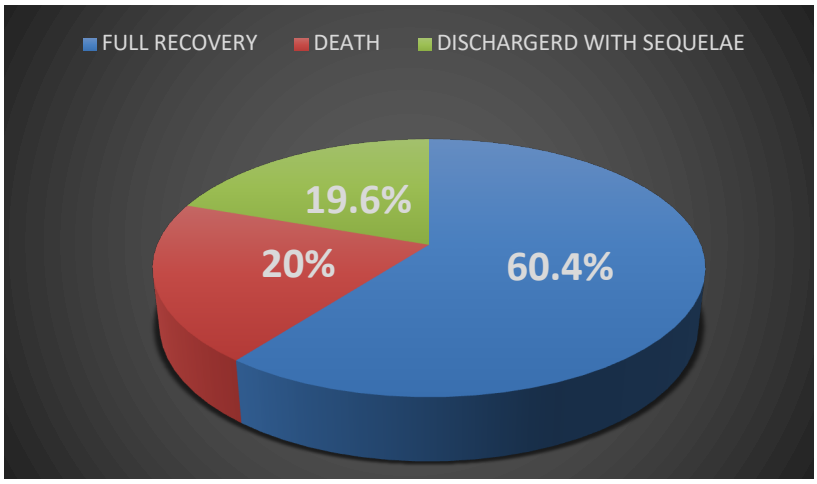

Figure 2: Outcome at discharge of AES cases

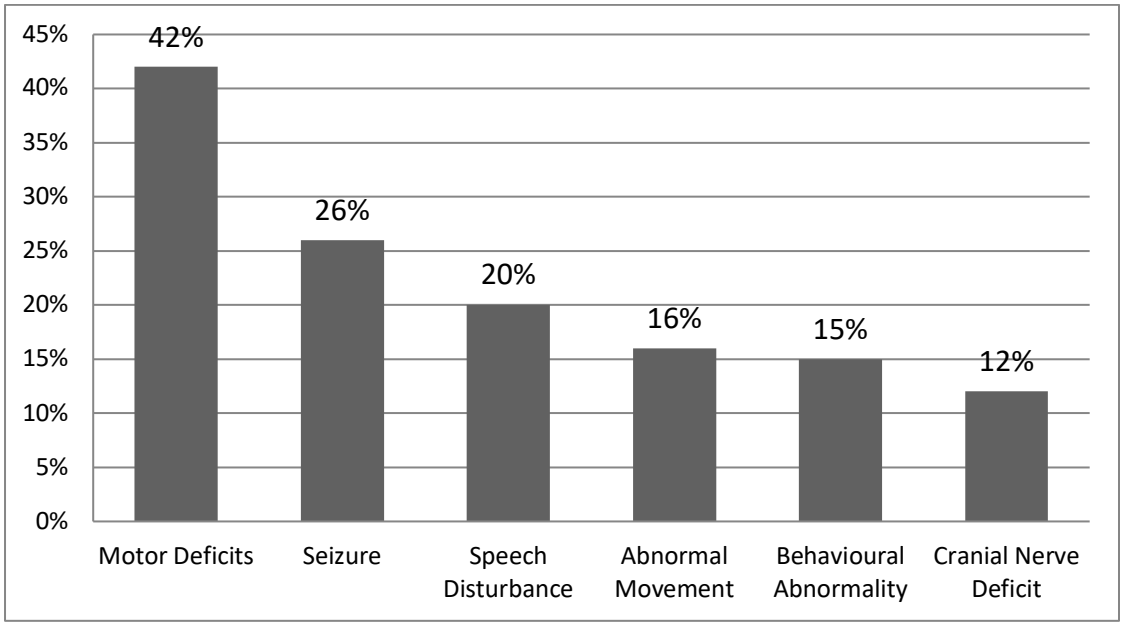

Figure 3: Sequelae at discharge in AES cases

Figure 4: Generalized dystonia as a sequelae in a child with JE (produced with permission)

Table 4: multivariate analysis of predictors of outcome in AES cases

				95%CI		p-value
PARAMETERS(predictors in univariate analysis)	β	SE	Z	Lower	Upper	
Intercept	-35.08	10.13	-3.463	-54.934	-15.225	<.001
Seizure	1.779	1.379	1.291	-0.923	4.481	0.197
Duration Of Altered Sensorium	-2.875	2.199	-1.308	-7.185	1.434	0.191
Days Of Fever Before Admission	0.436	1.299	0.336	-2.11	2.982	0.737
GCS At Admission	7.743	3.04	2.548	1.786	13.701	**0.011**
Tone	0.609	1.413	0.431	-2.16	3.378	0.666
Neurological Deficit	2.304	1.422	1.62	-0.483	5.092	0.105
Shock	4.037	2.113	1.91	-0.105	8.18	0.056
Abnormal Respiration	1.734	1.292	1.343	-0.797	4.266	0.179
Meningeal Sign	3.714	1.594	2.33	0.59	6.839	**0.020**
Abnormal NCCT Brain	1.354	1.497	0.904	-1.581	4.289	0.366
Length Of Hospital Stay	6.26	2.549	2.456	1.264	11.255	**0.014**

Discussion

This was a prospective observational study of 170 children aged 1 to 12 years with AES admitted as per hospital admission policy in the Department of Pediatrics and Neurology, GMCH, Guwahati. In our study, more than 50% of cases were between 6-12 years of age group with sex ratio (Male: Female) of 1.6: 1. The majority of the patients (76%) were from rural areas in our study. Previous studies had similar demographic profile [17,18,19,20]. In this study, the number of both JE and non-JE AES cases was higher between May and August, with a peak in July. Borkotoki U et al., [21] and Chakrabarty S et al., [22] also found similar seasonal variation.

In our study, 19.4% of the patients were seropositive for JE IgM. Jain A. et al., observed 16.2% of their patients to be seropositive [23] and Chakrabarti S et al., found JE seropositivity in 19% of AES cases [22]. Borkotoki U et al., in a study from Assam, found a decrease in JE-positive cases among AES patients in all the years from 2012 to 2014, when compared with 2011 (21). This decline in JE-positive cases among AES patients could be attributed to the extensive mass vaccination drives and intensive awareness programs. Etiological pro-

files were comparable in other earlier studies [23,24]. According to a prior study, COVID-19 can manifest as acute encephalitis syndrome [25].

In our study, 21.2% cases had low GCS (≤8). Mittal M et al., [26] and Kakoti G et al., [17] in their studies found low GCS in 30.8% and 40.3 % respectively. The average duration of fever before admission was 6 days in our study whereas the duration of altered sensorium was 5 days. Feng G et al., [27] and Rayamajhi et al., [28] had comparable findings.

NECT brain was done in all cases whereas MRI brain could be done in 40 patients (23.52%) only. CT brain was abnormal in only 10% of cases whereas MRI brain showed abnormality in 60% of cases. This is on par with the reports of Kalita J et al., [29] and Mishra UK et al., [30]. In our study thalami were the most commonly affected site radiologically, 52.9% of abnormal CT and half of abnormal MRI showed involvement of this area. The thalamic involvement was bilaterally symmetrical barring 2 cases where asymmetric involvement was noted. Cortical involvement was seen in 35.3% in CT and 45.8% in MRI. Similar findings were observed in the study conducted by Kalita J et al, [29] Mishra UK et al., [30] and Basumatary LJ et al., [31]. 20% of our cases died whereas full recovery was observed in 60.6% of cases. 19.6 % of AES cases were discharged with sequelae. Datta D et al., Chakrabarti S et al., Deepthi C et al., and Mittal M et al., had similar pattern of outcome with mortality of 32.4%, 27.7%, 12%, and 21.2% respectively [19,22,24,26]. The most common sequelae at discharge were motor deficits (42%), seizure (26%), speech disturbance (20%), behavioral abnormality (15%), cranial nerve deficit (12%), and abnormal movement (16%). Chakrabarti S et al., [22], Avabratha KS et al., [20], and Deepthi C et al., [24] had comparable outcome in their cases.

In our study, there was no statistically significant association between age and outcome. Similarly, the gender of the patients and the habitat of the patients were not significantly associated with outcome. Similar to our study, Ooi MH et al., [32], Avabratha et al, [20], Deepthi C et al., [24], Rayamajhi A. et al., [28] and Feng G. et al., [27] did not find age, sex or habitat to be a predictor of poor outcome. In our study, we found low GCS (≤8) as a strong predictor of poor outcomes with a p-value of 0.001. In multivariate analysis also poor GCS came out to be an independent predictor of poor outcome. Various studies from different parts of India and abroad showed similar results [17,20,27,28,30-33].

In our study, we found that prolonged fever and prolonged duration of altered sensorium as predictors of poor outcome. Rayamajhi A et al., also found prolonged duration of fever and altered sensorium to be a predictor of poor outcome (28). Basumatary LJ et al., [31], and Deepthi C et al., [24], observed prolonged duration of fever and altered sensorium to be a predictor of poor outcome respectively. We did not find any association between vomiting, headache, and irritability with the outcome. Previous studies also did not find such association [17,20,24,27,31]. We found that presence of seizures were associated with poor outcomes. Previous studies [27,31,32,33] had similar finding.

Patients in shock at admission had poor outcomes in our study. Ooi MH et al., [32] and Barbhuyan S et al., [33] also found shock to be a poor predictor. Abnormal respiration was also found to be associated with poor outcomes in our study. Tachypnea and irregular breathing are caused by metabolic acidosis and dehydration, which are brought on by inadequate fluid intake combined with altered sensorium and fever. Research by Avabratha KS et al., [20] also revealed that respiratory irregularity was a poor outcome predictor. In multivariate analysis, longer length of hospital stay came out to be an independent predictor of poor outcome. Misra UK et al., [34] and Feng G et al., [27] had similar observations.

In our study, there was a statistically significant correlation between poor outcome and abnormal tones of the patients. The abnormal tone was also linked to the worst prognosis, according to research by Ooi MH et al., [32]. We also observed that the presence of meningeal signs was associated with poor outcome in multivariate analyses. The study conducted by Avabratha KS et al., in Bellary, Karnataka, also revealed an association between mortality and meningeal signs [20].

In our study, there was a significant correlation between poor outcome and neurological deficit at presentation. The majority of focal neurological deficits in AES patients can be explained by frequent presentation of elevated intracranial pressure, brain herniation syndromes, and focal brain lesions on neuroimaging studies. A poor prognosis in patients with viral encephalitis can be predicted by focal neurological deficits, according to the reports of Feng G et al., [27] and Rayamajhi A et al., [28].

We found abnormal neuroimaging findings (CT and MRI brain) to be associated with poor outcome, which is in accordance with the previous studies [24,27]. However, there are contradictory results noted in the study by Basumatary LJ et al., [31] who did not find a statistically significant association. The small sample size of MRI patients in this study as well as variations in the timing and techniques of pertinent imaging exams could account for this discrepancy in observations. The role of radiological findings in the prognosis of AES

needs further study.

Conclusion

In our study, out of 170 children of AES, males were more commonly affected and majority of cases were found to be from rural background. Etiology remained unidentified in majority of cases (70.5%). JEV (Japanese Encephalitis Virus) was the most common pathogen identified. Fever, altered sensorium and seizures were most common symptoms whereas abnormal tone and motor deficit were predominant signs. MRI brain was found to be more sensitive in identifying parenchymal lesions than CT scan. Thalami followed by cortical regions were most commonly involved sites in neuroimaging. Poor GCS, meningeal signs and prolonged hospital stay were independent predictors of poor outcome in our study. Study of the predictors of poor outcome will help in focussed management and prognostication of patients. However, there is need of large multicentric study particularly to identify etiology of AES which can help in prevention and planning for better management. The need for mass public awareness programmes regarding AES is of utmost importance to save the lives of patients.

Bibliography

1. Solomon T, Thao TT, Lewthwaite P, et al. A cohort study to assess the new WHO Japanese encephalitis surveillance standards. Bull World Health Organ 2008; 86:178-86.
2. Jmor F, Emsley HC, Fischer M, Solomon T, Lewthwaite P. The incidence of acute encephalitis syndrome in Western Industrialised and Tropical Countries. Virol J. 2008; 5:134.
3. Kennedy PG. Viral encephalitis: causes, differential diagnosis, and management. J Neurol Neurosurg Psychiatry. 2004; 75:10-5.
4. Rayamajhi A, Singh R, Prasad R, Khanal B, Singhi S. Clinico-laboratory profile and outcome of Japanese encephalitis in Nepali children. Annals of tropical paediatrics. 2006 Dec 1;26(4):293-301.
5. Dutta P, Khan SA, Khan AM, Borah J, Sarmah CK, and Mahanta J, "Effect of Insecticide-Treated Mosquito Nets (ITMNs) on Japanese encephalitis virus seroconversion in pigs and humans," American Journal of Tropical Medicine and Hygiene, 2011; 84(3): 466–472, 2011.
6. Rayamajhi A, Singh R, Prasad R, Khanal B, and Singhi S. "Study of Japanese encephalitis and other viral encephalitis in Nepali children," Pediatrics International, 2007; 49(6): 978– 984, 2007.
7. Chen K.M, Tsai H.C, Sy C.L, et al., "Clinical manifestations of Japanese encephalitis in southern Taiwan," Journal of Micro- biology, Immunology and Infection, 2009 42(4): 296–302.
8. Clarke M, Newton RW, Klapper PE, Sutcli EH, Laing I, Wal- lace G. Childhood encephalopathy: Viruses, immune response, and outcome. Dev Med Child Neurol 2006; 48: 294–300.
9. World Health Organization (WHO), "Immunization, vaccines and biological," March 2013.
10. World Health Organization, "Japanese encephalitis vaccines," e Weekly Epidemiological Record, 2006; 81: 331–340.
11. Seay AR. Alpha virus and flavi virus diseases. In: Mckendall RR, Stroop WG, editors, Handbook of neurovirology, New York: Marcel Dekker, 1994; 391–411.
12. Zimmerman HM. Pathology of Japanese encephalitis. Am J Pathol 1946; 22:965 – 91.
13. Rose JW, Stroop WG, Mastuso F, Henkel J. Atypical herpes simplex encephalitis: neuropathologic evaluation. Neurology 1992; 42: 1809– 12.
14. Schrotch G, Gawehn J, Thron A, Vallbracht A, Voigt K. Early diagnosis of herpes simplex encephalitis by MRI. Neurology. 1987; 37:179 – 83.
15. Kumar S, Misra UK, Kalita J, et al. MRI in Japanese encephalitis. Neuroradiology. 1997; 39:180-184.
16. Sarika T, Singh RK, Tiwari R, Dhole TN. Japanese encephalitis: A review of the Indian perspective. Braz J Infect Dis. 2012; 16(6):564-73.
17. Kakoti G, Dutta P, Ramdas B, Borah J, Mahanta J. Clinical profile and outcome of Japanese encephalitis in children admitted with acute encephalitis syndrome. Biomed Res Int. 2013; 2013:152656.
18. Khinchi YR, Kumar A, Yadav S. Study of acute encephalitis syndrome in children, Journal of College of Medical Sciences-Nepal 2010; 6(1):7-13.
19. Datta D, Karmakar BC. A six years prospective epidemiological study of acute encephalitis syndrome among children admitted in a rural tertiary care center. Int J Contemp Pediatr. 2019; 6(5):2125-31.
20. Avabratha KS, Sulochana P, Nirmala G, Vishwanath B, Veerashankar M, Bhagyalakshmi K. Japanese encephalitis in children in Bellary, Karnataka, India: Clinical pro le and sequelae. International Journal of Biomedical Research. 2012;3(2):100-05.
21. Borkotoki U, Borkotoki S, Barua P, Das A, Rajkhowa A. Japanese encephalitis (JE) among acute encephalitis syndrome 27. (AES) cases— A hospital-based study from Upper Assam, India. Int J Health Sci Res. 2016; 6(5): 72–7.
22. Chakrabarti SK et al., Clinical Profile and Short Term Outcome of Acute Encephalitis

Syndrome; Journal of Clinical and Diagnostic Research. 2022 Mar;16(3): SC06-SC10.
23. Jain A, Jain P, Jain B. Etiology of acute encephalitis syndrome in North India. J Neuro infect Dis. 2015;6(2):01-02.
24. Deepthi C, Vasundhara A, Sourika P, Sravya GS. Acute febrile encephalopathy and its outcome among children in a tertiary care hospital, Andhra Pradesh, India. Int J Contemp Pediatr. 2018; 5(2):503-07.
25. Haider A, Siddiqa A, Ali N, Dhallu M. COVID-19 and the Brain: Acute Encephalitis as a Clinical Manifestation. Cureus. 2020 Oct 3; 12(10):e10784.
26. Mittal M, Kushwaha1 KP, Pandey AK, Gore MM. A clinico-epidemiological study of acute encephalitis syndrome with multi organ dysfunction. Int J Contemp Pediatr. 2017; 4(3): 745-50.
27. Feng G, Zhou L, Li F, Hu Y, Wang X, Tian X. Predictors of outcome in clinically diagnosed viral encephalitis patients: a 5-year prospective study. BioMed Research International. 2020 Jul 8; 2020.
28. Rayamajhi A, Ansari I., Ledger E, Bista KP, Impoinvil DE, Nightingale S, Kumar R, Mahaseth C, Solomon T, Griffiths MJ. Clinical and prognostic features among children with acute encephalitis syndrome in Nepal; a retrospective study. BMC Infectious Diseases. 2011; 11:294.
29. Kalita J, Misra UK. Comparison of CT and MRI findings in the diagnosis of Japanese encephalitis. Journal of the neurological sciences. 2000;174. 3-8.
30. Misra UK, Kalita J, Srivastava M., Prognosis of Japanese encephalitis: a multivariate analysis, Journal of the Neurological Sciences, Volume. 1998;161(2): 143-147.
31. Basumatary LJ, Raja D, Bhuyan D, Das M, Goswami M, Kayal AK. Clinical and radiological spectrum of Japanese encephalitis. J Neurol Sci. 2013; 325(1):15-21.
32. Ooi MH, Lewthwaite P, Lai BF, Mohan A, Clear D, Lim L, et al. The epidemiology, clinical features, and long-term prognosis of Japanese encephalitis in central sarawak, malaysia, 1997-2005. Clin Infect Dis. 2008; 47(4):458-68.
33. Barbhuiyan B et al. Int J Contemp Pediatr. 2021 Nov; 8(11):1798-1803.
34. Misra U.K., Kalita J., and Bhoi S.K., "Spectrum and outcome predictors of central nervous system infections in a neurological critical care unit in India: a retrospective review," Transactions of the Royal Society of Tropical Medicine and Hygiene, 2014; 108(3):141–146.