

Original research article

Study To Determine The Clinic-Etiologic Profile And Outcome Of AES In Hospitalized Children**Dr. Abu Irfan¹, Dr. Baibhav Prakash Sahay²****¹ Senior Resident, Department of Pediatric, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India****² Senior Resident, Department of Pediatric, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.****Corresponding Author: Dr. Baibhav Prakash Sahay****Abstract**

Background: 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, 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. The clinical definition of AES was introduced to facilitate surveillance for Japanese encephalitis (JE), mosquito-borne viral encephalitis. Most AES is considered to be due to a viral-encephalitis, virus like West Nile, Herpes simplex virus, Flavivirus like JE and dengue are more prevalent in South East Asia. Various subsequent studies confirmed that most AES in India are due to JE, which has been considered as the only major cause of AES in India.

Aim: this study was conducted for a better understanding and to determine the clinical profile and outcome of AES in hospitalized children and also to determine the etiology in all cases of AES.

Material and Methods: This Cross-sectional, observational study was done the Department of Pediatric, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, for 13 months. Children between age 1 month to 15 years with the acute onset of fever and a change in mental status such as confusion, disorientation, coma or inability to talk and/or new onset of seizures (excluding simple febrile seizure) were included in study. All cases were investigated Cerebrospinal Fluid (CSF) analysis, dengue serology, radiological investigation as per clinical presentation.

Results: out of 120 AES cases most of them were above 10 years of age (35.83%). Majority of them were males 77(64.17%), and 43(35.83%) were females. Most of the cases were reported during monsoon period 69(57.5%), followed by post-monsoon 39(32.5%) and pre-monsoon 12(10%). Out of 120 cases, all had fever; 89 (74.17%) had altered sensorium ; 71 (59.17%) had convulsion; 32 (26.67%) had headache; 49 (40.83%) had vomiting. On fundus examination 39 (32.5%) showed papilledema. Out of 120 cases 65(54.17%) had viral etiology, 29 (24.17%) had dengue, 7 (5.83%) had malaria, 5 (4.17%) bacterial etiology, 7 (5.83%) had tuberculosis, 6 (5%) had other causes. Those patients who had shock and need inotropes showed significant mortality (p-value: 0.014). Also those who required mechanical ventilation had significant mortality, out of 33 patients put on mechanical ventilation 19 died which was statistically significant with p -value 0.001.

Conclusion: Majority of cases were in the age-group of 1-5 years, with male predominance. The peak in occurrence of cases was during post-monsoon period (October-February).

Keywords: AES, CSF, Dengue, JE

Introduction

AES is known as 'acute febrile encephalopathy', 'viral encephalitis', 'infectious encephalitis', and 'brain fever', the concept of AES was introduced to facilitate surveillance for Japanese Encephalitis (JE), a mosquito borne viral encephalitis.¹ JE is a leading cause of viral encephalitis. It is a disease of major public health importance because of its epidemic potential and high case fatality rate.

Viral encephalitis is a globally distributed disease that seriously affects public health, threatening almost half of the world's population.² It may be sporadic like herpes simplex encephalitis (HSE), or epidemic such as Japanese B encephalitis (JE). The etiological agents are varied, and physicians treating such children often feel limited by the lack of availability of diagnostic testing for most of these agents. In developed countries, 50–60% of survivors of viral encephalitis with clear etiologies had a poor prognosis after long-term follow-up.³⁻⁷ At present, pathogen detection for viral encephalitis is not widely used for clinical diagnosis and treatment in India; the diagnosis is largely based on clinical data and auxiliary examination of patients.^{8,9} In addition, research shows that no more than 30–40 % of encephalitis cases can be pathogenically diagnosed, of which Japanese encephalitis (JE) is the most common cause in India.^{10,11} And more than half of pathogenically diagnosed viral encephalitis had a poor prognosis.¹² On the other hand, 10–30 % of patients with clinically diagnosed viral encephalitis also have a poor prognosis. In India except Jammu & Kashmir, Himachal Pradesh, and Uttaranchal, nearly all states have reported Japanese encephalitis.¹³ The Northeast part of India has been experiencing recurrent episodes of Japanese Encephalitis with different magnitude from July to October every year.¹⁴ we conducted a study of the patients admitted for acute encephalitis syndrome. The etiological agents are varied, and physicians treating such children often feel limited by the lack of availability of diagnostic testing for most of these agents. There are numerous lacunae in our knowledge, problems in epidemiological investigations, lack of diagnostic facilities, as well as difficulties in managing these critically ill children in smaller centers in our country. Therefore, study was conducted for a better understanding and to determine the clinical profile and outcome of AES in hospitalized children and also to determine the etiology in all cases of AES.

Material and methods

This Cross-sectional, observational study was done the Department of Pediatric, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 13 months .

Methodology

Children between age 1 month to 15 years with the acute onset of fever and a change in mental status such as confusion, disorientation, coma or inability to talk and/or new onset of seizures (excluding simple febrile seizure) were included in study. Those with febrile seizures, toxic encephalopathy and children with Central Nervous System (CNS) malformations and other major congenital anomalies predisposing to CNS infections, e.g spinal bifida, pilonidal sinus, CSF rhinorrhoea, meningocele etc. were excluded from this study. For patients fulfilling inclusion criteria, detailed history and clinical examination were done. All cases were investigated for baseline investigations as well as some specific investigations (Cerebrospinal Fluid (CSF) analysis, dengue serology, radiological investigation) as per clinical presentation. Patient's clinical course, treatment and outcome were noted.

Statistical analyses

Statistical analysis

The data obtained from the cases and controls was compiled and entered into Microsoft Excel case sheet. Statistical analysis was done by using descriptive and inferential statistics using chi square test and student's un-paired t-test and software used in the analysis were SPSS 22. Version and $p < 0.05$ was considered as level of significance.

Results

Table 1 indicates that among 120 AES cases most of them were above 10 years of age (35.83%). Majority of them were males 77(64.17%), and 43(35.83%) were females. Majority of them were Hindu 99(82.5%), followed by 15(12.5%) were Muslim. Most of them were from joint family 77(64.17%), agriculture 104(86.67%) is main occupation of parents of them. Most of them belongs to lower socioeconomic status 76(63.33%), 34(28.33%) from middle SES. table 2 shoe that Most of the cases were reported during monsoon period 69(57.5%), followed by post-monsoon 39(32.5%) and pre-monsoon 12(10%).

Table 1: Demographic Profile of Acute Encephalitis Syndrome Patients

Parameter	No. of patients (n=120)	Percentage
Gender		
Male	77	64.17
Female	43	35.83
Age		
Infancy	17	14.17
Toddler	28	23.33
Pre-school	32	26.67
School going	43	35.83
Religion		
Hindu	99	82.5
Muslims	15	12.5
Others	6	5
Parents occupation		
Agriculturists	104	86.67
Business	11	9.17
Unemployed	5	4.17
Socioeconomic class		
Upper	10	8.33
Upper middle	34	28.33
Lower middle	29	24.17
Upper lower	47	39.17
Potential vector breeding sites		
Indoor		
Present	75	62.5
Absent	45	37.5
Outdoor		
Present	82	68.33
Absent	38	31.67
Pigs/cattle sheds		
Present	66	55
Absent	54	45

Table 2: Distribution of patient's season basis

Season	No. of patients	Percentage
Pre- monsoon	12	10
Monsoon	69	57.5
Post-monsoon	39	32.5
Total	120	100

Table 3 depicts that out of 120 cases, all had fever; 89 (74.17%) had altered sensorium ; 71 (59.17%) had convulsion; 32 (26.67%) had headache; 49 (40.83%) had vomiting. On fundus examination 39 (32.5%) showed papilledema (Table 3)..

Table 3: clinical profile of patients

Clinical profile	No. of patients	Percentage (%)
Fever	120	100
Altered sensorium	89	74.17
Convulsion	71	59.17
Headache	32	26.67
Excessive cry	4	3.33
Altered behaviour	28	23.33
Vomiting	49	40.83
Neurodeficit	5	4.17
Extrapyramidal features	3	2.5
Cranial nerve palsy	4	3.33
Fundoscopy		
Normal	81	67.5
Papilledema	39	32.5
Other system abnormality:		
CVS	7	5.83
RS	7	5.83
Abdomen	10	8.33

Table 4 depicts that out of 120 cases 65(54.17%) had viral etiology, 29 (24.17%) had dengue, 7 (5.83%) had malaria, 5 (4.17%) bacterial etiology, 7 (5.83%) had tuberculosis, 6 (5%) had other causes. out of 120 AES patients neuroimaging was done for 40(33.33%) patients, in which majority had normal finding on neuroimaging, 13(10.83%) showed Encephalitis features while 7(5.83%) showed other features like Acute Disseminated Encephalomyelitis (ADEM) in 5(4.17%), 2(1.67%) Neurocysticercosis (NCC). In all cases of dengue encephalitis along with fever and cerebral involvement, anti-dengue IgM, NS1 were positive. Dengue encephalopathy cases were not included.

Table 4: AES Etiology of patients

AES Etiology	Number (n)	Percentage (%)
Viral etiology (other than dengue)	65	54.17
Pyogenic	5	4.17
Tuberculosis	7	5.83
Dengue encephalitis	29	24.17
Cerebral malaria	7	5.83
Other	6	5
Not known	1	0.83
Total	120	100

Table 5 shows correlation of various variables to the outcome. Those patients who had shock and need inotropes showed significant mortality (pvalue: 0.014). Also those who required mechanical ventilation had significant mortality, out of 33 patients put on mechanical ventilation 19 died which was statistically significant with p -value 0.001. Those patient had deranged Liver Function Test (LFT) profile also had significant higher mortality (p- value: 0.032). GCS on admission, leucocytes counts, serum sodium concentration and duration of hospital stay had no influence on outcome. Out of 120 children of AES admitted in Pediatric

Intensive Care Unit (PICU) 85(70.83%) were discharge, 25(20.83%) were succumbed, 10(8.33%) were got Discharge against Medical Advice (DAMA).

Table 5: Analysis of Outcome

Risk factors	Group	Death=25	Survivors=95	P
Age	Below 1years	5	17	0.323
	1-5years	3	22	
	5-10yrs	6	24	
	Above 10 years	11	32	
Sex	Male	17	60	0.638
	Female	8	35	
RBS on admission	<60 (mg/dl)	3	4	0.187
	60-145 (mg/dl)	22	86	
	>145 (mg/dl)	00	5	
Serum Na	<135 (meq/l)	10	21	0.426
	135-145 (meq/l)	15	65	
	>145 (meq/l)	00	9	
TLC	<4000 (cells/cumm)	2	18	0.088
	4000-11000 (cells/cumm)	14	57	
	>11000 (cells/cumm)	9	20	
Sr. creatinine	Normal			0.136
	Deranged			
	<1.5 times of baseline	17	66	
	>1.5 times of baseline	8	29	
LFT (SGPT)	Normal			0.032
	Deranged			
	<45 (U/L)	10	60	
	>45 (U/L)	15	25	
GCS on admission	<8	9	18	0.136
	>8	16	77	
Shock and ionotropes need	Yes	3	58	0.014
	No	22	37	
Mechanical ventilation need	Yes	19	14	< 0.001
	No	6	81	
Length of hospital stay	<7 days	7	29	0.188
	7-21days	18	66	

Discussion

In the present study, we have tried to analyze the clinical profile and factors determining the predictors of mortality in JE patients. This study demonstrates that JE is one of the leading forms of viral encephalitis of children in this part of the country. In the present study most of them were above 10 years of age (35.83%). Majority of them were males 77(64.17%), and 43(35.83%) were females. Similar results also found in studies done by Kakoti et al.¹⁵ and Kamble et al.¹⁶ whereas Sudhir et al.¹⁷ studied 92 cases where he found 70.6% were 1-5 years. In the present study, there is male preponderance which is in concordance with study done by Sudhir et al.¹⁷ In this present study Most of them belongs to lower socioeconomic status 76(63.33%), 34(28.33%) from middle SES. Similar results were found in Kamble et al.¹⁶ Beig et al.¹⁸ in U.P. also found that majority of AES cases that is 73.6% were from lower SES. Because of overcrowding in lower SES, poor maintenance of hygiene the transmission of viral and vector borne disease are more common. In the present study, Most of the cases were reported during monsoon period 69(57.5%), followed by post-

monsoon 39(32.5%) and pre-monsoon 12(10%). During monsoon and postmonsoon season, there is increase in number of mosquito breeding site thus it leads to increase in dengue, malaria and other vector born encephalitis. Similar results were found in studies by Kamble et al.¹⁶ and Sarkar et al.¹⁹ Study by Sudhir et al.¹⁷ showed highest number of AES cases i.e. 68.47% and were admitted in the month of June. However, contrary to this study, study by Yashodhara et al.²⁰ found that 71.42% of encephalitis cases occurred in winter season means post monsoon season.

In the present study, out of 120 cases, all had fever; 89 (74.17%) had altered sensorium; 71 (59.17%) had convulsion; 32 (26.67%) had headache; 49 (40.83%) had vomiting. On fundus examination 39 (32.5%) showed papilledema. Similar findings were done in studies by Kakoti et al.¹⁵ and Anuradha et al.²¹ Khinchi et al.²² showed all patients had fever and altered sensorium, 90% had seizures.

In the present study, on blood investigations for different parameters showed mean of Hb 10.9 ± 2.6 g/dl, total leucocyte count with mean of 9145.7 ± 5121.875 cells/cumm, RBS with mean 98.87 ± 21.12 mg/dl, SGPT with mean 107.91 ± 188.36 U/L. CSF examination done in about half of patients wherever possible. Mean CSF cell counts were 22.13 ± 66.98 cells/cumm, CSF sugar and protein were 26.6 ± 23.36 mg/dl and 15.64 ± 23.32 mg/dl respectively. Similar findings were also seen in study done by Kakoti et al.¹⁵ and Sambasivam et al.²³ in the present study out of 120 cases 65(54.17%) had viral etiology, 29 (24.17%) had dengue, 7 (5.83%) had malaria, 5 (4.17%) bacterial etiology, 7 (5.83%) had tuberculosis, 6 (5%) had other causes. out of 120 AES patients neuroimaging was done for 40(33.33%) patients, in which majority had normal finding on neuroimaging, 13(10.83%) showed Encephalitis features while 7(5.83%) showed other features like Acute Disseminated Encephalomyelitis (ADEM) in 5(4.17%), 2(1.67%) Neurocysticercosis (NCC). Similar results were found in study done by Kamble et al.¹⁶ showed out of 136 cases of AES, 84.5% had viral etiology, and 9.5% had other agents like pyogenic, tuberculosis. Thakur et al.²⁴ found that etiology of encephalitis include 27% viral and 47.6% were of unknown etiology. In studies done by Jain et al.²⁵ and Jain et al.²⁶ JE and dengue encephalitis were important etiologies. As JE is endemic in Andhra Pradesh, Assam, Bihar, Uttar Pradesh and West Bengal, it is the most common cause of AES in these regions. In other region, Enterovirus may be an important cause. In regions where dengue and malaria are endemic there dengue encephalitis and cerebral malaria are more common respectively. Serum NS1 and anti-dengue IgM plays important role in early diagnosis of dengue virus infection and encephalitis as shown by Manthalkar et al.²⁷

In the present study, Those patients who had shock and need inotropes showed significant mortality (pvalue: 0.014) Similar results were found by Sambasivam et al.²³ where those having shock had higher mortality, with significant p- value 0.010. In present study, Out of 120 children of AES admitted in Pediatric Intensive Care Unit (PICU) 85(70.83%) were discharge, 25(20.83%) were succumbed, 10(8.33%) were got Discharge against Medical Advice (DAMA). Present results are in concordance with previous observation in a hospital based study on AES by DuBray et al.²⁸ where 67.4% of cases discharged with full recovery. Study done by Khinchi et al.²² in Nepal found 40.6% encephalitis patients were discharged and 34.3% were expired. Kakoti et al.¹⁵ study in Assam showed 63.9% patients were completely recovered on discharge, 14.7% expired. In the present study, along with clinical profile, we have tried to analyse the factors determining the outcome of patients admitted to PICU with AES features. Death is higher in age group >10 years of age. In our study we found that three factors have statistical significant association with mortality. Hemodynamic status of patient, those who were having shock and on inotropic support had abnormal LFT and those who required mechanical ventilation had more mortality as compared to those who were hemodynamically stable and had normal liver function test. Similar results were found

in a study done by Sambasivam et al.²³ They found two factors have statistically significant association with mortality, one is shock and use of inotropes and another those who had hyponatremia have more mortality than those who are hemodynamically stable. Most of the specific etiological agent of encephalitis is remained unknown, due to higher cost of viral marker in CSF and serum. Follow up is lacking in our study which may be of help to find out long term neurological deficit and other sequelae in AES patients.

Conclusion

A total of 120 AES cases were formed as study subjects, occurrence of cases was peak during the months of OctFebruary (post monsoon). Most of cases were in the age group of 1-5years, with predominant cases being males, more than half of them were partially or unimmunized, residing in kuccha house with majority of them dwelling around potential outdoor vector breeding sites. They belong to upper lower group and most of their parents were agriculturists by occupation.

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