

Cross-sectional observational study to assess the clinic-demographic profile in children with Acute Encephalitis Syndrome

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Abstract

Aim: to evaluate the clinical profile and outcome of AES in hospitalized children. **Material and Methods:** This Cross-sectional, observational study was done the Department of Paediatrics, Vardhman Institute of Medical Science, Pawapuri, Nalanda, Bihar, India, for 1 year. 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:** among 100 AES cases most of them were above 10 years of age (34%). Majority of them were males 65(65%), and 35(35%) were females. Most of the cases were reported during monsoon period 55(55%), followed by post-monsoon 34(34%) and pre-monsoon 11(11%). Out of 100 cases, all had fever; 72 (72%) had altered sensorium, 57 (57%) had convulsion; 27 (27%) had headache; 43 (43%) had vomiting. On fundus examination 29 (29%) showed papilloedema. Out of 100 cases 55(55%) had viral etiology, 23(23%) had dengue, 6(6%) had malaria, 4 (4%) bacterial etiology, 6 (6%) had tuberculosis, 5 (5%) had other causes. Those patients who had shock and need inotropes showed significant mortality (p-value: 0.015). Out of 23 patients put on mechanical ventilation 10 died which was statistically significant with p -value 0.001. Those patients had deranged Liver Function Test (LFT) profile also had significant higher mortality (p- value: 0.027). Out of 100 children of AES admitted in Pediatric Intensive Care Unit (PICU) 69(69%) were discharge, 18(18%) were succumbed, 13(13%) were got Discharge against Medical Advice. **Conclusion:** Majority of cases were in the age-group of above 10 years, with male predominance. The peak in occurrence of cases was during post-monsoon period.

Keywords: AES, CSF, Dengue, JE.

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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, 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. AES was introduced to facilitate surveillance for Japanese encephalitis (JE), a mosquito-borne viral encephalitis. Japanese encephalitis is one of the most important forms of epidemic and sporadic encephalitis in the tropical regions of Asia, including Japan, China, Taiwan, Korea, Philippines, all of South eastern Asia, and India.[1,2] 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 Paediatrics, Vardhman Institute of Medical Science, Pawapuri, Nalanda, Bihar, India, for 1 year, after taking the approval of the protocol review committee and institutional ethics committee.

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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.

Results

Table 1 indicates that among 100 AES cases most of them were above 10 years of age (34%). Majority of them were males 65(65%), and 35(35%) were females. Majority of them were Hindu 84(84%), followed by 11(11%) were Muslim. Most of them were from joint family 65(65%), agriculture 83(83%) is main occupation of parents of them. Most of them belongs to lower socioeconomic status 63(63%), 30(30%) from middle SES. table 2 show that Most of the cases were reported during monsoon period 55(55%), followed by post-monsoon 34(34%) and pre-monsoon 11(11%).

Table 1: Demographic Profile of Acute Encephalitis Syndrome Patients

Parameter	No. of patients (n=100)	Percentage
Gender		
Male	65	65
Female	35	35
Age		
Below 1years	15	15
1-5years	24	24
5-10yrs	27	27
Above 10 years	34	34
Religion		
Hindu	84	84
Muslims	11	11
Others	5	5
Parents occupation		
Agriculturists	83	83
Business	12	12
Unemployed	5	5
Socioeconomic class		
Upper	7	7
Upper middle	30	30
Lower middle	22	22
Upper lower	41	41
Potential vector breeding sites		
Indoor		
Present	60	60
Absent	40	40
Outdoor		
Present	70	70
Absent	30	30
Pigs/cattle sheds		
Present	58	58
Absent	42	42

Table 2: Distribution of patients' season basis

Season	No. of patients	Percentage
Pre- monsoon	11	11
Monsoon	55	55
Post-monsoon	34	34
Total	100	100

Table 3 depicts that out of 100 cases, all had fever; 72 (72%) had altered sensorium ; 57 (57%) had convulsion; 27 (27%) had headache; 43 (43%) had vomiting. On fundus examination 29 (29%) showed papilledema (Table 3).

Table 3: Clinical profile of patients

Clinical profile	No. of patients	Percentage (%)
Fever	100	100
Altered sensorium	72	72
Convulsion	57	57
Headache	27	27
Excessive cry	3	3
Altered behaviour	25	25
Vomiting	43	43
Neurodeficit	5	5
Extrapyramidal features	2	2
Cranial nerve palsy	3	3
Fundoscopy		
Normal	69	69
Papilledema	29	29
Other system abnormality:		
CVS	6	6
RS	6	6
Abdomen	6	6

Table 4 depicts that out of 100 cases 55(55%) had viral etiology, 23(23%) had dengue, 6(6%) had malaria, 4 (4%) bacterial etiology, 6 (6%) had tuberculosis, 5 (5%) had other causes. out of 100 AES patients neuroimaging was done for 30(30%) patients, in which majority had normal finding on neuroimaging, 12(12%) showed Encephalitis features while 6(6%) showed other features like Acute Disseminated Encephalomyelitis (ADEM) in 4(4%), 2(2%) 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 (%)
Viraletiology (other than dengue)	55	55
Pyogenic	4	4
Tuberculosis	6	6
Dengue encephalitis	23	23
Cerebral malaria	6	6
Other	5	5
Not known	1	1
Total	100	100

Table 5 shows correlation of various variables to the outcome. Those patients who had shock and need inotropes showed significant mortality (pvalue: 0.015). Also those who required mechanical ventilation had significant mortality, out of 23 patients put on mechanical ventilation 10 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: 0.027). GCS on admission, leucocytes counts, serum sodium concentration and duration of hospital stay had no influence on outcome. Out of 100 children of AES admitted in Pediatric Intensive Care Unit (PICU) 69(69%) were discharge, 18(18%) were succumbed, 13(13%) were got Discharge against Medical Advice (DAMA).

Table 5: Analysis of Outcome

Risk factors	Group	Death=15	Survivors=85	P
Age	Below 1years	3	12	0.363
	1-5years	4	20	
	5-10yrs	4	23	
	Above 10 years	5	29	
Sex	Male	10	55	0.652
	Female	5	30	
RBS on admission	<60 (mg/dl)	2	5	0.177
	60-145 (mg/dl)	13	74	
	>145 (mg/dl)	00	6	
Serum Na	<135 (meq/l)	6	17	0.454
	135-145 (meq/l)	9	58	
	>145 (meq/l)	00	10	
TLC	<4000 (cells/cumm)	1	19	0.096
	4000-11000 (cells/cumm)	9	50	
	>11000 (cells/cumm)	5	16	
Sr. creatinine Normal	<1.5 times of baseline	10	60	0.146
	Deranged	>1.5 times of baseline	5	
LFT (SGPT)	Normal	6	62	0.027
	Deranged	>45 (U/L)	9	
GCS on	<8	5	15	0.144

admission	>8	10	70	
Shock and ionotropes need	Yes	3	56	0.015
	No	12	29	
Mechanical ventilation need	Yes	10	13	< 0.001
	No	5	72	
Length of hospital stay	<7 days	4	15	0.198
	7-21days	11	70	

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 (34%). Majority of them were males 65(65%), and 35(35%) 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 63(63%), 30(30%) 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 55(55%), followed by post-monsoon 34(34%) and pre-monsoon 11(11%). During monsoon and post monsoon 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 this study out of 100 cases, all had fever; 72 (72%) had altered sensorium; 57 (57%) had convulsion; 27 (27%) had headache; 43 (43%) had vomiting. On fundus examination 29 (29%) 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 10.7 ± 2.7 g/dl, total leucocyte count with mean of 9225.1 ± 5321.63 cells/cumm, RBS with mean 99.12 ± 22.02 mg/dl, SGPT with mean 104.77 ± 198.44 U/L. CSF examination done in about half of patients wherever possible. Mean CSF cell counts were 23.22 ± 64.25 cells/cumm, CSF sugar and protein were 27.1 ± 24.52 mg/dl and 15.88 ± 22.45 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 100 cases 55(55%) had viral etiology, 23(23%) had dengue, 6(6%) had malaria, 4 (4%) bacterial etiology, 6 (6%) had tuberculosis, 5 (5%) had other causes. out of 100 AES patients neuroimaging was done for 30(30%) patients, in which majority had normal finding on neuroimaging, 12(12%) showed Encephalitis features while 6(6%) showed other features like Acute Disseminated Encephalomyelitis (ADEM) in 4(4%), 2(2%) 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: 0.015) 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 100 children of AES admitted in Pediatric Intensive Care Unit (PICU) 69(69%) were discharge, 18(18%) were succumbed, 13(13%) 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 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.

Conclusion

Majority of cases were in the age-group of above 10 years, with male predominance. The peak in occurrence of cases was during post-monsoon period.

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