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Original Research Article

A cross-sectional study to evaluate the clinical profile and predictor of adverse outcome in children with acute encephalitis syndrome

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Abstract

Aim: to evaluate the clinical profile and predictors of outcome of acute encephalitis syndrome patients admitted in PICU.

Material and Methods: This Cross-sectional, observational study was done the Department of Paediatrics Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 12 months. 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:** out of 100 AES cases most of them were above 10 years of age (33%). Majority of them were males 62(62%), and 38(38%) were females. Most of them belongs to lower socioeconomic status 81(81%), 15(15%) from middle SES; and 15(15%). Out of 100 cases, all had fever; 74 (74%) had altered sensorium ; 70 (70%) had convulsion; 27 (27%) had headache; 41 (41%) had vomiting. On fundus examination 32 (32%) showed papilledema. out of 100 cases 52 (52%) had viral etiology, 25 (25%) had dengue, 6 (6%) had malaria, 4 (4%) bacterial etiology, 6 (6%) had tuberculosis, 6 (6%) had other causes. out of 100 AES patients neuroimaging was done for 36(36%) patients, in which majority had normal finding on neuroimaging, 10(10%) showed Encephalitis features while 6(6%) showed other features like Acute Disseminated Encephalomyelitis (ADEM) in 3(3%), 1(1%) Neurocysticercosis (NCC). Those patients who had shock and need inotropes showed significant mortality (pvalue: 0.012). Also those who required mechanical ventilation had significant mortality, out of 27 patients put on mechanical ventilation 16 died which was statistically significant with p -value 0.001. That patient had deranged Liver Function Test (LFT) profile also had significant higher mortality (p- value: 0.029). 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) 71(71%) were discharge, 21(21%) were succumbed, 7(7%) were got Discharge against Medical Advice (DAMA), 1(%) were referred other hospital because of their unaffordability to long duration of ICU stay for ventilator care.

Conclusion: AES is an important cause of morbidity and mortality especially during monsoon and post monsoon period. Fever, altered sensorium and convulsion were the important presenting features in AES cases. Viral encephalitis along with dengue encephalitis are important causes of AES. Early stabilization and institution of supportive.

Keywords: Acute Encephalitis Syndrome, Viral encephalitis, Dengue, Shock

Introduction

Patients with features of acute encephalitis syndrome have been one of the leading causes of PICU admissions. Viruses are one of the main causes of AES in India. [1,2] Apart from viral

encephalitis, severe form of leptospirosis and toxoplasmosis can cause AES. The causative agent of AES varies with season and geographical location, and predominantly affects population below 15 years.[3] Between 2000 and 2010, a dramatic change was observed in the AES scenario, which saw the rise in non-JE outbreaks mostly caused by viruses such as Chandipura virus (CHPV), Nipah virus (NiV), and other enteroviruses. After 2012, Japnese encephalitis is becoming the important viral pathogen causing AES.[4] Japnese encephalitis virus and Dengue virus are the chief causative agents of AES in North India according to Jain P et al. [5] Etiology of AES is an ongoing puzzle. Recently an association was found between ingestion of litchi fruit and encephalitis and death. Virologists found that death may be because of hypoglycemia. Another unconfirmed report says that alpha cypermethrin present in litchi fruit above permissible limits could be the reason.[4] An investigation of repeated AES outbreaks in Saharanpur in the early 2000s found that children were eating beans of the Cassia occidentalis plant which was causing acute hepatomyoencephalopathy. These patients were being misdiagnosed as AES cases.[6] Complications of acute encephalitis are many. They include motor in coordination, convulsive disorders, total or partial deafness, and behavioral disturbances. Visual disturbances like perceptual amblyopia may occur. Other severe complications include Guillain-Barre syndrome, hemiplegia, transverse myelitis and cerebellar ataxia. Prognostic factors implicated in the outcome of patients with AES include, age, specific cause and severity of clinical illness. HSV is one etiological agent where severe sequelae should be anticipated. Some literature suggests that infants with AES have poorer long term outcome than older children. There have been report of hydrocephalus with HSV I infection of CNS without even evidence of encephalitis.[7] Hyponatremia is one of the common dyselectrolytemia found in patients with AES. It has been variably associated with outcome. Common causes of hyponatremia in AES include syndrome of inappropriate secretion of antidiuretic hormone (SIADH), cerebral salt wasting (CSW). Mortality in AES may be due to various reasons. Age ≤18 months, marked elevation in serum lactate dehydrogenase (LD) and aspartate transaminase, diagnosis of either acute necrotising encephalopathy or haemorrhagic shock and encephalopathy syndrome and longer hypothermic periods were associated with increased risks of death or severe neurological deficit.[8]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 to assess clinical profile of AES and to assess risk factors for adverse outcome of AES in children.

Material and methods

This Cross-sectional, observational study was done the Department of Paediatrics, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 12 months.

Inclusion criteria

- Children between ages 1 month to 16 years with the acute onset of fever
- Patients change in mental status such as confusion, disorientation, Coma
- Patients with inability to talk
- New onset of seizures.

Exclusion criteria

- Patients with febrile seizures
- Toxic encephalopathy
- Children with Central Nervous System (CNS) malformations

- CSF Rhinorrhoea,
- Meningocele

Methodology

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 analysis

The SPSS 20 software was used for all statistical analyses. The descriptive variables were presented in percentages, means and standard deviations. Various variables were compared using Chi-square test or Fischer exact test. A p-value less than 0.05 was considered significant.

Results

Table 1 indicates that among 100 AES cases most of them were above 10 years of age (33%). Majority of them were males 62(62%), and 38(38%) were females. Majority of them were Hindu 84(84%), followed by 14(14%) were Muslim. Most of them were from joint family 92(92%), agriculture 70(70%) is main occupation of parents of them. Most of them belongs to lower socioeconomic status 81(81%), 15(15%) from middle SES; and 15(15%) out of 100 children had potential breeding site at their residing area. Most of the cases were reported during monsoon period 60(60%), followed by post-monsoon 24(24%) and pre-monsoon 16(16%).

Table 1: Demographic Profile of Acute Encephalitis Syndrome Patients

Variables	**Frequency (n)**	**Percentage (%)**
Religion		
Hindu	84	84
Muslim	14	14
Other	2	2
Type of Family		
Joint	92	92
Nuclear	8	8
Parents occupation		
Agriculturist	70	70
Business	8	8
Labourer	20	20
Unemployed	2	2
Socioeconomic status		
Upper	4	4
Middle	15	15
Lower	81	81
Potential breeding Site		
Present	15	15
Absent	85	85

Table 2 depicts that out of 100 cases, all had fever; 74 (74%) had altered sensorium ; 70 (70%) had convulsion; 27 (27%) had headache; 41 (41%) had vomiting. On fundus examination 32 (32%) showed papilledema (Table 2). Table 3 depicts that out of 100 cases 52 (52%) had viral etiology, 25 (25%) had dengue, 6 (6%) had malaria, 4 (4%) bacterial etiology, 6 (6%) had tuberculosis, 6 (6%) had other causes. out of 100 AES patients neuroimaging was done for 36(36%) patients, in which majority had normal finding on neuroimaging, 10(10%) showed Encephalitis features while 6(6%) showed other features like Acute Disseminated Encephalomyelitis (ADEM) in 3(3%), 1(1%) 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 2: Distribution of AES Patient according to Clinical Features

Clinical features	Frequency (n)	Percentage (%)
Fever	100	100
Altered sensorium	74	74
Convulsion	70	70
Headache	27	27
Excessive cry	4	4
Altered behaviour	23	23
Vomiting	41	41
Neurodeficit	4	4
Extrapyramidal features	2	2
Cranial nerve palsy	3	3
Fundoscopy		
Normal	68	68
Papilledema	32	32
Other system abnormality:		
CVS	6	6
RS	6	6
Abdomen	8	8

Table 3: Distribution of AES Patients according to Etiology

AES Etiology	Number (n)	Percentage (%)
Viral etiology (other than dengue)	52	52
Pyogenic	4	4
Tuberculosis	6	6
Dengue encephalitis	25	25
Cerebral malaria	6	6
Other	6	6
Not known	1	1
Total	100	100

Table 4 shows correlation of various variables to the outcome. Those patients who had shock and need inotropes showed significant mortality (pvalue: 0.012). Also those who required mechanical ventilation had significant mortality, out of 27 patients put on mechanical ventilation 16 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: 0.029). 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) 71(71%) were discharge, 21(21%) were succumbed, 7(7%) were

got Discharge against Medical Advice (DAMA), 1(%) were referred other hospital because of their unaffordability to long duration of ICU stay for ventilator care.

Table 4: Logistic Regression Analysis of Variables Affecting the Outcome

Risk factors	Group	Death	Survivors	P
Age	Below 1years	4	16	
	1-5years 5-10yrs	2 06	18 21	0.357
	Above 10 years	08	25	
Sex	Male62	14	48	0.720
	Female	06	32	
RBS on admission	<60 (mg/dl) 60-145 (mg/dl)	02 18	2 75	0.135
	>145 (mg/dl)	00	03	
Serum Na	<135 (meq/l) 135-145 (meq/l)	8 12	18 55	0.344
	>145 (meq/l)	00	7	
TLC	<4000 (cells/cumm) 4000-11000 (cells/cumm)	1 11	15 48	0.072
	>11000 (cells/cumm)	8	17	
Sr. creatinine Normal	<1.5 times of baseline	13	55	0.125
Deranged	>1.5 times of baseline	7	25	
LFT (SGPT) Normal	<45 (U/L)	8	50	0.029
Deranged	>45 (U/L)	12	30	
GCS on	<8	08	15	0.117
admission	>8	12	65	
Shock and	Yes	2	45	0.012
ionotropes need	No	18	35	
Mechanical	Yes	16	11	< 0.001
ventilation need	No	4	69	
Length of hospital stay	<7 days 7-21days	6 14	25 40	0.169
	>21 days	00	15	

Discussion

In the present study most of cases 33(33%) of AES occurred in more than 10 years of age group and between 5 to 10 years were 27 (27%). Similar results also found in studies done by Kakoti et al.[9] and Kamble et al.[10] whereas Sudhir et al.[11] 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.[11] In this present study out of 100 cases, Most of them belongs to lower socioeconomic status 81(81%), 15(15%) from middle SES; and 15(15%). Similar results were found in Kamble et al.[10] Beig et al.[12] 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 60(60%), followed by post-monsoon 24(24%) and pre-monsoon 16(16%). 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.[10] and Sarkar et al.[13] Study by Sudhir et al.[11] 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.[14] found that 71.42% of encephalitis cases occurred in winter season means post monsoon season.

In the present study, the main presentation was fever present in all patients, 74 (74%) had altered sensorium ; 70 (70%) had convulsion; 27 (27%) had headache; 41 (41%) had vomiting. On fundus examination 32 (32%) showed papilledema. Similar findings were done in studies by Kakoti et al.[9] and Anuradha et al.[15] Khinchi et al. [16]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 10.6 ± 2.4 g/dl, total leucocyte count with mean of 9306.5 ± 5225.765 cells/cumm, RBS with mean 99.21 ± 20.89 mg/dl, SGPT with mean 105.85 ±194.29 U/L. CSF examination done in about half of patients wherever possible. Mean CSF cell counts were 21.87 ± 66.29 cells/cumm, CSF sugar and protein were 26.1 ± 22.87 mg/dl and 15.16 ± 22.87 mg/dl respectively. Similar findings were also seen in study done by Kakoti et al.[9] and Sambasivam et al.[17] In the present study, among 100 children admitted in our PICU, out of 100 cases 52 (52%) had viral etiology, 25 (25%) had dengue, 6 (6%) had malaria, 4 (4%) bacterial etiology, 6 (6%) had tuberculosis, 6 (6%) had other causes. out of 100 AES patients neuroimaging was done for 36(36%) patients, in which majority had normal finding on neuroimaging, 10(10%) showed Encephalitis features while 6(6%) showed other features like Acute Disseminated Encephalomyelitis (ADEM) in 3(3%), 1(1%) Neurocysticercosis (NCC). Similar results were found in study done by Kamble et al.[10] showed out of 136 cases of AES, 84.5% had viral etiology, and 9.5% had other agents like pyogenic, tuberculosis. Thakur et al.[18] found that etiology of encephalitis include 27% viral and 47.6% were of unknown etiology. In studies done by Jain et al.[19] and Jain et al.[20] 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.[21]

In the present study, Those patients who had shock and need inotropes showed significant mortality (pvalue: 0.012) Similar results were found by Sambasivam et al.[17] 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) 71(71%) were discharge, 21(21%) were succumbed, 7(7%) were got Discharge against Medical Advice (DAMA), 1(%) were referred other hospital because of their unaffordability to long duration of ICU stay for ventilator care. Present results are in concordance with previous observation in a hospital based study on AES by DuBray et al.[22] where 67.4% of cases discharged with full recovery. Study done by Khinchi et al.[16] in Nepal found 40.6% encephalitis patients were discharged and 34.3% were expired. Kakoti et al.[9] 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.[17] 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 then 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

AES is an important cause of morbidity and mortality especially during monsoon and post monsoon period. Fever, altered sensorium and convulsion were the important presenting features in AES cases. Viral encephalitis along with dengue encephalitis are important causes of AES. Early stabilization and institution of supportive

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