

Original Research Article

Clinical profile and predictors of outcome in children admitted to PICU with acute encephalitis syndrome

Ekambaranath Sambasivam*, Jayakumar Muthaiyan, Shreedivya Mohan,
Aravind Malayappan Ayyavoo, Ganesh Jayachandran

Department of Pediatrics, Institute of Social Pediatrics, Government Stanley Medical College, Chennai, Tamil Nadu, India

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***Correspondence:**

Dr. Ekambaranath Sambasivam,
E-mail: eknath_dr@yahoo.com

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ABSTRACT

Background: Acute encephalitis syndrome (AES) is defined as the acute onset of fever and change in mental status (including symptoms such as confusion, disorientation, coma or inability to talk) and/or new onset seizures (excluding febrile seizures) in a person of any age at any time of the year. AES is reported mainly from Assam, Bihar, Tamil Nadu, Karnataka, Uttar Pradesh contributing approximately to 80% cases with case fatality rate of 20-25%. In view of paucity of clinical studies from Tamil Nadu, this study was undertaken to have a better insight on the clinical profile and prognostic indicators of AES in children. Objective of present work was to study the clinical profile and predictors of outcome of Acute encephalitis syndrome patients admitted in PICU

Methods: This retrospective study was conducted in children with AES admitted to PICU, Stanley medical college over a period of 1 year (May 2015-May 2016). 30 cases were studied. Clinical features, demography, immunisation status, and outcome were recorded. Results of blood investigations, peripheral smear, neuroimaging, CSF analysis and IgM ELISA for HSV, JE, CMV, Dengue were recorded and analysed.

Results: Mean age of cases was 3.5 ± 3.3 years. Male to female ratio was 1.1:1. Etiology included HSV (6.67%), malaria (3.33%), dengue (3.33%), tubercular meningitis (3.33%), AES of unknown origin (83.3%) 11. Most common presentation was seizures 21 (70%). 17 (56.6%) presented with GCS <8. 11 (36.6%) required inotrope support, 16 (53.4%) were ventilated. Laboratorial findings included, leukocytosis in 17 (66.7%), dysglycemia in 12 children (39.99%), hyponatremia in 10 (33.33%), hypernatremia in 8 (26.67%) Mortality was observed in 11 cases (36.67%). Hyponatremia ($p=0.02$) and cases requiring inotrope support on admission ($p=0.0003$) were significantly associated with mortality.

Conclusions: There was no case of Japanese encephalitis. Hyponatremia being significantly associated with mortality among children with AES, warrants detailed evaluation to define the etiology which will aid in appropriate management. Maintaining euvolesmia, prompt identification of shock and appropriate use of inotropes is of utmost importance. Varied and changing etiologies of AES poses a diagnostic challenge.

Keywords: Acute encephalitis syndrome, Hyponatremia, Outcome, Seizures

INTRODUCTION

Patients with features of acute encephalitis syndrome has been one of the leading cause 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, Japanese encephalitis is becoming the important viral pathogen causing AES.⁴ Japanese 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 incoordination, 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

METHODS

This is a retrospective study conducted in the PICU of Stanley Medical college in cases admitted over a period of 1 year, from May 2015-2016. Age group included was from 1 month to 12 years. All cases admitted with symptoms suggestive of AES were included in the study. Written informed consent was obtained from either the

patient or guardian. Detailed history was taken and relevant factors in history were documented. Demographic details were taken into consideration to find out the endemicity of any particular etiological agent. Thorough clinical examination was done and clinical findings were noted. Examination findings that could affect outcome were analysed.

Immunisation status was recorded in the proforma. Outcome which mainly includes the mortality and any sequelae was noted. Blood investigations like blood counts, electrolytes, peripheral smear were analysed. Neuroimaging done was analysed and abnormal findings documented. CSF analysis was done after getting consent from the parents. CSF was sent for cytology, biochemical analysis, AFB and gram stain. Viral analysis was done in CSF, which includes PCR for HSV and antibodies for JE, dengue, CMV and enterovirus.

Report was documented in proforma. IgM ELISA for HSV, JE, CMV, Dengue were done in serum also and analysed. Patients course in the hospital was monitored closely including the need for mechanical ventilation. Treatment given to the patient was analysed. Patients who survived were followed up for any neurological sequelae. The data are entered in excel sheet and analysed using epi info software version 7. Chi square test and fisher exact test were calculated for the variables.

RESULTS

Analysis of the results shows that; more cases are found in 1-5yr age group with mean age being 3.5 ± 3.3 years. There was no significant difference in death among the infants or older children. Male to female ratio was 1.1:1. Most common presentation was seizures 21 (70%) but it has no statistical significance with mortality. 17 (56.6%) presented with GCS < 8. Most of the patients presented in euglycemia. Dysglycemia was present in 12 patients (39.99). Assessment of etiology shows Herpes virus in 6.67%, dengue virus in 3.33%.

Non-viral etiologies include malaria in 3.33% and tuberculosis in 3.33%. JE virus could not be identified in any patient. 83.3% were of unknown origin. Those group of patients who had shock and required inotropes had significant mortality (0.0029). Also, the group of patients who had hyponatremia 10 (33.33%), the mortality was significantly high (p value 0.0105). Hypernatremia did not seem to influence the mortality significantly. Leucocyte counts, GCS on admission or duration of ventilation neither have any influence on outcome.

DISCUSSION

In present study, we have tried to analyse the factors determining the outcome of patients admitted to PICU with Acute Encephalitis Syndrome features. Case fatality is high in children under the age of 15 years.⁹ Seizures are the common presentation in many studies.¹⁰ We found

that two factors have statistical significant association with mortality. One is the hemodynamic status of the patient. Patients having shock and required inotropic

support have more mortality compared to those who are hemodynamically stable.

Table 1: Details of patients admitted for AES in PICU.

Risk factors	Group	Death*	Survivors*	pvalue#
Age	Less than 1 year	3(10)	6(20)	0.372
	1 to 5 year	6(20)	9(30)	
	More than 5 years	2(6.6)	4(13.3)	
Sex	Male	4(13.3)	12(40)	0.1497
	Female	7(23.3)	7(23.3)	
Seizure	Yes	6(20)	15(50)	0.1606
	No	5(16.6)	4(13.3)	
CBG on admission	<60mg/dl	0(0)	1(3.3)	0.2696
	60 to 150mg/dl	5(16.6)	13(43.3)	
	>150mg/dl	6(20)	5(16.6)	
Serum sodium	<135meq/l	7(23.3)	3(10)	0.0105
	135-145meq/l	3(10)	14(46.6)	
	>145meq/l	1(3.3)	2(6.6)	
Total leucocyte count	<4000cells/cumm	0(0)	0(0)	0.2432
	4000-11000/cumm	3(10)	9(30)	
	>11000/cumm	8(26.6)	10(33.3)	
Shock and ionotrope use	Yes	10(33.3)	6(20)	0.0029
	No	1(3.3)	13(43.3)	

*number(percentage).# pvalue<0.05 significant .CBG -capillary blood sugar

Directorate of National Vector Borne Disease Control in its guidelines on the clinical management of acute encephalitis syndrome, published in Aug 2009 identifies shock/ hypotension/ low bp/ feeble thready pulse as a danger sign and advises inotropes if shock persists after fluid resuscitation. Also, patients presenting with hyponatremia had more mortality. In a study by Misra et al it was found that hyponatremia was commonly associated with acute encephalitis syndrome and also, they had poor outcome.¹¹ In many cases death happens because of brain swelling caused by severe inflammation.¹² HSV is the common aetiological agent identified in present study. Other agents identified are malaria and tuberculosis. In present study, none of the patients tested positive for JE. One such outbreak of unknown aetiology occurred in 2012. None of the 334 patients tested positive for JE and at least 118 (35.3%) of them died.¹³ Etiology of AES varies in different studies. Jain A et al reported JEV 16%, Dengue virus 11%, Herpes simplex virus, Mumps virus and measles virus 9% each, and Varicella Zoster virus 4%. Total 42% cases were AES cases with unknown etiology.¹⁴ Thapa LJ et al in his study found only 4.07% patients were tested positive for JE.¹⁵

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Ethical approval: The study was approved by the Institutional Ethics Committee

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