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Clinico- etiopathological study and outcome of acute enchephalitis syndrome -a hospital based prospective observational study"

A S A M Srikanta[1], Ipsita sahoo[2], Payal Pradhan[3], Dillip kumar Dash[4],Braja Kishore Behera[5], Shivangi Maheshwari[6] ,Bibhudatta Dash[7]

[1]PG resident, Department of Pediatrics, Institute of Medical Science and SUM Hospital, Bhubaneswar,India
[2]Assistant Professor, Department of Pediatrics, Institute of Medical Science and SUM Hospital, Bhubaneswar,India
[3]Assistant Professor, Department of Pediatrics, Institute of Medical Science and SUM Hospital, Bhubaneswar,India
[4]Professor, Department of Pediatrics, Institute of Medical Science and SUM Hospital, Bhubaneswar,India
[5]Associate Professor Department of Pediatrics, Institute of Medical Science and SUM Hospital, Bhubaneswar,India
[6]PG resident, Department of Pediatrics, Institute of Medical Science and SUM Hospital, Bhubaneswar,India
[7]Associate Professor, Department of Pediatrics, Institute of Medical Science and SUM Hospital, Bhubaneswar,India

Abstract

Background & objectives: Acute encephalitis syndromeis aserious public health problem and mainly caused by viruses. The etiological diagnosis of acute encephalitis syndrome cases is essential for better patient management and policymaking. The present study was carried out to determine the clinicetio-pathological profile and outcome of acute encephalitis syndrome in tertiary center in Bhubaneshwar.

Methods:Serum and/or Cerebrospinal fluid were collected from acute encephalitis syndrome patients admitted at IMS & SUM Hospital, a tertiary care center, Bhubaneswar, Odisha between October 2019-september 2021. Cerebrospinal fluid and serum were tested for bacteriological culture and IgM antibodies against the HSV,Japanese encephalitis virus, dengue virus and scrub typhus by ELISA.

Results: Among the 128 cases 79.2% were suspected for viral etiology out of which HSV (5.88%), Japanese encephalitis (2%). Followed by bacterial (19.5%) out of which scrub typhus (38%), and tubercular meningitis (0.8%) were responsible for acute encephalitis syndrome.

Interpretation & conclusion:HSV, Dengue virus and Japanese encephalitis virus scrub typhus are most common causative etiological agents in our study, they are more prevalent during monsoon and post-monsoon seasons.

Keywords: Acute encephalitis syndrome; HSV,dengue virus; Japanese encephalitis virus; scrub typhus.

Introduction

Acute encephalitis is the clinical diagnosis of children with acute onset of symptoms and signs of inflammatory lesions in the brain[1,2]. Changes in sensorium, seizures and upper motor neuron type of altered muscle tone point to cerebral dysfunction [3,4]. Brain tissue would show the pathology, but at the bedside, inflammation is surmised from pleocytosis of the cerebrospinal fluid (CSF) to predominantly lymphocytes, since the etiology is mostly non-pyogenic infection [4,5,6]. The clinical picture usually consists of a prodromal phase (one to three days) with fever, malaise and headache and an encephalitic phase with continued fever, decreasing level of consciousness, seizures, abnormal movements or paralysis [7,8,9]. Signs of meningeal inflammation are absent or minimal. Many children may succumb, but others recover through a post-encephalitic phase, the fortunate ones more or less completely, but others with sequelae of cognitive deficiencies, muscle paralysis, abnormal movements etc.[9,10].

When features of encephalitis and meningitis co-exist, the disease is called meningoencephalitis.In recent years, a diagnosis of 'acute encephalitis syndrome' (AES) has crept into medical literature in India, with a definition at variance from that of acute encephalitis in pediatric textbooks.[11,12,13]. For example, AES was defined in one study as 'clinical neurologic manifestations caused by wide range of viruses, bacteria, fungus, parasites, spirochetes, chemicals and toxins [14,15]. Obviously, the clinical pictures of such various diseases cannot fit into one clinical diagnosis of acute encephalitis, either as a disease or as a syndrome.[16,17,18]

Methodology

Study design: cross-sectional study.
Study place: Department of Pediatrics, IMS&SUM Hospital,BBSR,Odisha.
Study subjects: Children who are between 1 month to 14 years, admits in pediatric department, IMS &SUM hospital with provisional diagnosis of AES

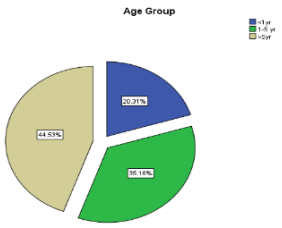
Duration of study:2 years.
Inclusion Criteria:
Children with provisional diagnosis of AES of ageing between 1 month to 14 years, during 2-year duration in pediatrics department of IMS &SUM Hospital, BBSR, Odisha, after obtaining informed consent from parents.

Exclusion Criteria:
1. Simple Febrile seizures
2. H/o Epilepsy
3. Trauma induced encephalopathy
4. Metabolic encephalopathy.

Data collected
1. Detailed past and present history
2. Signs& Symptoms at presentation
3. Detailed General & Systemic Examination
Data was analyzed using SPSS software (version 12) and the outcome was expressed in percentage.

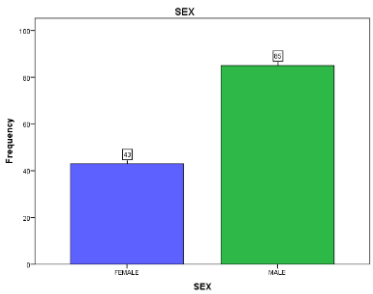
Results And Analysis

In our study which was conducted out of all pediatric admissions in IMS & SUM Hospital, Bhubaneshwar, Odisha 128 cases were taken as case population depending on presentation as acute encephalitis syndrome. Prevalence of AES in our study found out to be 1.2%



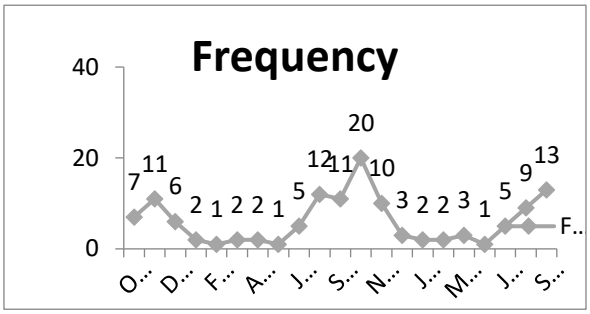
Age distribution; In our study out of 128 cases, 5years to 14 years age group are more affected (44.53%). (Chart :1)

Chart :1
Chart :2**Gender distribution**



Age group of 1 month to 14 years in 128 patients with diagnosis of AES based on clinical presentation, 85 patients were males (66.4%) and 43 patients were female (33.6%) with ratio of 1.9:1. (Chart :2)

Month of Admission and No of case
Chart :3



Frequency of AES cases showed seasonal variation. Peak of AES mostly seen in monsoon and post monsoon season. (Chart :3)

Symptomatology: The most common presenting symptom was fever (92.2%) followed by irritability (69.5%) and altered sensorium (53.9 %%). Vomiting (65.6%) being the commonest of meningeal symptom followed by headache (64.1%). (Table :1)

SymptomatologyTable :1

SYMPTOM		Frequency	Percent
SEIZURE	No	79	61.7
	Yes	49	38.3
FEVER	No	10	7.8
	Yes	118	92.2
COMA	No	118	92.2
	Yes	10	7.8
HYPOVOLEMIC SHOCK	No	102	79.7
	Yes	26	20.3
STATUS EPILEPTICUS	No	105	82.0
	Yes	23	18.0
HEADACHE	No	46	35.9
	Yes	82	64.1
VOMITING	No	44	34.4
	Yes	84	65.6
ALTERED MENTAL STATUS	No	59	46.1
	Yes	69	53.9
IRRATIBILITY	No	39	30.5
	Yes	89	69.5
FEEDING DIFFICULTY	No	63	49.2
	Yes	65	50.8
PHOTOPHOBIA	No	70	54.7
	Yes	58	45.3

Prehospital antibiotic therapy Table:2

Among 128 cases 82 patients (64.1%) admission and 46(45.9%) cases did not received antibiotics before getting receive any medication. (Table :2)

MEDICATION PRIOR ADMISSON		
	Frequency	Percent
No	46	35.9
Yes	82	64.1
Total	128	100.0

Meningial Signs Table:3

Sign	No	Yes
KERNIG SIGN	63(49.2)	65(50.8)

BRUDZINSKI SIGN	50(39.1)	78(60.9)
NECK STIFFNESS	41(32)	87(68)

Among 128 cases 65(50.8%) patients have kernig sign,78(60.9%) cases have Brudzinski sign and 87(68%)cases have meningeal sign. Neck stiffness being the commonest meningeal sign (68%).(Table :3)

Raised ICT features: Table:4

Features	Absent	Present
HYPERTONIA	105(82)	23(18)
BULGING FONTANELLE	107(83.6)	21(16.4)
VOMITING	44(35)	84(65)
HEADACHE	46(35.9)	82(64.1)

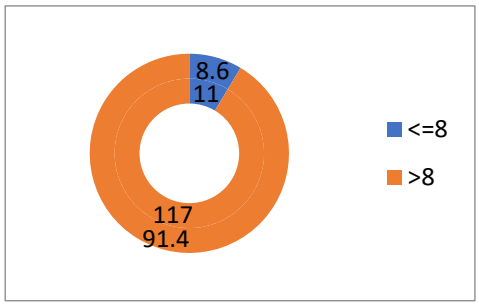
Out of 128 cases features of raised ICT was the most common sign. Vomiting was the most common complaint (65%).(Table :4)

Mechanical ventilation requirement Table :5

Mechanical Ventilation support		
	Frequency	Percent
No	108	84.4
Yes	20	15.6
Total	128	100.0

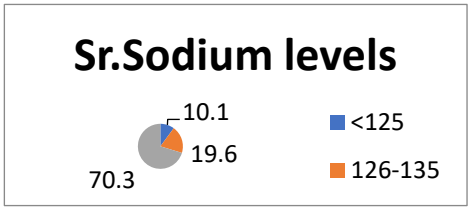
Among 128 cases of suspected AES, 20(15.63%) children required mechanical ventilator support for various reasons.(Table :5)

Chart:4 GCS



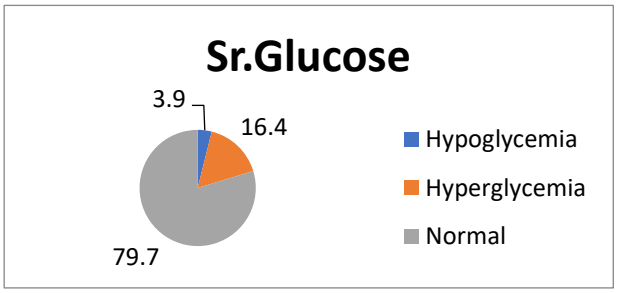
Out of 128 cases GCS was < 8 in 11 cases (8.6%) at the time of presentation. (Chart:4)

Hyponatremia: Chart:5



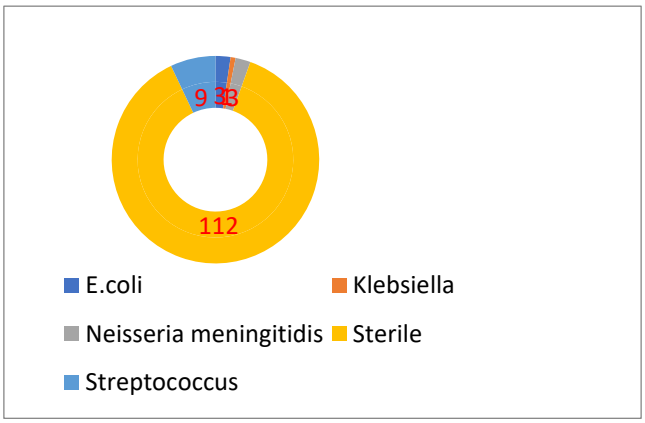
Hyponatremia was seen in 38 cases (29.7%), out of which <125 mEq/L was seen in 13 cases (10.1). (Chart:5)

DysglycemiaChart:6



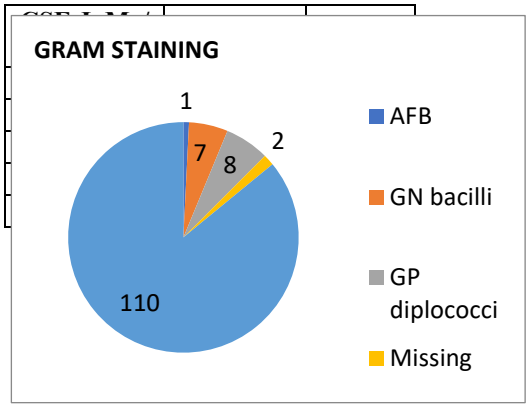
Dysglycemia was seen in 26 cases (20.3 %) at the time of presentation. Out of which Hypoglycemia was seen in 5 cases and Hyperglycemia was seen in 21 cases. (Chart:6)

CSF culture and sensitivity patter; Chart:7



In my study of 128 cases, bacterial meningitis was confirmed in 16 cases (12.5%) by CSF culture and gram stain. (Chart:7)

Gram staining Chart:8



Out of 128 cases, 16 (12.5%) cases were gram stain positive. (Chart:8)

ELISA results Table :6

SERUM IgM/ PCR		
	Frequency	Percent
Anti spike antibody	2	1.6
Dengue	2	1.6
EBV	1	.8
HSV	1	.8
JE	2	1.6
Measles	2	1.6
Mumps	2	1.6
Scrub	10	7.8
No	106	82.8
Total	128	100.0

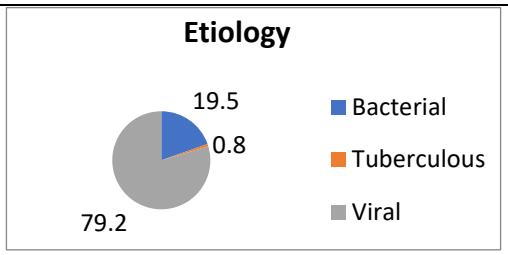
Serum IgM capture ELISA was done in128 suspected cases of AES, out of which scrub IgM was positive in 10 cases (7.8%) ,2 cases of each in dengue, Covid,JE,Measles,Mumps and 1 case each of EBV & HSV. (Table :6)

CSF IgM ELISA Table :7

CSF IgM / PCR	Frequency	Percent
HSV 1	5	3.9
JE	1	.8
No	122	95.3
Total	128	100.0

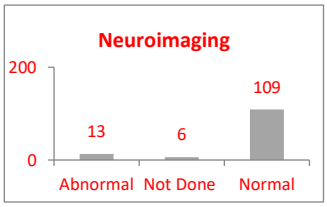
CSF IgM ELISA was positive in 6 cases of which 5 cases were HSV 1 and 1 case of JE. (Table :7)

Etiology Chart:9



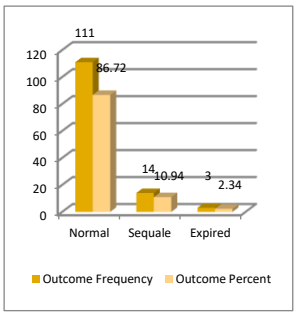
In total 128 cases Bacterial etiology was present in 25, tuberculous etiology in 1 case and Non-Bacterial etiology was found in 102 cases. Out of which confirmed Viral etiology was found in 17 cases. (Chart:9)

Neuroimaging Chart:10



Among 128 cases, Neuroimaging including MRI/CT was found to be normal in 109 cases, abnormalities were found in 13 cases. Imaging was not done in 6 cases because of monetary issues. (Chart:10)

Distribtion of outcome Chart:11



In total of 128 cases, Normal outcome was seen in 111 cases (86.7%) ,3 was expired (2.34%) &14 children discharged with sequalae (10.94%). (Chart:11)

COMPLICATION * Mechanical Ventilation

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
COMPLICATION * Mechanical Ventilation	128	100.0%	0	0.0%	128	100.0%

COMPLICATION * Mechanical Ventilation Cross tabulation

Count

		Mechanical Ventilation		Total
		No	Yes	
COMPLICATION	No	99	12	111
	Yes	9	8	17
Total		108	20	128

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	14.693[a]	1	.000		
Continuity Correction[b]	12.072	1	.001		
Likelihood Ratio	11.398	1	.001		
Fisher's Exact Test				.001	.001
N of Valid Cases	128				

a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 2.66.
b. Computed only for a 2x2 table

Statistical values suggest Complications were more commonly seen in children who received mechanical ventilation support.

Neuroimaging * COMPLICATION

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	%	N	%	N	%
Neuroimaging * COMPLICATION	128	100.0%	0	0.0%	128	100.0%

Neuroimaging * COMPLICATION Cross tabulation

Count

		COMPLICATION		Total
		No	Yes	
Neuroimaging	Abnormal	7	5	12
	Not done	6	0	6
	Normal	98	12	110
Total		111	17	128

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)

Pearson Chi-Square	9.851[a]	2	.007	.010
Likelihood Ratio	8.160	2	.017	.010
Fisher's Exact Test	7.316			.017
N of Valid Cases	128			
a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is .80.				

Statistical Values suggestive of Complications are more commonly seen in Children who were having abnormal findings in Neuroimaging.

GCS Score * COMPLICATION

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	%	N	%	N	%
GCS Score * COMPLICATION	128	100.0%	0	0.0%	128	100.0%

GCS Score * COMPLICATION Cross tabulation				
Count				
		COMPLICATION		Total
		No	Yes	
GCS Score	<=8	4	7	11
	>8	107	10	117
Total		111	17	128

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	26.494[a]	1	.000	.000	.000
Continuity Correction[b]	21.927	1	.000		
Likelihood Ratio	17.543	1	.000	.000	.000
Fisher's Exact Test				.000	.000
N of Valid Cases	128				
a. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 1.46.					
b. Computed only for a 2x2 table					

Statistical Values suggestive of Complications are more commonly seen in Children who were having low GCS at the time of admission.

Discussion

Age Distribution: Acute Encephalitis Syndrome is one among common CNS diseases in pediatric age groups.Most common age group affected was 5 to 12 years. In our study results of most common group effected are similar to Baswati et all [19]**.**and saumyen de et all. [20]**.** My study results are similar to other studies as Khinchi et all [21]**.**Manish kakkar et all [22]**.**Sneha et all[23]**.** in which males are outnumbered than females**.** Fever, altered sensorium and seizure are the most common symptoms. In our study results are similar to other study like Khinchi et all. Bhaswati bandyopaghyay et all and Manish kakkar et all .In our study 26 (20.3%) children had dysglycemia which is similar to the study done by Manish kakkar et all(21.4%) . Among them most of the cases had sugar levels more than 140 which may be considered as stress related hyperglycemia. Studyby Pramit Shrivastavaet all [24]**.**shows more incidence of Dysglycemia than our study.Hyponatremia in our study seen in 29.7% cases. Results are comparable to previous studiesi.eAjit Rayamajhiet all(33.3%)[25]**.**Hyponatremia associated with adverse outcome in our study. Glasgow coma scale at the time of admission <8 was found in 8.6%cases in the present study which is comparatively less compared to study by Khinchi et al (29.5%), Ajit Rayamajhi et all (56.6%) and Joshi R, Kalantriet all (25%)[29] .children with GCS <8 on admission the CFR was 27.5%.CSF study in our study was in consistence with viral encephalitis in79.7%, Bacterial meningitis in19.5% and TBM in 0.8%.Above results were predicted based on cell count, sugar and protein in CSF and were found to be similar to most of the previous studies as mentioned below.

STUDY	VIRAL ENCEPHALITIS	BACTERIAL MENINGITIS	TBM
Sneha et al	69	75.1	3.7
Khinchi et al	36	40.9	-
R.Jayakarthika	76	8.9	5.4
Present study	79.7	19.5	0.8

CSF culture and sensitivity pattern in acute encephalitis syndrome: Our study results shows 16% which is more as compared to study by Rakesh Kumar et al (3.5%) **[26].** and Joshi R, Kalantriet all(8.9%).In our study conducted on 128 cases, bacterial etiology was confirmed in 25 cases by CSF culture and sensitivity, TBM in 1 case and confirmed viral etiology in 17 cases. Out of these 17 viral cases, 6 cases turned out to be positive for HSV by IgM ELISA, 2 cases showed positive results for JE IgM ELISA as studied by Shresta SR, et al [30]and 2 cases had MRI features suggestive of covid related encephalitis along with anti-spike antibodies.

Study	**Result**
Bhaswati bandyopadhyay et all	None
Khinchi et all	JE (18%)
Sneha et All	Viral JE & Dengue (84.5), Pyogenic,TB& varicella(9.5%),Unknown(5.8%)
Rakesh kumar et all	Viral JE(29%),Viral Non JE (57.5),Bacterial(8.5%) Cerebral Malaria(5%)
Jain et al	Dengue(10.8%),JE(16.2%)HSV(9.3%),Measles(8.9%),VZV(4. 4%)
Joshi et al	Non Viral (16.9%),Viral (11.2%),Unknown (79.6%)
Rathore k et al[27]	Measles(2.6%) ,HSV (16.1%) JE(1.5%),VZV(0.38%)
Sen TK et al	Pyogenic(8.9%),TBM(5.4%),VZV(5.4%),,ProbableJE(3.5%), AES unknown etiology(67%)
PRESENT STUDY	Bacterial :19.5%(SCRUB-38%), TBM (0.8%) VIRAL:79.7% (HSV-5.88% JE, DENGUE, MUMPS, MEASLES, SARS-COVID-2%, EBV-1%)

In terms of immediate outcome our study shows a promising result as compared to other previous studies as mentioned below.

Study	Normal	Sequelae	Death
Rakesh kumar et al[26]	72.5%	10.5%	13%
Shresta SR et al [30]	61%	18%	13%
Present study	86.72%	10.94%	2.34%

Poor Outcome in Our Study Implicated To1. Poor GCS (<8) at the time of admission 2. Need for mechanical ventilation 3. Hyponatremia 4. Abnormal neuroimaging.

Conclusion

Acute Encephalitis Syndrome is one among common CNS diseases in pediatric age group, in which we need early diagnosis, management to Prevent Morbidity and Mortality. In most of the cases confirmed etiology was not identified. In our observational study we found out that the prevalence of Acute encephalitis syndrome during our study period was 1.2 %. Among all pediatric age groups affected by AES,our study showed children belong to 5-14 years more commonly Males area effected. Our study showed seasonal variation in number of AES cases, most being in monsoon and post monsoon period of the year. In our observation in all Acute encephalitis syndrome cases, the most common symptom at the time of presentation was found to be Fever (92.2%), followed by irritability (69.5%) and altered sensorium (53.9%).Dyselectrolytemia was seen in most of the cases in which Hyponatremia being most commonly encountered.Neuroimaging was done to confirm our diagnosis of AES and found out abnormal MRI findings were present in 10.2% cases with hyperintensities in temporal lobe being common. In our study Confirmed Viral etiology was found in 17 cases (13.3%) in which 6 children were infected by HSV-1 and 2 cases were JE, confirmed by CSF viral markers. Our study showed in cases of all Acute Encephalitis syndrome the outcome and prognosis depend on Low Glasgow coma scale score at the time of presentation, Abnormal findings in neuro imaging, PICU admission and mechanical ventilation support and Dyselectrolytemia. With preventive measures and early detection, it is possible to tackle the menace of encephalitis to a large extent.

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