

Prospective Analysis of Acute Encephalitis Syndrome: Clinical Characteristics and Patient Outcomes in a Tertiary Care Pediatric Setting

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Abstract:-

➤ *Background:*

One of the most frequent neurological emergencies in pediatrics, central nervous system infections cause a considerable amount of death and morbidity. Especially in newborns, the symptoms are frequently modest, therefore a strong index of suspicion is needed to make the diagnosis. Inadequate or delayed treatment may result in fatalities or other severe consequences.

➤ *Objective:*

To ascertain the frequency, clinical characteristics, and etiological makeup of kids hospitalized in tertiary PICU due to acute encephalitis syndrome.

Results of kids referred to tertiary PICUs with acute encephalitis symptoms.

➤ *Study Design:*

Hospital based prospective study.

➤ *Participants:*

Children with AES from one month up to 18 years of age admitted in PICU of hospitals.

➤ *Intervention:*

Thorough clinical assessments were completed, and blood samples will be sent for various baseline biochemical analyses. In every instance, samples of blood and urine were sent for sensitivity and culture while adhering to strict aseptic protocol. In every incidence of fever with altered sensorium, neuroimaging and CSF analysis will be carried out. The history, clinical examination, and pertinent laboratory investigations are used to determine the etiology of AES.

➤ *Results:*

Out of the one hundred cases that were examined, five had J.E., thirty had rickettsia, twenty had dengue, one had varicella, twelve had COVID-19, five had measles, four were pyogenic, one had tuberculosis, twelve had ADEM, and nine were undiagnosed. A total of 45

patients were lost to follow-up throughout the follow-up period. Of the patients, 16 had hearing loss, 10 had speech loss, 15 had extra pyramidal abnormality, 21 had behavioral abnormality, and 21 had cranial nerve impairments.

➤ *Conclusion:*

AES is a persistent public health issue that requires immediate attention, as well as cooperation and support from other sectors. Strengthening primary health care is urgently needed to provide access to both routine and emergency care, both of which are essential for better results.

Keywords:- Acute Encephalitis Syndrome; Cerebrospinal Fluid Analysis; Clinical Profile; Glasgow Outcome Score.

I. INTRODUCTION

One of the most frequent neurological emergencies in pediatrics, central nervous system infections cause a considerable amount of death and morbidity. Especially in newborns, the symptoms are frequently modest, therefore a strong index of suspicion is needed to make the diagnosis. Inadequate or delayed treatment may result in fatalities or other severe consequences. 1. One such serious CNS ailment that affects children across the nation with notable morbidity and mortality is acute encephalitis syndrome, which is also one of the most frequent reasons for admission to the pediatric intensive care unit (PICU). 2.

An acute inflammatory process that affects the brain is referred to as encephalitis. AES may manifest as meningoencephalitis, meningoencephalitis, or meningitis. Mycobacteria, rickettsia, viruses, or bacteria may be the cause of AES, while toxoplasma is less common. 3,4 The most frequent and significant cause of encephalitis is viral infections, of which JE and HSV are primarily responsible for the epidemic and sporadic etiologies, respectively. South East Asia has a higher prevalence of dengue and JE. 4

Since the initial report of AES from Vellore, Tamil Nadu, in 1955, the history of the virus has followed that of the Japanese encephalitis virus (JEV) in India. In the West Bengali district of Bankura, the first JEV outbreak was documented in 1973. Subsequently, the primary cause of AES-related early fatalities in India has been isolated instances and outbreaks.⁴

According to reports, the annual incidence of acute encephalitis in children worldwide ranges from 10.5 to 13.8 per 1,000,000.5. The NVBDCP estimates that the incidence rate in India is between 3.5 and 7.4 per 1,000 children. Based on the information at hand, pathogen detection for encephalitis has not yet been extensively employed in India for clinical diagnosis and treatment. On the other hand, clinical information and additional patient examinations form the majority of the diagnosis. Furthermore, studies reveal that only 30–40% of cases of encephalitis could be pathogenically detected, with Japanese encephalitis (JE) accounting for the majority of cases in India among all known encephalitis-causing organisms.

Therefore, routine diagnostic investigations such as CT and MRI are needed to uncover the etiology and assess the amount of inflammation, as well as to analyze blood for inflammatory markers. Clinicians confront the issue of a limited window of time between diagnosis and therapy, given the variety of causative agents and the rapid rate of neurological deterioration resulting from pathogenesis.

The current research shows how the perception of AES has evolved in India over time, based on findings from a review of several surveillance and epidemic investigations. As we have shown, there have been changes in both the clinical and etiological variations from demographic areas.

Hence, the present study was conducted to determine the incidence, clinical as well as etiological profile of the children admitted with acute encephalitis syndrome.

II. METHODOLOGY

A. Source of Data:

This was a hospital based prospective study conducted in 100 children with AES from one month upto 18 years of age admitted in PICU were included in the study for the period of one and a half year. The study was approved by the Institutional Ethics Committee.

B. Inclusion Criteria:

All cases of fever with altered sensorium from > 4 hours but < 2 weeks (according to Glasgow coma scale) between the age of 1 month to 18 years admitted in Pediatric Intensive Care Unit.

C. Exclusion Criteria:

Children with – Metabolic encephalopathy, head injury, mental retardation, space occupying lesion, granuloma, endocrinal encephalopathy, febrile seizure and post hypoxic ischemic encephalopathy.

D. Method:

A case proforma including detailed history and clinical examination was noted. Each patient was studied in a methodical manner in predesigned structural proforma after obtaining written consent from parents or guardians regarding their willingness to participate in the study.

After admission, detailed history was taken and management of fever, raised ICP and seizure were carried out simultaneously. Detailed clinical examinations were done and blood samples was sent for different baseline biochemical tests. Neuroimaging and CSF analysis was performed in all cases of fever with altered sensorium. The clinical variables recorded was heart rate, respiratory rate and respiratory patterns, blood pressure (average of three recordings, using mercury sphygmomanometer, by auscultatory method), temperature, sensorium (using modified Glasgow Coma Scale), pupillary size and response to light, extra ocular movement, posture, motor pattern (recorded subjectively by assessing the passive tone), seizure if any, type of seizure, involuntary movement and fundus picture. The etiology of AES was determined on the basis of history, clinical examination and relevant laboratory investigations.

The outcome of patients was graded with a functional outcome score (Glasgow Outcome Scale, GOS), as follows: Grade I –death, Grade II-Severe sequelae greatly impairing function and incompatible with independent living, Grade III -Moderate sequelae mildly affecting function (including seizures), but compatible with independent living, Grade IV-Minor sequelae including altered personality or clinical signs not affecting functions, Grade V- full recovery and normal neurologic examination findings.

The investigations such as random blood sugar (RBS), Complete blood count (CBC), Serum electrolytes, C-reactive protein, Urine routine, Blood culture, Cerebrospinal fluid analysis, CT/MRI brain, Renal function test, Dengue serology, Prothrombin time / Activated prothrombin time (PT/APTT), Random diagnostic test – Malarial parasite (RDT-MP), viral analysis of CSF – IgM ELISA for JE, IgG ELISA for HSV and measles and RT-PCR for enterovirus.

E. Statistical Analysis

- **SPSS (Statistical Package For Social Sciences)** version 20. (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis
- Data was entered in the excel spread sheet.
- Descriptive statistics of the explanatory and outcome variables were calculated by frequency and proportions for qualitative variables.

III. RESULTS

Table 1: Distribution of the Subjects Based on Demographic Details

		Frequency	Percent
Age Groups	1 month to 1 yr	16	16.0
	1 to 5 yrs	47	47.0
	5 to 17 yrs	37	37.0
Gender	Males	50	50.0
	Females	50	50.0
Location	Urban	53	53.0
	Rural	47	47.0
Religion	Hindu	87	87.0
	Muslim	12	12.0
	Christian	1	1.0
Parents Occupation	Agriculture	35	35.0
	Services	47	47.0
	Labourer	12	12.0
	Unemployed	6	6.0
SES	Upper class	6	6.0
	Middle Class	66	66.0
	Lower Class	28	28.0
Potential Breeding Site	Present	70	70.0
	Absent	30	30.0

Based on age group, 16 patients (16%) belonged to the age group of 1 month to 1 year, 47 patients (47%) belonged to the age group of 1 year to 5 years and 37 patients (37%) belonged to the age group of 5 years to 17 years. 50 (50%) were males and 50 (50%) were females.

Based on urbanization, 53 patients (53%) belonged to urban area and 47 patients (47%) belonged to rural area. The

occupation of patients parents was agriculture for 35 patients (35%), services for 47 patients (47%), labourer for 12 patients (12%) and unemployed for 6 patients (6%). According to socioeconomic status, 6 patients (6%) were upper class, 66 (66%) were middle class and 28 (28%) were lower class. 70 patients (70%) had potential breeding site.

Table 2: Distribution of the Subjects Based on Chief Complaints

Chief Complaints		Frequency	Percent
Fever	Present	99	99.0
	Absent	1	1.0
Confusion	Present	63	63.0
	Absent	37	37.0
Disorientation	Present	49	49.0
	Absent	51	51.0
Inability to talk	Present	47	47.0
	Absent	53	53.0
Lethargy	Present	23	23.0
	Absent	77	77.0
Obtundation	Present	2	2.0
	Absent	98	98.0
Semi Coma	Present	1	1.0
	Absent	99	99.0
Coma	Present	11	11.0
	Absent	89	89.0
Convulsions	Present	77	77.0
	Absent	23	23.0
Headache	Present	40	40.0
	Absent	60	60.0
Excessive Cry	Present	21	21.0
	Absent	79	79.0
Vomiting	Present	38	38.0
	Absent	62	62.0

Loose Stools	Present	21	21.0
	Absent	79	79.0
Rashes	Present	82	82.0
	Absent	18	18.0
Bleeding manifestations	Present	17	17.0
	Absent	83	83.0
Breathlessness	Present	21	21.0
	Absent	79	79.0
Swelling of the body	Present	17	17.0
	Absent	83	83.0
Limb weakness	Present	31	31.0
	Absent	69	69.0
Shock at admission	Present	46	46.0
	Absent	54	54.0
Aspiration syndrome	Present	24	24.0
	Absent	76	76.0
GCS	< 8	32	32.0
	> 8	68	68.0

➤ *Inference:*

According to symptoms, 99 had fever, 63 had confusion, 49 had disorientation, 47 had inability to talk, 23 had lethargy, 2 had obtundation, 1 were in semi coma, 11 were in coma, 77 had convulsions, 40 had headache, 21 had

excessive cry, 38 had vomiting, 21 had loose stools, 82 had rashes, 17 had bleeding manifestations, 21 had breathlessness, 17 had swelling of the body, 31 had limb weakness, 46 had shock at admission, 24 had aspiration syndrome and 32 had GCS <8.

Table 3: Distribution of the Subjects Based on CNS Examination

			Frequency	Percentage
GCS		< 8	32	32.0
		> 8	68	68.0
Signs of Meningeal irritation		Neck sign	1	1.0
		Leg Sign	8	8.0
		Both	71	71.0
		Normal	20	20.0
Cranial Nerve involvement		Yes	35	35.0
		No	65	65.0
Pupil	Normal	0	12	12.0
		1	88	88.0
	Abnormal	0	84	84.0
		R1	3	3.0
		R2	13	13.0
Fundus (papilledema)		1	40	40.0
		2	60	60.0
Tone		Hypertonia	6	6.0
		Hypotonia	56	56.0
		Normal	38	38.0
Neurological deficits		Yes	32	32.0
		No	65	65.0
DTR		Brisk	50	50.0
		Diminished	25	25.0
		Normal	25	25.0
Plantar		Extensor	14	14.0
		Flexor	79	79.0
		Unequivocal	7	7.0
Cerebellar Sign		Yes	20	20.0
		No	80	80.0
Extra Pyramidal Sign		Yes	14	14.0
		No	86	86.0
F/S/O raised ICT		Yes	59	59.0
		No	41	41.0

Coma/sensorium severity	Grade 1	10	10.0
	Grade 2	79	79.0
	Grade 3	11	11.0

➤ *Inference:*

- Based on CNS examination, 32 patients had a GCS of <8 and 68 patients had a GCS of > 8.
- According to signs of meningeal irritation, 1 patient had neck sign, 8 patients had leg sign and 71 had both.
- 35 patients (35%) had cranial nerve involvement.
- 12 patients had a 0-normal pupil and 88 patients had 1-normal pupil.
- 41 patients had as score of 1 on fundus examination and 2 for 60 patients.
- 6 had hypertonia, 56 had hypotonia and 38 had normal tone.
- 32 had neurological deficits.
- The deep tendon reflex was brisk in 10 patients, diminished in 25 patients and normal in 25 patients.
- Based on plantar reflex, 14 had extensor reflex, 70 had plantar reflex and 7 had unequivocal reflex.
- 20 patients had cerebellar sign. 14 patients had extrapyramidal sign. 59 patients had raised ICT.
- 10 patients had grade 1 Coma/sensorium severity, 79 patients had grade 2 Coma/sensorium severity and 11 patients had grade 3 Coma/sensorium severity.

Table 4: Distribution of the Subjects Based on Investigations

			Frequency	Percent
RBS on admission		< 60 mg/dl	14	14.0
		60 to 150 mg/dl	78	78.0
		> 150 mg/dl	8	8.0
CBC	HB	< 8	14	14.0
		8.1 to 10	69	69.0
		> 10	17	17.0
	TC	< 4000 cells/ m3	13	13.0
		4000 to 11000 cells/m3	69	69.0
		> 11000 cells/m3	18	18.0
	Platelet Count	< 50k	17	17.0
		50k to 1 L	61	61.0
		> 1 L	22	22.0
LFT	SGPT	< 45	29	29.0
		> 45	71	71.0
	Serum protein	< 3.5 g/dl	29	29.0
		> 3.5 g/dl	71	71.0
Electrolytes	Sodium	< 135 mEq/L	19	19.0
		135 to 145 mEq/L	64	64.0
		> 145 mEq/L	17	17.0
Blood Serology	Dengue Serology	Yes	23	23.0
		No	77	77.0
	Malarial Smear	Yes	1	1.0
		No	99	99.0
	Chikungunya	Yes	2	2.0
		No	98	98.0
	Weil Felix	Yes	33	33.0
		No	67	67.0
	COVID-19 antibodies	Yes	17	17.0
		No	83	83.0
	Ig M ELISA	Yes	5	5.0
		No	95	95.0
CSF Characteristics	CSF Cell count	N	26	26.0
		Y	74	74.0
	CSF Protein	N	26	26.0
		Y	74	74.0
	CSF glucose	N	26	26.0
		Y	74	74.0
	IgG	IgG ELISA for measles	1	1.0
		Rickettsial	33	33.0

CSF serology		IgM ELISA for JE=	3	3.0
		Non pathological	63	63.0
	CSF RTPCR	Enterovirus	1	1.0
		Chikungunya	2	2.0
		COVID-19	15	15.0
		Non pathological	82	82.0

➤ *Inference:*

Based on RBS, 14 patients had <60 mg/dl on admission, 78 patients had 60 to 150 mg/dl and 8 patients had > 150 mg/dl. 14 patients had <8 Hb, 69 patients had 8.1 to 10 Hb and 17 patients had >10 Hb. The total count was <4000 cells/m³ in 13 patients, 4000 to 11000 cells/m³ in 69 patients and > 11000 cells/m³ in 18 patients. The platelet count was < 50k in 17 patients, 50k to 1 L in 61 patients and >1 lakh in 22 patients. 29 patients had SGPT <45 and 71 patients had SGPT >45. 29 patients had serum protein < 3.5 g/dl and 71 patients had serum protein > 3.5 g/dl. 19 patients had sodium value < 135 mEq/L, 64 patients had sodium value 135 to 145 mEq/L and 17 patients had sodium value >145 mEq/L. 23 patients had positive dengue serology and 1 patient had positive malarial smear. 2 patients had chikungunya, 33 patients had Weil Felix, 17 patients had positive COVID-19 antibodies, 5 patients had positive Ig M ELISA. 74 patients had positive CSF cell count, CSF Protein and CSF glucose. 1 patient had positive IgG ELISA for measles, 33 patients for Rickettsial and 3 patients for IgM ELISA for JE and 63 patients were non-pathological. 1 had enterovirus, 2 had chikungunya, 15 had COVID 19 and 82 were non pathological.

IV. DISCUSSION

Acute encephalitis is the clinical diagnosis of children with acute onset of symptoms and signs of inflammatory lesions in the brain. Changes in sensorium, seizures and upper motor neuron type of altered muscle tone point to cerebral dysfunction.⁷

In the present study, based on age group, 16 patients (16%) belonged to the age group of 1 month to 1 year, 47 patients (47%) belonged to the age group of 1 year to 5 years and 37 patients (37%) belonged to the age group of 5 years to 17 years. Similarly, in a study by Adhikari *et al.*,⁸ the age group mainly affected was 5 to 12 years and the youngest one was 5 months old. Majority of the Kakoti G, *et al.*, reported higher incidence among 5-12 years age group.⁹

A male : female ratio of 1.1:1 was reported by Jain P, *et al.*¹⁰ Our results were in concurrence with the findings of Jain P, *et al.*,¹⁰ In the present study, based on gender, 50 (50%) were males and 50 (50%) were females.

In the present study, based on urbanization, 53 patients (53%) belonged to urban area and 47 patients (47%) belonged to rural area. On the contrary, a study by Adhikari *et al.*,⁸ showed that mostly affected children were from rural areas (90%) and belong to low socioeconomic group (63%). This correlated well with the earlier studies by Potula R, *et al.*,¹¹ and Kumar R, *et al.*,¹² where the patients were children of farmers or farm laborers of low socioeconomic group residing in rural areas. This may be due to favorable

epidemiological factors like presence of water logged paddy field supporting profuse breeding of vector mosquitoes, piggeries in close proximity to residence, non use of bed nets and outdoor playing habits of children.

The low income group community people become directly or indirectly exposed to JEV infection and this kind of data also satisfies that low economic status is one of the important risk factors in relation to JE incidences, corroborating with the earlier observation by Badari *et al.*¹³ and Luo D, *et al.*¹⁴ In the present study, 70 patients (70%) had potential breeding site. This may be due to favorable epidemiological factors like presence of water logged paddy field supporting profuse breeding of vector mosquitoes, piggeries in close proximity to residence, non use of bed nets and outdoor playing habits of children.

According to symptoms, 99 had fever, 63 had confusion, 49 had disorientation, 47 had inability to talk, 23 had lethargy, 2 had obtundation, 1 were in semi coma, 11 were in coma, 77 had convulsions, 40 had headache, 21 had excessive cry, 38 had vomiting, 21 had loose stools, 82 had rashes, 17 had bleeding manifestations, 21 had breathlessness, 17 had swelling of the body, 31 had limb weakness, 46 had shock at admission, 24 had aspiration syndrome and 32 had GCS <8. Kakoti G, *et al.*,⁹ also reported fever (100%), altered sensorium (83.58%) and seizures (82.08%) as most common. Whereas, Mittal M, *et al.*,¹⁵ described significantly higher proportion of headache (25.8% vs 10.74%) in the JE category, and generalised oedema (6.5% vs 24.8%) in the non JE category.⁵¹ Signs of meningeal irritation were frequently observed in more than half of the study patients as recorded in other studies by Potula R, *et al.*¹¹ and Gourie-Devi M, *et al.*¹⁶

Use of mechanical ventilation, lower Glasgow coma score (GCS) and concurrent seizures are good predictors of poor outcome in acute encephalitis syndrome. So we should manage the patient aggressively when these poor prognostic factors present without wasting golden hours irrespective of etiology. Children with Glasgow Coma Score less than 8 should preferably be intubated; mechanical ventilation should be provided in case the breathing efforts are not adequate.

Our study has clearly established the existence of AES etiology in the sporadic JE incidences by performing antibody captured ELISA method against the JEV specific antigen. JE risk was significantly associated with the rural residents living in close proximity to irrigated rice fields (preferred breeding place for vector mosquito of JE) and pig-rearing places. To avoid the risk of AES, these rural residents should take personal protection by using of mosquito repellent, insecticide-treated bed nets and deet-permethrin soap, in order to reduce the mosquito bite or vector exposure.

In addition, the larvae of the vector mosquito should be controlled by some biological control strategies.

V. CONCLUSION

This study provides an explanation of the current etiology, clinical manifestation, and immediate result of AES. In these patients, the need for mechanical breathing, a lower GCS score, and concomitant seizures are risk factors for a bad prognosis. Nonetheless, the substantial number of instances with unclear etiologies and the paucity of information regarding long-term results all point to the necessity of additional research in this area. Encouraging all instances to be reported and given the proper investigation will improve AES surveillance and significantly lower the illness's morbidity and death rate.

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