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Clinico-etiological profile and outcome of acute encephalitis syndrome in children

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Abstract: Acute Encephalitis Syndrome (AES) is a significant cause of mortality and morbidity in children in endemic regions. While viruses have been the primary etiological agents attributed to AES in India, other microbes and toxins have also been reported in recent years. This study aimed to determine the etiology, clinical features, and outcomes of AES in children. This prospective observational study was conducted in the pediatric department of Jorhat Medical College and Hospital of Assam over a period of one year. The study included 49 diagnosed cases of AES in children aged between one month to 12 years as per the WHO case definition. Clinical features, etiology, and outcomes (recovery without or with neurological sequelae or death) were recorded for each patient. The study found that fever (100%) and altered sensorium (100%) were the most common clinical presentations in AES cases. Seizure (63%), headache (34.7%), vomiting (26.5%), diarrhea (22.4%), and other symptoms such as excessive crying and irritability (22.4%) were also observed. Japanese Encephalitis (JE) was the most common cause of AES (28.6%), followed by Herpes Simplex Virus (4.1%), pyogenic meningitis (4.1%), and tubercular meningitis (2%). The majority of cases (61.2%) were of unknown etiology. Among the 49 cases, 27 (55.1%) recovered without neurological sequelae, 8 (16.8%) had neurological sequelae, and 14 (28.6%) died during hospital treatment. The most common neurological sequelae was motor deficit (37.5%), followed by behavioral disorders and aphasia (25% each). Cranial nerve palsy was observed in one case (25%). Of the eight AES cases with neurological sequelae, five were JE positive and three were caused by other agents. The study concludes that AES cases commonly present with fever, altered sensorium, seizure, headache, vomiting, and signs of meningeal irritation. JE remains a major cause of AES in children in this region of India. These findings highlight the need for global attention to combat the menace of this arboviral encephalitis and save the lives of children.

Keywords: Acute encephalitis; Syndrome; Meningitis; Glasgow coma scale.

1. Introduction

Acute Encephalitis Syndrome (AES) is a major public health issue in many countries, particularly in the developing world, where it affects a large number of children. AES is characterized by the acute onset of fever and encephalitis, with or without seizures, and can lead to high mortality and neurological sequelae. The cause of AES varies based on season and geographical location, with viruses being the most commonly attributed cause in India. However, other microbes and toxins have also been reported as causative agents in AES cases [1,2].

It is critical to evaluate AES cases immediately to reduce mortality and morbidity. Children with AES often require admission to intensive care units and need specialized care, including monitoring of vital signs, hydration, nutrition, and management of seizures. However, there is no specific treatment for AES, and management is primarily supportive, see [3–9].

This study aims to investigate the etiology, clinical features, and outcomes of AES in children in a hospital setting. The findings of this study can help in the development of effective treatment and management protocols to reduce the disease burden of AES. The study was conducted in the pediatric department of Jorhat Medical College and Hospital in Assam over a period of one year, and 49 diagnosed cases of AES were included

in the study. Clinical features, etiology, and outcomes were recorded in these patients, and the results of the study are expected to provide important insights into the management of AES in children.

2. Materials and Methods

2.1. Study Sites

Jorhat Medical College and Hospital, established in 2009, is a tertiary care hospital and serves as a surveillance center for Acute Encephalitis Syndrome (AES).

2.2. Study Design

This was a hospital-based observational study.

2.3. Timeline of the Study

The study was conducted from June 1st, 2020 to May 31st, 2021.

2.4. Sample Size

All children admitted to the Pediatric Department of Jorhat Medical College and Hospital during the study period and diagnosed with AES, who fulfilled the inclusion and exclusion criteria, were included in the study.

2.5. Inclusion Criteria

The following criteria were used to include patients in the study:

- Children diagnosed with AES according to the WHO case definition.
- Children aged between 1 month and 12 years whose parents or legally acceptable representatives (LAR) provided written informed consent.

2.6. Exclusion Criteria

The following criteria were used to exclude patients from the study:

- Children with a history of simple febrile seizure.
- Patients with pre-existing neurological deficits prior to the onset of AES.
- Neonates (aged from birth to 28 days).

2.7. Method of Study

This observational study was conducted at the Pediatric Department of Jorhat Medical College and Hospital over a period of one year. Ethics committee (Human) approval was obtained before the study commenced. Each patient was studied in a systematic manner using a pre-designed structural proforma, with written informed consent obtained from their parents or guardians. Clinical variables such as heart rate, respiratory rate and patterns, blood pressure, temperature, sensorium using the modified Glasgow Coma Scale, pupillary response to light, posture, motor pattern (assessed subjectively by assessing passive tone), seizures (if any), type of seizure, and involuntary movement were recorded.

The etiology of AES was determined based on history, clinical examination, and relevant laboratory investigations. Under aseptic and antiseptic precautions, 2ml of blood and 1 ml of CSF were collected and immediately sent to the central clinical laboratory of Jorhat Medical College and Hospital. Laboratory investigations included serology for Japanese encephalitis using the IgM Capture ELISA kit provided by the National Institute of Virology (NIV) and Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) for tubercular meningitis. Rapid diagnostic tests and peripheral blood smears for malaria parasites were performed depending on the clinical presentation. The etiology of AES was classified into Japanese encephalitis, bacterial meningitis, tubercular meningitis, cerebral malaria, and AES of unknown etiology. The outcome was recorded as recovery without neurological sequelae at the time of discharge, recovery with neurological sequelae at the time of discharge, or death.

2.8. Data Analysis

Descriptive statistical methods were used to present the clinico-epidemiological characteristics of the study population. The Statistical Package for Social Sciences (SPSS) software, IBM SPSS version 21, was used for all statistical analyses.

2.9. Ethical Consideration

Ethical approval was obtained before the study began. The patients and their parents were informed about the purpose, design, risks, benefits, voluntary participation, and confidentiality of data. Written informed consent was obtained from the parents or guardians of all participants in the study. All information obtained was kept confidential.

3. Results

3.1. Demographic Profile

A total of 49 cases of Acute Encephalitis Syndrome (AES) were admitted to the hospital. Of these, 29 (59%) were male and 20 (41%) were female. Children aged between 1 month to 1 year accounted for 9 cases (18%), those aged between 1 year to less than 5 years accounted for 21 cases (43%), and those aged between 5 years to 12 years accounted for 19 cases (38%).

3.2. Clinical Profile

Fever was present in all 49 cases (100%), and altered sensorium was also present in all cases. Seizures were reported in 31 cases (63%), headache in 17 cases (34.7%), vomiting in 13 cases (26.5%), and diarrhea in 11 cases (22.4%). Other symptoms reported included excessive crying and irritability, which were observed in 11 cases (22.4%).

3.3. Etiological Profile

Japanese encephalitis was the most common cause of AES, accounting for 14 cases (28.6%), followed by HSV in 2 cases (4.1%), pyogenic meningitis in 2 cases (4.1%), and tubercular meningitis in 1 case (2%). The majority of cases, 30 (61.2%), had an unknown etiology.

3.4. Outcome of AES Patients

Among the 49 cases of AES, 27 (55.1%) recovered without any neurological sequelae, 8 cases (16.8%) suffered from neurological sequelae, and 14 cases (28.6%) expired during hospitalization. Motor deficit was the most common neurological sequelae observed in 3 cases (37.5%), followed by behavioral disorders and aphasia in 2 cases each (25%). Cranial nerve palsy was observed in 1 case (12.5%). Out of the 8 cases with neurological sequelae, 5 were positive for Japanese encephalitis and 3 had other causes.

3.5. Tables

Table 1 shows the age distribution of AES patients, Table 2 shows the sex distribution of AES patients, Table 3 shows the urban and rural distribution of AES patients, Table 4 shows the clinical profile of children with AES, Table 5 shows the distribution of AES patients according to etiology, Table 6 shows the outcome of children with AES at the time of discharge, and Table 7 shows the type of neurological sequelae observed at the time of discharge.

Table 1. Age distribution of AES patients (n=49)

Age	AES	Percentage
1 Month - <1 Year	9	18.4%
1Year to <5 Year	21	42%
5 Year to 12 Year	19	38%

Table 2. Sex distribution of AES patient (n=49)

SEX	AES	Percentage
Male	29	59.2%
Female	20	40.8%

Table 3. Urban and Rural distribution of AES patients (n=49)

RURAL/URBAN	Number	Percentage
URBAN	8	16.3%
RURAL	41	83.7%

Table 4. Clinical profile of children with AES (n=49)

Clinical profile	Number	Percentage
Fever	49	100%
Altered sensorium	49	100%
Seizure	31	63.3%
Headache	17	34.7%
Vomiting	13	26.5%
Diarrhea	11	22.4%
Others	11	22.4%

Table 5. Distribution of AES patients according to etiology

Etiology	Frequency(n=49)	Percentage %
JE Positive	14	28.6%
HSV	2	4.1%
Pyogenic meningitis	2	4.1%
Tubercular meningitis	1	2%
Unknown	30	61 .2%

Table 6. Outcome of children with AES at the time of discharge

Outcome	AES(n=49)	Percentage%
Recovered without neurological sequelae	27	55.1%
Recovered with neurological sequelae	8	16.3%
Death	14	28.6%

Table 7. Type of Neurological sequelae at the time of discharge

Neurological sequelae	AES	Percentage%
Aphasia / incomprehensible sound	2	25%
Motor deficit	3	37.5%
Cranial nerve palsy	1	12.5%
Behavioral disorders	2	25%

4. Discussion

4.1. Demographic profile of AES patients

In the present study, most AES cases were recorded in the age group of 1 year to 5 years, with a mean age group of 5.12 ($\pm$ 3.76) years and a median age group of 4 years. These findings are consistent with earlier studies by Karmarkar SA *et al.* (2008) [3] and Dutta D *et al.* (2019) [4], which also found that the most

common age group affected by AES was 1-5 years, with mean age groups of 3.21 ($\pm$ 2.9) and 5.10 ($\pm$ 3.6) years, respectively. This observation highlights the vulnerability of young children to AES and emphasizes the need for targeted preventive measures.

Regarding gender distribution, our study found that AES cases were more common in males (59.2%) than females (40.8%). This observation is consistent with earlier studies by Sarkar AH *et al.* (2017) [5], Khound M *et al.* (2017) [6], and Kakoti G *et al.* (2020) [1]. The reason for this gender difference is not clear and warrants further investigation.

4.2. Clinical profile of AES cases

The present study found that the most common clinical symptoms of AES were fever (100%) and altered sensorium (100%), followed by seizure (63.3%), headache (34.7%), vomiting (26.5%), and diarrhea (22.4%). These findings are consistent with earlier studies by Khinchi YR *et al.* (2010) [7] and Basu R *et al.* (2018) [8], which also reported fever and altered sensorium as the most common symptoms of AES in children. These clinical features are non-specific and can be caused by a variety of etiologies. Therefore, accurate diagnosis of the underlying cause of AES is crucial for appropriate management and prognosis.

4.3. Etiological profile of AES patients

Our study found that the most common known cause of AES was viral encephalitis, with Japanese encephalitis (28.6%) being the most frequent viral cause and HSV (4.1%) being the second most common viral cause. Pyogenic meningitis (4.1%) and tubercular meningitis (2%) were the most common non-viral causes of AES. However, the majority of cases (61.2%) remained undiagnosed. These findings are consistent with an earlier study by Basu R *et al.* (2018) [8], which reported that viral encephalitis was the most common cause of AES, followed by bacterial meningitis and tubercular meningitis. Accurate diagnosis of the underlying cause of AES is crucial for appropriate management and prognosis. Therefore, efforts should be made to improve the availability and accessibility of diagnostic facilities in resource-limited settings.

4.4. Outcome of AES cases at the time of discharge

In the present study, out of 49 AES cases, the majority of cases (55.1%) recovered without neurological sequelae, 8 (16.8%) recovered with neurological sequelae, and 14 (28.6%) expired during treatment. Observation found by earlier study De S *et al.*,(2015) [9], as 6(25%) recovered without neurological sequelae, 11(45.83%) recovered with neurological sequelae and 7(29.16%) cases expired during treatment.

Khound M *et al.*, (2017) [6]found in earlier study most common neurological sequelae was aphasia(41%), followed by behavioral abnormality (24%), motor deficit(20%), cranial nerve palsy(9%), extrapyramidal abnormal movements (4%).Basu R *et al.*, [8]found in earlier study extrapyramidal abnormality (63.63%), followed by speech loss (51.51%), behavioral abnormality (21.21%), hearing loss(9.03%) and cranial nerve palsy (6.06%).

5. Conclusion

The current study identifies fever, altered sensorium, seizure, headache, vomiting, and signs of meningeal irritation as the most frequently observed clinical presentations in AES cases. Notably, Japanese encephalitis (JE) continues to be a major cause of AES in children, causing significant morbidity and mortality in this region of India. These findings highlight the urgent need for global attention to combat the spread of this arboviral encephalitis and save the lives of children. Comprehensive strategies should be implemented to prevent, diagnose and treat JE in a timely manner, including vaccination programs, improved surveillance and early detection, and prompt clinical management. Such efforts are crucial to reduce the burden of AES and improve the overall health outcomes of affected individuals and communities.

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Conflicts of Interest: "Nil."

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