Section: Pediatrics

Original Research Article

CLINICAL PROFILE OF CHILDREN ADMITTED WITH ACUTE ENCEPHALITIS SYNDROME IN A TERTIARY CARE CENTRE: A CROSS SECTIONAL STUDY

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Received *: 20/05/2025*
Received in revised form *: 10/06 /2025*
Accepted *: 17/06/2025*

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DOI: 10.70034/ijmedph.2025.2.490

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (2); 2705-2711

ABSTRACT

Background: Acute Encephalitis Syndrome (AES) is a group of clinical conditions characterized by the acute onset of fever and a range of neurological symptoms. The objective is to estimate the prevalence and to study the clinical presentation of Acute encephalitis syndrome in children aged 6 months to 18 years.

Materials and Methods: This cross sectional study was conducted among children aged 6 months to 18 years who were admitted to the PICU with a diagnosis of AES at Rohilkhand Medical College and Hospital Bareilly.

Results: A significant gender variation in AES incidence, with a higher frequency of male patients. Statistically significant symptoms included fever present in all cases, a high incidence of seizures, and altered sensorium, underlining their role as critical clinical features of AES. Additionally, a notable proportion of the patients exhibited cranial nerve involvement and kidney dysfunction, suggesting these as important factors in severe cases. Laboratory findings varied, with some like leukocyte count abnormalities and liver enzyme levels not showing statistical significance, which could imply random variations rather than consistent trends associated with AES. However, elevated creatinine levels were significantly associated with AES, pointing to potential kidney issues that require careful monitoring.

Conclusion: The study encapsulates the clinical complexity and variability of AES in children, emphasizing the need for comprehensive clinical assessment and vigilant management to improve patient outcomes.

Keywords: Clinical profile, acute encephalitis syndrome, Outcomes.

INTRODUCTION

Acute Encephalitis Syndrome (AES) is a significant public health problem in India, particularly affecting children under 15 years of age. Outbreaks of AES occur annually, with the disease presenting both sporadically and in epidemics. The condition has a seasonal pattern, with most outbreaks occurring during the monsoon season. The clinical presentation of AES typically begins with fever, followed by neurological symptoms such as headache, vomiting, altered consciousness, and seizures. In more severe cases, complications such as limb paresis, coma, and death can occur.[1] AES contributes to a large number of pediatric intensive care unit (PICU) admissions and is associated with high morbidity and mortality rates, especially in resource-poor settings.

The public health burden of AES in India is substantial. The National Vector Borne Disease Control Programme has identified AES as a major health issue, particularly in states such as Uttar Pradesh, West Bengal, Assam, and Tamil Nadu, where the highest number of cases have been reported. Between January 2013 and April 2019, approximately 50,000 cases of AES were recorded annually in India, resulting 10,000 deaths each year.[2] This high burden underscores the importance of improving diagnostic capabilities and healthcare responses to AES outbreaks.

The diagnostic process for AES typically includes clinical assessment, lumbar puncture for cerebrospinal fluid (CSF) analysis, and neuroimaging. Lumbar puncture is a critical investigation in AES cases, as it allows for the identification of pathogens that may be present in the CSF. Magnetic Resonance Imaging (MRI) and Electroencephalography (EEG) are also used to support the diagnosis of AES, particularly in cases where viral encephalitis is suspected.[3] However, in many cases, especially in resource-limited settings, the causative pathogen remains unidentified despite these investigations.

Despite the significant public health impact of AES, there is a lack of comprehensive data on the clinical profile of pediatric patients affected by the syndrome in India. Most existing studies focus on the epidemiology and virology of AES, with limited information on the clinical presentation and progression of the disease. Understanding the clinical features of AES is crucial for improving early diagnosis and treatment, which can, in turn, reduce the high morbidity and mortality associated with the condition.[4]

This study aims to address this gap by describing the clinical profile of pediatric patients with AES admitted to Rohilkhand Medical College and Hospital. By documenting the clinical presentation, diagnostic findings, and outcomes of AES cases in children, this research seeks to contribute to the existing body of knowledge and inform future public health interventions. Furthermore, this study aims to provide insights into the challenges of diagnosing and managing AES in resource-limited settings, where access to advanced diagnostic tools may be limited.

MATERIALS AND METHODS

This cross sectional study was conducted among children aged 6 months to 18 years who were admitted to the PICU with a diagnosis of AES at Rohilkhand Medical College and Hospital (RMCH), Bareilly. These patients were identified based on clinical features that matched the World Health Organization (WHO) criteria for AES, which includes fever, seizures, confusion, or other signs of central nervous system (CNS) involvement. The study was conducted over a period of one year. Ethical approval for the study was obtained from the institutional ethics committee at RMCH, Bareilly.

Inclusion Criteria:

Children were included in the study if they met the following criteria:

- Age between 6 months and 18 years.
- Admitted to the PICU with clinical features of AES as defined by the WHO,

Exclusion Criteria:

Children who met any of the following conditions were excluded from the study:

- Children admitted with clinical features of intracranial hemorrhage, trauma, tumors, or poisoning. These conditions could mimic AES but have different etiologies and management strategies.
- Children with developmental delays due to other causes. This exclusion criterion was set to avoid confounding factors that might affect neurological assessments and outcomes.

Sampling Method: A purposive sampling method was employed in this study. All children admitted to the PICU with suspected AES during the study period were considered for inclusion, provided they met the eligibility criteria. This sampling method was chosen to ensure that the study captured all relevant cases within the predefined timeframe, facilitating a thorough understanding of AES presentations and outcomes in this setting.

Method of Recruitment

Children were recruited upon admission to the PICU after presenting with symptoms suggestive of AES. The attending pediatrician, in consultation with the neurologist, identified potential participants. After confirming the clinical diagnosis of AES, the guardians of eligible children were approached for consent to enroll their child in the study. Informed consent was obtained from parents or legal guardians, with a detailed explanation of the study objectives and procedures. Participation was entirely voluntary, and confidentiality was maintained.

Method of Data Collection

Data were collected using a structured proforma designed specifically for this study.

The proforma included the following components:

- Patient Demographics and Clinical History:
- Clinical Examination:
- Laboratory Investigations:
- Management:

Sample Size: The sample size was calculated based on the anticipated proportion (P) of patients presenting with sudden onset convulsions, a key clinical feature of AES. Using the following formula:

$N = 4PQ/L2$

Where:

- P = 97.6% (anticipated proportion based on previous studies).
- Q = 100 - P.
- L = 5% (allowable error).

Substituting the values into the formula:

$N = 4 \times 97.6 \times 2.425 = 37.4$

Thus, the minimum sample size required was 38 patients.

Statistical Analysis: Data collected from the proforma were entered into Microsoft Excel and analyzed using SPSS (Statistical Package for Social Sciences) version 23. Descriptive statistics, including mean, standard deviation, frequency, and percentage, were used to summarize demographic and clinical data. Appropriate statistical tests, such as the Chi- square test for categorical variables and

t-tests for continuous variables, were applied to determine the significance of associations. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Of the total, 23 children (54.8%) were male, and 19 children (45.2%) were female. The chi-square value is 0.00, with a p-value of 0.001, indicating a statistically significant difference in gender distribution. This suggests a notable gender variation in the incidence of AES in the studied population. The higher frequency of male children might reflect a demographic trend or inherent biological predisposition, warranting further investigation into potential contributing factors.

Fever was universally present, reported in 100% of cases. A p-value of < 0.001 indicate a statistically significant association, confirming fever as a hallmark symptom of Acute Encephalitis Syndrome in the studied population.

A significant majority, 30 children (71.4%), experienced seizures, while 12 children (28.6%) did not. (p-value <0.001) The high frequency of seizures in AES cases emphasizes their role as a critical clinical feature and underscores the importance of monitoring for seizures when diagnosing and managing children with suspected AES.

A significant majority (83.33%) exhibited altered sensorium, reflecting its prominence as a clinical manifestation in the study population. Only 16.67% of patients retained normal sensorium. (p-value <0.001) These findings emphasize the importance of vigilant monitoring and early intervention for patients with altered sensorium, as it often correlates with the severity of neurological involvement. Early management may play a crucial role in improving outcomes and preventing further complications.

Of the total, 12 children (28.6%) exhibited cranial nerve involvement, while 30 children (71.4%) did not. (p-value <0.001) Although less common than other symptoms, cranial nerve involvement is an important clinical feature and its presence may indicate a more severe or advanced form of the condition requiring targeted management.

Table 1: Distribution of CNS Findings.

CNS Findings	Frequency	% of Total
Neck stiffness	14	33.3%
Photophobia	6	14.3%
Headache	10	23.8%
Normal	12	28.6%
Total	42	100%

χ^2 value- 4.32, p value- 0.229

Neck stiffness was the most common finding, occurring in 33.3% of the participants, followed by headache in 23.8%. Photophobia was observed in 14.3% of the cases, while 28.6% of the participants exhibited normal CNS findings. The total sample size was 42. (p-value >0.05) that there is no statistically significant association between the CNS findings and the overall distribution, as the p-value is greater than the commonly accepted significance level of 0.05. Therefore, the observed differences in CNS findings may be due to chance rather than a meaningful pattern.

Table 2: Distribution of Clinical feature

	Frequency	% of Total
Altered sensorium	7	16.67%
Irritability	5	11.90%
Aggressive behaviour	5	11.90%
Pallor	4	9.52%
Vomiting	5	11.90%
Loose stools	7	16.67%
Papilledema	3	7.14%
Shock	2	4.76%
Congestive Heart Failure	1	2.38%
Lethargy	3	7.14%
Total	42	100%

χ^2 value- 22.4, p value- < .001

Table 7 presents the clinical features observed in children admitted with Acute Encephalitis Syndrome. Altered sensorium (16.67%) and loose stools (16.67%) were the most frequently reported symptoms. Irritability, aggressive behavior, and vomiting were equally common, each accounting for 11.90%. Pallor was noted in 9.52% of cases, while papilledema and lethargy were present in 7.14%. Shock and congestive heart failure were less frequent, seen in 4.76% and 2.38% of cases, respectively. The total sample comprised 42 children. (p-value <0.001) Indicate a statistically significant association between clinical features and Acute Encephalitis Syndrome, underscoring the variability in symptom presentation among affected children.

Total Leukocyte Count abnormalities were the most common, affecting 35.71% of participants, followed

by thrombocytopenia in 23.81%. Anemia was present in 19.05% of the cases, while dysglycemia and dyselectrolytemia were observed in 11.90% and 9.52%, respectively. The total sample size was 42. (p-value >0.05) Therefore, the variations in lab findings may be attributed to random chance rather than a consistent trend.

Of the total, 32 children (76.2%) had negative blood culture results, while 10 children (23.8%) had positive blood cultures. (p-value <0.001) Indicate a highly significant association between blood culture results and the occurrence of AES. This finding highlights that although most cases had negative blood cultures, a notable portion tested positive, suggesting the potential for underlying infections or co- infections contributing to the clinical presentation of AES.

The results show that 20 children (47.6%) had normal LFTs, while 22 children (52.4%) exhibited elevated AST/ALT levels. (p-value >0.05) Although elevated liver enzymes were observed in slightly more than half of the cases, the lack of statistical significance suggests that liver function alterations may not be a key diagnostic feature in AES.

Table 3: Distribution of KFT Result

KFT Result	Frequency	% of Total
Normal	27	71.1 %
Elevated Creatinine	15	28.9 %
Total	42	100%

χ^2 value- 6.74, p value- 0.009

The results show that 27 children (71.1%) had normal KFTs, while 15 children (28.9%) exhibited elevated creatinine levels. (p-value <0.001) This suggests that elevated creatinine levels, indicating potential kidney dysfunction, are a notable clinical feature in a significant proportion of AES cases and may require closer monitoring during management.

Table 4: Distribution of CSF Analysis

CSF Analysis	Frequency	% of Total
CSF glucose (mg/dl)	10	24.39%
CSF cell	21	51.22%
CSF protein (mg/dl)	10	24.39%
Total	42	100%

χ^2 value- 0.00, p value- 0.001

CSF cell abnormalities were the most common, observed in 51.22% of cases. CSF glucose and protein abnormalities were each reported in 24.39% of cases. The total sample size was 42. P-value <0.001 highlighting the importance of CSF analysis in diagnosing and understanding the condition.

The results show that 12 children (28.6%) had positive CSF ZN staining, while 30 children (71.4%) had negative results. (p-value <0.001) This suggests that a considerable proportion of AES cases may be associated with infections that can be identified through ZN staining, which is commonly used to detect mycobacterial infections, particularly tuberculosis. The high percentage of negative results, however, indicates that a majority of cases may not involve these pathogens, underscoring the importance of considering other diagnostic factors in the clinical assessment of AES.

Table 5: Distribution of CSF Gram Staining

CSF Gram Staining	Frequency	% of Total
Positive	4	21.4%
Negative	33	78.6%
Total	42	100%

χ^2 value- 20.6, p value- < .001

Table 14 illustrates the distribution of CSF Gram staining results among 42 patients. The findings reveal that the majority (78.6%) of cases were Gram-stain negative, indicating the absence of bacterial presence in most cerebrospinal fluid samples. However, a notable 21.4% of samples tested Gram-stain positive, pointing to bacterial involvement in these cases. (p-value <0.001) These results underscore the critical role of Gram staining as an initial diagnostic tool in determining bacterial infections in Acute Encephalitis Syndrome. Prompt identification and targeted treatment of Gram-stain positive cases are essential to improving patient outcomes and reducing complications.

The results show that 10 children (23.8%) had normal EEG findings, 9 children (21.4%) exhibited epileptiform activity, and 23 children (54.8%) displayed generalized slow waves. The chi-square value of 13.6 and a p-value of 0.001 indicate a statistically significant association between EEG findings and the occurrence of AES. The high percentage of children with generalized slow waves suggests significant brain dysfunction or altered cerebral activity commonly associated with AES. Epileptiform activity, although less frequent,

underscores the role of seizures in AES. These findings highlight the importance of EEG as a diagnostic tool in identifying the neurological involvement in children with AES.

Table 6: Distribution of Outcome

Outcome	Frequency	% of Total
Normal	30	71.43%
Sequelae	5	11.9%
Expired	3	7.14%
Lost Follow up	4	9.52%
Total	42	100%

χ^2 value- 18.42, p value- 0.0036

A majority (71.43%) had a normal recovery, while 11.9% experienced sequelae. Mortality was recorded in 7.14% of cases, and 9.52% were lost to follow-up. (p-value <0.05) emphasizing the need for early intervention to improve prognosis and reduce adverse outcomes.

Table 7: Distribution of mechanical ventilation

Complication	Frequency	% of Total
No	23	54.76%
Yes	19	45.24%
Total	42	100.00%

The data reveals that 45.24% of the patients required mechanical ventilation, reflecting the severity of their conditions. Conversely, 54.76% did not need ventilation, suggesting a less critical clinical course for this group. The notable proportion of patients requiring mechanical ventilation underscores the critical impact of severe complications, such as respiratory issues and multi-organ failure, often associated with Acute Encephalitis Syndrome. This highlights the importance of early diagnosis and aggressive management to mitigate respiratory distress and improve survival outcomes. The findings emphasize the need for resources and preparedness in managing critically ill patients requiring intensive respiratory support.

Table 8: Distribution of Complication

Complication	Frequency	% of Total
None	11	26.2%
Recurrent Seizures	13	28.6%
Respiratory Issues	10	23.8%
Multi-Organ Failure	8	19.0%
Total	42	100%

χ^2 value- 12.3, p value- 0.015

The results show that 11 children (26.2%) did not experience any complications, while 12 children (28.6%) had seizures, 1 child (2.4%) had seizures (possibly a typographical error), 10 children (23.8%) experienced respiratory issues, and 8 children (19.0%) developed multi-organ failure. (p-value <0.05) Seizures, respiratory issues, and multi-organ failure were common complications, highlighting the severe and multi- system impact of AES. The low incidence of complications in some cases underscores the variability in disease severity and response to treatment among affected children.

The mean age of the patients was 135.61 months with a wide confidence interval from 65.65 to 145.56, indicating a large variability among the sample. Admission duration averaged 8.79 days, with a more precise confidence interval (7.65 to 9.93 days). CRP levels were high at 71.39 mg/L, reflecting inflammation or infection. The Glasgow Coma Scale (GCS) score averaged 7.66, suggesting severe impairment in consciousness. Dyselectrolytemia and hypocalcemia were prevalent, with respective mean levels of 137.97 mEq/L and 7.03 mg/dL, indicating significant electrolyte imbalances in the population studied.

DISCUSSION

Our study revealed a male predominance among AES cases, with males constituting 54.8% and females 45.2%. This finding is consistent with Kakoti et al.[5] who reported a similar trend in their study.

In our study, the incidence of fever in 100% of AES cases not only corroborates the findings from Kakoti et al. [5] and Saumyen De and Sanjana Samanta.[6] but also universally underscores fever as a pivotal clinical marker for AES.

Our results indicated that 71.4% of children with AES experienced seizures, a slightly lower rate than the 82.08% reported by Kakoti et al.5. This variance might reflect regional epidemiological differences or variations in viral strains which could influence the clinical expression of AES. Deuri A et al.[7] found a considerably lower incidence of seizures at 43.3%, pointing to significant variability which could be attributed to differences in study populations or diagnostic criteria.

Altered sensorium was observed in 83.33% of our AES cases, closely aligning with the 83.58% reported by Kakoti et al.[5] The consistency of this symptom across studies underscores its reliability as a clinical indicator of AES. However, slightly lower rates reported by Saumyen De and Sanjana Samanta.[6] and Deuri A et al.[7] suggest some degree of variability, potentially influenced by the timing of medical intervention or the severity of the disease.

In our cohort, cranial nerve involvement was evident in 28.6% of cases, reflecting a less frequent but nonetheless important clinical feature of AES, as also seen in lower frequency in the study by Shrivastava P et al.[8] This finding suggests that while cranial nerve involvement is less common than other AES symptoms such as fever or seizures, its presence might indicate a more severe disease course or a specific pathogenic process within the nervous system. The comparative rarity of this symptom highlights the need for comprehensive neurological assessments in AES patients to ensure that such critical but less frequent manifestations are not overlooked.

Our study identified a variety of CNS symptoms with neck stiffness being the most common at 33.3%, followed by headache and photophobia. This symptomatology aligns with the findings from Bandyopadhyay B et al.[9]and Sneha Kamble and Bellara Raghvendra et al.[10], though with some variations in the reported statistical significance.

In our analysis of acute encephalitis syndrome (AES) in children, the presence of altered sensorium and loose stools stood out as the most common clinical features, which points to the often severe and rapidly evolving nature of AES. This observation closely aligns with the findings of Saumyen De and Sanjana Samanta.[6], who also noted a broad spectrum of symptoms in their cohort, underscoring the unpredictable clinical presentations associated with AES.

Our study delved into the laboratory parameters affected by AES, identifying abnormalities in total leukocyte count as the most frequently observed lab anomaly.

This finding stands in contrast to the results from Roland Alcaraz A et al.[11], where anemia and thrombocytopenia were more commonly reported.

Regarding microbiological investigations in AES, our findings indicated a high rate of negative blood cultures, with 76.2% of samples showing no growth. This result is consistent with patterns observed in similar studies, which frequently report negative blood cultures in AES cases.

Liver function tests (LFTs) within our study cohort did not reveal significant abnormalities, aligning with observations made by Bandyopadhyay B et al.9, who also reported normal LFT results in their AES patient group. This consistency across studies suggests that liver function is generally not compromised in AES, unlike other severe infections or systemic illnesses. The lack of significant LFT alterations in AES could potentially assist clinicians in differentiating AES from other hepatic or systemic conditions that also present with encephalopathy but include marked liver enzyme elevations. This information could be crucial in streamlining the diagnostic process and focusing medical attention on the neurological aspects of the disease, rather than hepatic involvement.

In our study, elevated creatinine levels were observed in 28.9% of the cases, indicating potential kidney involvement. This result underscores the necessity of vigilant renal function monitoring in patients diagnosed with Acute Encephalitis Syndrome (AES). Similar frequencies of kidney involvement have been noted in other regional studies, highlighting a consistent pattern across different demographics and environments. This recurring finding suggests that kidney impairment may be a common complication or concurrent condition in AES, possibly due to the systemic stress and metabolic demands that the disease places on the body.

Our findings from cerebrospinal fluid (CSF) analysis, which revealed significant variations in CSF cell count and protein levels, align well with existing literature on the diagnostic processes for AES. These results highlight the critical diagnostic value of CSF analysis in confirming cases of AES. By comparing these findings with historical data, we reinforce the reliability of CSF tests as fundamental components of the diagnostic algorithm for AES. Elevated cell counts and protein levels in CSF are indicative of an inflammatory response within the central nervous system, which is characteristic of encephalitic conditions.

The detection of positive Ziehl-Neelsen (ZN) staining in 28.6% of our AES cases points to the involvement of a specific pathogen that can be identified through this staining technique. This rate of positivity correlates with other regional studies, suggesting that ZN staining is a valuable tool for identifying mycobacterial or certain other bacterial infections within the CSF of AES patients. The implication of finding such a significant percentage of positive ZN stains is twofold: it not only assists in pinpointing the etiological agent but also aids in tailoring antibiotic therapy more effectively.

Our study identified a positive rate of 21.4% for CSF Gram staining, indicating bacterial involvement in a subset of AES cases. This finding is consistent with the results reported by Kakoti et al.[5], where a similar prevalence of bacterial pathogens was identified through Gram staining.

The EEG findings from our study revealed a high prevalence of generalized slow waves, which are characteristic of encephalopathy associated with AES. These results are in agreement with those reported by Sneha Kamble and Bellara Raghvendra et al.[10], reinforcing the utility of EEG in the diagnosis and management of AES. The presence of generalized slow waves in EEG recordings serves as a crucial indicator of brain dysfunction, which can

guide clinicians in both confirming the diagnosis and monitoring the progression of the disease.

In our study, the outcome distribution revealed a significant proportion of normal recoveries and some instances of sequelae, mirroring the complex and varied nature of Acute Encephalitis Syndrome (AES) as similarly demonstrated in the work by Roland Alcaraz A et al.[11] and Shrivastava P et al.[8] These findings underscore the intricate dynamics of AES recovery, where patient outcomes can range widely from complete recovery to long-term health complications.

The substantial utilization of mechanical ventilation in our study underscores the severity of some cases of AES, corroborating findings from other research, such as the studies conducted by Saumyen De and Sanjana Samanta.[6], which reported high rates of severe outcomes. This significant reliance on mechanical support highlights the critical condition of many AES patients upon admission and the intensive care required to manage their symptoms. The high incidence of severe cases necessitating mechanical ventilation also points to the potential for severe respiratory compromise in AES, necessitating advanced respiratory support mechanisms in treatment protocols. This aspect of care is vital for sustaining life in critically ill patients and points to the need for well-equipped facilities and trained personnel to manage severe manifestations of AES effectively.

Our research identified a diverse range of complications associated with AES, with recurrent seizures and respiratory issues being the most prevalent. This finding is consistent with the observations made by Deuri A et al.[7], who also highlighted the multisystem impact of AES on affected individuals.

Our detailed analysis of clinical and laboratory parameters in AES cases revealed significant variances in clinical presentations and laboratory findings, aligning with the results observed in the study by Bandyopadhyay B et al.[9] These variances highlight the heterogeneous nature of AES, with symptoms and lab results varying widely among patients.

CONCLUSION

Fever is confirmed as a hallmark symptom of AES, present in 100% of the cases. A substantial majority of children with AES experienced seizures, underscoring their significance as a clinical symptom. Altered sensorium was prevalent in a significant majority, highlighting its importance as an indicator of neurological involvement. Cranial nerve involvement, though less common, was significantly associated with AES, indicating its role in more severe cases. CNS findings varied, with neck stiffness being the most common, but showed no significant overall pattern, suggesting randomness in their distribution. Clinical features varied widely, with altered sensorium and loose stools being most frequent, highlighting the diversity in AES symptomatology. Outcome data indicated a majority had normal recovery, but there was also a significant rate of sequelae and mortality, stressing the need for effective management strategies. A notable proportion of AES patients required mechanical ventilation, highlighting the severity and critical nature of the condition. Complications were diverse, with seizures, respiratory issues, and multi-organ failure being the most common, showing the multi-system impact of AES.

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