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Acute Encephalitis Syndrome- Clinicoetiological Presentation and Survival in Non-Japanese Encephalitis Patients

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Abstract

Acute Encephalitis Syndrome (AES) is a complex neurological condition characterized by brain inflammation, presenting a significant challenge in diagnosis and management due to its diverse etiology and high mortality rates.

This prospective study aimed to comprehensively investigate the clinical features, etiological spectrum, and survival outcomes of AES in adult patients in a Western Indian population. Over a period of 1 year and 6 months, 60 adult patients with Non-Japanese AES were enrolled in this open-labeled, prospective study conducted at a tertiary care center. Detailed clinical data, including demographic information, clinical manifestations, and outcomes, were meticulously collected using standardized protocols. Cerebrospinal fluid (CSF) samples were systematically analyzed for the identification of etiological agents utilizing polymerase chain reaction (PCR) and other laboratory tests.

The study unveiled a diverse range of etiological factors contributing to AES. Among the diagnosed infective cases, Scrub Typhus Encephalitis emerged as the predominant etiology, with a substantial proportion of patients also presenting with Epstein Barr Encephalitis, Parvo Virus Encephalitis, and Dengue virus encephalitis. Furthermore, a subset of patients exhibited undiagnosed infective etiology, non-infective etiology, and unknown causes, underscoring the complexity of AES etiology in this population.

Clinical manifestations of AES varied, with fever, altered sensorium, irritability, and abnormal behavior being the most prevalent features observed. The study reported a notable case fatality rate of 41.7%, highlighting the urgent need for enhanced diagnostic tests and evidence-based management strategies to

improve outcomes for AES patients. The findings emphasize the critical importance of developing tailored diagnostic tools and management protocols to mitigate the morbidity and mortality associated with AES in this region.

This study provides valuable insights into the intricate clinical and etiological landscape of AES in a Western Indian population, emphasizing the pressing need for refined diagnostic approaches and optimized management strategies. Further research endeavors are warranted to deepen our understanding of AES pathogenesis and to advance personalized diagnostic and therapeutic interventions tailored to the specific characteristics of this population.

Keywords: Acute Encephalitis Syndrome, Clinical Features, Etiology, Case Fatality Rate, Cerebrospinal Fluid Analysis, Polymerase Chain Reaction.

Introduction

Acute Encephalitis Syndrome (AES) is a severe neurological condition characterized by inflammation of the brain. The etiology of AES is diverse, encompassing viral, bacterial, and non-infectious causes. The clinical presentation of AES varies widely, making diagnosis and management challenging. AES is associated with high morbidity and mortality rates, particularly in resource-limited settings. Understanding the clinical features, etiological agents, and survival outcomes in patients with AES is crucial for improving diagnostic and management strategies. This prospective study aimed to address these gaps by conducting a comprehensive investigation of AES in adult patients.

Methods

This open-labeled, prospective study was conducted at a tertiary care center over a period of 1 year and 6 months. A total of 60 adult patients with Non-Japanese AES were included in the study. Clinical data, including demographic information, clinical features, and outcomes, were collected using standardized protocols. CSF samples were collected from all patients and analyzed for the identification of etiological agents using polymerase chain reaction (PCR) and other laboratory tests. The clinical and laboratory data were analyzed to determine the etiological spectrum, clinical features, and survival outcomes in patients with AES.

Results

Clinical Features: Clinical signs and symptoms with which the patients presented to the tertiary care hospital is depicted in Table no 1. Fever, altered sensorium, irritability, abnormal behaviour, headache were most common clinical findings observed in the patients. All the 60(100%) patients had fever. Altered sensorium was seen in 43(71.6%) patients followed by irritability in 42(70%), behavioural abnormality in 28(46.6%), headache in 27(45%), seizures in 20(33.3%) and focal neurological deficit and vomiting in 15(25%) cases.

Table 1: Clinical Features Seen Among Study Population (N=60)

Clinical Features	Number Of Patients	Percentage
Fever>39c	60	100 %
Altered Sensorium	43	71.6%
Irritability	42	70%
Behavioural Abnormality	28	46.6%
Headache	27	45%
Seizure	20	33.3%
Focal Neurological Deficit	15	25%
Vomiting	15	25%
Loose Motion	12	20%
Jaundice	9	15%
Swelling Over Body	8	13.3%
Psycosis	2	3.4%

General Examination

The table no. 2 shows the most common findings during the general examination of the patients in the study population. Pallor, Tachycardia and tachypnea were the most common findings observed. Pallor was seen in 40(66.7%) patients followed by tachycardia in 36(60%) patients, tachypnea in 18(30%) patients, and hypertension in 13(21.7%) patients.

Table 2: Findings During General Examination of Study Population (N=60)

General Examination Findings	No. of Patients	Percentage
Pallor	40	66.7%
Tachycardia	36	60%
Tachypnea	18	30%
Hypertension	13	21.7%
Icterus	9	15%

CNS Examination

Table no 3. shows the findings observed during the central nervous system (CNS) examination. Low Glass Glow Coma scale, hypotonia and abnormal movements were the most common findings. Glass Glow Coma scale less than equal to 7 was seen in 34(56.7%) patients out of 60. Hypotonia was in 20(33.3%) patients and abnormal movements was seen in 11(18.3%) patients.

Table 3: Findings During CNS Examination of the Study Population (N=60)

CNS Examination Findings	No. of Patients	Percentage
Gcs<=7	34	56.7%
Hypotonia	20	33.3%
Abnormal Movement	11	18.3%
Neck Rigidity	4	8.3%
Hypertonia	3	5%
Planter Extension	3	5%

Etiology

Table no.4 represents the distribution of the study population according to the etiological findings.

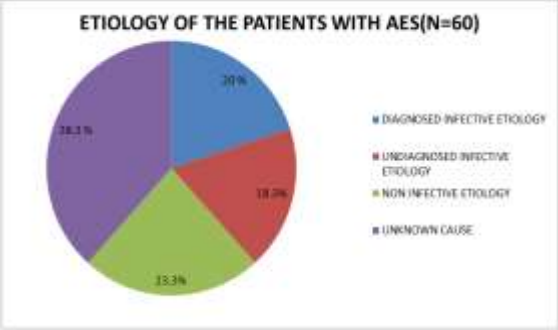
1. From all patients with AES, definitive diagnosis (using bacterial and fungal culture, scrub typhus ELISA and multiplex PCR for virus, real time PCR for dengue virus) could be made in 12 cases and these cases were called Diagnosed Infective Etiology cases.
2. In 11 patients with CSF R/M suggestive of bacterial/viral infection, causative organism for AES was identified but it could not be identified in 11 patients with CSF R/M suggestive of infective etiology, and they were termed as Undiagnosed Infective Etiology cases.
3. 1.66% 98.33% real time PCR for detection of dengue virus (n=60) patients positive for dengue negative 128. Rest 38 patients out of 60 had normal CSF R/M findings.
4. One of the 38 cases with normal CSF R/M had diagnosed infective etiology ie dengue virus encephalitis.
5. Presence of underlying diseases or systemic illness which may lead to encephalitis were observed in 38 patients out of 60 with normal CSF findings.
6. In 14 patients out of 38 with normal CSF findings, underlying diseases and systemic illness including hepatic encephalitis, acute kidney injury, chronic renal failure, electrolyte imbalance, diabetic ketoacidosis, autoimmune diseases and others were found to cause AES, hence these were labelled as Non Infective Etiology cases.
7. Also, in 23 patients out of 38 with normal CSF findings, there was no other systemic illness or underlying disease, all tests done in this study were

negative hence, the etiology remained unknown and were named as Unknown Etiology cases.

Table 4: Etiology among the Study Population Suffering from AES (N=60)

Etiology	No. Of Patients	Percentage
Diagnosed Infective Etiology	12	20%
Undiagnosed Infective Etiology	11	18.3%
Non Infective Etiology	14	23.3%
Unknown Cause	23	38.3%

Graph 1:



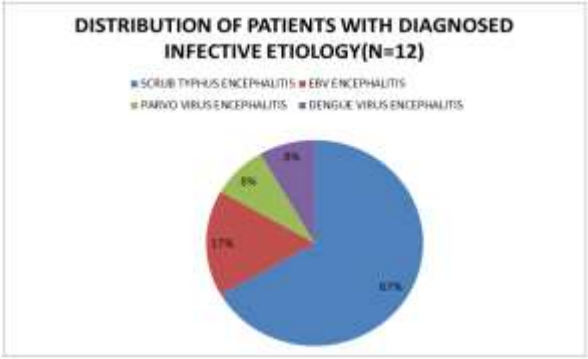
Etiology among Diagnosed Infective Cases

Table no. 5 shows the distribution of study population with diagnosed infective etiology. Among 12 patients in above category, Scrub Typhus Encephalitis was diagnosed in 8(66.6%) patients using serum sample, Epstein Barr Encephalitis was seen in 2(16.6%) patients and Parvo Virus Encephalitis was seen in 1(8.3%) patient using CSF sample. Also, Dengue virus encephalitis was observed in 1(8.3%) using serum sample.

Table 5: Distribution of Study Population with Diagnosed Infective Etiology (N=12)

Etiology Among Diagnosed Infective Cases	No. Of Patients	Percentage
Scrub Typhus Encephalitis	8	66.66%
EBV Encephalitis	2	16.66%
Parvo Virus Encephalitis	1	8.33%
Dengue Virus Encephalitis	1	8.33%

Graph 2:



Association between CSF- R/M Examination with Etiology

Table no 6 to 8 represents the association of CSF R/M examination findings with the Scrub Typhus IgM ELISA findings and Multiplex PCR results of the patients and real time PCR for dengue virus results with AES. In 22 patients out of 60 CSF R/M was s/o infective etiology and 38 patients had normal CSF R/M finding. Table no 6. Shows association between CSF- R/M examination s/o bacterial infection with etiological findings. Out of 22 cases s/o infective etiology, 17 CSF samples were suggestive of bacterial infection. Out of these 17 cases, 8(47.1%) were diagnosed as Scrub typhus encephalitis. None of the Scrub Typhus encephalitis patients had normal CSF. This difference was statistically significant (p value=0.001).

Graphical Representation of Diagnosis According to Etiology

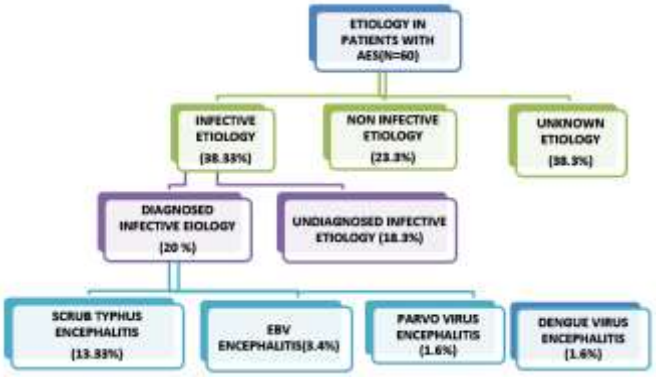


Table 6: Association between CSF- R/M Examination S/O Bacterial Infection with Etiological Finiding

Diagnosis	CSF- R/M Examination Bacterial infection (N=17)		P-value
	No	%	
Scrub typhus encephalitis	08	47.1	0.01*
Unknown bacterial infection	09	52.9	NS

Association Between CSF- R/M Examination S/O Viral Infection with Etiological Finding

Table no 7. shows the association between CSF- R/M examination s/o viral infection with etiological findings. Out of 22 cases s/o infective etiology, 5 CSF samples were suggestive of viral infection. Out of these 5 cases, 2 cases were diagnosed with EBV Encephalitis and 1 case was diagnosed with Parvo Virus Encephalitis but difference was not statistically significant.

Table 7: Association between CSF- R/M Examination S/O Viral Infection with Etiological Finiding

Diagnosis	CSF- R/M EXAMINATION Viral infection (N=05)		P-Value
	No	%	
EBV encephalitis	02	40.0	NS
Parvo virus encephalitis	01	20.0	NS
Unknown viral infection	02	40.0	NS

Association between CSF- R/M Examination S/O Normal CSF Report with Etiological Finding

Table no 8. Shows the Association between CSF- R/M examination with normal CSF report with etiological findings. Out of 38 patients with normal CSF findings, 1 patient was diagnosed as dengue virus encephalitis while 14 patients had non infective etiology and 23 patients had unknown etiology. In the patients with normal CSF R/M, 60.5% cases had unknown etiology, 36.8% had non infective etiology and 2.65% had dengue virus encephalitis.

Table 8: Association Between CSF- R/M Examination S/O Normal CSF Report with Etiological Finding

Diagnosis	CSF- R/M Examination Normal (N=38)		P Value
	Number	Percentage	
Dengue Virus Encephalitis	1	2.6%	NS
Non Infective Etiology	14	36.8%	NS
Unknown Etiology	23	60.5%	

Outcome

Table no 9. shows the outcome of the disease among the study population. The case fatality rate of AES observed in the study was 41.7% i.e. 25 among 60 patients died and only 35(58.3%) patients survived.

Table 9: Outcome among The Study Population Suffering from AES (N=60)

Outcome	Number Of Patients	Percentage
Survived	35	58.3%
Death	25	41.7%

Association between Diagnoses with Outcome

Table no 10 and 11 shows the association between diagnosis of the patient and the outcome.

1. Maximum patients who died had unknown etiology which implies an urgent need to implement additional pathogen testing by Molecular methods.
2. Also, 62.5% of Scrub typhus encephalitis cases died which was alarming but not statistically significant and this could be prevented by specific and timely diagnosis and treatment.
3. None of the patient with Parvovirus encephalitis and dengue virus encephalitis had fatal outcome.
4. Both the patients with EBV Encephalitis died owning to 100% mortality, but due to less number of patients with viral encephalitis it was not statistically significant.
5. 18.9% of patients with undiagnosed Infective etiology died which were significantly less than 81.8% who survived (p value=0.01) which implies that patients with infective etiology can have good outcome, also diagnosis and specific treatment can help in decreasing mortality and morbidity.

Table 10: Diagnosis with Outcome

Diagnosis	Total No. of Cases	No. of Cases Survived	No of Cases Died
Scrub typhus encephalitis	08	03	05
EBV encephalitis	02	00	02
Parvovirus encephalitis	01	01	00
Dengue virus encephalitis	01	01	00
Undiagnosed infective etiology	11	09	02
Non infective cause	14	06	08
Unknown cause	23	14	09

Table 11: Association between Diagnosis with Outcome

Diagnosis	No.	Outcome				P Value
		Survived		Death		
		No	%	No	%	
Scrub typhus encephalitis	08	03	37.5	05	62.5	NS
EBV encephalitis (viral)	02	-	-	02	100.0	NS
Parvovirus encephalitis (viral)	01	01	100.0	-	-	NS
Dengue virus encephalitis(viral)	01	01	100.0	-	-	NS
Undiagnosed Infective etiology	11	*09	81.8	02	18.2	0.024
Non infective etiology	14	06	42.9	08	57.1	NS
Unknown	23	14	60.8	09	39.1	NS

Graph 3:

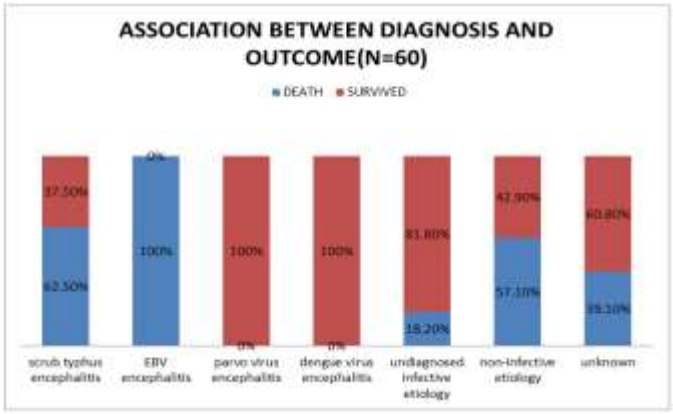
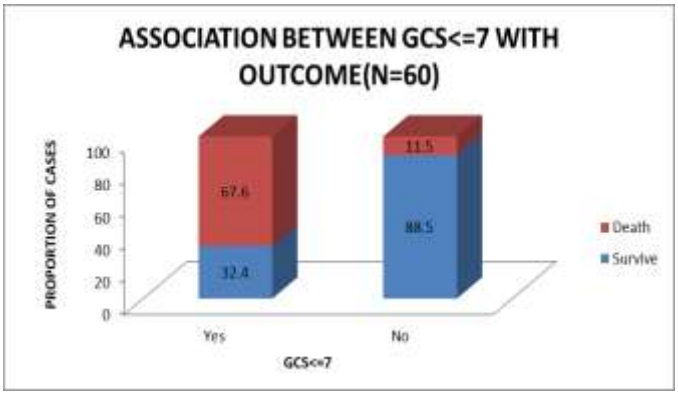


Table 12: Association Between Gcs<=7 With Outcome

GCS<=7	Outcome				P Value
	Survived		Death		
	No	%	No	%	
Yes(N=34)	11	32.4	23	67.6	*0.001
No(N=26)	23	88.5	03	11.5	

Graph 4:



Association between Gcs<=7 With Outcome

Table no. 12. depicts the association between GCS <= 7 and outcome. The below table states that 67.6% of cases with GCS<=7 died which was significantly more as compared to 32.4% of the cases with GCS<=7 who Survived.

Conclusion

The study concluded that AES presents a diagnostic and management challenge due to its diverse etiology and high case fatality rate. The findings underscore the urgent need for improved diagnostic tests and evidence-based management algorithms for AES. The lack of published data from western India regarding AES etiology emphasizes the need for further research and understanding of the disease. The study provides valuable insights into the clinical and etiological aspects of AES, highlighting the urgent need for improved diagnostic and management strategies.

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