

Original Research Article

# Predictors of Outcome in Children with Acute Encephalitis Syndrome: A Prospective Study

**Authors: Dr. Ankita Marathe<sup>1</sup> (Postgraduate Resident), Dr. Prachi Goyal<sup>2</sup> (Assistant Professor) & Dr. Nirbhay Mehta<sup>3</sup> (Professor)**

Department of Paediatrics, Mahatma Gandhi Memorial Medical College and Maharaja Yeshwantrao Hospital, Indore, Madhya Pradesh, India<sup>1,2&3</sup>

Corresponding Author: Dr. Prachi Goyal

## ABSTRACT

**Background:** Acute encephalitis syndrome (AES) is an important cause of mortality and morbidity in children. We undertook this study for better understanding of predictors of outcome in terms of neurological sequelae in children with AES.

**Methods:** It was a prospective observational study. We studied 100 patients of AES admitted in PICU of Maharaja Yeshwantrao Hospital Indore from June 2021 to July 2022. WHO case definition of AES was adopted while enrolling cases. All the demographic details, clinical characteristics and laboratory parameters were noted in a predesigned proforma. We evaluated their clinical characteristics, laboratory features and outcomes at the time of discharge. Modified Rankin Scale was used to assess the neurological disability at the time of discharge. Outcomes were assigned score between 0 and 6. The outcome was correlated with above mentioned variables.

**Results:** Out of 100 patients, 54/100(54%) patient high mRS score of 5 and 6 (poor outcome) 12/100(12%) of the patients had score of 3-4 and 34/100(34%) patients had mRS score of 0-2 (good outcome). Low GCS at admission, shock and inotrope requirement and need of mechanical ventilation were significantly associated with high mRS and poor outcome. Deranged Biochemical parameters like blood glucose abnormalities, deranged liver enzymes and deranged electrolytes were associated with high mRS and poor outcome.

**Conclusions:** This study explains correlation of clinical presentation, laboratory parameters and therapeutic intervention required with neurological outcome of AES. Low Glasgow coma score, deranged biochemical parameters, Shock and inotrope requirement and need of mechanical ventilation are predictors of a poor outcome.

**Keywords:** AES, Glasgow coma scale, Modified Rankin scale

## 1. INTRODUCTION

Acute encephalitis syndrome (AES) refers to a clinical syndrome characterized by the acute onset of fever along with changes in mental status (disorientation, delirium, confusion, and coma) and/or new onset of seizures (excluding simple febrile seizures).<sup>(1)</sup> AES is characterized by high case fatality rate, occurring in seasonal outbreaks every year, taking heavy toll of human life mostly affecting children below 15 years of age.<sup>(2)</sup> The presentation being acute with a rapidly deteriorating clinical course is leading cause of death within few hours. Those who survive may have long lasting disability affecting quality of life. The Modified Rankin Scale is used to measure the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability. The Modified Rankin Score (mRS) is a 6 point disability scale with possible scores ranging from 0 to 5. A separate category of 6 is added for death<sup>(3,4)</sup>. This study is done for a better understanding and to determine the clinical profile and neurological outcome of AES in hospitalized children.

## 2. MATERIALS AND METHODS

### Study Setting

The present study was conducted in pediatric intensive care unit of Department of Pediatrics of Maharaja Yeshwantrao Hospital Indore, Madhya Pradesh.

### Study Period

The study was conducted for a period of one year from June 2021 to July 2022 in the Department of Paediatrics, Maharaja Yeshwantrao Hospital Indore, Madhya Pradesh

### Study Design

A prospective observational study

### Study population

The children of 1 month to 14 years of age clinically diagnosed with acute encephalitis syndrome as per WHO definition, admitted in Pediatric Intensive Care unit (PICU) , Maharaja Yeshwantrao Hospital , Indore, Madhya Pradesh were included in the study.

### Study Sample

Study sample size is calculated using formula

$$N=4PQ/d^2$$

Where P is prevalence, Q = 100-Prevalance, d is allowable error.

100 cases were enrolled in the study.

### Inclusion Criteria

All pediatric patients admitted in PICU of MY Hospital, Indore clinically diagnosed with AES.

### Exclusion criteria

1 Patients diagnosed with pre-existing CNS conditions like cerebral palsy and Inborn error of metabolism

2 Children admitted with past history of simple febrile seizure.

### Methodology

Children aged 1 month to 14 years admitted in PICU meeting inclusion criteria were included in the study after taking informed consent.

On admission, basic patient details such as age, gender, socioeconomic status, address and duration of illness were entered in a predesigned proforma . All the enrolled cases were clinically examined on the day of admission. These patients were investigated and treated as

per unit protocol. All the investigations and treatment details were entered in the proforma. The final outcome in form of discharge or death was noted in the proforma. Patients with neurological disability were given score according to Modified Rankin Scale between 0 to 5. Death was given score of 6.<sup>(3)</sup>

Score	Description
0	No symptoms at all
1	No significant disabilities despite symptoms in clinical examination; age appropriate behaviour and further development
2	Slight disability; unable to carry out all previous activities, but same independence as other age- and sex-matched children (no reduction of levels on the gross motor function scale )
3	Moderate disability; requiring some help, but able to walk without assistance; in younger patients adequate motor development despite mild functional impairment (reduction of one level on the gross motor function scale)
4	Moderately severe disability; unable to walk without assistance; in younger patients reduction of at least 2 levels on the gross motor function scale
5	Severe disability; bedridden, requiring constant nursing care and attention
6	Dead

### Statistical Analysis

All statistical analysis were performed with the use of Statistical Package for Social Sciences (SPSS) software, IBM SPSS - version 20. Chi-square tests were performed to test for differences in proportions of categorical variables. *P* values of less than 0.05 were considered as statistically to be significant.

### 3. RESULTS

In this study, 100 patients clinically diagnosed with AES (according to WHO case definition) were enrolled. Table 1 depicts the demographic profile of the AES patients. The majority of patients were of age between 1 year to 5years (55%) and 26(26%) patients were in the age group above 5 years. The patients aged less than 1 year were 19(19%). Out of 100 patients, 57 were male and 43 were female. No significant preponderance was noted according to the area of residence .51(51%) patients were from Urban Areas and 49(49%) were from Rural Areas.

Table 1: Demographic Profile of AES Patients

Variables	Frequency(n)	Percent(%)
Age < 1year	19	19
1-5 years	55	55
> 5 years	26	26
Sex Male	57	57
Female	43	43
Area Urban	51	51
Rural	49	49

Clinical profile of the patients are summarized in table 2. 100% of the patients had fever at presentation. 86 (86%) of the patients had fever of duration more than 24 hours and 14(14%) of the patients had fever of less than 24 hours duration.61% of the patient presented with status epilepticus. Headache and vomiting were among the clinical symptoms in 12 and 36 patients respectively. Impaired level of consciousness( GCS<8) at presentation was found in 52 patients(52%). 48(48%) patients had GCS>8 at presentation. About 59(59%) patients had shock requiring inotrope support during the hospital stay.

Table 2: Clinical Characteristics of patients with AES

Clinical Features	Number(n=100)	Percent
Duration of fever <24 hours	14	14
>24 hours	86	86
Status Epilepticus	61	61
Vomiting	36	36
Headache	12	12
GCS* <8	52	52
>8	48	48
Shock	59	59

Table 3 depicts the outcome of patients with AES at the time of discharge or death. Modified Rankin Scale score was assigned to each patient on the basis of physical dependence at the time of discharge. Out of 100 patients, 54 (54%) patient had score of 5-6.12(12%) patients had disability score of 3-4 and 34 (34%) of the patient had good outcome with score of 0-2.

Table 3 Outcome According to Modified Rankin scale

Score	Number	Percent(%)
0-2	34	34
3-4	12	12
5-6	54	54

Table 4 depicts correlation between various parameters and outcome according to mRS score. Fever was present as a chief complaint in 100% of the cases. 14 (14%) of the patients had duration of less than 24 hours and 86(86%) patients had fever of more than 24 hours. No statistically significant correlation was found between duration of fever and final outcome in patients with AES. 61 out of 100 patients presented with status epilepticus. 30 patients had mRS 5-6, 8 patients had mRS 3-4 and 23 had mRS 0-2 (good outcome). Low GCS (<8) was found in 52 patients, 47 of which had high mRS and poor outcome. GCS (>8) was found in 48 patients. 33 patients had mRS 0-2 and good outcome (p value=0.00). Shock requiring inotrope support was present in 59 patients. 54 patients had poor outcome with mRS 5-6 (p value=0.00). Mechanical ventilation was required in 60 (60%) patients. 54 patients out of 60 had poor outcome with mRS 5-6(p value=0.00). Blood glucose abnormalities were found in 37 patients. 30 patients out of 37 had high mRS 5-6 and poor outcome (p value =0.26). Deranged biochemical parameters like liver enzymes and serum electrolytes were associated with high mRS and poor outcome (p value 0.00 and 0.01 respectively). CSF analysis was done in 68 patients. CSF pleocytosis was found in 42 patients, 23 out of which had high mRS. No significant association was found between CSF analysis and final outcome. Neuroimaging was done in 32 patients out of 100 cases enrolled during the study. 21 patients had abnormal findings in neuroimaging. 13 patients had high mRS of 5-6, 4 patients had mRS 3-4 and 4 patients had mRS 0-2.

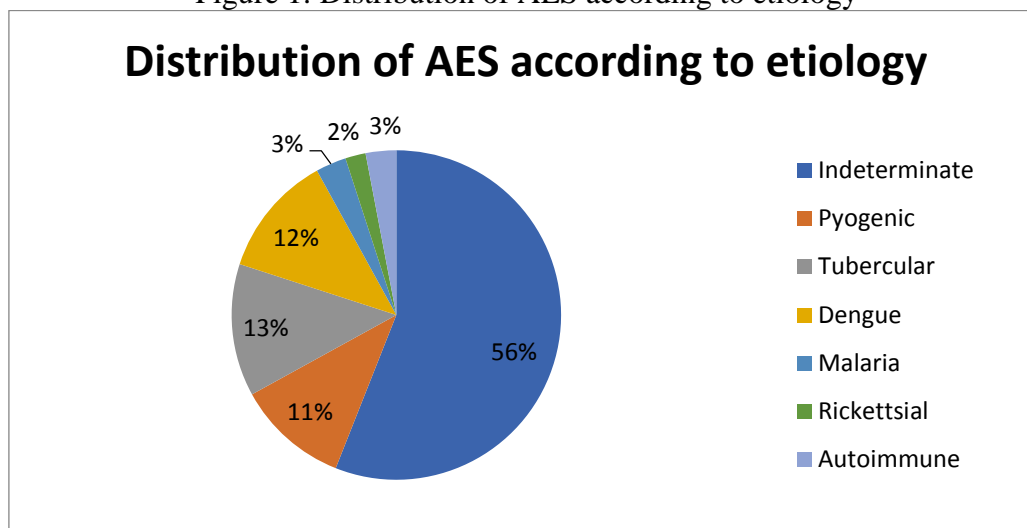
Table 4 correlation between variables and outcome according to mRS

Variable	mRS 0-2	mRS 3-4	mRS 5-6	P- value
Duration of fever				
<24 hours	06	01	07	0.28 Not significant
>24 hours	28	11	47	
Status Epilepticus (n=61)	23	08	30	0.06 not significant
GCS <8	01	04	47	0.000 significant
>8	33	08	07	
Inotrope Required	01	04	54	0.000 significant
Not Required	33	08	00	
Mechanical Ventilation				
Not Required	32	08	00	0.000 significant
Required	02	04	54	
Rbs <60mg/dl	02	01	08	0.026 significant
60-150	30	09	24	
>150	02	02	22	
TLC <4000	02	03	08	0.06 not significant
4000-11000	26	06	33	
>11000	06	03	13	
Normal Platelet	29	08	20	0.07 Not
Thrombocytopenia(<	05	04	34	

1.5 lac)				significant
Liver Enzymes				0.000
Normal	33	11	32	significant
Deranged	01	01	22	
Serum Electrolytes				0.01 significant
Normal	28	09	29	
Deranged	06	03	25	
CSF				
Pleocytosis(n=68)	12	07	23	0.06 not significant
Neuroimaging (n=32)				
Normal(n=11)	08	01	02	0.07 not significant
Abnormal(n=21)	04	04	13	

Figure 1 depicts distribution of AES according to etiology. Out of 100 cases, 56 (56%) cases had indeterminate etiology . 11 (11%) cases of pyogenic meningitis and 13 (13%) case of Tubercular meningoencephalitis. Besides this 12(12%) cases were dengue encephalitis, 3(3%) cases of cerebral malaria , 3(3%) autoimmune encephalitis and 02 cases of Rickettsial etiology.

Figure 1: Distribution of AES according to etiology



#### 4. DISCUSSION

The study included 100 patients clinically diagnosed with AES admitted in Pediatric Intensive Care Unit of Maharaja Yeshwantrao hospital, Indore. We have analyzed the clinical profile and factors determining the outcome in AES patients.

The modified Rankin Scale (mRS) was used to measure the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability.<sup>(5)</sup>

In the present study, Modified Rankin Scale Score was used to determine neurological outcome of the patients with AES. The patients were assessed at the time of discharge or death. Outcomes have been assigned score of 0 to 6. Score 0-2 denote good outcome, 3 and 4 moderate outcome and 5 and 6 is suggestive of poor outcome. Most of the patients were 1 to 5 years of age (55%). This tallies with findings of Sambasivam et al (50%) and Karmakar et al 45.7%<sup>[6,7]</sup>. The least number of cases that is, in the age group of 1 month to less than 1 year constituted 9.26% of the total cases. This finding closely resembles the finding of Kakoti et al (2.98%)<sup>[8]</sup>. Age group between 5 and 14 years were found to be affected mostly in the studies conducted by Verma et al (92.85%)<sup>(53)</sup>, Yashodhara et al<sup>(9)</sup> (73.3%), Kakoti et al<sup>(8)</sup> (65.66%) Khinchi et al (50.8%). In the present study, 57 cases were male and 43 were female. Out of 100 patients, 54(54%) of the patient had poor outcome with mRS score of 5 and 6. 34(34%) patients had good outcome mRS score of 0-2 and 12(12%) of the patients had score of 3-4. 86% of the patients had fever duration of more than 24 hours. 61% patients presented with status epilepticus. 52% patients had GCS <8 on admission. 59% patient had shock and inotrope requirement. One retrospective study by Ooi et al concludes that low perfusion; GCS score below 8, and convulsions were associated with poor prognosis.<sup>(10)</sup> Another study done by Adhikari et al in 2020 also concluded that need of mechanical ventilation, lower GCS score, and concurrent seizures are predictors for a poor outcome in these patients.<sup>(11)</sup>

56 (56%) cases had indeterminate etiology. 11 (11%) cases of pyogenic meningitis and 13 (13%) case of Tubercular meningoencephalitis. Besides this 12(12%) cases were dengue encephalitis, 3 (3%) cases of cerebral malaria and autoimmune encephalitis and 02 cases of Rickettsia etiology. In our study, 54% patients had high mRS score and poor outcome, 12 % had neurological sequelae with mRS 3 -4. 34% patients got discharged without any neurodisability.

In the study, we observed that neuroimaging was done in 32 patients. 21 of them had abnormal findings and 11 had normal findings.

11 patients had normal neuroimaging studies, 8 amongst those had score of 0-2 and good outcome, 1 patient had mRS 3-4 and 4 had poor outcome with mRS 5-6. MRI abnormality was found in 21 patients. 4 patients had features of leptomenigeal and basal cisternal enhancement with periventricular infarcts and ventriculomegaly along with hydrocephalus suggestive of tubercular-meningo encephalitis. 2 patients were discharged having mRS 3-4 and residual neurological sequel. 15 patients had hyperintensities and restricted diffusion in T2W scan. 3 patients had findings suggestive of intraparenchymal haemorrhage. These patients had poor outcome with mRS 5-6.

Low GCS at admission, shock and inotrope requirement and need of mechanical ventilation was strongly associated with high mRS and poor outcome. Deranged Biochemical parameters like blood glucose abnormalities, deranged liver enzymes and deranged electrolytes are associated with high mRS and poor outcome.

## 5. CONCLUSION

We conclude that most common affected group in AES is between 1 year to 5 years of age. Low GCS at admission, shock and inotrope requirement and need of mechanical ventilation are predictors of poor outcome and high mortality. Deranged blood glucose level, liver functions and serum electrolytes are also associated with poor outcome. In our study, etiology was undetermined in majority of cases. Early diagnosis and treatment of AES patients and

attempts to detect exact etiology could improve their outcomes. The findings of our study can help to identify and predict outcome in children with Acute encephalitis Syndrome on the basis of above mentioned clinical and biochemical laboratory parameters.

#### LIMITATION

1. Due to financial constraints and the non-availability of confirmatory tests like PCR etiology was not confirmed in most of the cases.
2. The long-term outcome with regard to neurological recovery was not studied.

#### Author's Contribution:

**AM** - Interpreted the results; reviewed the literature and manuscript preparation; **NM** - Concept and design of the study, prepared first draft of manuscript; **PG** - Concept, coordination, statistical analysis and interpretation

**Conflicting Interest:** None

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