

## Original Research Article

# A study of the outcome of acute encephalitis syndrome in children

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## ABSTRACT

**Background:** Acute encephalitis syndrome (AES) is defined as a person of any age, at any time of the year, with acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, inability to talk) and/or new onset of seizures (excluding simple febrile seizures) [WHO]. Japanese encephalitis (JE) is one of the leading causes of AES affecting children and adolescents in the tropical countries. Objective of the study were to study the outcome of children with AES. The study was conducted in the department of pediatrics, Gauhati medical college and hospital, Guwahati from 1<sup>st</sup> July 2016 to 30<sup>th</sup> June 2017.

**Methods:** Patients admitted in the pediatrics department of Gauhati medical college and hospital, Guwahati with diagnosis of AES during the study period were taken into account based on inclusion and exclusion criteria.

**Results:** It has been observed that age, awareness among caregivers, poor GCS, multiple seizures, shock are important factors in the outcome of AES.

**Conclusions:** From the present study, prognosis of the cases may be predicted and measures taken to improve outcome

**Keywords:** AES, JE, Outcome

## INTRODUCTION

Acute encephalitis syndrome (AES) is defined as a person of any age, at any time of the year, with acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, inability to talk) and/or new onset of seizures (excluding simple febrile seizures) [WHO]. AES constitutes a group of clinical and neurological manifestations caused by a wide range of viruses, bacteria, fungi, parasites, spirochetes, chemicals and toxins. The common causes of acute viral encephalitis worldwide are JE virus, West Nile virus, Eastern equine encephalitis virus, Western equine encephalitis virus, Venezuelan equine encephalitis virus, Handra virus, enterovirus, Chandipura virus, Nipah virus, dengue virus, Kyasanur forest disease virus, St.

Louis encephalitis virus, herpes simplex virus, polio virus and measles virus.<sup>1</sup> JE is one of the leading causes of AES affecting children and adolescents in the tropical countries.<sup>2</sup> Keeping in mind, the wide range of causal agents and the rapid rate of neurological impairment due to pathogenesis, clinicians face the challenge of a small window period between diagnosis and treatment. A confirmed etiology is generally not required for clinical assessment of AES.

## METHODS

The study was conducted in the department of pediatrics, Gauhati medical college and hospital, Guwahati. Duration of study was 1 year, starting from 1<sup>st</sup> July 2016 to 30<sup>th</sup> June 2017. It was a cross sectional hospital-based study.

**Case definition used (WHO):** Clinically, a case of AES is defined as “a person of any age, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) AND/OR new onset of seizures (excluding simple febrile seizures)”.

**Study population (Sample size):** All the patients admitted in the pediatrics department of Gauhati medical college and hospital, Guwahati with diagnosis of AES during the study period.

#### **Inclusion criteria**

Children from 1 month to 12 years of age admitted in pediatric ward of GMCH with AES were included WHO definition of AES was used.

#### **Exclusion criteria**

Children having other severe infections other than in the CNS-Malignancy, brain infarction or cerebral hemorrhage, diagnosis of delirium or encephalopathy secondary to sepsis, toxins or metabolic causes and patients with pre-existing neurological deficit prior to the onset of the disease (AES) and neonates.

#### **Informed consent**

It was taken from all parents/guardians in a specially designed form for the purpose.

All patients admitted to the department of pediatrics who fulfilled the inclusion criteria were selected and their outcome was evaluated. The various data were gathered and were entered in the specially designed proforma. The data obtained was tabulated and analyzed statistically using the software IBM PASW 21.0 version. The socio-economic status of the patients (that is of the parents/guardians) has been evaluated as per modified B. G. Prasad scale (2016) into lower, lower middle, middle, upper middle and upper classes.

## **RESULTS**

A total of 5119 cases were admitted in the department of pediatrics, Gauhati medical college and hospital out of which 162 cases were AES. This constituted 3.1% of the total admission.

The outcome of the patients with AES who were admitted in the department of pediatrics, Gauhati medical college and hospital during the period from 1<sup>st</sup> July 2016 to 30<sup>th</sup> June 2017 were properly recorded. The outcome of the patients was noted under four headings: Discharge without sequelae, discharge with sequelae, death and leave against medical advice (LAMA).

Table 1 shows the outcome of children with AES. 63 (38.9%) of the patients were discharged without any

sequelae whereas 44 patients were discharged with sequelae, comprising 27.2% of the cases. A total number of 50 patients expired during hospital stay. This constituted 30.9% of the cases. Five cases left the hospital against medical advice without completing treatment. This comprised 3.0% of the cases.

To analyse the significance of various parameters in the outcome of AES cases, 5 cases which left against medical advice were excluded from 162 cases and 157 cases were taken into account.

The correlation between age and outcome of AES is shown in the Table 2. From Table 2, the following observations have been made-(a) In the first age group, out of a total of 14 patients, the maximum number of patients were discharged without sequelae (64.3%), 21.4% were discharged with sequelae and only 14.3% expired, (b) In the second age group, out of total of 64 cases, 43.8% of the patients were discharged without sequelae, 37.5% of the patients died and 18.8 % of the patients were discharged with sequelae and (c) In the third age group out of the total of 79 cases, 32.9% of the cases were discharged without sequelae. The 30.4% of the patients expired. The 36.7% of the patients were discharged with sequelae.

The number of deaths was least in the first age group and maximum number of patients were discharged without sequelae. Therefore, this age group was found to have better outcome compared to the other two age groups. In the above analysis  $p=0.047(<0.05)$  which is significant.

Table 3 shows the correlation of sex with the outcome of AES patients. Among the 105 male patients, 35 expired constituting 33.3% and 41 (39%) were discharged without sequelae. Among the 52 female patients, 15 (28.8%) expired and 22 (42.3%) were discharged without disability. Sex of the patient has no significant relation with the outcome of AES cases since  $p=0.848(>0.05)$ .

Table 4 shows the relation between socioeconomic status and outcome of AES cases. The maximum number of discharges with sequelae (44.4%) was in the lower class followed by middle class (36%). Death was maximum in the upper class (44.4%) followed by lower class (38.9%). So, the outcome of AES varies with socio economic status. Poor socioeconomic classes have poorer prognoses in terms of death and discharge with disability than higher classes but the result is not significant at 5% significance level as the  $p=0.078(>0.05)$ .

Table 5 shows the relation between awareness of the disease and outcome of AES patients. Six out of 32 patients, that is 18.8% cases expired whose parents/guardians had awareness of the disease. Also 19 out of 32, that is 59.4% of this group were discharged without sequelae. But among the cases, whose parents/guardians were not aware of this disease entity, 44 out of 125 expired; comprising 35.2% and 35.2% were

discharged without sequelae. It has been observed that awareness of disease is associated with better outcome (less deaths and more discharge without disability). This association is significant as  $p=0.040$  ( $<0.05$ ).

Table 6 shows the relation between GCS at presentation and outcome. The 41 out of 59 patients whose GCS was less than or equal to 8 died, constituting 69.5%. Among these 59 patients, only 4 could be discharged without sequelae, that is 6.8%. From the 98 patients whose GCS was more than 8, only 9 (9.2%) expired and 59 (60.2%) were discharged without sequelae. Thus, it has been observed that poor GCS on admission is associated with poor outcome, that is more deaths and more disability. This association is significant since  $p=0.0001$  ( $<0.05$ ).

Table 7 shows the relation between seizures and outcome. Out of the 121 patients who had multiple seizures, 39 expired comprising 32.2% and 50 were discharged without sequelae constituting 41.3%. On the other hand, out of the 18 patients, who had single episode of seizure, only 1 (5.6%) expired and 9 (50%) were discharged without any sequelae. So, it was seen that who had multiple episodes of seizure had poor outcome

compared to those who had single episode of seizure. This relation is significant as the  $p=0.026$  ( $<0.05$ ).

Table 8 shows the relation between shock and outcome in AES cases. Out of the 29 patients who presented in shock, 26 expired that is 89.7% and 1 was discharged without sequelae constituting 3.4%. Among 128 patients who were not in shock at the time of admission, 24 (18.8%) died and 62 (48.4%) were discharged without any sequelae. So, it has been observed that shock is associated with poor outcome. This is significant as  $p=0.001$  ( $<0.05$ ).

**Table 1: The outcome of AES patients.**

Outcomes	No.	Percentage (%)
Discharge without sequelae	63	38.9
Discharge with sequelae	44	27.2
Death	50	30.9
Leave against medical advice	05	3.0
Total	162	100

**Table 2: Age group versus outcome in AES.**

Age groups (Years)	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
1 month to less than 1, (n=14)	3	21.4	9	64.3	2	14.3	0.047 ( $<0.05$ )
1 to <5, (n=64)	12	18.8	28	43.8	24	37.5	
5 to 12, (n=79)	29	36.7	26	32.9	24	30.4	
Total	44	28.0	63	40.1	50	31.9	

**Table 3: Sex versus outcome of AES cases.**

Sex	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
Male, (n=105)	29	27.6	41	39.0	35	33.3	0.848 (>0.05)
Female, (n=52)	15	28.8	22	42.3	15	28.8	
Total, (157)	44	28.0	63	40.1	50	31.9	

**Table 4: Socioeconomic status vs outcome of AES cases.**

Socioeconomic status	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
Low class, (n=18)	8	44.4	3	16.7	7	38.9	0.078 (>0.05)
Lower middle class, (n=48)	7	14.6	27	56.3	14	29.2	
Middle class, (n=50)	18	36	19.0	38.0	13	26.0	
Upper middle class, (n=23)	6	26.0	10	43.5	7	30.4	
Upper class, (n=18)	5	27.8	5	27.8	8	44.4	
Total (157)	44	28.0	63	40.1	50	31.9	

**Table 5: Awareness of the disease versus outcome of AES cases.**

Awareness of the disease	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
Present, (n=32)	7	21.9	19	59.4	6	18.8	0.040 ( $<0.05$ )
Absent, (n=125)	37	29.6	44	35.2	44	35.2	
Total (157)	44	28.0	63	40.1	50	31.9	

**Table 6: GCS versus outcome of AES cases.**

GCS	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
Less than or equal to 8, (n=59)	14	23.7	4	6.8	41	69.5	0.0001 ( $<0.05$ )
More than 8, (n=98)	30	30.6	59	60.2	9	9.2	
Total (157)	44	28.0	63	40.1	50	31.9	

**Table 7: Episodes of seizure versus outcome of AES cases.**

Episodes of seizure	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
Multiple, (n=121)	32	26.4	50	41.3	39	32.2	0.026 ( $<0.05$ )
Single, (n=18)	08	44.4	09	50.0	01	5.6	
Total (139)	40	28.8	59	42.4	40	28.8	

**Table 8: Shock versus outcome of AES cases.**

Shock	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
Present (on admission), (n=29)	02	6.9	01	3.4	26	89.7	0.001 ( $<0.05$ )
Absent, (n=128)	42	32.8	62	48.4	24	18.8	
Total (157)	44	28.0	63	40.1	50	31.8	

**Table 9: JE versus outcome of AES cases.**

JE	Outcome						P value
	Discharge with sequelae		Discharge without sequelae		Death		
	No.	%	No.	%	No.	%	
Negative, (n=127)	31	24.4	55	43.3	41	32.3	0.090 (>0.05)
Positive, (n=30)	13	43.3	08	26.7	09	30.0	
Total (157)	44	28.0	63	40.1	50	31.8	

Table 9 shows relation of JE positivity with outcome. Out of 127 JE negative cases, 41 (32.3%) expired and 55 (43.3%) were discharged without sequelae. Out of the 30 JE positive, 9 (30%) expired, 8 (26.7%) were discharged without disability. There is no significant relationship between JE and outcome of AES as  $p=0.090$  ( $>0.05$ ).

## DISCUSSION

It has been observed that most of the cases belonged to five to 12 years of age constituting 49.38% of the AES

cases. This finding tallies with the findings of Verma et al (92.85%), Yashodhara et al (73.3%), Kakoti et al (65.66%) Khinchi et al (50.8%).<sup>3-6</sup> The finding does not tally with the findings of Sambasivam et al (20%) and Karmakar et al (25%).<sup>7</sup> This age group is followed by the 1 to 5 years age group which constituted 41.36%. This tallies with findings of Sambasivam et al (50%) and Karmakar et al 45.7%.<sup>7,8</sup> The least number of cases that is, in the age group of 1month 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>5</sup> This may be attributed to older children being more exposed to

mosquito bites during outdoor activities like playing, school.

In the age group of 1 month to less than 1 year, out of a total of 14 patients, the maximum number of patients were discharged without sequelae (64.3%), 21.4% were discharged with sequelae and only 14.3% expired. In the second age group of 1 year to less than 5 years, out of a total of 64 cases, 43.8% of the patients were discharged without sequelae. The 37.5% of the patients died and 18.8% of the patients were discharged with sequelae. In the third age group of 5 to 12 years, out of the total of 79 cases, 32.9% of the cases were discharged without sequelae, 30.4% of the patients expired. The 36.7% of the patients were discharged with sequelae. The number of deaths was least in the first age group and maximum number of patients were discharged without sequelae. Therefore, this age group was found to have better outcome compared to the other two age groups. In the above analysis the  $p=0.047$  ( $<0.05$ ) which is significant. Similarly, Rayamajhi et al in their study found that older age group of children was associated with bad outcome.<sup>9</sup>

Gogoi et al in their study found that more deaths occurred among the children of higher age group. Song et al found that acute JE at younger age was a marker for unfavorable outcomes (sequelae or fatal). But in our study, younger age of 1 m to less than 1 year was found to be associated with better prognostic outcome.<sup>10,11</sup> Burke et al also did not find any association between age and outcome in AES patients.<sup>12</sup>

Among the 105 male patients, 35 expired constituting 33.3% and 41(39%) were discharged without sequelae. Among the 52 female patients, 15 (28.8%) expired and 22 (42.3%) were discharged without disability. Sex of the patient has no significant relation with the outcome of AES cases since the  $p=0.848$  ( $>0.05$ ). Burke et al also did not find any association between sex and outcome in AES patients.<sup>12</sup>

It has been observed that, the maximum number of discharges with sequelae (44.4%) was in the lower class and followed by middle class (36%). Death was maximum in the upper class (44.4%) followed by lower class (38.9%). So, the outcome of AES varies with socioeconomic status. Poor socioeconomic classes have poorer prognoses in terms of death and discharge with disability than higher classes but the result is not significant at 5% significance level as the  $p=0.078$  ( $>0.05$ ). Baruah et al in their study found poor socio-economic status to be associated with a bad outcome.<sup>13</sup>

Six out of 32 patients, that is 18.8% cases expired whose parents/guardians had awareness of the disease. Also 19 out of 32, that is 59.4% of this group were discharged without sequelae. But among the cases, whose parents/guardians were not aware of this disease entity, 44 out of 125 expired; comprising 35.2% and 35.2% were discharged without sequelae. Therefore, it has been

observed that awareness of the disease is associated with better outcome (less deaths and more discharge without disability). This association is significant as the  $p$  value is 0.040 ( $<0.05$ ). None of the studies reviewed showed any relation between awareness of the disease among the caregivers with the outcome of AES.

It has been observed that 41 out of 59 patients whose GCS was less than or equal to 8 died, constituting 69.5%. Among these 59 patients, only 4 could be discharged without sequelae, that is 6.8%. From the 98 patients whose GCS was more than 8, only 9 (9.2%) expired and 59 (60.2%) were discharged without sequelae. Thus, it has been observed that poor GCS on admission is associated with poor outcome, that is, more deaths and more disability. This association is significant since the  $p=0.0001$  ( $<0.05$ ). This is in concurrence with the findings of De et al who found  $GCS < 8$  to be a factor for poor outcome ( $p=0.0085$ ).<sup>14</sup> Luo et al found in their study that deep coma was associated with a poor outcome. Kumar et al<sup>2</sup> in their study found mortality was significantly related to deep coma, abnormalities in tone and decerebrate posturing.<sup>2,11</sup>

It has been observed that out of the 121 patients who had multiple seizures, 39 expired comprising 32.2 % and 50 were discharged without sequelae constituting 41.3%. On the other hand, out of the 18 patients, who had single episodes of seizure, only 1 (5.6%) expired and 9 (50%) were discharged without any sequelae. So, it was seen that patients who had multiple episodes of seizure had poor outcome compared to those who had single episode of seizure. This relation is significant as the  $p=0.026$  ( $<0.05$ ). This is in conformity with the findings of De et al who found recurrent seizures to be a poor prognostic factor ( $p=0.05$ ).<sup>14</sup>

It has been observed that out of the 29 patients who presented in shock 26 expired that is 89.7% and 1 was discharged without sequelae constituting 3.4%. Among the 128 patients who were not in shock at the time of admission, 24 (18.8%) died and 62 (48.4%) were discharged without any sequelae. So, it has been observed that shock is associated with poor outcome. This is significant as the  $p=0.001$  ( $<0.05$ ). None of the reviewed literature mentioned the correlation of shock with the outcome of AES.

### Limitation

The study took into consideration data of only one center. Only nine factors were studied.

### CONCLUSION

It has been observed that age, awareness among caregivers, poor GCS, multiple seizures, shock are important factors in the outcome of AES. This study may help to predict outcomes of the AES cases and help to take measures to improve outcomes.



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