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A Study on Clinical Outcome in Children with Acute Febrile Encephalopathy Admitted in Nilratan Sircar Medical College and Hospital, Kolkata

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KEYWORDS

Acute Febrile Encephalopathy, Paediatric Neurology, Clinical Outcomes, Infectious Diseases, Prognostic Factors

ABSTRACT:

Introduction: Acute febrile encephalopathy (AFE) in children is a serious neurological condition characterized by fever and altered mental status, with a range of etiologies including infectious, metabolic, and autoimmune causes. Understanding the clinical outcomes in these patients is crucial for improving management strategies and prognostication.

Aims: To study various clinical features of AES, find out possible etiologies of acute encephalitis syndrome and to determine outcome and effect of different prognostic markers in outcome of acute encephalitis syndrome at the time of end of hospital stay

Materials and methods: This is a Prospective Observational Study, it's conducted from one and half year (1st March 2021 to 31st August 2022). All the cases of fever with altered sensorium from >4 hour but <2 weeks, aged 1 months to 12 years admitted in Paediatric Medicine ward of NRS Medical College & Hospital. 95 patients were including in this study.

Result: A positive JE IgM serology was found in 5 (5.26%). One patient (1.05%) had a positive MPDA. A CSF study revealed pleocytosis in 92 cases (96.44%) and polymorphic predominance in 81 cases (85.26%). CSF protein levels ranged from 40–100 mg/dl in 24 cases (25.66%) and above 100 mg/dl in 71 instances (74.74%). In 23(24.21%) and 72(75.79%) cases, the CSF sugar level was less than 40 mg/dl. Five (5.26%) of the CSF samples tested positive for JE IgM.

Conclusion: The clinical outcomes in children with acute febrile encephalopathy at Nil Ratan Sircar Medical College and Hospital reflect a significant risk of severe neurological sequelae and mortality. Early diagnosis, prompt treatment, and targeted management based on etiology are critical for improving outcomes. Future studies should focus on prospective data collection and explore targeted interventions to enhance recovery and reduce long-term effects.

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INTRODUCTION

Encephalitis is defined as an inflammatory process of central nervous system with dysfunction of brain.[1] Encephalitis was first discovered by the pathologist as well as naturalist Sir John Burton Cleland (1878-1971) in 1916.According to WHO, clinically, a case of acute encephalitis syndrome (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). Other early clinical findings can include an increase in irritability, somnolence or abnormal behaviour greater than that seen with usual febrile illness.[2]

CLASSIFICATION OF AES: [2]

Suspected case: A case that meets the clinical case definition for AES. Suspected cases are then further classified into one of the following four groups. Laboratory-confirmed JE: A suspected case that has been laboratory- confirmed as JE. Probable JE: A suspected case that occurs in close geographic and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak.

Acute encephalitis syndrome – other agent: A suspected case in which diagnostic testing is done and an etiological agent other than JE virus is identified. Acute encephalitis syndrome – unknown: A suspected case in which no diagnostic testing is done, or in which testing identified no etiological agent, or in which the test results were indeterminate.

ETIOLOGY/CAUSES OF AES:

(1) Viruses:

- RNA viruses: Mumps, Measles, Rubella, Enteroviruses
- DNA viruses: Herpes Simplex virus(HSV), Cytomegalo virus(CMV) , Epstein Barr Virus(EBV), Pox Virus
- Others: Japanese B, Dengue virus, Rabies virus, West Nile, Equine viruses.

(2) Bacteria: Tuberculosis meningitis, pyogenic meningitis.

(3) Fungi: Cryptococcus.
(4) Protozoa: Malaria.
(5) Toxins.
(6) Chemicals.
(7) Unknown causes.
In general population the incidence of acute encephalitis syndrome ranges between 3.5 and7.4cases per 100,000 patient-years .

[3]According to a population-based study in the United Kingdom, herpes simplex virus (HSV) was the most common virus diagnosed, and the proportion of cases with an identified etiology was significantly lower in children (33%) than in adults (45%). [4]

MATERIAL AND METHODS

- **Study Design –** Prospective Observational Study
- **Study Area**- Department of Paediatric Medicine, NRS Medical College & Hospital, Kolkata
- **Study Period** –One and half year (1st March 2021 to 31st August 2022)
- **Study Population** - All the cases of fever with altered sensorium from >4 hour but <2 weeks, aged 1 months to 12 years admitted in Paediatric Medicine ward of NRS Medical College & Hospital.
- **Sample Size –** 95
- **Inclusion criteria**-
  - All patients of age group between 1months and 12 years, with fever with altered sensorium from >4 hour but <2 weeks, admitted in Paediatric Medicine ward of NRS Medical College & Hospital.
- **Exclusion criteria**-
  - Metabolic encephalopathy
  - History of head injury
  - Mentally retarded child,
  - Intracranial space occupying lesion, granuloma
  - Endocrinal encephalopathy
  - Febrile seizure

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RESULTS AND ANALYSIS

Table 1: Clinical symptoms on admission in AFE cases

Symptoms	No. of cases	Percentage
Fever	95	100%
Altered sensorium	95	100%
Seizure	69	72.63%
Vomiting	42	44.21%
Loose stool	18	18.95%
Rash	2	2.11%
Bleeding manifestation	3	3.16%
Oedema	8	8.42%

Table 2: Investigation reports of AES cases

Investigations	No. of AES cases	Percentage
Hemoglobin (gm/dl)		
< 7	4	4.21%
>7	91	95.79%
TLC (Cells/mm3)		
< 4000-12000	73	76.48%
>12000	22	23.16%
Serum sodium (mg/dl)		
<135	51	53.68%
135-145	36	37.89%
> 145	8	8.42%
Serum calcium(mg/dl)		
<8	16	16.48%
>8	79	83.16%
Serum JE IgM	5	5.26%
MPDA	1	1.05%

Table 3: Distribution of total cases of AFE according to Etiology

Etiology		No. of AES cases	Percentage
Viral	JE	7	7.36%
	Non-JE	48	50.52%
Pyogenic		21	22.10%
Tubercular		9	9.47%
Cerebral malaria		1	1.05%
ADEM		5	5.26%
Undiagnosed		4	4.21%
Total		95	100.00%

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Table 4: Outcome of the AES cases on the basis

Outcome	No. of AES cases	Percentage
Death	18	18.94%
Discharge with sequelae	21	22.10%
Discharge without sequelae	56	58.94%
Total	95	100.00%

As the most prevalent symptom, fever with altered sensorium was observed in 95 (100%) of the cases. Other symptoms that were frequently linked to this illness included oedema in 8 (8.42%) cases, loose stool in 18 (18.95%) cases, vomiting in 42 (44.21%), and seizures in 69 (72.63%). Following blood examinations, findings indicated that 4 (4.21%) instances had haemoglobin levels less than 7 gm/dl, 22 (23.16%) had leucocytosis, 51 (53.68%) and 16 (16.48%) had serum sodium and calcium less than 135 mg/dl. A positive JE IgM serology was found in 5 (5.26%). One patient (1.05%) had a positive MPDA. A CSF study revealed pleocytosis in 92 cases (96.44%) and polymorphic predominance in 81 cases (85.26%). CSF protein levels ranged from 40–100 mg/dl in 24 cases (25.66%) and above 100 mg/dl in 71 instances (74.74%). In 23(24.21%) and 72(75.79%) cases, the CSF sugar level was less than 40 mg/dl. Five (5.26%) of the CSF samples tested positive for JE IgM.

Diffuse cerebral oedema was the most often observed brain finding in 16(16.84%) CT/MRI cases. Additional findings included multiple hyper-intensities in T2 images in white matter in 4(4.21), diffuse basal enhancement with basal exudates in 16(16.84%), and hyper-intensity lesion on T2WI in thalami, brain stem, cerebellum, and cortex in 13(13.68%) cases. In 7(7.36%) cases, MRI changes corroborated with ischemic changes. However, in 27 cases (28.42%), neuroimaging was either not done or was normal. Acute viral encephalitis accounted for 55 (57.89%) instances of AFE, of which 7 (12.73%) cases were Japanese encephalitis. This was the most prevalent cause of AFE. Pyogenic meningitis 21 (22.11%) was the second most frequent cause, followed by tubercular meningitis 9 (9.47%) and ADEM 5 (5.26%). Four cases (4.21%) were still undiagnosed. Of the 95 cases, 18 (18.94%) had died and 77 (81.05%) had survived; of these, 21 (22.10%) had been discharged with complications and 56 (589.94%) had recovered completely.

DISCUSSION

Acute encephalitis syndrome is a major illness affecting children of West Bengal and other part of country with significant mortality and morbidity. AES is one of the most common causes of PICU admission in our hospital.

In our hospital total 95 cases of AES (3.38% of total admission) were admitted in 1 year (1st April 2021-31st march 2022). Though **J. Granerodet al**. [3] showed in their study that in general population the incidence of AES ranges between 3.5 and 7.4 cases per 100,000 patient-years.

In our study out of 95 children from age group 1month to 12 years.62 (65.26%) cases were boys and 33(34.74%) cases were girls. Maximum patients 37 (38.95%) were from age group of 5years to 12 years. This finding is consistent with, **Bansal A et al [5].**

Majority of the parents of the patients were from the low socioeconomic group, that is 66(69.47%), were literate 66(69.47%) and 51 (53.68%) cases were from the person residing in mud house. **Farzana K. Beig et al [6]** showed in their study that the maximum patient was from low socioeconomic group.

Out of 95, most of the cases 83 (87.37%) were from rural areas where as 12(12.63%) cases from urban areas, it may be because of most of the cases admitted in our hospital were referred from Murshidabad, Malda, south 24 parganas and Nadia district, but similar result was also found by **Bhaswati Bandyopadhyay et al [7].**

Most of the cases were seen in the post monsoon period that is out of 95 cases 47(49.47%) cases were seen in the month of August to September**,** because mosquito density increased in this season. similar observation was reported from other studies like **Bhaswati Bandyopadhyay et al [7].**

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A study from School of Tropical Medicine by **Bhaswati Bandyopadhyay et al [7],** showed that fever with altered sensorium were most common presenting features approximately in 100% of the cases, the finding of our study was also same. Other clinical features we found were seizure 69 (72.63%), vomiting 42 (44.21%), loose stool 18(18.95%), breathlessness 15(15.79%) and features of shock in 8 (8.42%). On examination we found that at the time of admission GCS was below 8 in 24(25.26%) which was similar to the study like **C M Bokade et al [8]** other important finding was presents are signs of meningeal irritation 41(43.16%), cranial nerve involvement 25(26.31%), abnormal pupil 57(60.00%), planter extension 74(77.89%), papilledema11(11.58%), neurological deficit 13(13.68%), features of raised ICT 45(47.36%) and extrapyramidal signs in 9 (9.47%). Similar finding was also found by **Dongol S et al [9].**

Out of 95 subjects 55 (57.89%) were diagnosed as viral encephalitis among them 7(7.37%) were Japanese encephalitis, 21(22.11%) as pyogenic meningitis, 9 (9.47%) were tubercular meningitis, 5(5.26%) were ADEM, and 1(1.05%) case were cerebral malaria. There were 4(4.21%) cases remained undiagnosed**.** In a study on non-traumatic coma in children by **BansalAet al. [5]** they found viral encephalitis in 30%, 26.66% as pyogenic meningitis, 31.66% as tuberculosis meningitis and cerebral malaria in 3.33%.

We found mortality in 18(18.94%) cases and 77 (81.05%) cases survived, among them 21(22.10%) had sequelae and 56 (58.94%) patients discharged with complete recovery**.** Similar outcome that is mortality in 19.31% and sequelae in 26.70% were found in a study by **CM Bokade et al. [8]**

In our study higher mortality was seen in age group of 1month to 1 year, that is 7(38.88%) and maximum 12(57.14%) sequelae were seen in age group of 1 year to 5 years while least mortality 5(27.78%) was seen in age group of 5-12 years but sex wise Maximum 13(72.22%) mortality and sequelae 12(57.14%) both was seen in male than female**.** Also, in the study by **CM Bokade et al. [8]** maximum mortality was found in age group of up to 3 years but maximum mortality in female.

Out of 21 cases with sequelae, 4(19.04%) cases developed severe (GOS- II) sequelae, while 9(42.85%) moderated (GOS-III) and 8(38.09%) mild (GOS-IV) sequelae. Out of 4 severe sequelae, etiology wise 3(75.00%) were of Japanese encephalitis cases, but age wise 2 (50.00%) were from age group 1month to 1year and 2(50.00%) were from age group of 1-5 years and sex wise 3(75.00%) were seen in female**.**

In our study out of 95 cases, 7(7.75%) cases were diagnosed as Japanese Encephalitis, among them 6 positive cases were diagnosed by serum and CSF testing positive for anti- JEV IgM antibodies and in 1 case only in serum. Among the JE positive cases 3 cases were male and 4 cases female. The predominant age group affected was 2-12 years but the youngest child affected was 3years old. In a 2 years 2011-2012 study at Kolkata by **Bhaswati Bandyopadhyay et al. [7],** found that 22.76% of AES cases were JE IgM positive in 2011 but it sharply decreased to 5% in 2012.

We found maximum mortality 7(38.89%) in viral encephalitis and least in ADEM 1(5.55%). Maximum sequelae 6(28.57%) were also due to viral encephalitis while least 1(5.55%) was due to **.CM Bokade et al. [8]** also found the maximum mortality (44.11%) in viral encephalitis but least14.07%) in pyogenic meningitis while maximum sequelae (36.17%) were found in tuberculous meningitis and least (6.38%) in cerebral malaria.

Out of 21 cases of sequelae Most common type of sequelae in 13(61.90%) were extrapyramidal abnormality, followed by behavioural abnormality in 11(52.38%) cases**.** This observation was not similar to **Avabratha et al. [10]**, who found that most common type of sequelae was speech disturbances in 36.64% and motor deficit in 33.58%.

In our study, Out of 13 independently significant variables, only 6 variables that is GCS <8, severe anaemia, raised ICT, meningeal sign, use of mechanical ventilator and severity of sensorium were found to be significant ($p<0.05$). Other variables like age, sex, seizures, shock, JE IgM, papilledema and tone were not found significant, which was similar to the previous studies like **CM Bokadeet al. [8]**

In present study, GCS<8 had higher risk of death and was found to be statistically significant ($p=<0.001$). This study was in accordance with previous study like **CM Bokade et al. [8]**

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Presence of refractory seizures was significantly associated with mortality which is seen in study of **Sahin M et al. [11]** But here the p value is .086.

In our study we found that presence of variables like meningeal sign (p=0.001), severity of coma grade (p=<0.001), features of raised ICT (p=0.001) and use of mechanical ventilator (p=<0.001) had higher risk of death and statistically significantly, which was similar to the studies like **CM Bokade et al. [8]**

CONCLUSION

The majority of the children were between 1 and 5 years old, with a notable prevalence of AFE in males compared to females. The common presenting symptoms included high fever, seizures, and altered mental status. The treatment protocols varied based on the underlying etiology. Antiviral and antimicrobial therapies were administered as per the infectious agent, while supportive care, including antiepileptics and intravenous fluids, was essential for overall management. The clinical outcomes showed that while many children recovered with minimal sequelae, a significant number experienced persistent neurological impairments. The recovery rate was positively correlated with early intervention and the absence of severe complications at presentation. The findings underscore the importance of early recognition and prompt treatment in improving outcomes for children with AFE. The variability in outcomes highlights the need for personalized treatment approaches based on individual patient profiles and etiological factors. There is a need for continued investment in advanced diagnostic tools and facilities to ensure accurate and timely diagnosis of AFE. Developing and implementing standardized treatment protocols based on the latest evidence could improve management and outcomes. Regular follow-up and long-term monitoring of patients who recover from AFE should be emphasized to address any emerging neurological sequelae early. Additional research is recommended to explore the long-term outcomes of AFE and the impact of various treatment modalities on recovery and quality of life. In conclusion, while the study highlights some promising outcomes with current management strategies, it also calls for ongoing efforts to enhance diagnostic accuracy, treatment efficacy, and patient follow-up to optimize care for children with acute febrile encephalopathy.

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