

Original Research Article

Clinical profile and outcome of acute febrile encephalopathy in children

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ABSTRACT

Background: This prospective observational study aims at studying clinical profile of patients with acute febrile encephalopathy.

Methods: This study was conducted in patients of acute febrile encephalopathy admitted in PICU at tertiary care centre during November 2019 to May 2021 in age group one month to 18 years. 35 patients satisfied the inclusion criteria.

Results: 51.4% children belonged to age group less than 60 months and 40% children belonged to age group 61-120 months. Other than fever and altered sensorium (diagnostic criteria), seizures (74.3%), vomiting (60%), headache (22.9%) and refusal to feed (17.1%), were the major complaints. Raised ICT was found in 20 (57.1%). 20 (57.1%) patients had hyponatremia ($\text{Na}^+ < 135$). MRI brain abnormalities were found in 13 patients with majority finding being edema 8 (61.5%). 15 (62.5 %) patients had CSF cell count between 5-100/ μl . 16 (45.7%) children presented with GCS score 10-12. In the present study, most common diagnosis was rickettsia encephalitis in 10 patients (28.6%) followed by Dengue encephalitis 6 (17.1%) and probable Viral encephalitis 6 (17.1%). There was no mortality in the present study.

Conclusions: Seizure, headache and vomiting were the other common presenting features in a case of acute febrile encephalopathy. This indicates raised intracranial tension. Rickettsia followed by Dengue and probable Viral encephalitis were the common etiological diagnosis. Many cases are viral in nature and since no particular or highly effective therapy is available, early diagnosis, emergent treatment of raised intracranial pressure and hyponatremia and implementation of aggressive supportive care may reduce mortality and morbidity as in present study.

Keywords: Acute febrile encephalopathy, Viral encephalitis, Children, Clinical profile

INTRODUCTION

Acute febrile encephalopathy is a common and potentially serious neurological condition seen in children. It is associated with altered mental status that either accompanies or follows short febrile illness. In children it is associated with mortality and morbidity. It is a medical emergency warrants rapid and accurate diagnosis.¹ The clinical features are nonspecific and aetiological diagnosis is seldom possible on basis of these. Pathogen-specific microbiological investigations being not freely available,

etiological diagnosis remains elusive in a considerable proportion of cases.² On one end of the spectrum of presentation are children that present with innocuous fever without neurological manifestation at the onset and on the other hand are a set of children that present in comatose state. Outcome ranges from uncomplicated course to serious complications, devastating neurological sequelae and mortality. Commonest aetiology is viral encephalitis but remains elusive in majority of cases febrile encephalopathy. There is paucity of study on Acute febrile encephalopathy from western Maharashtra. This observational prospective study aims at studying clinical

profile of patients with acute febrile encephalopathy, analysing course of disease, its complication and correlation of clinical profile, investigations, and outcome.

METHODS

This observational prospective study was conducted in patients of acute febrile encephalopathy admitted in PICU at Ashwini Sahakari Rugnalaya and Sanshodhan Kendra, Solapur, Maharashtra state, a tertiary care center. Informed written consent was taken from the patient/guardian. Patients were recruited if they fulfilled the inclusion criteria.

Study design duration and sample

Current study is an observational descriptive. The duration of study was from November 2019 to May 2021. All children of age 1 month to 18 year of age group who had Acute Febrile Encephalopathy admitted in PICU at tertiary care center during November 2019 to May 2021 and who satisfied the inclusion and exclusion criteria and were enrolled in the study. 35 patients constituted the study sample.

Inclusion criteria

Patients between 1 month to 18 year of age group admitted in PICU with altered state of consciousness lasting for >15 minutes and with fever ≤ 2 weeks duration with or without seizure were included in the study.

Exclusion criteria

Patients with diagnosis of Simple febrile seizure, Space occupying lesion, Metabolic encephalopathy and Endocrinal encephalopathy were excluded from the study.

In this study demographic data and detailed history of patient was taken and it includes age, gender, duration of illness and time of presentation.

Operational definitions

Acute febrile encephalopathy: acute febrile encephalopathy is term commonly used to identify the condition in which altered mental status either accompanies or follows short febrile illness. **Seizure:** Transient occurrence of signs and symptoms resulting from abnormal excessive and or synchronous neuronal activity in the brain. **Simple febrile seizure:** Generalized seizure lasting less than 15 minutes, not recurring during 24-hour period that occur between the ages of 6 and 60 months with temperature of 38°C (100.4 F) or higher, that are not the result of CNS infection or any metabolic imbalance, and that occur in the absence of history of prior afebrile seizure. **Pediatric/neonate cerebral performance categories/PCPC Scale:** PCPC 1: normal, PCPC 2: mild cerebral disability, PCPC 3: moderate cerebral disability,

PCPC 4: severe cerebral disability, PCPC 5: coma or vegetative state, PCPC 6: brain death.

Method of data collection

Method of collection of data included demographic data, presenting complaints, past history and clinical features. All data was collected from patient in prescribed proforma.

Clinical features

Clinical features of the patients in the study were: seizure, fever, headache, vomiting, refusal to feed, skin lesions, altered sensorium (evaluated by modified Glasgow Coma Scale), increased intracranial pressure, involuntary movements, cranial nerve palsy and tone disturbances

Clinical examination

Standard general and systemic clinical examinations of the patients was done with special attention to examination to central nervous system.

Investigations

Investigations undertaken among the patients in this study included: Complete Blood Count (CBC) & Peripheral Smear Study, Blood Glucose level on admission, Urine-Routine and Microscopy, Serum Creatine level, Serum Bilirubin, SGOT, SGPT, Prothrombin time, Serum Electrolyte- Na^+ , K^+ , Mg^{++} , Blood Culture, Dengue NS1, IgM, IgG, Rickettsia IgM, Japanese Encephalitis IgM, CSF- Routine, Microscopy and culture, CSF testing for HSV and PCR, Neuroimaging (USG Cranium, MRI Brain, CT Brain) and Biofire CSF Panel.

Treatment

All children who participated in the study received treatment according to the standard guidelines of management for acute febrile encephalopathy. Treatment for cerebral decongestion specifically focused upon.

Outcome

Outcome was measured with three distinct clinical outcomes viz: Cured with no neurological complications, discharged with morbidities like neurological deficit, seizures or behavioural abnormality and mortality.

Data analysis

The Demographic and baseline characteristics such as age, gender, past medical history, type of fever, clinical features, presenting complaints and laboratory investigations parameters were summarized using the descriptive statistics. Categorical variables were summarized by frequency distribution for each categorical component (relative frequencies and percentage). For continuous variables, results were reported as mean $\pm$

standard deviation. The data analysis was performed using statistical package for the social sciences (SPSS) vs.20.

RESULTS

This study aimed to assess the clinical profile of acute febrile encephalopathy in children between 1 month to 18 year of age group. All the demographic and baseline characteristics were summarized using the descriptive statistics. In the present study, majority of children belonged to age group 61-120 months (40%). The average age (months) was 63.29±48.50. There was a slight female preponderance (male: female=1:1.3).

Table 1: Age distribution.

Age (months)	N	%
≤6	5	14.3
7-12	6	17.1
13-60	7	20.0
61-120	14	40.0
121-180	3	8.6
Average age	63.29±48.50	

Table 2: Clinical features.

Clinical features	N	%
Cranial nerve palsy	0	0.0
Refusal to feed	6	17.1
Playful	5	14.3
Sick	1	2.9
Lethargic	5	14.3
Drowsy (Altered sensorium)	22	62.9
Pallor	3	8.6
Icterus	0	0
Cyanosis	0	0
Edema	2	5.7
LN	0	0

Average duration of fever was 3.97±2.40 in days. Average duration of altered sensorium was 19.07 hours whereas the illness duration was 16.2±7.9 days.

Table 3: Presenting complaints.

Presenting complaints	N	%
Fever	35	100
Headache	8	22.9
Vomiting	21	60.0
Seizure	26	74.3
Altered sensorium	27	77

Table 4: Signs.

Signs	N	%
Meninges - neck rigidity	6	17.1
ICT	20	57.1
Hypotension	8	22.9

Majority of the patients were seen during November to January i.e., in winter period (60%). Due to increased virulence of viruses during that period, viral meningitis and malaria are very common which leads to increased incidence. After fever (100%) and altered sensorium (77%), which are diagnostic criteria for Acute febrile encephalopathy, seizure (74.3%), vomiting (60%), headache (22.9%) and refusal to feed (17.1%), were the major complaints.

Table 5: Serum electrolyte Na+.

Na+	N	%
<135	20	57.1
135-145	14	40.0
>145	1	2.9

Table 6: MRI.

MRI	N	%
Edema	8	61.5
Caudate nucleus	1	7.7
Subthalamic nuclei	1	7.7
Striate nuclei	1	7.7

Table 7: EEG.

EEG	N	%
Normal	11	30.6
Positive	2	5.6

Table 8: Glasgow coma scale (GCS).

GCS	N	%
<7	0	0
7-9	15	42.9
10-12	16	45.7
>12	4	11.4

Table 9: Diagnosis.

Diagnosis	N	%
Acute pyogenic meningitis	1	2.9
Atypical febrile seizure	1	2.9
Chikungunya encephalitis	2	5.7
Dengue encephalitis	6	17.1
Acute febrile encephalopathy	4	11.4
FIRES with multiorgan dysfunction	1	2.9
Meningitis with dengue fever	1	2.9
Meningitis pneumococcal	1	2.9
PRESS hypertension encephalopathy	1	2.9
Recurrent meningitis	1	2.9
Rickettsia encephalitis	10	28.6
Viral encephalitis	6	17.1

Most common signs found in the present study was raised ICT (57.1%) followed by hypotension (22.9%) and neck

rigidity (17.1%). Average hemoglobin level was 10.43 ± 1.84 g/dl. Average serum electrolyte Na^+ and K^+ was recorded as 132.80 ± 8.80 meq/l and 5.94 ± 1.47 meq/l and 5.94 ± 1.47 , respectively. In present study, 20 (57.1%) patients serum Na^+ less than 135 meq/l. 14 (40%) patients had serum sodium between 135-145 meq/l and only 1 (2.9%) patient had >145 meq/l. Imaging was done in all the patients. Abnormalities were found in 13 patients. Majority finding was cerebral edema 8 (61.5%). Abnormalities were also reported one each in region of caudate nucleus (7.7%), subthalamic nuclei (7.7%), and striae nuclei (7.7%).

Table 10: Outcome.

Outcome	N	%
Cured	28	80
Discharged against medical advice	7	20
Mortality	0	0

In present study, abnormal EEG was found in 2 cases (5.6%). CSF was done in 29 patients (82.9%). In present study, 6(25 %) patients had <5 cells/microl. 15 (62.5 %) patients had cells between 5-100/microl. 1 (4.2 %) patient had 100-200 cells/microl. 2 (8.3 %) patients had >200 cells/microl in CSF. The average CSF cell count was 71 ± 160.8 /microl. In present study, 23 (82.1 %) patients had CSF protein <45 mg/dl, 4 (14.3%) patients had CSF protein between 46-200 mg/dl, 1 (3.6%) patient had CSF protein >200 mg/dl. The average CSF Protein count was 41.6 ± 51 . In present study, 3 (10.7 %) patients had CSF glucose level <45 mg/dl. 22 (78.6 %) patients had CSF glucose level between 45-80 mg/dl. 3 (10.7 %) patients had glucose level in CSF >80 mg/dl. The average CSF Glucose was 63.5 mg/dl ± 18 . In present study, positive CSF culture was found in only 1 case (3.7%). Majority of children 16 (45.7%) presented with GCS score 10-12 and 15 (42.9%) with 7-9 score. None of children had a GCS score of less than 7. In the present study, most common diagnosis was observed Rickettsia encephalitis 10 patients (28.6%) followed by Dengue encephalitis 6 (17.1%) and Viral encephalitis 6 (17.1%). 28 (80%) cases were cured and 7 (20%) cases refused continuation of treatment midway and were discharged against medical advice. No mortality was found in the present study.

DISCUSSION

Fever with altered mental state, also known as Acute Febrile Encephalopathy, is a constellation of symptom and signs that leads to hospitalizations in both adults and children in our country. Central nervous system infections are the most prevalent cause of non-traumatic coma in children according to several studies. There is paucity of studies in the region of western Maharashtra. Keeping these facts in the mind, the present study was undertaken to assess clinical features of acute febrile encephalopathy among children and to determine the correlation of the

clinical features, investigation finding and outcome of the disease.

In this prospective observational study, we analyzed clinical features, etiology, and outcome of 35 children admitted in PICU at tertiary care center with AFE during November 2019 to May 2021 between one month and 18 years of age group. There was a slight female preponderance (male: female = 1:1.3) and average age was 63.29 ± 48.50 months. In a study by Debnath et al in Pune, India, in children <12 years of age, 74.68% were <5 years of age; 46.8% were infants, 27.9% were 1-5 years old, and male-female ratio was 1:1.82 with average age was 31 months. In the study by Mani et al from 1996 to 2005, the male-female ratio was reported as 1: 3.18 and Deepthi et al reported a ratio of 1:1.6.⁷⁻⁹ After fever and altered sensorium, which are diagnostic criteria for AFE, seizure (74.3%), vomiting (60%), headache (22.9%) and refusal to feed (17.1%), were the major complaints. Similar findings were also observed in viral encephalitis cases by Karmakar et al and Deepthi et al.^{3,9} Also, similar complaints apart from fever and altered sensorium, headache and vomiting were also observed in acute febrile encephalopathy in children presenting to a tertiary care referral center of Eastern Nepal by Singh et al.⁴ Average duration of fever was 3.97 ± 2.40 in days. The average duration of fever was comparable to the study done by Sharma et al who found mean duration of 4.4 ± 3.57 days.⁷ The average duration of fever reported was slightly more in study done by Biswas et al who found mean duration of 4.62 days.¹⁴ In our study, average duration of altered sensorium was 19.07 hours whereas the illness duration was 16.2 ± 7.9 days. In the present study, refusal to feed was seen in only 6 patients (17.1%). Whereas in study by Gupta reported that, the most common clinical features were refusal to feed 63 (70%).^{12,13} Most common signs found in the present study was raised ICT 20 (57.1%) followed by hypotension (22.9%) and neck rigidity (17.1%). Similar findings of ICT also observed in 47.6% cases by Deepthi and 58% cases by Biswas et al.⁷ Whereas Singh reported neck rigidity (57% cases) as the most common sign in their study. Deepthi reported neck stiffness in 44 (52.4%) cases.^{9,14}

In the month of November maximum cases 8 (22.9%) were seen. Most of the cases were reported during monsoon period, followed by post-monsoon and pre-monsoon. During monsoon and post monsoon season, there is increase in number of mosquito breeding sites and this leads to increase in dengue, malaria and other vector born encephalitis. Similar results were found in studies by Kamble et al as 62 (45.4%) and Sarkar et al a 46.9%. Study by Sudhir et al reported that highest number of acute encephalitis syndrome cases i.e., 68.47% were admitted in the month of June. However, contrary to this study, study by Yashodhara et al found that 71.42% of encephalitis cases occurred in winter season.¹⁵⁻¹⁸ In our study, in 16 cases, CSF cell count was abnormal. In a study by Anga et al 66 out of 129 patients had a normal CSF cell count.³ In our study, majority of children 16 (45.7%) presented with GCS score 10-12 and 15 (42.9%) with 7-9 score. None of

children had a GCS score of less than 7, whereas study done by Gupta et al found that, 47.8% having a Glasgow Coma Score (GCS) <8.¹² Deepthi reported that majority of children 17.8% presented with a GCS score of 9.⁹ GCS score of >9 was reported in 21.4% cases, score of 7-9 in 40.5% cases, score of 4-6 in 28.6% cases. 9.5% cases showed GCS score of 3. Modi et al have reported in their study, the Glasgow Coma Scale (GCS) score at the time of presentation was ≤ 7 in 21 (17.5%) patients, while 99 (82.5%) patients had a GCS of >7 .¹⁸

In present study, 51.4% cases were found to have elevated TLC. Similar results were found in studies by Singh et al 48.6%.⁴ In our study, in one case CSF Pathogen panel test revealed pneumococcal species (3.7%) and rest cases CSF culture showed no growth. Slightly more CSF culture results were reported as 7 (15.5%) in studies by Singh et al.⁴ This might be owing to many patients receiving antibiotics outside of our hospital prior to arrival. In our study, MRI brain was done in 28 patients and abnormality was found in 13 (46.4%) patients. The main findings were cerebral edema, oedema in the region of basal ganglia. In our study, the most frequent diagnosis was Rickettsia encephalitis in 10 cases (28.6%) followed by Dengue encephalitis 6 (17.1%) and Viral encephalitis 6 (17.1%). Karmarkar et al found that, Pyogenic meningitis was the most frequent diagnosis 51 (33.8 %) followed by tubercular meningitis 12 (7.9 %), and cerebral malaria 8 (5.2 %) in the patient group of non-viral causes and 57 cases (37.3%) were suspected as viral encephalitis.² Whereas Viral encephalitis as most frequent diagnosis was reported in studies done by Deepthi (38%), Bokade (46.59%), Bansal (30%).^{1,9,13}

This difference can be attributed to geographical variability. Infective pathology being most common cause of AFE in India serology should be performed in all patients of acute febrile encephalopathy in order to make the appropriate diagnosis, as clinical presentation alone is not specific for this diagnosis. In our study no case mortality was seen, 28 (80%) cases were cured, and 7 (20%) cases refused continuation of treatment midway and were discharged against medical advice. In their study Biswas have reported 156 (55%) discharges without sequelae, 50 (17.7%) discharges with sequelae and 65 (23%) deaths.¹⁴ Similar findings of mortality also reported by Bokade.²

Limitations

Some shortcomings were identified in this study. The study's sample size was small, limiting the analysis's power. Because it was a tertiary care center-based study, referral bias could not be ruled out. Specific microbiological investigations for many viral etiologies of AFE and autoimmune encephalitis were not done. The children were not followed up on for long-term complications and sequelae. Viral studies like Bio fire panel of CSF could not be done due to cost restrictions of

the families in 6 cases and so viral etiology cannot be established with certainty.

CONCLUSION

Acute febrile encephalopathy is a serious neurological condition in children. Infective aetiology is most common and it varies geographically and seasonally. In our study the most common aetiology was Rickettsia and Dengue. Because many cases are viral in nature and no particular or highly effective therapy is available (apart from for herpes), early implementation of aggressive supportive care may be able to reduce death and long-term morbidity. The combination of fever and altered sensorium in children should make one suspect Acute febrile encephalopathy. Presence of headache, vomiting and refusal of feeds are ominous signs and indicate raised intracranial tension. Many children with Acute Febrile Encephalopathy can recover completely if raised intracranial tension is emergently treated along with aggressive supportive care. Hyponatremia needs timely appropriate correction We believe that these were the main reason for no mortality in our study. Common treatable infections in the geographical area should be investigated for. If possible advanced microbiological investigations should be done for viral aetiology.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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