

# Study on clinical profile and etiology of acute febrile encephalopathy in children aged between 2 months to 14 years attending to a tertiary care hospital, Eluru, Andhra Pradesh, India

Deepthi A.<sup>1</sup>, Bekkam M.<sup>2</sup>

<sup>1</sup>Dr. Anusha Deepthi C.H, Assistant Professor, <sup>2</sup>Dr. Manohar Bekkam, Assistant Professor, Department of Pediatrics, Alluri Sitaramaraju Academy of Medical Sciences, Eluru, Andhra Pradesh, India.

**Corresponding Author:** Dr. Manohar Bekkam, Assistant Professor, Department of Pediatrics, Sitaramaraju Academy of Medical Sciences, Eluru, Andhra Pradesh, India, Email: drbmanohar@gmail.com

## Abstract

**Background:** Acute febrile encephalopathy (AFE) is a common condition leading to hospitalization of children in India. CNS infections are commonest cause of non-traumatic coma in children. Although AFE is one of the major causes of hospital admissions of children and adults in India, only a few studies have been done on it so far. So this study was conducted to study the clinical profile and etiology of AFE in children. **Methods:** This prospective study was carried out on 84 children between 2 months to 14 years, with fever duration of <14 days, GCS  $\leq$  12 at the time of admission and altered sensorium in the pediatric intensive care unit over a period of 12 months from August 2017 to August 2018. Clinical profile and etiology were evaluated. **Results:** The present study, has identified viral encephalitis (38%) and pyogenic meningitis (34.5%) as the major causes of Acute febrile encephalopathy in the study population. Most common symptoms apart from fever and altered sensorium were vomiting (58.3%), convulsions (45.2%), headache (35.7%), jaundice (8.3%), and most common presenting clinical signs apart from fever and GCS < 12 were neck stiffness (52.4%), signs of raised ICT (47.6%), positive Kernig's sign (39.2%), and motor tone abnormalities (34.5%). **Conclusion:** In this study, we observed that CNS infections are the most common cause of febrile encephalopathy in children. Early recognition of the clinical signs and immediate and appropriate treatment will combat the problem and improve the survival rate.

**Keywords:** Acute febrile encephalopathy (AFE), Central nervous system (CNS) infections, GCS

## Introduction

Acute febrile encephalopathy (AFE) is a term commonly used to identify the condition in which altered mental status either accompanies or follows short febrile illness [1,2]. Acute febrile encephalopathy is a common condition leading to hospitalization of children in India. CNS infections are commonest cause of non-traumatic coma in children [3]. The profile of AFE varies across different geographic regions. Despite much epidemiological investigation, the presentation with acute onset fever and altered sensorium has often remained mystery, especially in Indian states [3,5,6].

Acute infections of central nervous system in hospitalized children are associated with high mortality especially in developing countries, where there is a lack of intensive care facilities. AFE is one of the major

causes of hospital admissions of children and adults in India, and only a few studies have been done so far [4]. In spite of large burden of AFE in pediatric age group and high mortality associated with it, there is paucity of studies from India regarding clinical profile and etiology in these children.

Most acutely ill febrile children with encephalopathy can make complete neurological recovery once the underlying cause is identified and treated promptly and appropriately.

## Aims and Objectives

1. To study the clinical profile of Acute febrile encephalopathy in children aged between 2 months to 14 years.
2. To find out the etiology of Acute febrile encephalopathy in these children.

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## Materials and Methods

This prospective study was conducted on 84 children aged 2 months to 14 years who were admitted with fever and altered sensorium in the pediatric intensive care unit of Alluri SitaramaRaju Academy of Medical Sciences (ASRAM) Hospital, Eluru, Andhra Pradesh, India over a period of 12 months from August 2017 to August 2018.

### Inclusion criteria

- Children in the age group between 2 months to 14 years with fever of duration <14 days and GCS (modified score) of  $\leq 12$  at the time of admission.
- Children of metabolic encephalopathy if precipitated by fever.

### Exclusion criteria

- Children with traumatic coma.
- Children with febrile convulsions.
- Children with cerebral palsy and epilepsy.
- Children below 2 months and above 14 years of age.

## Results

**Age and Sex distribution of study population:** A total of 84 children were observed in this study. Among these 54.7% were of 6-14 years age group, which is the commonest age group. Second largest group was 1-5 years age group which contributes 33.3% of the total study population. Remaining 12% cases were of 2months-1year age group. Among the 84 children of study group 60.7% (n=51) were boys and 39.3% (n=33) were girls. Sex incidence was more common in males.

Data was collected according to the pre-structured proforma after getting consent from parents/guardians of children. Clinical profile was recorded at admission and children were followed throughout the course of illness in the hospital. Immediate resuscitative measures were taken, and specific treatment was started and changed according to patient's course in the hospital. Children were followed daily till discharge/death to study the clinical profile and etiology. Depth of coma was evaluated with reference to modified Glasgow coma scale.

The etiology was determined on the basis of history, clinical examination and relevant laboratory investigations like, complete blood counts, blood culture, blood sugar, CSF analysis, CT scan or MRI scan of brain, electro encephalogram, smear for malarial parasite or QBC or rapid malarial antigen test (HRP-II/p LDH), ABG analysis, liver function tests, urinalysis, urine ketone bodies, mantoux test and chest x- ray, echocardiography and other investigations according to clinical suggestions. Descriptive statistics were expressed as number and percentages. Data was analyzed using SPSS statistical software.

**Table 1: Etiology of Acute febrile encephalopathy in the study population**

Etiology	No. of Patients	Percentage
Viral Encephalitis	32	38%
Pyogenic Meningitis	29	34.5%
Cerebral Malaria	8	9.5%
Tuberculous (TB) Meningitis	6	7.2%
Aseptic Meningitis	2	2.4%
Brain Abscess	2	2.4%
Diabetic Ketoacidosis	2	2.4%
Hepatic Encephalopathy	1	1.2%
Enteric Encephalopathy	1	1.2%
Septicemia with toxic encephalopathy	1	1.2%
<b>Total</b>	<b>84</b>	<b>100%</b>

Among the 84 patients studied 32 cases (38%) were Viral encephalitis which is the most common etiology for acute febrile encephalopathy in present study followed by pyogenic meningitis (34.5%), cerebral malaria (9.5%) and TB meningitis (7.2%). Aseptic meningitis, brain abscess, diabetic ketoacidosis each accounted for 2.4% each whereas hepatic encephalopathy, enteric encephalopathy and septicemia accounted in 1.2% cases each.

**Table 2: Presenting symptoms in the study population.**

Presenting Symptoms	No. of cases	Percentage
Fever	84	100%
Altered sensorium	84	100%
Vomiting	49	58.3%
Convulsions	38	45.2%
Headache	30	35.7%
Jaundice	7	8.3%
Blurring of vision	2	2.4%

As per criteria fever and altered sensorium are pre-requisite for selection of cases in present study. Associated symptoms apart from fever and altered sensorium in the order of frequency are vomiting in 49 cases (58.3%), convulsions in 38 cases (45.2%), headache in 30 cases (35.7%), jaundice in 7 cases (8.3%) and blurring of vision in 2 cases (2.4%).

**Table 3: Clinical signs of the study population.**

Signs	No. of cases	Percentage
Fever	84	100%
GCS <12	84	100%
Neck stiffness	44	52.4%
Signs of Raised Intra cranial tension (ICT)	40	47.6%
Kernig's Sign	33	39.2%
Motor tone abnormalities	29	34.5%
Pallor	15	17.8%
Abnormal Respiratory pattern	15	17.8%
Pupillary size abnormality	14	16.6%
Abdominal Findings	13	15.5%
Decerebrate posture	12	14.3%
Cranial nerve palsy	12	14.2%
Icterus	11	13%
Pupillary reaction abnormality	11	13%
Decorticate posture	8	9.5%
Cardiac Findings	2	2.4%

Apart from fever and GCS < 12 which were pre-requisite for criteria most common presenting clinical signs in present study in order of frequency are : neck stiffness in 52.4%, signs of raised ICT in 47.6%, positive Kernig's sign in 39.2%, motor tone abnormalities in 34.5%, pallor and abnormal respiratory pattern in 17.8% cases each, pupillary size abnormalities in 16.6%, abdominal findings in 15.5%, decerebrate posture in 14.3%, cranial nerve palsies in 14.3%, pupillary reaction abnormalities and icterus in 13% cases each, decorticate posture in 9.5% cases and cardiac findings in 2 (2.4%) cases.

**Table 4: Coma severity in the study population.**

GCS score	No. of patients	Percentage
11	7	8.4%
10	11	13%
9	15	17.8%
8	10	12%
7	9	10.7%
6	8	9.5%
5	9	10.7%
4	7	8.4%
3	8	9.5%
<b>Total</b>	<b>84</b>	<b>100%</b>

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A GCS score of less than 12 was taken as coma. Majority of children 17.8% presented with a GCS score of 9, followed by 13% with a score of 10 and 12% children with GCS score of 8. 10.7% each presented with GCS score of 7 and 5. 9.5% children presented with score of 3 and 6 each. 8.4% each presented with GCS 11 and 4.

**Table 5: Clinical profile of viral encephalitis cases in the study population.**

Clinical feature	No. of cases of viral Encephalitis(32)"	Percentage
Meningeal Signs	18	56.2%
Vomiting	17	53.1%
Brisk deep tendon reflexes	15	46.8%
Headache	12	37.5%
Convulsions	11	34.3%
Raised ICT signs	10	31.2%
Hypertonia	7	21.8%
Cranial nerve palsy	4	12.5%

Among the 32 cases diagnosed as viral encephalitis, positive meningeal signs is the most common feature accounting for 18 cases (56.2%). Other features in order of frequency are vomiting in 17(53.1%), brisk deep tendon reflexes in 15 (46.8%), headache in 12(37.5%), convulsions in 11(34.3%), signs of raised ICT in 10 (31.2%), hypertonia in 7 (21.8%) cases and cranial nerve palsy in 4 cases (12.5%).

**Table 6: Clinical profile of pyogenic meningitis cases in the study population.**

Clinical feature	No.of pyogenic meningitis cases (N:29)	Percentage
Bulging anterior fontanelle	3	10.3%
Convulsions	12	41.3%
Cranial nerve palsy	5	17.2%
Headache	10	34.4%
Hypertonia	5	17.2%
Meningeal signs	20	69%
Signs of raised ICT	14	48.2%
Vomiting	20	69%

Among 29 cases diagnosed as pyogenic meningitis, the most common presenting clinical feature was positive meningeal signs and vomiting each accounting for 20 cases constituting 69% cases. Other clinical features in order of frequency are positive signs of raised ICT 14(48.2%), convulsions 12(41.3%), headache 10(34.4%), cranial nerve palsy and hypertonia (17.2%) and bulging anterior fontanelle in 3(10.3%) cases.

**Clinical profile of tuberculous meningitis cases in the study population-** Among the 6 cases diagnosed as tuberculous meningitis in study population, the most common presenting feature was vomiting present in 100% cases. Other features in order of frequency are convulsions in 5(83.3%), meningeal signs and headache each in 4 (66.6%) and blurring of vision and cranial nerve palsy each accounting for 2 cases (33.3%).

## Discussion

Fever with altered mental status is commonly produced by bacterial meningitis, viral encephalitis, cerebral malaria, typhoid encephalopathy, and fulminant hepatic failure due to viral hepatitis [7]. Various studies in children with non-traumatic coma have shown that CNS infections are the commonest cause of non-traumatic

coma [3]. In the present study, we have tried to evaluate the common presenting clinical manifestations, common etiologies of acute febrile encephalopathy encountered in children in a tertiary care hospital. Age-wise prevalence of present study showed majority of cases between 6-14 years (54.7%) followed by 1-5

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years (33.3%) and 2months-1year (12%). Similar prevalence found by Rupa R. Singh et al [8] with 66.6% cases are >5years of age and 33.3% case were < 5 years of age. Among the 84 children of study group 60.7% (n=51) were boys and 39.3% (n=33) were girls. Sex incidence was more common in males. Male: Female ratio is 1.6:1. Similar sex prevalence ratio (M:F=1.7:1) observed by S.A. Karmarkar et al [9].

**Common etiologies:** Among the 84 patients studied, 32 cases (38%) were viral encephalitis which was the commonest etiology for acute febrile encephalopathy in the present study. Similar observations were found in S.A Karmarkaretal [9] which showed 37.3% viral encephalitis in the study population.

29 cases are of Pyogenic meningitis which constituted to 34.5% cases of present study. Similar observations found in S. A Karmarkar et al [9] who found 33.8% cases. Cerebral malaria accounted for 8 cases (9.5%) in present study. Similar observations found in studies of Rupa R. Singh et al [8] (7.5%) and Anga Get al (7.1%) [10].

TB meningitis accounted for 6 cases (7.2%) in the present study, which showed similar observation to that of S.A Karmarkar et al [9], 2008 of 7.9%.

Aseptic meningitis, brain abscess and diabetic ketoacidosis each accounted for 2 cases (2.4%) in the present study. Both children with brain abscess have congenital cyanotic heart disease. Similar incidence for diabetic ketoacidosis of 2% seen in study of S.A Karmarkar et al [9]. Hepatic encephalopathy, enteric encephalopathy and septicemia accounted in 1 case (1.2%) each. Similar observations are seen in the study of S. A Karmarkar et al [9] 2008.

**Clinical Presentation:** Apart from fever and altered sensorium which were pre-requisite for selection of cases in the present study, associated symptoms in order of frequency were vomiting in 49 cases (58.3%), convulsions in 38 cases (45.2%), headache in 30 cases (35.7%), jaundice in 7 cases (8.3%) and blurring of vision in 2 cases (2.4%). Similar observations were seen in study of Rupa R. Singh et al [8] where headache and vomiting were the most common presenting symptoms and convulsions was reported in 50% of cases.

A GCS score of less than 12 was taken as coma. Majority of children 17.8% presented with a GCS score of 9. GCS score of >9 found in 21.4% cases, score of 7-9 present in 40.5% cases, score of 4-6 present in 28.6% cases. 9.5% cases showed GCS score of 3.

Apart from febrile and GCS < 12 which were pre-requisite criteria, most common presenting clinical signs in present study was neck stiffness seen in 52.4% cases. Second most common presenting sign is signs of raised intracranial tension which was seen in 47.6%.

Positive Kernig's sign present in 39.2%. Abnormal motor responses (34.5%), include hypotonia (12%) and hypertonia (22.5%). Cranial nerve palsies in 14.2% of cases. Most of them were found in pyogenic meningitis and viral encephalitis. Pallor was present in 17.8% cases. Most of them are seen in cerebral malaria.

Abnormal respiratory pattern seen in 17.8% cases, of which Cheyne-stokes or ataxic breathing seen in 12.6% cases. Pupillary size abnormalities in 16.6%, of which pupils were constricted in 3.6% cases and dilated in 13% cases. Abdominal findings in the form of hepatomegaly or splenomegaly were present in 15.5% cases; most of them were in cerebral malaria.

Decerebrate posture present in 14.3%, pupillary reaction abnormalities and icterus in 13% cases each and decorticate posture seen in 9.5% cases. Comparative observations seen in study by Rupa R. Singh et al [8] which observed neck rigidity in 57%, Kernig's sign in 43.9%, hypertonia in 22.4% of cases.

Out of the 32 cases diagnosed as viral encephalitis, positive meningeal signs was the most common feature accounting for 18 cases (56.2%). Other features in order of frequency are vomiting in 17(53.1%), brisk DTR in 15(46.8%), headache in 12(37.5%), convulsions in 11(34.3%), signs of raised ICT in 10(31.2%), hypertonia in 7(21.8%) and cranial nerve palsy in 4 cases (12.5%). Similar observations found in studies of S.A. Karmarkar et al [9] which found meningeal signs in (59.6%) and in Sanjay verma et al [11] which showed vomiting in 54.8% and brisk DTR in 54.8% cases.

Out of 29 cases of pyogenic meningitis, the most common presenting clinical features were positive meningeal signs and vomiting each accounting for 20 cases constituting 69%. Other clinical features in order of frequency are positive signs of raised ICT 14 (48.2%), convulsions 12 (41.3%), headache 10 (34.4%), cranial nerve palsy and hypertonia (17.2%) each and bulging anterior fontanelle in 3(10.3%) cases.

Similar findings were present in studies of Elased MF et al [12] and S. Curtis et al [13] where neck stiffness, convulsions, vomiting and bulging anterior fontanelle were common presenting features. Out of 8 cases diagnosed as cerebral malaria in study population, the

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most common presenting clinical features were pallor, icterus and abdominal signs (hepatomegaly or splenomegaly) seen in 100% cases. Convulsions are seen in 5 cases (62.5%). Decerebrate posturing and abnormal breathing pattern each accounts for one-fourth cases (25%) and cranial nerve palsy, hepatic dysfunction, shock in 1(12.5%) cases. Splenomegaly present in 100% cases but hepatomegaly was present in 75% cases. Similar percentages of hepatomegaly seen in Sushant et al[14] (2012) and that of shock and hepatic dysfunction seen in G.S Tanwaret al [15] (2011) studies.

Among the 6 cases diagnosed as tuberculous meningitis in study population, the most common presenting feature was vomiting, present in 100% cases. Other features in order of frequency were convulsions in 5(83.3%), meningeal signs and headache each in 4 (66.6%) and blurring of vision and cranial nerve palsy each accounting for 2 cases (33.3%). Similar observations were found in study of Thilothamal et al [16] where convulsions account for 79% cases and meningeal signs account for 65% of cases.

### Conclusion

In the present study, we observed that CNS infections are the most common cause of febrile encephalopathy in children. Preventive strategies like immunization with Hemophilus influenza vaccine, Japanese encephalitis vaccine and proper sanitation can be done to decrease the incidence of CNS infections. Early recognition of illness by common clinical presentation and administration of early and appropriate antimicrobial treatment can make complete neurological recovery and can decrease morbidity and mortality from Acute febrile encephalopathy.

### Contributions

Dr. Anusha Deepthi wrote the first draft of the manuscript, Dr. Manohar Bekkam helped in data collection, Dr. Anusha Deepthi helped in writing manuscript and did primary corrections in the manuscript, Dr. Manohar Bekkam made final corrections of manuscript before submission, Both authors approved the submission of this version of the manuscript and takes full responsibility for the manuscript. None of the authors have any conflict of interest.

### What this study adds to existing knowledge?

Central nervous system infections are the most common causes of acute febrile encephalopathy in children and

appropriate antimicrobial therapy can reduce the morbidity and mortality from acute febrile encephalopathy.

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