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Original Research Article

Clinical and Etiological Profile of Acute Febrile Encephalopathy in South Rajasthan, India

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Abstract

Objective: To study the clinical and etiological profile of Acute Febrile Encephalopathy (AFE) in South Rajasthan.
Methods: Children in the age of 1 month to 18 year with acute febrile encephalopathy were enrolled in the study. The investigations included CBC with PBF , ESR, Malarial parasite, blood sugar, kidney function test, electrolytes, liver function test, calcium, CSF examination, urine examination, X-ray chest PA view. ABG, serum ammonia, blood culture for bacteriological and virological studies and CT/ MRI brain were performed whenever required.
Results: 85 patients were admitted with fever and loss of sensorium. Other clinical features included convulsion (64.70%), vomiting (45.88%), headache (16.47%), skin lesion (2.35%), parotid swelling (1.17%), signs of raised intracranial tension (21.17%), signs of meningeal irritation (18.82%), cranial nerve palsy (4.70%), abnormal involuntary movement (2.35%), hepatomegaly (55.29%), splenomegaly (38.82%), anemia (41.17%) and clinical icterus (7.05%). Cerebral malaria was the commonest cause 32 (37.64%) of AFE followed by bacterial meningitis 16 (18.82%) and Suspected Viral Encephalitis 15 (17.64%). Reye's syndrome was seen in 14 (16.47%) patients. Other etiologies were Tubercular meningoencephalitis and Hepatic encephalopathy 2 (2.35%) each, Meningococcemia, Mumps meningoencephalitis, Acute Disseminated Encephalomyelitis and Dengue encephalopathy 1 (1.17%) each.
Conclusion: Cerebral Malaria was the leading cause of AFE followed by Bacterial Meningitis and Suspected viral encephalitis. While determining the etiology of AFE in a malaria endemic area, Cerebral Malaria should be considered in all patients. Reye's syndrome should also be considered and all patients of AFE should be evaluated to diagnose /rule out this entity.

Keywords: Acute Febrile Encephalopathy, Cerebral Malaria**,** Suspected Viral Encephalitis, Reye's syndrome.

1. Introduction

Encephalopathy is a diffuse disease of brain that alters its structure or function may be caused by a variety of infective, metabolic, toxic, ischemic / hypoxic, nutritional causes or trauma [1]. Acute febrile encephalopathy defined as fever associated with acute depression of consciousness or mental deterioration with or without seizure, motor and/ or sensory deficit and total duration of illness one week or less [2].

Several unrelated disorders such as cerebral malaria, bacterial and viral infections of the CNS, Reye's syndrome and electrolyte imbalance may present as acute febrile encephalopathy in children. Often no definitive cause can be assigned and a provisional diagnosis of 'viral encephalitis' is made. In India, the illness would need to be distinguished from other CNS infections such as cerebral malaria, bacterial meningitis and tubercular meningitis. There is paucity of systemic study from our country for establishing diagnosis in patients with AFE. Hence this study was conducted to find out the clinical and etiological profile of Acute Febrile Encephalopathy in south Rajasthan.

2. Material and Methods

All Children (> 1 month & < 18 year) presenting with fever, altered sensorium with or without seizure, motor and/or sensory deficit and total duration of illness 1 week or less were admitted in Balchikitsalay of RNT Medical College, Udaipur (Rajasthan) from July 2015 to December 2015, were included in the study. Neonates and patients of simple febrile seizures were excluded from the study.

The clinical and the demographic information were recorded based on a pre-structured proforma, together with the detail history & physical examination at the time of admission with informed consent. The investigations included CBC with PBF, ESR, Malarial parasite {card, slide, MP (QBC)}, blood sugar, kidney function test, electrolytes, liver function test, calcium, CSF examination, urine examination,

X-ray chest PA view. ABG, serum ammonia, blood culture for bacteriological and virological studies and CT/ MRI brain were performed whenever required. Patients were classified into broad groups of Cerebral Malaria, Bacterial Meningitis, Suspected Viral Encephalitis, Reye's syndrome and other clinical syndrome on the basis of predesigned diagnostic criteria (Table 1).

Table 1: Diagnostic criteria used for different etiologies of AFE

Disease	Diagnostic criteria
Cerebral Malaria	Fever with altered sensorium + blood smear positive for malarial parasite[1]
Pyogenic Meningitis	Fever with altered sensorium +/-neck signs+ CSF cytology (mainly polymorphs) & biochemistry
Suspected Viral Encephalitis	Fever with altered sensorium + CSF normal or mild pleocytosis+ absence of bacteria on direct microscopy or culture + no other alternative diagnosis
Reye's syndrome	Fever with altered sensorium + protracted vomiting + raised liver enzymes (>3 fold), raised serum ammonia, abnormal coagulogram and anicteric [3]
TBME	Fever with altered sensorium + typical CSF picture (mainly lymphocytes) with or without abnormal neuroimaging study.
Hepatic Encephalopathy	Fever with altered sensorium + deep icterus, raised liver enzymes (>3 fold), abnormal coagulogram and raised ammonia level.
Meningococcemia	Fever with altered sensorium + signs of meningeal irritation, petechial or purpuric rash and hypotension with shock with typical CSF picture[1]
Mumps meningoencephalitis	Fever with altered sensorium + bilateral parotid swelling with usually normal CSF picture.
ADEM	Fever with altered sensorium + characteristic MRI features with a preceding history of respiratory infection, exanthema or vaccination[4]
Dengue Encephalopathy	Fever with altered sensorium + maculopappular rashes with Dengue IgM ELISA positive/ NS_1 Antigen reactive[5]

3. Results

A total of 85 cases with the diagnosis of AFE were admitted in Balchikitsalay of Udaipur. Most of the children (35.71%) were in the age group of 5-10 year followed by 1-5 year (32.85%) with mean age group was 6.3 year. Male to female ratio was 1.8:1. Clinical profile of patients with acute febrile encephalopathy is given in Table 2.

Table 2: Clinical Profile of Patients with Acute Febrile Encephalopathy

S. No.	Clinical features	No. of cases (%)
1	Fever	85 (100%)
2	Loss of sensorium	85 (100%)
3	Convulsion (Generalized)	50 (58.82%)
4	Convulsion (Focal)	05 (5.88%)
5	Headache	14 (16.47%)
6	Vomiting	39 (45.88%)
7	Signs of raised ICT	18 (21.17%)
8	Signs of Meningeal Irritation	16 (18.82%)
9	Cranial Nerve Palsy	04 (4.70%)
10	Abnormal Involuntary movements	02 (2.35%)
11	Skin lesions	02 (2.35%)
12	Hepatomegaly	47 (55.29%)
13	Splenomegaly	33 (38.82%)
14	Anemia	35 (41.17%)
15	Icterus	06 (7.05%)
16	Parotid swelling	01 (1.17%)

Investigations revealed Leucocytosis (TLC count > 11000/mm^3) in 50 (58.82%), hypoglycemia (blood sugar < 50 mg/dl) in 18 (21.17%), Urea > 50 mg/dl in 40 (47.05%), Creatinine > 1.5 mg/dl in 15 (17.64%), hypernatremia (Sodium level > 150 Meq/L) in 4 (4.70%), hyponatremia (Sodium level < 135 Meq/L) in 40 (47.05%) patients.

The most common illness presenting as acute febrile encephalopathy was Cerebral Malaria seen in 32 (37.64%) patients. Plasmodium falciparum was detected in all cases of Cerebral Malaria. Bacterial meningitis was second most common diagnosis responsible for 16 (18.82%) cases. Blood culture was positive in 3 (18.75%) & CSF culture was positive in 1 (6.25%) cases of Bacterial meningitis. Others include Suspected Viral Encephalitis 15 (17.64%), Reye's syndrome 14 (16.47%), Tubercular meningoencephalitis 2 (2.35%), Hepatic encephalopathy 2 (2.35%), meningococcemia 1(1.17%), Mumps meningoencephalitis 1(1.17%), Acute Disseminated Encephalomyelitis 1(1.17%), and Dengue encephalopathy 1(1.17%). All patients of Reye's syndrome were anicteric, SGPT >1000 IU/L and raised ammonia level.

4. Discussion

In the present study, Cerebral Malaria was the most common cause (37.64%) of acute febrile encephalopathy followed by Bacterial Meningitis (18.82%), Suspected Viral Encephalitis (17.64%) and Reye's syndrome (16.47%). Others were Tubercular meningoencephalitis (2.35%), Hepatic encephalopathy (2.35%), Meningococcemia (1.17%), Mumps meningoencephalitis (1.17%), Acute Disseminated Encephalomyelitis (1.17%), and Dengue encephalopathy (1.17%). Earlier studies from several regions of India have documented the pyogenic meningitis to be most common diagnosis in such children. Kumar *et al* [6] from Lucknow, India studied a total of 740 consecutive children aged between 6 months and 12 years who presented with acute encephalopathic illnesses during a three year period were assessed both clinically and by laboratory investigations. A firm diagnosis was established in 278 patients (38%). Pyogenic meningitis (n = 134), measles encephalopathy (n = 38), and electrolyte imbalance (n = 23) were important causes in this group, cerebral malaria (n = 4) was uncommon and

there were no cases of Reye's syndrome. A similar study by Anga *et al* [7] 149 children were enrolled in the study. 129 had a lumbar puncture and CSF examination; 66 had a normal CSF white cell count. A clinical or laboratory-based diagnosis was possible for 140 children, but a definite pathogen was identifiable in only 55 (37%). The diagnoses included bacterial meningitis in 33 (S. pneumonia 16, H. influenza 13 and N. meningitides 4), tuberculous meningitis (5), probable tuberculous meningitis (18), malaria (10), cryptococcal meningitis (1), flavivirus encephalitis (5), rubella encephalitis (1), hepatic encephalopathy (1) and HIV encephalopathy (1). Mehrotra *et al* [8] found pyogenic meningitis in 49.1% and viral causes in 11.4%. In comparison to these studies, Cerebral Malaria was more common in our study. This could be due to the fact that southern Rajasthan is endemic for malaria.

In another study of 151 children by Karmarkar *et al*, viral encephalitis was the most common etiology seen in 57 patients. A diagnosis other than viral encephalitis was reached in 94 (62.3%) patients. Pyogenic Meningitis was the most frequent diagnosis (33.8%), followed by TBM (7.9%) and cerebral malaria (5.2%) in the patient group of non-viral etiology [1]. In our study, results were a bit different. Cerebral malaria was the most common cause (37.64%) followed by Bacterial meningitis (18.82%). No specific etiology was found in 17.64% cases included in the present study, these were labeled as suspected viral encephalitis. It is possible that a more detailed diagnostic work up such as serology and antigen detection by PCR for viruses could have picked more etiologies.

Singh *et al* [9] conducted a study on clinical and etiological profile of acute febrile encephalopathy in children presenting to a tertiary care referral center of Eastern Nepal. The most common presenting complaints apart from fever and altered sensorium were headache and vomiting. Convulsions, neck rigidity, hypertonia, brisk deep tendon reflexes, extensor plantar response and focal neurological deficits were seen in 50%, 57%, 22.4%, 28%, 39.3% and 9.3% of the subjects, respectively. The diagnoses based on clinical presentation and laboratory findings were pyogenic meningitis in 45 (42%), non JE viral encephalitis in 26 (25%), JE in 19 (18%), cerebral malaria in 8 (7%), herpes encephalitis and tubercular meningitis in 4 (4%) each, and typhoid encephalopathy in 1 case. In the present study, clinical profile includes fever and loss of sensorium (100%), convulsion (64.70%), vomiting (45.88%), headache (16.47%), skin lesion (2.35%) and parotid swelling (1.17%). Clinical examination revealed most common stage of encephalopathy on admission was stage 3 coma (35.71%) followed by stage 2 coma (34.28%), signs of raised intracranial tension (21.17%), signs of meningeal irritation (18.82%), cranial nerve palsy (4.70%), abnormal involuntary movement (2.35%), hepatomegaly (55.29%), splenomegaly (38.82%), anemia (41.17%), and clinical icterus (7.05%).

Our study is limited by the facts that firstly, polymerase chain reaction (PCR) was not done for diagnosis of viral encephalitis. Secondly, the complete serological screening for viral etiologies was not available to us, and hence we could not identify the culprit virus in a substantial number of our patients

5. Conclusion

In this study, Cerebral Malaria was the leading cause of AFE followed by Bacterial Meningitis, Suspected Viral Encephalitis and Reye's syndrome. Cerebral malaria needs special consideration and a high index of suspicion, especially in the post-monsoon period. Reye's syndrome should be considered in all patients of AFE & all children with acute encephalopathy should be evaluated to diagnose and/or rule out this disorder. Larger systemic studies on AFE in children are required for systemic data generation & this should essentially include workup to identify viruses responsible for encephalitis and to identify factors leading to Reye's syndrome.

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