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Profile of acute febrile encephalopathy in children

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ABSTRACT

An attempt was made to study the etiology, clinical spectrum, laboratory data and mortality / morbidity in children with acute febrile encephalopathy.A prospective hospital based study conducted on 40 patients admitted in Department of Pediatrics, PGIMS Rohtak during the period from March 2013 to August,2014 based on the following inclusion criteria: (1) Age more than 1 month to 14 years and (2) A diagnosis of acute febrile encephalopathy, based on following criteria: (i) fever (ii) acute depression of consciousness for more than 12 hours with or without motor or sensory deficit and (iii)Total duration of illness at time of admission 1 week or less. The final study group comprised of 40 patients with mean age of 5.84±3.93 years. Maximum number of patients had fever (100%) as presenting complaint followed by convulsions (67.5%) and loss of consciousness (32.5%).Pyogenic meningitis was the major diagnosis seen in 40% followed by tubercular meningitis in 15%,cerebral malaria and septicemia in 10% and diabetic ketoacidosis in 7.50%. A total of nine patients (22.5%) had significant findings on CT Scan. A total of 10 patients out of 22 meningitis patient were found to have neurological sequelae while only two non-meningitis patients had sequelae. The most common sequelae was developmental delay found in seven patients

The etiology of acute febrile encephalopathy varies from infectious to non-infectious disorders.The study emphasizes the need for better rehabilitation and disability services in developing countries close to where children live.

INTRODUCTION

Acute encephalopathy refers to a state of rapid deterioration of brain function, usually presenting as an alteration in state of consciousness, with or without focal neurological signs.[1] It is a clinical term used to describe patients presenting with a short febrile illness with altered mental state.[2] Encephalopathy is a diffuse disease of brain which alters its structure or function and it may be caused by variety of infective, metabolic, toxic, ischaemic /hypoxic, nutritional causes or trauma. In febrile illnesses, encephalopathy may result from pathogenic mechanisms affecting central nervous system (CNS) directly or indirectly causing systemic complications e.g. Hypoglycaemia, hyponatremia, hyperpyrexia, hypoxia, anaemia, hepatic/renal failure and bleeding.[3] Several unrelated disorders such as bacterial and viral infections of the CNS, Reye's syndrome and electrolyte imbalance may present as febrile encephalopathy in children.[4]

CNS infections are most common cause of non-traumatic coma in children. A study of non traumatic coma in children has indicated that TBM, pyogenic meningitis and encephalitis together constitute >90 % of cases.[5] There is a challenge of emergency management, identification of its cause, treatment not only to ensure survival but also to treat long term sequelae, neurological or otherwise.[3]

In view of varied aetiologies, presentations and outcome, an effort has been made in present study to analyse the causes, clinical and laboratory spectrum and morbidity/mortality pattern in patients of acute febrile encephalopathy in children.

MATERIALS AND METHODS

It was a hospital based prospective study conducted on 40 children admitted in the Department of Pediatrics, Pt. B.D Sharma PGIMS, Rohtak during study period of eighteen months from March, 2013 to August, 2014.Inclusion criteria included age more than one month and less than 14 years and a diagnosis of acute febrile encephalopathy based on following criteria: a) Fever

b) Acute depression of consciousness or mental deterioration for more than 12 hours with or without motor or sensory deficit and c) Total duration of illness less than or equal to 1 week. Exclusion criteria included patients patients already with neurological deficits; patients with stroke,brain hypoxia/anoxia; patients with Reye's syndrome; patients with idiopathic inflammatory diseases of the CNS or disorders of demyelination of CNS (e.g. ADEM, Multiple sclerosis),since they present days to weeks after recovery from an infectious illness suggesting autoimmune phenomenon triggered by infections. . Neonates were excluded from the study because frequently they have generalized diseases in which encephalopathy is only one aspect not a distinct entity.[6]

METHODS

Following criteria for diagnosis of various conditions of acute febrile encephalopathy(AFE) were adopted [7] (Table A):

History was taken on admission and the information was entered on a pre-structured proforma, together with the results of physical examination. A careful record of the patient's progress in hospital was maintained. The modified Glasgow coma scale was used to assess the patients' sensorium on admission and thereafter at regular intervals.

An attempt was made to determine the cause of illness from the results of the following investigation which were performed in all patients namely complete hemogram, renal function tests, random blood glucose, liver function tests, serum electrolytes, C-reactive protein, peripheral blood film for malarial parasite, plasmodium falciparum/vivax antigen test, lumbar puncture for CSF, urine examination, chest x-ray,blood culture and sensitivity, and patients with suspected viral encephalitis were subjected to following viral studies:(i) Viral identification (by PCR or quantitative or qualitative DNA amplification techniques) (ii)Viral Serology (by rapid serological assays e.g. IgM capture ELISA). Samples of CSF were stored in the freezing compartment of the refrigerator and serum samples were stored at 4^0C in the refrigerator. CSF and serum samples of these patients were transported to and analyzed at the National Institute of Communicable Diseases, New Delhi. CECT and/or MRI brain was done in almost all patients and EEG was done as per requirement.

The patients were treated according to the standard treatment protocols followed in the hospital. This included supportive care eg. inotropic agents if the patient was hemodynamically compromised, decongestive therapy for treatment of raised intracranial tension, intravenous antibiotics and anticonvulsive agents as and when required. The patient's progress in the hospital, response to treatment, and state of consciousness was monitored and recorded vigilantly. A careful note was made of any neurological sequelae at the time of discharge. Statistical analysis was performed with SPSS version 16.

RESULTS

A total of 40 cases with acute febrile encephalopathy were studied out of which maximum i.e. 42.5% were in the age group 1-5 years with mean age of all patients as 5.84±3.93 years. Males were 57.5% and females were 42.5%. Maximum number of patients had fever (100%) as presenting complaint followed by convulsions (67.5%) and loss of consciousness (32.5%). Majority of patients had a combination of presenting complaints (fever with convulsions) which was seen in 27(67.5%) of patients.(Table 1)

The mean GCS score of all patients with AFE during first week was 9.57±1.78, during 2nd week it was 11.27±1.93 and

Table A

Disease	Criterion
Pyogenic meningitis	Fever with altered sensorium (without focal symptoms/signs) ± neck Signs + CSF cytology (predominantly polymorphs) + meningeal enhancement on either CT scan or MRI
Meningoencephalitis	Fever with altered sensorium (without focal symptoms/signs) ± neck signs + CSF cytology (predominantly lymphocytes) + EEG / MRI / CT + evidence of parenchymal disease
Tubercular meningitis	Fever with altered sensorium (with or without focal symptoms / signs) + CSF compatible with chronic meningitis + CSF ADA >12
Cerebral Malaria	Fever with altered sensorium (without focal symptoms/signs) with peripheral smear/HRP antigen test for malaria.
Septic encephalopathy	Underlying sepsis syndrome with normal CSF analysis, CT and MRI scan.

Table 1 : Combination of complaints

Fever + Convulsions	27 (67.5%)
Fever+ Altered sensorium	16(40%)
Convulsions + Altered sensorium	7(17.5%)

Table 2 : Diagnosis

	No. of patients	Percentage
Cerebral malaria	4	10.00
Diabetic ketoacidosis	3	7.50
Dyselectroletimia	2	5.00
Hepatic encephalopathy	2	5.00
Herpes encephalitis	1	2.50
Japanese encephalitis	2	5.00
Pyogenic meningitis	16	40.00
Septicemia	4	10.00
Tubercular meningitis	6	15.00

during 3rd week it was 12.02±1.84 while mean GCS score of the patients presenting with altered sensorium was poorer. During first week of illness, it was 8.5±1.78, during second week it was 9.87±1.36 and during third week it was 10.5±1.15.

Pyogenic meningitis was the major diagnosis in the present study i.e. 40% followed by tubercular meningitis in 15% and cerebral malaria and septicemia in 10% each.(Table 2)

A total of 10 patients out of 22 patients diagnosed as meningitis were found to have neurological sequelae while only two patients of acute febrile encephalopathy with diagnosis other than meningitis had sequelae.(Figure 1)

DISCUSSION

Out of total 40 patients in present study, Pyogenic meningitis was the major diagnosis seen in 40% followed by tubercular meningitis 15%. Cerebral malaria and septicemia were present in 10% of the cases followed by diabetic ketoacidosis which was present in 7.50% cases. In a comparative study conducted by Karmarkar et al (2008), out of total 151 patients studied, viral encephalitis was found as cause in 57(37.7%) cases. A diagnosis other than viral encephalitis was reached in 94 patients (62.3%). Pyogenic meningitis being the most frequent diagnosis in 51 patients (53.7%) followed by Tubercular meningitis seen in 12 patients (12.6%).[4] In our study, viral cytology revealed Japanese encephalitis in 2 cases i.e. 5% and Herpes Simplex virus in 1 i.e. 2.5% cases. In study done by Beig et al(2010), a viral etiology was diagnosed in a total of 21.8% cases with most common etiological agent as enterovirus 71 present in 42.3% cases followed by measles in 21.1% cases.[8] In a study done by Singh et al(2009) on a total of 107 patients, diagnosis based on clinical features and lab investigations were Pyogenic meningitis in a maximum of 45(42 %) cases, non JE viral encephalitis in 26(25%) cases, Japanese encephalitis in 19(18%) cases, cerebral malaria in 8(7%) cases, herpes encephalitis and TBM in 4(4%) cases each and typhoid encephalopathy in 1% cases.[9] In a similar study done by Modi et al(2012) on 120 patients, pyogenic meningitis was the most common cause accounting for 36.7%, followed by acute viral encephalitis in 28.33% of patients (Japanese B encephalitis in 12.5%, herpes simplex viral encephalitis in 3.33% and other undetermined viral etiology in 12.5% cases). Cerebral malaria, sepsis associated encephalopathy and tuberculous meningitis were diagnosed in 21.7%, 9.17%, 4.2% of cases respectively.[10] In a study done by Anga et al(2010), the most common diagnosis was bacterial meningitis (22%).[11]

The proportion of children having seizures and focal neurological deficits in the present study was lower in comparison to an earlier study from Lucknow done by Kumar et al.[12] This seems to be related to more virulent strains of viruses in the Lucknow study. Significant number of viral encephalitis cases can be prevented by providing universal coverage of MMR vaccine, JE vaccine (in endemic areas) and limiting mosquitoes' breeding. Sequelae and mortality can be reduced if patients are referred in time for supportive interventions at proper place.

In our study, a total of nine patients i.e. 22.5% had significant findings on contrast enhanced CT Scan. Four Patients (25%) with pyogenic meningitis had meningeal enhancement while rest 75% had normal CT Scan findings. Therefore, the results of an imaging study do not exclude or prove the presence of acute

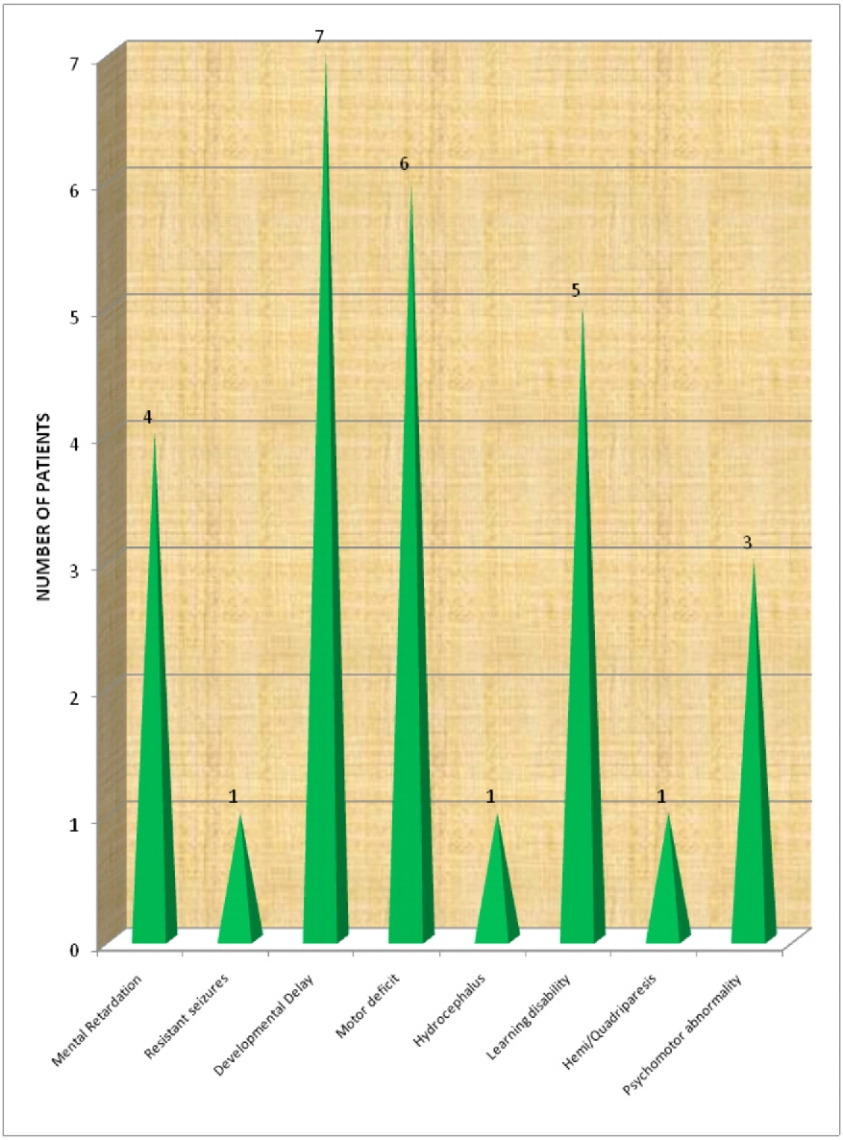

Figure 1: Sequelae in Meningitis Patients

meningitis. Four out of six (66.66%) patients having Tubercular Meningitis had ring enhancing lesions with basal exudates. Japanese encephalitis was characterized by panda sign. mMRI Brain was done in present study where findings of CT scan and CSF were inconclusive. In a study done by Kashinkunti et al(2013), only 31 patients out of 100 had shown abnormalities on imaging, CT or MRI. Meningeal enhancement was seen in 45.5% patients with pyogenic meningitis. Bilateral T2 thalamic hyperintensity was seen in one patient with JE.[13]

Sequelae were significantly more in meningitis patients ($p<0.01$) than other cases of acute febrile encephalopathy. In a study done by Beig et al (2010), children with a GCS score >12 had no sequelae i.e. the outcome was good.[8] Khinchi et al in their study found that children with a GCS score of >12 had no sequelae i.e. outcome was good.[14] In a study done by Bokade et al, maximum sequelae was found in tubercular meningitis and least in cerebral malaria.[15] Most of the patients in our study i.e. 11 out of 12(91.66%) with sequelae had a GCS score of less than 12. No relation of prolonged hospitalization or sequelae was seen in our study with severe initial manifestations of shock, hypotension, refractory seizures or clinical features of raised ICT.

Long term follow-up was difficult as families lacked the resources to return for further assessment. This study provides details on the nature and frequency of neurological sequelae, and emphasizes the need for better rehabilitation and disability services for children in developing countries and the importance of providing these services close to where children live.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

CONCLUSION

The study was conducted in the Department of Pediatrics, Pt.B.D. Sharma PGIMS Rohtak from March 2013 to August 2014 (eighteen months).Forty cases of acute febrile encephalopathy were studied. Maximum number of patients had rural background i.e.77.5%.Maximum number of patients had fever as presenting complaint followed by convulsions and loss of consciousness. Majority of patients had a combination of presenting complaints as fever with convulsions. Mean GCS score of the patients presenting with altered sensorium was poorer. Cranial nerve

palsies were seen in 3 patients out of which 2 had seventh nerve palsy while one had third nerve palsy. A total of six patients had findings suggestive of papilloedema and five were found to have early papilloedema. Meningeal signs could be elicited in 15 patients.Pyogenic meningitis was the major diagnosis in the present study i.e. 40% followed by tubercular meningitis 15%. Cerebral malaria and septicemia were present in 10% of the cases followed by diabetic ketoacidosis which was present in 7.50%. Dyselectroletimia, hepatic encephalopathy and japanese encephalitis were diagnosed in 2(5%) patients each. Sequelae and mortality can be reduced if patients are referred in time for supportive interventions at proper place. This study provides details on the nature and frequency of neurological sequelae, and emphasizes the need for better rehabilitation and disability services for children in developing countries and the importance of providing these services close to where children live.

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