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CLINICAL PROFILE OF ACUTE FEBRILE ENCEPHALOPATHY IN A TERTIARY CARE CENTER IN ROHILKHAND REGION

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ABSTRACT

Introduction. Acute Febrile encephalopathy (AFE) term is commonly used to describe the clinical syndrome of Acute onset fever which is either accompanied or followed by altered mental status.

Objective. To study clinical profile and analyze the cause of acute febrile encephalopathy in adult patients presenting to tertiary care center in Rohilkhand region

Methods. 97 patients (aged > 18 yr) presenting to the emergency with fever (> 38 0 C) of less than 2 wk duration with altered sensorium with/ or without seizure were prospectively investigated for etiological cause. The investigations included blood and CSF counts, blood and CSF cultures, peripheral smear and serology for malarial parasite, and dengue and typhoid serology. Other investigations included EEG and CT or MRI wherever indicated.

Results. Of the total 97 patients viral encephalitis was the most common accounting for 38.1% ,bacterial meningitis in 11.3%, tubercular meningitis in 21.6%, cerebral malaria in 8 (8.2%),8% had septic meningitis, Dengue encephalopathy was seen in 4.1% and 4 patient had non-infectious febrile encephalopathy .

Conclusion. viral encephalitis and tubercular meningitis are the most common causes of acute presentationwith fever and encephalopathy. Preventive strategies must be directed keeping these causes in mind.

KEYWORDS :

INTRODUCTION

Acute Febrile encephalopathy (AFE) term is commonly used to describe the clinical syndrome of Acute onset fever which is either accompanied or followed by altered mental status.[1] This syndrome is frequently encountered by doctors in the emergency department.It is always a challenge to identify the etiology of this syndrome because it has very important implications on the management and the outcome of the patient.[2] Usually, this syndrome is thought to be caused by various infectious etiology[2], however in clinical practice we see that there are other several non-infectious etiologies that can present like this syndrome for example heat syndrome .Therefore Understanding the different non-infectious etiology help in early diagnosis and prompt initiation of effective and appropriate treatment for early recovery of the patient and its better outcome.

Acute febrile encephalopathy has different spectrum of infectious etiology like viral, fungal, bacterial, protozoa which is needed to be studied for better understanding of disease spectrum and early start of effective empirical treatment, any delay in starting of therapy will have a serious complication and neurological squeal and increase morbidity and mortality.[1]

In this study we have tried to look at the different clinical presentation of various etiology of acute febrile encephalopathy including both infective and no infective etiology in tertiary health care center in SRMS-IMS hospital.

MATERIALS AND METHODOLOGY

The present study was conducted over 18 months time period September 2018 to March 2020. It is a prospective observational type of study. Inclusion criteria were patient with age more than 18 Years, patient with fever <2 Weeks duration and altered sensorium either at the onset or following the fever. Exclusion criteria were age<18 Years, altered sensorium attributable to the metabolic cause, Cerebrovascular accidents followed by fever, Known case of CKD on hemodialysis, Space occupying lesion of brain and Trauma.

Clinical features, laboratory investigations, and brain imaging was done in all the patient meets the inclusion criteria as mentioned above, during the study period. A proforma is prepared which included a detailed history, clinical examination, and requisite investigations available in the hospital. After taking informed consent from the patient, history, and clinical findings attributable to the acute febrile encephalopathy are collected in detail.

Investigations like complete hemogram, routine urine analysis, blood sugar, serum electrolytes, serum creatinine, blood urea, liver function tests, blood cultures, chest X-ray, Electrocardiogram, MP antigen, Typhi dot, dengue serology, CSF analysis(CSF sugar, protein, total count, differential count, Gram stain, bacterial culture, Z.N stain for AFB, India ink stain for Cryptococcus, CT or MRI brain were done in all patients. Investigations like CSF PCR studies were done in the patients as required.

Depending on the patient's clinical presentation, duration of illness, CSF analysis, and brain imaging findings, patients were classified into their etiology. Patients are examined clinically in detail and their severity is assessed based on the clinical grounds, laboratory investigations, and brain imaging findings. CECT or 3T/ 1.5 Tesla MRI was done in all patients.

Various etiologies of acute febrile encephalopathy were classified as an infectious and non-infectious group. The infectious group includes viral, tubercular, bacterial, septic, protozoal, and fungal causes and the non-infectious group includes metabolic, toxic, and drug induced acute febrile encephalopathy.

Table 1:diagnostic Criteria Used For Various Etiologies Is As Follows

1. Acute viral encephalitis [2]
• Acute febrile encephalopathy +/- Meningitis with CSF pleocytosis of more than 5 WBC/cumm in addition to the following criteria

• Absence of detectable bacterial pathogen on CSF smear/culture or blood culture AND/OR
• EEG/MRI/CT evidence of parenchymal disease AND/OR
• CSF for HSV PCR positive
• Negative CSF for AFB
2. Bacterial meningoencephalitis[2]
• Acute febrile illness +/- Meningitis with CSF pleocytosis >10 wbc/cumm with neutrophilic predominance with clinical features of meningitis and CSF sugar <50% of RBS AND/OR
• Gram staining of CSF positive for meningitis causing bacteria OR
• A CSF culture positive for a known bacterial pathogen
3. Tuberculous meningitis[2]
• Acute febrile illness with clinical features of altered mental status+/- meningismus
• Ziehl-Neelsen stain of CSF positive for acid fast bacilli OR
• A CSF culture positive for tuberculous bacilli OR
• CSF Xpert-MTB RT-PCR analysis positive for TB OR
• Neuroimaging (CT/MRI scan) consistent with TB meningitis (hydrocephalus, basal meningeal enhancement etc.) OR
• Any other source positive for tuberculosis (lymph node biopsy / sputum smear / tissue biopsy / bone marrow biopsy / Chest x ray findings etc.) AND/OR
• Clinician's decision about the diagnosis
4. Septic encephalopathy[2]
• Fever with altered mental status AND Features of sepsis include infection (documented or suspected) and some of the following feathers of SIRS as (Temperature>38.3 or <36, HR >90, RR>20 and altered mental status).
• Features of systemic inflammation like (WBC>12000, leukopenia WBC<4000, CRP>2 SD, Plasma procalcitonin >2SD.
• Feathers of organ dysfunction like Arterial hypoxemia(PaO2/FiO2<300),Acute oliguria(<0.5 ml/hr for >2 hr despite fluid resuscitation, creatinine rise ,creatinine rise >0.5 mg/dl, INR>1.5, Paralytic ileus, Thrombocytopenia(platelet count <100000), Hyperbilirubinemia (>4mg/dl).

5. Other Causes

Cerebral malaria, Dengue encephalitis and Leptospirosis were diagnosed in patients who present with febrile encephalopathy and were positive for Malaria antigen or on peripheral smear, Dengue Elisa & leptospirosis serology respectively. Non-infectious etiology was diagnosed in the patients having normal CSF examination and Neuroimaging findings.

RESULTS & OBSERVATIONS

The minimum age of patients was 18 years and the maximum was 81 years with a mean of 40.5 years+-10.92 years. Among 97 patients in the present study, the majority of patients (79.23%) were from the age group of less than 60 years. 18.58 % of patients belonged to the age group of 60-79 years. The majority of patients i.e 60 patients were (62%) males and 37 patients were females. Hypertension and Diabetes mellitus was the common comorbidities seen in study patients. 3.2% of patients had a history of diabetes mellitus and 6.6% of patients had a history of hypertension.

As per Table 2- among 97 patients in the study group, the common initial presenting symptoms were fever, headache, and altered sensorium as shown in Table 2. The mean GCS score at admission was 9.11 with a median of 9.

Table 2- Depicting the characterstics of patients with Acute Febrile Encephalopathy in different etiologies

Column1	VIRAL	PYOGENIC	TUBERCULAR	SEPSIS	CEREBRAL MALARIA
FEVER	37 (100)%	11(100%)	21(100 %)	8(100 %)	8(100)%
ALTERED SENSORIUM	37 (100)%	11(100%)	21(100 %)	8(100 %)	8(100)%
SEIZURE	17 (45.94)%	3(27.27%)	7(33.33 %	3(37. 5%)	2(25%)
CSF TLC	64.17 +- 65.23	1375.417 +- 1336.58	278.90+ - 395.77	1.25+ - 2.5	35.62+- 87.072
PROTEIN	105.44+- 57.18	394.69+ -346.91	289.26+- 325.03	82.75+ -56.97	63.15+-43.72
SUGAR	67.72+- 27	48.92+- 28.69	49.70+- 40.46	90.28+ -35.74	54.37+-12.55
CT/MRI FINDINGS	8(21.6%)	3(27.27 %)	5(23.80%)	ALL NORMAL	ALL NORMAL

Among 97 patients 76% of patients have normal neuroimaging. (4.12%) patients had hydrocephalus. Hyper and hypodensity on neuroimaging were seen in (8.24%) patients. The vasculitic infarct is seen in (8%) of patients, and only (2%) patients had granuloma brain on MRI.

As per Table 3- Among 97 patients in the study, 37 i.e. 38.1%of patients were diagnosed with viral encephalitis. (21.6%) of patients were diagnosed as Tubercular meningitis followed by (11.3%) of patients diagnosed with pyogenic meningitis and only (8.2%) of patients were diagnosed as Septic encephalitis. Among the 37 patients with viral meningoencephalitis, we did HSV PCR testing in 18 patients, and out of 18, only 8 patients were HCV PCR positive in CSF. The remaining were negative and were diagnosed with viral encephalitis based on CSF and MRI findings.

Table 3: Etiology Of Acute Febrile Encephalopathy

Row Labels	Count of FINAL DIAGNOSIS
VIRAL ENCEPHALITIS	37
TUBERCULAR MENINGITIS	21
PYOGENIC MENINGITIS	11
SEPTIC ENCEPHALOPATHY	8
CEREBRAL MALARIA	8
DENGUE ENCEPHALOPATHY	4
HEAT STROKE	2
LEPTOSPIROSIS	3
SUSPECTED AUTOIMMUNE ENCEPHALITIS	1
FEBRILE DELIRIUM	1
CRYPTOCOCAL MENINGITIS	1

The patient who presented with subacute meningitis, CSF lymphocytic pleocytosis, elevated CSF protein, and absent cryptococcal antigen in CSF were diagnosed as probable tuberculous meningitis; MRI evidence of basal meningeal exudates, hydrocephalus, tuberculous granuloma in the brain helped to reach the diagnosis of tuberculous meningitis. One patient had cryptococcal meningitis (patient with HIV infection). 3 Patients were diagnosed with leptospirosis, 8 patients were having Cerebral malaria 4 patients were having Dengue encephalopathy.4 patients belong to another sub-group which is collectively grouped under the non-infectious group of febrile encephalopathy comprising heat stroke, febrile delirium, and autoimmune encephalitis.

DISCUSSION

In present study the predominant etiology of acute febrile encephalopathy was infectious (96%). Among the infectious, our study found that infection of the central nervous system was the most common cause which included acute bacterial meningitis (12%), tubercular meningitis(22%), viral meningitis or meningoencephalitis (38%), septic meningitis (8%) and protozoal meningitis(8%).

There was no difficulty in diagnosing patients with acute pyogenic meningitis. All 11 patients presented with sudden onset of fever, headache, and rapidly deteriorating conscious level within 1-2 days of symptoms onset. All patients had altered sensorium with a reduction in the conscious level. Patients were diagnosed with pyogenic meningitis based on typical CSF findings. All patients had high protein, low sugar, and very high neutrophil count in the CSF (> 400cells/cm2)

All patients received empirical antibiotic therapy with Inj. ceftriaxone 2gm IV BD and Inj. Vancomycin 1gm IV bd was continued throughout the illness irrespective of sensitivity reports (Due to the high incidence of penicillin resistance for pneumococci in the recent reports). Early recognition and prompt treatment resulted in decreased morbidity and mortality as shown in other studies.18

We diagnosed viral encephalitis based on CSF analysis and brain imaging features; viral etiology was considered when CSF had slightly

elevated protein, low normal blood sugar, and moderately elevated lymphocyte count. Bacterial cultures, gram-stain, and India ink stain were negative in these patients.

Tubercular meningitis can mimic viral meningitis, especially when the presentation is acute. Some patients who were treated for viral meningitis came back to the hospital, with tuberculous meningitis. 32 Tuberculous meningitis can have lymphocytic pleocytosis in the CSF and can be misdiagnosed as viral meningitis in the initial evaluation.32 So a treating physician must follow up with the patient regularly.[11]

In present study, though we are unable to isolate the organisms in 29 out of 37 patients with presumed viral encephalitis, we were able to rule out tuberculous or fungal etiology in these patients. Because these patients recovered well without specific antibiotics, antituberculosis and antifungal therapy and they were asymptomatic during follow up which confirmed the diagnosis of probable viral etiology.

Tubercular meningitis is often diagnosed based on clinical, CSF findings, and radiological correlation. Elevated protein and lymphocytic pleocytosis in CSF, presence of basal meningeal exudates, presence of tuberculoma, hydrocephalus, and typical distribution of vasculitic infarcts in the capsuloganglionic region in brain imaging suggested the diagnosis of probable tuberculous meningitis in these patients. Tuberculous meningitis commonly presents as either subacute or chronic meningitis, but we found that a proportion of our 21 patients(22%) presenting with this syndrome had tuberculous etiology which was less than 10 % in most other studies.[12]

This could be attributed to this being a referral center and the higher prevalence of tuberculosis in the community. Early diagnosis of TBM is crucial because early initiation of treatment will prevent disability and irreversible complications. Empirical anti-tuberculous therapy should be started in the setting of compatible clinical, epidemiological, and laboratory findings. With early appropriate anti-tuberculous therapy and steroids, all patients in this study recovered well without neurological deficits.

Four patients had dengue virus encephalitis. Sepsis-associated encephalopathy though is not a primary CNS infection presented with this syndrome in 8 % of patients which was slightly less compared with a few studies which had mentioned sepsis-associated encephalopathy as an etiology.[9] The non-infectious etiology comprises only 4% and were heat stroke, febrile delirium, and autoimmune encephalitis in which CSF and CT/MRI both were normal.

In our study we also looked at various admission parameters including clinical symptoms, signs, comorbidities, vital status, and laboratory parameters both hematological, biochemistry, and CSF findings would predict the diagnosis particularly infectious and non-infectious as we know that early diagnosis and prompt treatment can prevent mortality and morbidity. So early diagnosis and prompt treatment resulted in early recovery and less post neurological sequelae.

CONCLUSION

Acute febrile encephalopathy is a challenging clinical entity for the physicians in the emergency department because of the wide spectrum of etiology causing it and the high mortality and morbidity associated with it.

In this study, we attempted to look at the entire spectrum of patients presenting with AFE including both the infectious and non-infectious. Detailed history taking and examination will help identify symptoms and signs that can predict diagnosis. Viral encephalitis was the most common overall cause in this study Early diagnosis and prompt treatment resulted in the early recovery of the patients presented with this syndrome. High mortality and morbidity associated with this syndrome makes it more challenging and also warrants more research to identify the etiology as many cases we found remained undiagnosed.

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