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## A STUDY ON ETIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND PROGNOSIS IN ACUTE FEBRILE ILLNESS

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### ABSTRACT:

**Background:** Acute febrile encephalopathy (AFE) is a clinical term used to an altered mental state that either accompanies or follows a short febrile illness and is characterized by a diffuse and nonspecific brain insult manifested by a combination of coma, seizures, and decerebration.

**Materials and Methods:** A prospective observational study was done in patients aged 13 years or above who were admitted with AFE at a Tertiary Care Center in Government General Hospital, Dept of General Medicine, Kurnool Medical College, Kurnool, Andhra Pradesh. The non-infectious causes of unconsciousness were excluded and then only a diagnosis of AFE was considered. Cerebrospinal fluid (CSF) analysis and imaging of brain was done to determine the possible etiology. Outcome was assessed at 1 month of follow up after discharge by using modified Rankin Scale (MRS). Data were analyzed and presented as mean, median, and percentages.

**Results:** Among the 50 patients 33 (66%) are male patients. 43 patients (86%) were young adults. The common presenting symptoms are fever in 41 patients (82%), headache in 29 patients (58%), altered sensorium in 19 patients (38%). Out of 50 patients studied acute febrile encephalopathy was common in males when compared to female, more common in age group 30-40 years. Acute viral encephalitis was the most common cause accounting for 36 percentage in which Herpes Simplex Encephalitis 24 percentage Japanese encephalitis 4 percentage and other undetermined viral etiology count for 10 percentage followed by pyogenic meningitis 28 percentage followed by tuberculous meningitis 12 percentage, cerebral malaria diagnosed 2 percentage sepsis associated encephalopathy 10 percentage in which 6 percentage leptospirosis and 4 percentage scrub typhus were diagnosed. Of all the total cases 2 patient died in which one patient with HIV associated Cryptococcus meningitis other patient with pyogenic meningitis. MRS at discharge were five in pyogenic meningitis three in viral meningitis after one month, MRS was 2 in pyogenic meningitis and the rest it was less than one

**Conclusions:** In the present study we found that, most of the patients with meningoencephalitis were males and young adults in this study viral meningo encephalitis was the leading cause of acute febrile encephalopathy followed by pyogenic meningitis and tuberculous meningitis. The outcome in cases with pyogenic meningitis can be fatal or more disabling than other aetiology.

**Keywords:** AMS -- Altered Mental Sensorium, CrAg -- Cryptococcal Antigen

**INTRODUCTION** Acute febrile encephalopathy is term clinically used for altered mental status that follows short febrile illness characterised by diffuse nonspecific brain insult with clinical manifestations of coma, seizures and decerebration. The most common cause may be due to meningitis or encephalitis is non traumatic cases. Meningitis is a clinical syndrome characterized by inflammation of meninges.

The classic triad of meningitis consists of fever, headache and neck stiffness<sup>1</sup>

Bacterial meningitis occurs in about 3 people per 100,000 annually in western countries. Population-wide studies have shown that viral meningitis is more common at 10.9 per 100,000 population. Bacterial (pyogenic) meningitis is a pyogenic inflammation of meninges and subarachnoid cerebrospinal fluid (CSF) and is characterized by neutrophilic pleocytosis in CSF<sup>2</sup>. Pneumococcal meningitis is caused by streptococcus pneumonia, a gram

positive coccus and is the most common bacterial cause of meningitis. Meningococcal meningitis is caused by gram-negative diplococcus – Neisseria meningitides. Most patients recover completely if appropriate antibiotic therapy is instituted promptly<sup>2</sup> Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment<sup>3</sup>. Tuberculous meningitis should be a strong consideration when a patient presents with clinical picture of meningoencephalitis, especially in high risk groups, including persons with malnutrition, those with alcohol abuse or drugs and patients with known retroviral infection. Death may occur as a result of missed diagnosis and delayed treatment<sup>4</sup>.

#### **AIM & OBJECTIVES-**

To identify to etiology, clinical manifestations of various acute febrile encephalopathy

To evaluate for diagnosis and to asses prognosis in acute febrile encephalopathy.

#### **MATERIALS AND METHODS**

This is prospective study conducted at Department of General Medicine, Govt. General

Hospital (GGH) Kurnool Medical College, Kurnool, Andhra Pradesh during the period from October 2019 to October 2021. All patients above the age group of 13 years to 65 yrs who presented to the hospital with acute febrile encephalopathy with neurological manifestations and admitted in the Department of Medicine at GGH. Kurnool with fever of less than two weeks duration along with altered sensorium with or without seizures were enrolled in the study after taking consent from each subjects

#### **INCLUSION CRITERIA:**

All children over the age of 13 and all adults up to the age of 65 are included patients with an acute febrile illness lasting less than 2 weeks and any of the clinical neurological manifestations of altered consciousness level, headache, disorientation, vomiting, focal neurological deficit, blurring of vision, and diarrhoea, vomiting, chills, and rigors. A total of 50 patients were enrolled in the study

#### **EXCLUSION CRITERIA:**

Patients with non-infectious causes of unconsciousness, such as traumatic brain injury, chronic encephalopathy, and vascular (vasculitis, SLE, SAH, SDH, stroke, and behcets) with a history of neurological disorders such as seizures and whose persistent altered mental status could be attributed to dearranged condition was excluded. Patients with metabolic (hepatic renal failure, diabetes) encephalopathy with metabolic parameters such as hypoglycemia, Dyselectrolytemia with hyponatremia, space occupying lesion (SOL) or endocrinopathies such as addison's, hypothyroidism and hashimotos encephalopathy were excluded from the study. Patients with a history of psychiatric illness or pharmacological treatment for other neurological illnesses were not included in the study

After taking informed consent from the patient, history and clinical findings attributable to the meningitis and meningoencephalitis 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, CSF analysis(CSF sugar, protein, total count, differential count, gramstain, bacterial culture, Z.N stain for AFB, India ink stain for Cryptococcus, Cryptococcal antigen test, automated

culture for AFB, CT or MRI brain<sup>5</sup> were done in all patients. Investigations like CSF PCR studies<sup>6</sup> were done in the patients as required. According to patients clinical presentation, duration of illness, CSF analysis and brain imaging findings, patients were classified according to their etiology. Patients are examined clinically in detail and their severity is assessed based on the clinical grounds, laboratory investigations and brain imaging

findings. To assess the clinical outcome of the patients, modified Rankin Scale was used. Based on this scale. Patients functional evaluation was done at the end of the first month. The results were analysed to assess the clinical presentation, etiology, and clinical outcome in these patients diagnosed with meningoencephalitis.

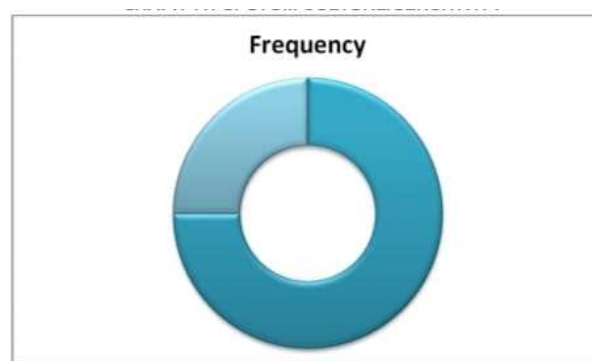
**Statistical tools:** The data collected from the patients is tabulated using Microsoft Excel. The data are reported as the mean +/- SD or the median, depending on their distribution. The differences in quantitative variables between groups were assessed by means of the unpaired test. Comparison between groups was made by the non-parametric Mann-Whitney test. A Chi square test was used to assess differences in categoric variables between groups. P value of 0.05 using two tailed test was taken as being of significance for all statistical tests. All data were analysed with a statistical software package (SSPS version 16.0 for window)

**OBSERVATIONS:**

**TABLE 1: SPUTUM CULTURE/SENSITIVITY & AFB**

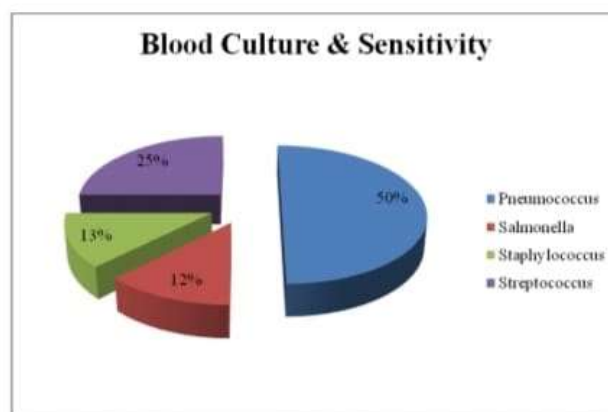
Sputum Culture/Sensitivity	Frequency	Percent
Mycobacteria	3	6.0

Sputum culture sensitivity seen in 6 % cases in the study



**TABLE 2: BLOOD CULTURE & SENSITIVITY**

Blood Culture & Sensitivity	Frequency	Percent
Pneumococcus	4	8.0
Salmonella	1	2.0
Staphylococcus	1	2.0
Streptococcus	2	4.0



**TABLE 3 : CSF PROTEIN & GLUCOSE VALUES**

Protein(mg/dl)	Frequency	Percent
<40	18	36.0
40-100	26	52.0
>100	6	12.0
Glucose (mg/dl)		
<40	28	56.0
>40	22	44.0

CSF Gram Stain Positivity	Frequency	Percent
Streptococci	2	4.0
Staphylococci	2	4.0
Nesseria meningococci	1	2.0
Mycobacterium Tuberculosis	3	6.0
pneumococcus	2	4.0

TABLE 4:CSF GRAM STAIN POSITIVITY

**DISCUSSION:** In this study we analyzed 50 consecutive patients of meningo encephalitis admitted in GGH, Kurnool between October 2019 to October 2021. Although epidemiological studies are not available to analyze the accurate incidence of meningo encephalitis, several epidemiological data are available separately for bacterial, viral and fungal infections of the central nervous system. This study is unique that we analyzed all the cases of meningo encephalitis and we are able to produce small epidemiological data about the incidence of common organisms responsible for meningo encephalitis in a tertiary care center level. Vigorous supportive therapy and avoidance of complications are very important in managing these patients<sup>7</sup>

#### Limitations of the study: -

However, as the study was limited to a small population, analysis of a larger group would definitely give an insight into the various causative factors leading to hyper homocysteinemia and its role in CAD amongst the young Indian population.

#### CONCLUSION

Acute febrile encephalopathy is a heterogenous syndrome. Many causative agents can result in a very similar kind of presentation. This study was prospective and observational study aimed to detect etiology and clinical features of acute febrile encephalopathy. The current study highlighted the following findings: The mean age of presentation in current study was between 30 - 40 years. The younger age group in the present study is correlating with other studies such as Modi et al. Males predominate in the current study with male to female ratio 3:2 which is

accordance with Modi et al. In a study Panagaria

CSF Culture Sensitivity	Frequency	Percent
Bacteria	14	28.0
Mycobacterium Tuberculosis	3	6.0
Fungus	1	2.0

et al have shown similar trend of male predominance in HSV encephalitis. Although none of CNS infection are known to have a male predominance, this apparent male predominance can be attributed to be male dominated social system where sick male gets preferential medical attention

Most common presentation in present study are fever and headache which is lower in present study compared to other studies like Ashish et al. Most common sign in the current study –neck rigidity (34%) which is slightly lower than when compared to other studies by Joshi et al. This indicates that absence of fever or neck stiffness does not exclude the possibility of infectious meningoencephalitis

Most common etiology in the present study presented was viral meningoencephalitis followed by pyogenic meningitis followed by tuberculous meningitis. This observation is similar to the Western literature where viral etiology in the most common one in western population where as Modi et al study had pyogenic meningitis being common etiology.

Out of 50 patients 23 had acute viral meningoencephalitis, 14 patients had acute pyogenic bacterial meningitis, 6 patients had acute presentation of tuberculous meningitis, 1 patient was diagnosed as Cryptococcal meningitis and remaining 1 had cerebral malaria while 3 had leptospirosis and 2 had rickettsial disease which was comparable to Ashish et al<sup>8</sup>.

Among acute viral encephalitis in current study Herpes Simplex encephalitis (36%) was the most common cause followed by Japanese encephalitis (4%) and other undetermined viral etiology (10%) which is in contrast to other studies as many of them were done by western people. Pyogenic meningitis (28%) in current

study where as Modi et al<sup>9</sup> study showed 36.7% of pyogenic meningitis. Tuberculous meningitis was 12% in present study which is less when compared to the other studies such as Modi et al. due to exclusion of subacute and chronic presentation from tuberculous meningitis. Septic encephalopathy was 10% in present study which is comparable with other studies like Ashish et al. Overall mortality rate in present study was 4% which is very less compared to other similar studies by Modi et al., Ashish et al.,.

Modified Rankin score at time of discharge was five in pyogenic meningitis three in viral meningitis after one month, MRS was two in pyogenic meningitis and the rest it was less than one. The outcome in cases with pyogenic meningitis was fatal or more disabling than other aetiology which is contrast to Modi et al<sup>10</sup> where more fatal outcome seen in acute viral encephalopathy

The current study is similar to many Indian studies with respect to younger age of presentation, gender difference and etiology of acute febrile encephalopathy but varied with respect to symptoms and signs and mortality rate. In tropical countries like India, viruses transmitted by arthropod constitute very important cause like JE<sup>11</sup>. Other important cause like cerebral malaria and rickettsial disease should be considered. Western studies have higher presentation of other viral meningoencephalitis like enterovirus as the clinical profile of acute febrile encephalopathy varies across different geographic region

Many acute febrile patients with encephalopathy may recover completely once the underlying cause is treated. Hence large studies are necessary for understanding the epidemiology etiological spectrum , factors affecting mortality and morbidity of acute febrile encephalopathy

## DECLARATIONS

**Conflict of interest:** There was no conflict of interest.

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## REFERENCES

1. Ginsberg L, Kidd D. Chronic and recurrent meningitis. *Pract Neurol*. Dec 2008;8(6):348-61
2. Moses S. Meningitis: Acute bacterial <http://www.fpnotebook.com/neuro/ID/Mngts.htm>. meningitis.
3. Rich AR, McCordick HA. The pathogenesis of tuberculous meningitis. *Bulletin of John Hopkins Hospital*. 1933;52:5-37.
4. World Health Organization. Tuberculosis. WHO Organization. <http://www.who.int/mediacentre/factsheets/fs104/en/>.
5. Demaerel P, Wilms G, Robberecht W, Johannik K, Van Hecke P, Carton H, et al. MRI of herpes simplex encephalitis. *Neuroradiology* 1992;34:490-3.
6. Fujiwara K, Yokosuka O, Fukai K, Imazeki F, Saisho H, Omata M, et al. Analysis of full-length hepatitis A virus genome in sera from patients with fulminant and self-limited acute type A hepatitis. *J Hepatol* 2001;35:112-9.
7. Landry ML, Greenwold J, Vikram HR. Herpes simplex type-2 meningitis: presentation and lack of standardized therapy. *Am J Med*. Jul 2009;122(7):688-91.
8. Ashish Bhalla, Vikas Suri, Paramjeet Singh, Subhash Varma, Niranjana Khandelwal. Imaging in adult patients with acute febrile encephalopathy : What is better Computerized Tomography or Magnetic Resonance Imaging. *Indian Journal of Medical Sciences*, 2011;65:193-202
9. Aniyang Modi, Virendra Atam, Nirdesh Jain, Manish Gutch, Rajesh Verma. The etiological diagnosis and outcome in patients of acute febrile
10. Aniyang Modi, Virendra Atam, Nirdesh Jain, Manish Gutch, Rajesh Verma. The etiological diagnosis and outcome in patients of acute febrile encephalopathy: A prospective observational study at tertiary care center. *Neurol India* 2012; 60:168-73.

11. Shrestha, S. R., Awale, P., Neupane, S., Adhikari, N. & Yadav, B. K. Japanese Encephalitis in Children admitted at Patan Hospital. *J. Nepal Paediatr. Soc.* 29, 17–21 (2009).