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**Original Research Article**

# Clinical profile and outcome of patients with meningoencephalitis in a tertiary care hospital

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## ABSTRACT

**Background:** Encephalitis is an important cause of morbidity, mortality, and permanent neurologic sequelae globally. Causes are diverse and include viral and non-viral infections. In the emergency setting differentiating the bacterial from other causes such as viral, fungal, tubercular, toxic or autoimmune causes is extremely difficult. Although plenty of literature is available on meningitis, the clinic-etiological profile and outcome with meningoencephalitis remains not that well studied, except for in paediatric population.
**Methods:** The present prospective observational study included 75 patients who presented with acute encephalitis syndrome in tertiary care hospital, Bengaluru. All patients were subjected to complete clinical evaluation and appropriate investigations to study the etiology, clinical profile and outcome in them.
**Results:** Among 75 patients, majority of them were <60 years constituting about 73.2%, mean age being 49.14 years with female preponderance. 30 (40%) patients had viral meningoencephalitis where aetiology was confirmed in 15 patients, remaining were presumed to be of viral aetiology. 12 (16%) had tubercular meningitis and 8 (10.6%) had bacterial meningitis followed by cryptococcal meningitis 7 (9.3%). In about 18 (24%) patients, aetiology was not identified and were treated based on syndromic approach. The most common presentation was fever and altered sensorium. Thrombocytopenia was common among viral and bacterial aetiologies and those in unspecified etiological group. Mortality was highest among cryptococcal meningitis (71.4%) followed by tubercular (66.7%) and bacterial meningitis (62.5%).
**Conclusions:** A large number of number of cases where aetiology cannot be identified maybe benefited by a syndromic approach and better diagnostic modalities.

**Keywords:** Meningoencephalitis, Syndromic approach, Mortality

## INTRODUCTION

Meningitis is a clinical syndrome characterized by inflammation of the meninges surrounding the brain and spinal cord. The classic triad of meningitis consists of fever, headache and neck stiffness.[1] Although encephalitis by definition involves the brain parenchyma, it may also involve the meninges as well, which is termed as meningoencephalitis.

The clinical presentation is encephalopathy with diffuse or focal neurological symptoms, including behavioural and personality changes, decreased level of consciousness, neck pain/stiffness, photophobia, lethargy, generalised focal seizures, acute confusion or amnestic states and flaccid paralysis.[2]

The most common bacterial pathogens are *Streptococcal pneumonia*, *Neisseria meningitides*, *H. influenza*, *Listeria monocytogens* and *Staphylococcus aureus*. Tubercular meningitis is caused by *Mycobacterium tuberculosis*.

Among the viral infections, the common cause includes herpes simplex virus (HSV), entero-virus, arboviruses like dengue, chikungunya and Japanese encephalitis virus.

In the emergency setting differentiating the bacterial from other causes such as viral, fungal, tubercular, neoplastic, toxic or autoimmune causes is extremely difficult. If a diagnosis of meningitis is made, it is prudent to start the patient on empirical antibiotics until the cultures and other results are awaited.[3]

Although plenty of literature is available on meningitis, the clinic-aetiological profile and outcome in patients with meningoencephalitis remains not that well studied, except for in paediatric population.[4]

## METHODS

This was a prospective observational study conducted on patients admitted under medicine department between February 2020 and February 2021 at Victoria Hospital, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India. Approval and clearance were obtained from the institutional ethics committee dated 29/01/2020, BMCRI/PS/210/2019-20.

The study included those patients who presented with altered mental status in the form of decreased or altered level of consciousness, lethargy, or behavioral change lasting more than or equal to 24 hours with no alternative cause identified. Exclusion criteria included patients not willing to give informed consent, brain imaging showing structural or vascular lesions and altered mental status secondary to deranged metabolic parameters. Further investigations included cerebrospinal fluid (CSF) examination, i.e., biochemical and cytological analysis and CSF for virological analysis, brain computed tomography (CT) or magnetic resonance imaging (MRI), blood investigations such as complete blood count, renal function tests, and liver function tests with serological investigation for virus and bacteria. Other appropriate investigations were done as per the patient's clinical presentation. A total of 75 patients were studied.

Sample size estimation where, n is no of sample size, p is proportion=26, and d is 10% relative risk on substitution.

$$n = 4pq/d^2$$

$$q = 100 - p = 100 - 26 = 74$$

$$n = 4 \times 26 \times 74/(10)^2 = 77$$

### *Statistical analysis*

Statistical package for social sciences (SPSS) version 20 (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis.

Data was entered in the excel spread sheet.

Descriptive statistics of the explanatory and outcome variables were calculated by mean and standard deviation for quantitative variables, frequency and proportions for qualitative variables.

Inferential statistics like Chi-square test was applied for qualitative variables.

Analysis of variance (ANOVA) was applied to compare the lab parameters; duration of hospital stays among the groups.

The level of significance is set at 5%.

## RESULTS

### *Demographics*

The study included 75 patients with acute meningoencephalitis. Among 75 patients, 45(60%) were females and 30(40%) were males (Table 1). The majority of them were <60 years constituting about 73.2% with mean age being 49.14 years (Table 2).

**Table 1: Distribution of the subjects based on gender.**

| Variables | Frequency (%) |
|---|---|
| **Gender** | |
| Females | 40 (53.3) |
| Males | 35 (46.7) |
| Total | 75 (100.0) |

**Table 2: Distribution of subjects based on age.**

| Age group | Frequency |
|---|---|
| 18-20 | 1 |
| 21-30 | 12 |
| 31-40 | 11 |
| 41-50 | 15 |
| 51-60 | 15 |
| 61-70 | 13 |
| 71-80 | 5 |

50% of patients each for bacterial and viral meningoencephalitis came from Bangalore district. Tumkur district contributed about 40% of the patients with viral meningoencephalitis and 38.8% among those meningoencephalitis cases where etiology was not identified (Table 3).

### *Clinical profile and presentation*

The common initial presenting symptoms were fever (85%), headache and altered mental status (82.7%) among all types of meningoencephalitis with fever and altered sensorium being most common among bacterial, viral and unspecified etiology of meningoencephalitis. Headache and altered sensorium were the commonest presentations among patients with tubercular meningitis. About 4

patients with viral meningoencephalitis had seizures; 3 had generalised tonic clonic while focal seizures were noted in 1 patient.

***Aetiological distribution***

The most common cause found in the present study was of viral etiology constituting 30 (40%) cases followed by unidentified etiology 18 (24%). Tubercular meningitis constituted around 12 (16%) of total cases. Bacterial meningitis and cryptococcal meningitis constituting around 8 (10.6%) and 7 (9.3%) respectively.

***Lab parameters***

Thrombocytopenia was noted in viral, bacterial and unspecified aetiology mean value being 1.32, 1.27 and 1.47 lakhs respectively which was statistically significant (Table 5).

**Imaging**

Imaging of the brain (CT/MRI) was normal in majority of the patients. Leptomeningeal enhancement was found in 9 patients with viral and 2 patients with cryptococcal meningitis. Among tubercular meningitis, 5 patients had basal exudates, 2 had ring enhancing lesions in cerebellar and caudate lobes. 2 patients each with bacterial meningitis and cryptococcal meningitis had hydrocephalus (Table 6).

***Outcome***

Death was highest among patients with cryptococcal meningitis (71.4%) followed by tubercular meningitis (66.7%) and viral meningoencephalitis (36.7%) (Table 7).

With the average length of stay being least for bacterial (3.5 days), viral (3.8 days) and unspecified aetilogy (3.7 days) (Table 8).

**Table 3: Association of the etiology with location.**

| Location | Etiology | | | | | Total |
|---|---|---|---|---|---|---|
| | Viral | Bacterial | Tubercular | Cryptococcal | Unknown | |
| **Bangalore** | | | | | | |
| Count | 15 | 4 | 7 | 6 | 5 | 37 |
| % | 50.0 | 50.0 | 58.3 | 85.7 | 27.8 | 49.3 |
| **Chikkaballapura** | | | | | | |
| Count | 0 | 1 | 0 | 0 | 2 | 3 |
| % | 0.0 | 12.5 | 0.0 | 0.0 | 11.1 | 4.0 |
| **Hassan** | | | | | | |
| Count | 1 | 0 | 0 | 0 | 2 | 3 |
| % | 3.3 | 0.0 | 0.0 | 0.0 | 11.1 | 4.0 |
| **Kolar** | | | | | | |
| Count | 2 | 0 | 2 | 0 | 2 | 6 |
| % | 6.7 | 0.0 | 16.7 | 0.0 | 11.1 | 8.0 |
| **Others** | | | | | | |
| Count | 0 | 2 | 1 | 0 | 1 | 4 |
| % | 0.0 | 25.0 | 8.3 | 0.0 | 5.6 | 5.3 |
| **Tumkur** | | | | | | |
| Count | 12 | 1 | 2 | 1 | 6 | 22 |
| % | 40.0 | 12.5 | 16.7 | 14.3 | 33.3 | 29.3 |
| **Total** | | | | | | |
| Count | 30 | 8 | 12 | 7 | 18 | 75 |
| % | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

Chi-square value=26.67; p value=0.145

**Table 4: Association of the symptoms with etiology.**

| Symptoms | | Etiology | | | | | Total | Chi square value | P value |
|---|---|---|---|---|---|---|---|---|---|
| | | Viral | Bacterial | Tubercular | Cryptococcal | Unknown | | | |
| **Fever** | | | | | | | | | |
| - | Count | 3 | 0 | 2 | 5 | 1 | 11 | 21.15 | 0. 001* |
| | % | 10.0 | 0.0 | 16.7 | 71.4 | 5.6 | 14.7 | | |
| + | Count | 27 | 8 | 10 | 2 | 17 | 64 | | |
| | % | 90.0 | 100.0 | 83.3 | 28.6 | 94.4 | 85.3 | | |

Continued.

| Symptoms | | Etiology | | | | | Total | Chi square value | P value |
|---|---|---|---|---|---|---|---|---|---|
| | | Viral | Bacterial | Tubercular | Cryptococcal | Unknown | | | |
| **Rash** | | | | | | | | | |
| - | Count | 28 | 7 | 12 | 7 | 16 | 70 | 2.36 | 0.669 |
| | % | 93.3 | 87.5 | 100.0 | 100.0 | 88.9 | 93.3 | | |
| + | Count | 2 | 1 | 0 | 0 | 2 | 5 | | |
| | % | 6.7 | 12.5 | 0.0 | 0.0 | 11.1 | 6.7 | | |
| **Altered sensorium** | | | | | | | | | |
| - | Count | 4 | 1 | 4 | 1 | 3 | 13 | 2.66 | 0.616 |
| | % | 13.3 | 12.5 | 33.3 | 14.3 | 16.7 | 17.3 | | |
| + | Count | 26 | 7 | 8 | 6 | 15 | 62 | | |
| | % | 86.7 | 87.5 | 66.7 | 85.7 | 83.3 | 82.7 | | |
| **Seizure** | | | | | | | | | |
| - | Count | 26 | 8 | 12 | 6 | 17 | 69 | 3.42 | 0.49 |
| | % | 86.7 | 100.0 | 100.0 | 85.7 | 94.4 | 92.0 | | |
| + | Count | 4 | 0 | 0 | 1 | 1 | 6 | | |
| | % | 13.3 | 0.0 | 0.0 | 14.3 | 5.6 | 8.0 | | |
| **Headache** | | | | | | | | | |
| - | Count | 24 | 6 | 5 | 6 | 15 | 56 | 8.52 | 0.07 |
| | % | 80.0 | 75.0 | 41.7 | 85.7 | 83.3 | 74.7 | | |
| + | Count | 6 | 2 | 7 | 1 | 3 | 19 | | |
| | % | 20.0 | 25.0 | 58.3 | 14.3 | 16.7 | 25.3 | | |

**Table 5: Comparison of the mean lab parameters based on type of infection using ANOVA.**

| Lab parameters | Etiology | N | Minimum | Maximum | Mean | SD | P value |
|---|---|---|---|---|---|---|---|
| **Hb** | Viral | 30 | 2.58 | 15.10 | 11.26 | 2.42 | 0.224 |
| | Bacterial | 8 | 10.80 | 15.20 | 13.01 | 1.60 | |
| | Tubercular | 12 | 8.60 | 16.10 | 11.08 | 2.19 | |
| | Cryptococcal | 7 | 9.40 | 14.20 | 12.44 | 1.90 | |
| | Unknown | 18 | 6.30 | 15.40 | 11.09 | 2.62 | |
| **TC** | Viral | 30 | 2345.00 | 18100.00 | 9957.43 | 4557.89 | 0.209 |
| | Bacterial | 8 | 7865.00 | 21700.00 | 12082.75 | 4776.50 | |
| | Tubercular | 12 | 4600.00 | 12400.00 | 9608.33 | 2275.87 | |
| | Cryptococcal | 7 | 5300.00 | 14700.00 | 9271.43 | 3297.04 | |
| | Unknown | 18 | 1996.00 | 22570.00 | 12373.11 | 4845.09 | |
| **Platelets** | Viral | 30 | 0.20 | 3.21 | 1.32 | 0.87 | 0.008* |
| | Bacterial | 8 | 0.31 | 3.42 | 1.27 | 0.97 | |
| | Tubercular | 12 | 0.80 | 5.04 | 2.54 | 1.20 | |
| | Cryptococcal | 7 | 0.90 | 3.00 | 1.83 | 0.82 | |
| | Unknown | 18 | 0.16 | 3.57 | 1.47 | 1.05 | |
| **Creatinine** | Viral | 30 | 0.45 | 6.00 | 1.68 | 1.39 | 0.140 |
| | Bacterial | 8 | 0.40 | 15.80 | 3.03 | 5.22 | |
| | Tubercular | 12 | 0.20 | 1.80 | .92 | .44 | |
| | Cryptococcal | 7 | 0.50 | 1.90 | .91 | .46 | |
| | Unknown | 18 | 0.50 | 5.30 | 1.21 | 1.07 | |

**Table 6: Association of the imaging with etiology.**

| Imaging | | Etiology | | | | | Total |
|---|---|---|---|---|---|---|---|
| | | Viral | Bacterial | Tubercular | Cryptococcal | Unknown | |
| **Basal exudates** | | | | | | | |
| Count | | 0 | 0 | 2 | 0 | 0 | 2 |
| % | | 0.0 | 0.0 | 16.7 | 0.0 | 0.0 | 2.7 |
| **Chronic infarcts** | | | | | | | |
| Count | | 5 | 1 | 0 | 0 | 2 | 8 |

Continued.

| Imaging | Etiology | | | | | Total |
|---|---|---|---|---|---|---|
| | Viral | Bacterial | Tubercular | Cryptococcal | Unknown | |
| % | 16.7 | 12.5 | 0.0 | 0.0 | 11.1 | 10.7 |
| **Communicating hydrocephalus** | | | | | | |
| Count | 0 | 1 | 0 | 2 | 0 | 3 |
| % | 0.0 | 12.5 | 0.0 | 28.6 | 0.0 | 4.0 |
| **Cortical atrophy** | | | | | | |
| Count | 1 | 1 | 1 | 0 | 1 | 4 |
| % | 3.3 | 12.5 | 8.3 | 0.0 | 5.6 | 5.3 |
| **Diffuse cerebral atrophy** | | | | | | |
| Count | 0 | 0 | 0 | 0 | 1 | 1 |
| % | 0.0 | 0.0 | 0.0 | 0.0 | 5.6 | 1.3 |
| **Diffuse cerebral edema** | | | | | | |
| Count | 0 | 0 | 0 | 0 | 1 | 1 |
| % | 0.0 | 0.0 | 0.0 | 0.0 | 5.6 | 1.3 |
| **Meningeal enhancement** | | | | | | |
| Count | 9 | 0 | 1 | 2 | 1 | 13 |
| % | 30.0 | 0.0 | 8.3 | 28.6 | 5.6 | 17.3 |
| **Normal** | | | | | | |
| Count | 15 | 4 | 5 | 3 | 12 | 39 |
| % | 50.0 | 50.0 | 41.7 | 42.9 | 66.7 | 52.0 |
| **Obstructive hydrocephalus** | | | | | | |
| Count | 0 | 1 | 0 | 0 | 0 | 1 |
| % | 0.0 | 12.5 | 0.0 | 0.0 | 0.0 | 1.3 |
| **Ring enhancing lesion** | | | | | | |
| Count | 0 | 0 | 3 | 0 | 0 | 3 |
| % | 0.0 | 0.0 | 25.0 | 0.0 | 0.0 | 4.0 |
| **Total** | | | | | | |
| Count | 30 | 8 | 12 | 7 | 18 | 75 |
| % | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

Chi-square value=67.81, p value=0.024*

**Table 7: Association of the etiology with outcome.**

| Outcome | Etiology | | | | | Total |
|---|---|---|---|---|---|---|
| | Viral | Bacterial | Tubercular | Cryptococcal | Unknown | |
| **Death** | | | | | | |
| Count | 11 | 5 | 8 | 5 | 6 | 35 |
| % | 36.7 | 62.5 | 66.7 | 71.4 | 33.3 | 46.7 |
| **Discharge** | | | | | | |
| Count | 19 | 3 | 4 | 2 | 12 | 40 |
| % | 63.3 | 37.5 | 33.3 | 28.6 | 66.7 | 53.3 |
| **Total** | | | | | | |
| Count | 30 | 8 | 12 | 7 | 18 | 75 |
| % | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

Chi-square value=6.95, p value=0.139*

**Table 9: Comparison of the mean duration of hospital stay based on type of infection using ANOVA.**

| Etiology | N | Minimum | Maximum | Mean | SD | P value |
|---|---|---|---|---|---|---|
| **Viral** | 30 | 1.00 | 8.00 | 3.83 | 2.00 | |
| **Bacterial** | 8 | 1.00 | 8.00 | 3.50 | 2.56 | |
| **Tubercular** | 12 | 5.00 | 20.00 | 8.83 | 4.36 | 0.001* |
| **Cryptococcal** | 7 | 2.00 | 10.00 | 7.14 | 2.79 | |
| **Unknown** | 18 | 1.00 | 7.00 | 3.77 | 1.73 | |

## DISCUSSION

### *Demographic distribution*

The present study included 75 adult patients with meningoencephalitis. The AES spectrum includes patients of all age groups and both sexes. In our study, the mean age was 41.6years with female preponderance. The demonstrated mean age from another similar study by Joshi et al conducted in rural central India was found to be 40.2 (SD: 18.3) years.[5]

Majority of the patients came from rural parts of Tumkur and Bangalore districts. However significant urban and periurban transmission was also seen.

### *Etiological distribution*

In 76% of the patients, infective etiology was established based on CSF analysis report. On the other hand, unspecified etiology constituted about 24% where CSF analysis was inconclusive but symptoms were suggestive of infective etiology. In comparison to the study done by Roy et al; where the etiology unspecified constituted 46%.[6] In our study majority of the patients were classified as having viral meningoencephalitis where specific etiology was established in about 15 patients. The identified pathogens included Dengue (6), Chikungunya (3), and Herpes simplex virus (6).

This under recognition of an etiology maybe contributed by the varied etiological agents and the lack of availability of diagnostic testing for most of these agents. There are numerous lacunae in our knowledge, problems in epidemiological investigations, lack of diagnostic facilities, as well as difficulties in managing these critically ill patients.

Acute encephalitis syndrome (AES) is a group of clinical neurologic manifestation caused by wide range of viruses, bacteria, fungus, parasites, spirochetes, chemicals and toxins.

The most common causes of acute viral encephalitis are Japanese encephalitis virus, West Nile virus (WNV), Eastern equine encephalitis virus (EEEV), Western equine encephalitis virus (WEEV), Venezuelan equine encephalitis virus (VEEV), Hendra virus (HeV), enteroviruses (ENV), Chandipura virus (CHPV), Nipah (NiV), Kyasanur forest disease (KFD), St. Louis encephalitis virus, Herpes simplex, poliovirus and measles virus.

It is a major public health concern in India. Large outbreaks of AES, occur annually in the country post monsoon from July to November. JEV is the major cause of AES in India (ranging from 5-35%), the etiology in a large number of cases however remains unidentified.

8 patients were diagnosed with pyogenic meningitis based on typical CSF findings that showed high protein, low sugar and very high neutrophil count in the CSF. CSF culture was positive only in 1 patient which showed growth of *E. coli*. For the remaining patients, the cultures were sterile possibly due to prior antibiotic exposure.

Tubercular meningitis constituted about 16% of the total cases. Among them, 3 patients were positive for Retroviral disease who had the highest mortality.

7 cases were diagnosed as cryptococcal meningitis who were positive for CSF India ink test. 6 out of 7 cases were retroviral disease positive, while 1 case did not have any immunocompromised condition. Several case reports on cryptococcal meningitis in an immunocompetent patient have been reported which highlighted the fact that these patients may have subclinical or minor immunosuppression which should be explored.[8]

### *Symptomatology*

Most common presenting features were fever and altered mental status with seizures and headache being common in viral meningoencephalitis and tubercular meningitis respectively. A similar study done by Petchiappan et al on clinical profile and outcome of meningoencephalitis patients highlighted that fever was the most common presenting symptom followed by headache and altered sensorium.[9]

### *Lab parameters and imaging*

Thrombocytopenia was common with viral and bacterial etiologies which points towards arboviral etiology and sepsis. In a study done by Thejaswini et al; 50% of the patients with febrile thrombocytopenia were positive for arboviral infection.[10]

Majority of the patients had normal brain imaging. 17% of the patients had leptomeningeal enhancement. Hydrocephalus was most common among patients with cryptococcal meningitis which is similar to findings of study done by Zhang et al; where hydrocephalus in cryptococcal meningitis patients is associated with poor outcome.[11]

Basal exudates followed by ring enhancing lesions were common in tubercular meningitis.

### *Course in the hospital and outcome*

The mean duration of stay was approximately 3-4 days for viral, bacterial and unknown etiologies with bacterial meningitis having highest mortality. Overall mortality was highest for cryptococcal meningitis (71.4%) followed by tubercular meningitis (66.7%) and bacterial meningitis (62.5%) which could be due to late presentation to health care facility. Majority of them died due to secondary

complications like aspiration pneumonia, sepsis and multiorgan dysfunction.

Specific therapy was administered if the etiology was confirmed. Empirical antibacterial therapy was started for suspected bacterial meningitis and antiviral therapy with acyclovir for HSV encephalitis patients. Syndromic approach was used where patients with fever, rash and thrombocytopenia were started on doxycycline and ceftriaxone which infact reduced the mortality in etiology unspecified group. A study by Mishra et al on diagnosis and management of acute infectious encephalitis where a syndromic approach to treatment was used where etiological confirmation being awaited showed significant reduction in cost and effective treatment outcomes.[12]

### *Limitations*

Complete CSF encephalitis panel was not obtained in some patients due to short hospital stay. Follow up of investigations in response to treatment was not studied.

## CONCLUSION

A large number of number of cases where etiology cannot be identified maybe benefited by a syndromic approach and a better diagnostic modality.

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