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CLINICAL PROFILE OF MENINGITIS IN ADULTS

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Abstract

Background and Aim: Meningoencephalitis is a syndrome leading to fatality and neurological damages. Worldwide, infection of the central nervous system is the most common cause of meningoencephalitis. In encephalitis, a leptomeningeal involvement along with inflammation of brain parenchyma is invariably present and the clinical symptoms reflect both diffuse and focal cerebral pathology as well as meningitis. This study is done to emphasize the importance of early diagnosis, so that prompt management is given at appropriate time.

Material and Methods: The prospective observational study was conducted on patients attending at the Department of Medicine, Gujarat Adani Institute of Medical Sciences, Bhuj, Kutch, Gujarat, India. A total of 70 patients were studied. All patients were subjected to complete clinical evaluation and appropriate investigations to study the etiology, clinical profile and outcome in them.

Results: 53 patients in our study were young adults (<50 years of age group). Among the 70 patient with meningo-encephalitis in this study, the common initial presenting symptoms were fever, headache and altered sensorium. Among 70 patients, 41 patients were diagnosed as Tuberculous meningitis. 11 patients were diagnosed as pyogenic meningitis; 12 patients were diagnosed as viral meningo encephalitis.

Conclusion: Meningoencephalitis is a disease with high morbidity and mortality and considered as medical emergency. In this study, most of the patients with meningoencephalitis were males and young adults. Tuberculous meningitis was the most common overall cause in this study.

Key Words: Central Nervous System, Fever, Meningoencephalitis, Tuberculous Meningitis

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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]

Bacterial (pyogenic) meningitis is a pyogenic inflammation of meninges and subarachnoid cerebrospinal fluid (CSF) and is characterized by neutrophilic pleocytosis in CSF.[3] Pnemococcal 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 - Neiserria meningitides. Most patients recover completely if appropriate antibiotic therapy is instituted promptly. Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment.[4] Tuberclous meningitis should be a strong consideration when a patient presents with clinical picture of meningoencephalitidis, especially in high risk groups, including persons with malnutrition, those with abuse alcohol or drugs and patients with known retroviral infection. Death may occur as a result of missed diagnosis and delayed treatment. World-wide causes of viral meningitis include enterovirus, herpes, mumps, measles and HIV. Enterovirus is the most common cause of viral meningitis.[5]

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. As there are fewer developments in therapies for viral meningitis and there remain no effective therapies for most pathogens, this study is done to emphasise the importance of early diagnosis, so that prompt management is given at appropriate time.

This study is done to emphasize the importance of early diagnosis, so that prompt management is given at appropriate time.

Objectives of the study are

To Study Organism of meningitis in adults, to study Risk factors of meningitis in adults and to study Outcome and Complications of meningitis in adults

Material and Methods

The prospective observational study was conducted on patients attending at the Department of Medicine, Gujarat Adani Institute of Medical Sciences, Bhuj, Kutch, Gujarat, India.

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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 70 patients were studied.

Sample size calculation was done by using the following formula,

Population under study N 240 considering confidence level 95% Z = 1.96 for 95 % CI Margin of error (c) -10% Response distribution 50% Predicted sample size n=by the following formula n=[z2*p(1-p)]/c2 =[1.92*0.5(1-0.5)]/(0.1)2 =(3.8*0.5*0.5)/0.01 = 76 For finite population correction n is adjusted

n (adjusted) = (N*n)/(N+n) (240*96)/(240+96) 23040/336 68.57

Hence 70 patients were included in study.

Patient's demographic and medical details were entered in preformed proforma sheet designed for the study. Detailed history was taken, clinical examination was done and mental status was assessed. The investigations included complete hemogram, urine routine examination, blood urea, serum creatinine, blood glucose levels, liver function test and estimation of serum electrolytes like sodium, potassium, calcium and magnesium. Special investigations like lumbar puncture, CSF routine micro, CSF ADA, CSF cbnaat, CSF culture serological tests, CT scan/MRI brain, EEG were done in selected cases.

According to the patient's duration of illness, patients were sub classified into acute, subacute and chronic. According to patient's 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, the barthel index was used. Based on this index patient's functional evaluation was done at the end of the first month.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described as means and standard deviations or median and interquartile range based on their distribution. Qualitative variables were presented as count and percentages. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

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Results

The study included 70 patients with acute meningoencephalitis. 53 patients in our study were young adults (<50 years of age group). 14 patients were in the 50-60 years age group; Only 3 patients were elderly adults. (Table 1)

Among the 70 patient with meningo-encephalitis in this study, the common initial presenting symptoms were fever, headache and altered sensorium. Fever was the most common initial presenting symptom. 58 patients had fever and 51 patients had headache. (Table 2)

Table 1: Age wise Distribution of study participants

AGE	MALE	FEMALE	TOTAL	(%)
18 -30	16	8	24	34.28%
31 – 50	20	9	29	41.42 %
51 – 60	4	10	14	20%
>60	3	0	3	4.28%
Total	43	27	70	100%

Headache was associated with vomiting in some of the patients. 40 patients had both fever and headache. 37 patients had altered sensorium in the course of illness, varying from drowsiness to deep coma. Only 23 patients had all the three triad – headache, fever and altered sensorium.

Table 2: Prevalence of Positive Clinical Presentation

CLINICAL PRESENTATION	N	(%)
Headache	51	72.85%
Fever	58	82.85 %
Seizures	9	12.85%
Vomiting	34	48.57%
Altered mental status	44	62.85%

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CSF Rhinorrhea	6	8.5 %
Hemiparesis	6	8.5 %
Speech Disturbances	3	4.2 %
Cranial Nerve Palsy	6	8.5 %

Among the 9 patients only one patient had parenchymal lesion in the MRI (granuloma). Other 4 patients had only meningeal enhancement and 3 patients had normal MRI.

Only 29 patients had neck stiffness. Remaining 41 patients did not have neck stiffness, even though there is meningeal involvement. Fundus examination showed papilledema in only 8 patients. Only 10 patients had neurological deficits. 5 patients had hemiparesis, one patient had hemiparesis and aphasia. 6 patients had cranial nerve paralysis. Among patient with altered sensorium, 14 patients had significant deterioration in consciousness with Glascow coma scale less than 10; one patient with Pyogenic Meningitis had deep coma with GCS 3/15 throughout the hospitalization with poorly reacting pupils.; Among the remaining 14 patients only 4 patients had normal MRI. 10 patients had abnormal MRI with meningeal enhancement , granuloma or hydrocephalus; All these 14 patients were on ventilatory support in ICU, until the consciousness improved.

Table 3: Prevalence of MRI Findings

MRI FINDINGS	F	(%)
Meningeal Enhancement	35	50%
Hydrocephalus	9	12.85 %
Granuloma	8	11.75%
Vasculitic infarcts	8	11.75

6 patients had CSF rhinnorhea as the cause of their meningitis. 5 patients had CSF rhinorrhea due to past head injury. One patient had non traumatic CSF rhinorrhea.

In our study, etiology of meningo encephalitis and the probable organisms responsible for meningoencephalitis was diagnosed on the basis of CSF analysis and MRI brain findings. Gram

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stain and CSF culture and sensitivity helped to isolate the bacteria in case of pyogenic meningitis; Patient's 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.

CSF PCR technique helped to reach diagnosis in patients with Herpes simplex encephalitis, Aspergillus Meningitis and some cases of tuberculous meningitis. Among 70 patients, 41 patients were diagnosed as Tuberculous meningitis. 11 patients were diagnosed as pyogenic meningitis; 12 patients were diagnosed as viral meningo encephalitis. Among the 12 patients with viral meningoencephalitis, 3 patients had positive HSV PCR in the CSF. No organism could be found in the remaining 7 patients. 3 patients had cryptococcal meningitis. 3 patients had cerebral toxoplasmosis and one patient had aspergillus meningitis.

Table 4: Etiology

ETIOLOGY	N	(%)
Tuberculous Meningitis	41	58.57 %
Acute Pyogenic Meningits	11	15.71 %
Viral MeningoEncephalitis	12	17.14%
Cryptococcal Meningitis	3	4.2 %
Cerebral Toxoplasmosis	3	4.2 %
Aspergillus Meningits	1	1.42%
Total	50	100%

Outcome at the end of one month by Barthel index Scoring was done. Among 70 patients, 66 patients recovered completely without neurological deficits. 1 case had Barthel index zero. Another 3 patients had rapidly progressive fulminant course and were succumb to the illness by the end of 1 month.

Discussion

Meningitis and encephalitis constitute more than 95% of all CNS infections. Remaining small percentage of CNS infections involves the spinal cord and spinal meninges alone and result in myelits, myeloradiculitis or spinal meningitis. In our study, we tried to analyze the major portion of CNS infections i.e. Meningitis and encephalitis. Clinical presentations are almost similar in meningitis and encephalitis that include fever, headache, seizures and altered sensorium. Signs of meningeal irritation, like neck stiffness and positive kernig sign occurs in most of the patients with meningitis and is often absent in patients with predominant encephalitis. Sometimes, neck stiffness may be absent in patients with predominant meningitis especially in subacute meningitis

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and meningitis in infants and elderly adults. So, the term meningitis and encephalitis are not exclusive.

In this study we analyzed 70 consecutive patients of meningo encephaliti admitted in Department of Medicine, Gujarat Adani Institute of Medical Sciences, Bhuj, Kutch, Gujarat, India. The AES spectrum includes patients of all age groups and both sexes. In our study, the mean age was 41.8 years 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.[6]

The common presenting symptoms were fever, Headache and altered sensorium. A similar study done by Petchiappan et al[7] on clinical profile and outcome of meningoencephalitis patients highlighted that fever was the most common presenting symptom followed by headache and altered sensorium. In a study done by Khan FY et al.[8] including 110 study participants, 9 (7.7%) patients had diabetes mellites, 4 (3.4%) patients had history of substance abuse in the form of alcohol intake, i.v. drug abuse and smoking, 2 (1.7%) patients had immunosuppression and 5 (4.3%) had history of otitis media. In a study done by Tan K et al[9] including 116 study participants, 12 (10%) patients had diabetes mellites, 6 (5%) patients had history of substance abuse in the form of alcohol intake and smoking, 32 (34%) patients had immunosuppression and none had history of otitis media.

Patients were diagnosed as pyogenic meningitis on the basis of typical CSF findings. All patients had high protein, low sugar and very high neutrophil count in the CSF (> 1000 cells/mm3 in most of the patients). The probability of visualizing bacteria on a gramstain depends on the specific bacterial pathogen, CSF concentration of bacteria and technique. In many cases of presumed viral encephalitis, the responsible organism could not be identified, despite detailed diagnostic testing. In the California Encephalitis Project, 334 patients with encephalitis were studied from 1998 – 2000. Etiological organism was not identified in 208 of 334 patients (62%), despite extensive testing and evaluation.[10]

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.[11]

Tuberculous meningitis can mimic viral meningitis, especially when the presentation is acute. Some patients who were treated as viral meningitis came back to the hospital, with tuberculous meningitis. Both fungal and tuberculous meningitis can have lymphocytic pleocytosis in the CSF and can be misdiagnosed as viral meningitis in the initial evaluation. In our study, though we are unable to isolate the organisms in 8 out of 12 patients with presumed viral meningo encephalitis, we were able to rule out tuberculous or fungal etiology in these patients. Because, these patients recovered well without specific antibiotics, antituberculous and antifungal therapy and they were

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totally asymptomatic during follow up which confirmed the diagnosis of probable viral etiology. In a study by Tan k et al.[9], in which 116 patients were recruited, tubercular aetiology was found in 3.4%, bacterial cause in 31.0%, viral cause in 53.4%, fungal cause in 12.06% and other causes in 5.1%. In a study by Modi S and Anand AK[12], in which 120 patients were recruited, tubercular aetiology was found in 4.2%, bacterial cause in 36.7%, viral cause in 28.3%, fungal cause in none of the cases and other causes in 30.8%. In a study by Pandey D and Mahale RL[13], in which 100 patients were recruited, tubercular aetiology was found in 54%, bacterial cause in 38.0%, viral cause in 8%, and fungal cause in none of the cases. In a study by Yerramilli A et al[14], in which 147 patients were recruited, tubercular aetiology was found in 28%, bacterial cause in 28.1%, viral cause in 39%, fungal cause in 3% and other causes in 2.1%. In the present study, in which 184 patients were recruited, tubercular aetiology was found in 51.6% (n=95), bacterial cause in 21.19% (n=39), viral cause in 25% (n=46), fungal cause in 2.17% (n=4). In the present study, Tuberculosis was the major cause of meningoencephalitis which is in concordance with study done by Pandey D and Mahale RL[13] and is in discordance with study done by Tan K et al.[9]

In our study 20 patients had basal meningeal exudates in brain imaging (MRI Brain). Few patients underwent only CT scan which revealed basal meningeal enhancement. Hydrocephalus was present in 8 patients. With repeated sequential examination of CSF, kennedy and fallon reported tubercle bacilli in 87% of patients. In their study, AFB was visible in stained CSF sediments in 37% patients during initial examinations, but the yield was 87% when the CSF from four serial spinal taps was examined.[15] In another study bacteriological diagnosis was made in 107 of 132 adults in clinically suspected TBM. To increase the protein yield, centrifuged sediment of more than 10 ml of CSF should be used for acid fast staining and 200-500 high power fields should be examined of each specimen for at least 30 minutes, preferably by more than one observer. Serial CSF examination and examination of ventricular CSF will increase the yield further.[16] The sensitivity of CSF PCR testing was only 60% in patients classified as having definite or probable TM. In another meta analysis of PCR assay in TBM, the sensitivity was 56% and specificity was 98%.49 In a study done by Pandey D and Mahale RL[13] imaging (CT/ MRI Brain) findings suggestive of tuberculoma was seen in 26% cases, vasculitic infarcts seen in 10% cases, hydrocephalus in 8%, features suggestive of meningitis in 89% cases.

Among 70 patients, 66 patients recovered completely without neurological deficits. All these 66 patients had barthel Index 100, at the end of one month. Two patients with pneumoncoccal meningitis and a patient with cryptococcal meningitis had rapidly progressive fulminant course and they succumb to the illness at the end of 1 week despite appropriate drug treatment.

Limitations of the study were 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.

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Conclusion

Meningoencephalitis is a disease with high morbidity and mortality and considered as medical emergency. In this study, most of the patients with meningoencephalitis were males and young adults. Surprisingly, tuberculous meningitis was the most common overall cause in this study. Both viral meningo encephalitis and pyogenic meningitis constituted most of the cases of acute Meningoencephalitis. Tuberculous meningitis was the most common cause in patient with subacute meningitis. Diagnosis of tuberculous meningitis was challenging; clinical presentation, CSF studies, and brain imaging features helped to make a diagnosis of tuberculous meningitis. All patients with chronic presentation (> 4 weeks) had tuberculous meningitis. Early recognition and if treated appropriately increases the survival rate and also neurological sequelae secondary to meningoencephalitis can be minimised to some extent which adds on to the quality of patients life. In tertiary care centers where referred and critical cases are more, detailed history and clinical examination along with appropriate investigations are necessary to confirm the diagnosis of meningoencephalitis. Sensitive, rapid and affordable investigations are required for the accurate and early diagnosis.

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