Original Research Article

# Clinical profile in chronic meningitis patients: A prospective study at tertiary care center

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## Abstract

**Background:** Early diagnosis and appropriate therapy of chronic meningitis is important in improving the overall outcome and to prevent long-lasting sequels. As many etiological agents lead to the development of chronic meningitis, it is important to develop a systematic approach to the diagnosis; taking clues from history, examination and laboratory tests, to make an accurate diagnosis and institute appropriate therapy. **Aim:** To document clinical profile and diagnostic modalities of patients with chronic meningitis. **Material and Methods:** A total of 90 patients with chronic meningitis were included. Clinical features were noted and CNS examination was done and investigations such as Gene X-pert-CBNAAT, Chest X-Ray, CSF analysis, Computed Tomography Scan and Magnetic resonance imaging were done. **Results:** Among the 90 patients in this study, the common initial presenting symptoms were fever, headache, neck stiffness and altered sensorium. Fever was the most common initial presenting symptom. 73 patients (81.1%) had fever and 66(73.3%) patients had headache. Most common etiology of the chronic meningitis in the study was tuberculous meningitis with 65 (72.2%) patients. There was a single patient of Aspergillus and 2 patients of bacterial meningitis. Number of deaths was highest in TB meningitis (10.77%) and the proportion of the mortality was highest in viral meningitis(18.75%) cases. **Conclusion:** Chronic meningitisis an important neurological disease. Although most patients require clinical evaluation and CSF analysis, CT scan and Gene X-pert (CB-NAAT) study of CSF is also necessary to rule out structural intracranial lesions and tuberculous meningitis.

**Key Word:** Chronic meningitis, symptoms, tuberculous meningitis, Gene X-pert (CB-NAAT), outcome

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Received Date: 21/01/2019 Revised Date: 02/03/2019 Accepted Date: 10/04/2019
DOI: https://doi.org/10.26611/102110114

| Access this article online | |
|---|---|
| Quick Response Code: | Website: www.medpulse.in |
| | Accessed Date: 22 April 2019 |

## INTRODUCTION

Chronic meningitis is a common clinical problem. Early diagnosis and appropriate therapy is important in improving the overall outcome and to prevent long-lasting sequels. As many etiological agents lead to the development of chronic meningitis, it is important to develop a systematic approach to the diagnosis; taking clues from history, examination and laboratory tests, to make an accurate diagnosis and institute appropriate therapy.[1,2] This study was conducted to focus on the clinical and diagnostic approach towards the commonly encountered situation of chronic meningitis. The classical triad of clinical features of the meningitis(fever, headache and neck stiffness) whilst seen in upto 85% of the patients presenting with acute bacterial meningitis is far less commonly seen in Chronic meningitis.[3,4,5] Focal neurological signs with cranial palsy and abnormal CT brain findings are more commonly seen in chronic meningitis.[6] With recent advancement in serologic and CSF diagnostic testing, specific infectious, neoplastic, or autoimmune etiologies of chronic meningitis can be identified. Eliminating previous diagnostic uncertainty of chronic inflammation in the CNS has led to rapid and specific treatment regimens that ultimately improve patient outcomes. The present study was done with an aim at documenting the patients presenting with chronic meningitis, their clinical profile and diagnostic modalities.

How to cite this article: Kapil Shesherao More, Aruna Kondibarao Pohare, Avinash. Clinical profile in chronic meningitis patients: A prospective study at tertiary care center. *MedPulse International Journal of Medicine*. April 2019; 10(1): 52-55.
https://www.medpulse.in/Medicine/

## MATERIAL AND METHODS

This prospective study was included patients who were admitted in General Medicine Ward and in medical intensive care unit and had given such written informed consent (consent was obtained from relatives in case patient was not in condition). There were total 90 patients who were diagnosed to have chronic meningitis during study time.

**Inclusion criteria**

- Patient aged >18years old admitted with the classic features of meningitis (fever, headache, meningismus).
- Willingnesstoparticipateinthestudyandready/abletogiveaninformedconsent(or with a relative who was willing to give consent in the setting of altered mental status of the patient).

**Exclusion criteria**

- Patient who had meningitis recently (in the last month)
- The patients /relatives who were not ready to participate in the study.

## METHODOLOGY

Detailed clinical history was taken from patients and/or relatives after admission in the hospital. After this thorough clinical general and systemic examination was carried out. CNS examination was done in detail. Following this, investigations were carried out wherever necessary such as complete blood count, liver and kidney function test, Erythrocyte sedimentation rate, VDRL and HIV Test. Sputum Microscopy, Gene X-pert-CBNAAT, Chest X-Ray, CSF analysis, Computed Tomography Scan and Magnetic resonance imaging was also done.

**Ethical considerations:** All ethical considerations and necessary approvals were taken from Institutional Ethical Committee. After the approval, all the study participants were interviewed and necessary examinations were done.

**Statistical analysis:** Following the above procedures, the findings were recorded in the proforma (Case record form). These findings were entered in Microsoft Excel 2010.The results were compiled by using suitable tables and graphs wherever necessary. The variations were analyzed as a percentage of the total and reported. Data analysis is done with the help of appropriate SPSS Software version 20.Qualitative data is presented with Frequency and Percentage tables.

## RESULTS

Among the 90 patients, 59 patients were (65.6%) males and 31(34.4%) patients were females. 68 patients in our study were young adults (≤50 years of age group). 19 patients were in the 51-60 years age group; Only 3 patients were elderly adults (one 63, one 64 years, and another 86 years). Among the 90 patients in this study, the common initial presenting symptoms were fever, headache, neck stiffness and altered sensorium. Fever was the most common initial presenting symptom. 73 patients (81.1%) had fever and 66(73.3%) patients had headache. Headache was associated with vomiting in some of the patients. 57(63.3%) patients had both fever and headache. 53 (58.9%) patients had altered sensorium in the course of illness, varying from drowsiness to deep coma. Only 58 (64.44%) patients had all the three of triad – headache, fever and neck stiffness.

**Table 1:** Clinical presentation in the study subjects

| Clinical Presentation | N | (%) |
|---|---|---|
| Headache | 66 | 73.3% |
| Fever | 73 | 81.1% |
| Seizures | 39 | 43.3% |
| Vomiting | 24 | 48% |
| Altered mental status | 53 | 58.9% |
| Hemiparesis | 7 | 7.8% |
| Speech Disturbances | 4 | 4.4% |
| Cranial Nerve Palsy | 7 | 7.8% |
| Neurological deficit | 13 | 14.4 |
| Neck Stiffness | 64 | 71.1% |

Out of total 39(43.3%) patients having seizure, 22(24.4%) were of focal type and 17 (18.9%) were GTCS, remaining 51(56.7%) patients had no seizure. In MRI/ CT scan were normal in 15 patients (16.7%) findings. There were more than 51% patients showing meningeal enhancement on MRI/CT scan.11 patients showed typical findings of hydrocephalus. There were each 9 scans that showed granuloma and vasculitic infarcts.

**Table 2:** CT/ MRI findings

| MRI/CT findings | No. of patients (n=90) | (%) |
|---|---|---|
| Meningeal Enhancement | 46 | 51.1% |
| Hydrocephalus | 11 | 12.2% |
| Granuloma | 09 | 10% |
| Vasculitic infarcts | 09 | 10% |
| Normal | 15 | 16.7% |

There were total 19 (21.1%) patients with HIV positive status and rest were negative. Out of these 19 (21.1%) patients of HIV 14(73.68%) were of TB meningitis and 5(26.32%) were Cryptococcal meningitis.

**Table 3:** Etiology of the chronic meningitis in the study subjects

| Etiology | N | (%) |
|---|---|---|
| Tuberculous meningitis | 65 | 72.2% |
| Viral meningitis | 16 | 17.8% |
| Cryptococcal meningitis | 6 | 6.7% |
| Aspergillus meningitis | 1 | 1.1% |
| Bacterial meningitis | 2 | 2.2 |
| Total | 90 | 100% |

Most common etiology of the chronic meningitis in the

study was tuberculous meningitis with 65 (72.2%) patients followed by viral meningitis in 16 (17.8%) cases, 6 (6.7%) were cryptococcal meningitis. There was a single patient of Aspergillus and 2 patients of bacterial meningitis. Out of total X rays, 49 (54.5%) were appeared to be normal. 20 (22.2%) were of post TB fibrotic changes, pleural effusion 7(7.8%), Miliary TB 3(3.3%) and cavitatory changes were 8(8.9%). Three patients of viral meningitis showed changes of aspiration pneumonitis on X-ray.

**Table 4:** CSF analysis in the study subjects

| Parameter | Interpretation | N | (%) |
|---|---|---|---|
| CSF Protein | Normal | 29 | 32.2% |
| | Increase | 61 | 67.8% |
| CSF Glucose | Low Glucose | 74 | 82.3% |
| | Normal | 16 | 17.7% |
| CSF TLC | Pleocytosis | 65 | 72.2% |
| | Marked pleocytosis (>1000/mm$^3$) | 25 | 27.8% |
| CSF DLC | Lymphocytic | 69 | 76.7% |
| | Neutrophilic | 21 | 23.3% |

Out of total 90 patients, 7 (7.77%) CSF culture was positive, in 7 patients of which 6 were cryptococcal as viewed on India Ink preparation and one was positive for Aspergillus (outside CSF culture report which was positive for Aspergillus) and 83 (92.23%) was negative for culture. Gene X-pert (CB-NAAT) done on CSF of 90 patients, 56(62.2%) sample detected MTB and rest were found not detect MTB. As per the ESR findings of the study subjects, in 71 patients had raised ESR and rest 19 were found to be normal. There were 69 patients in the study who were reactive to C reactive protein. Out of total 90 patients 69(75.6%) study subjects had raised leucocyte count in the blood. Out of 65 patients of TBM, 51 patients in whom sputum microscopy was done, 39(76.47%) were found to detect acid fast bacilli of TB in the sputum. No sputum in remaining.

**Table 5:** Etiology and outcome of the chronic meningitis

| Etiology | Recovered/Alive | Not recovered/death |
|---|---|---|
| Tuberculous meningitis (n=65) | 58(89.23%) | 7(10.77%) |
| Viral meningitis (n=16) | 13(81.25%) | 3(18.75%) |
| Cryptococcal meningitis (n=6) | 5(83.35%) | 1(16.7%) |
| Aspergillus meningitis (n=1) | 1 (100%) | 0 (0%) |
| Bacterial meningitis (n=2) | 2 (100%) | 0 (0%) |
| Total (n=90) | 79 (87.8%) | 11 (12.2%) |

Though the number of deaths was highest in TB meningitis 7 (10.77%), the proportion of the mortality was highest in the case of viral meningitis(18.75%). There was a single death in case cryptococcal meningitis in the study.

## DISCUSSION

Meningitis can be categorized as acute, subacute, or chronic based on duration of inflammation. This study focuses on the most common causes of chronic meningitis. Chronic meningitis is commonly defined as inflammation evolving during weeks to months without resolution of CSF abnormalities. Determining the time course of meningitis is important for creating a differential diagnosis. Most organisms causing acute meningitis rarely persist more than a few weeks. Most common etiology of the chronic meningitis in the study was tuberculous meningitis with 65 (72.2%) patients followed by viral meningitis in 16 (17.8%) cases, 6 (6.7%) were cryptococcal meningitis. There was a single patient of Aspergillus and 2 patients of bacterial meningitis. In a study in Ethiopia, 53 patients of chronic meningitis were diagnosed of which majority (48 patients) were HIV positive. Commonest cause was cryptococcal meningitis (8 patients), followed by tuberculosis (TB), Toxoplasma gondii, Brucella and Neisseria meningitides infections.[7] In a study from Thailand, among 114 patients of chronic meningitis commonest etiology was again cryptococcus (54%) followed by TB (37%) meningitis. Amongst the patients with cryptococcal and TB meningitis, 79% and 7% respectively were HIV positive.[8] Among the 90 patients in this study, the common initial presenting symptoms were fever, headache, neck stiffness and altered sensorium. Fever was the most common initial presenting symptom. 73 patients (81.1%) had fever and 66(73.3%) patients had headache.The classic triad of clinical features of meningitis (fever, neck stiffness, headache), whilst seen in up to 85% of patients presenting with acute bacterial meningitis is far less commonly seen in chronic meningitis.[3,4,5] In our study, there were more than 51% patients showing meningeal enhancement on MRI/CT scan.11 patients showed typical findings of hydrocephalus. There were each 9 scans that showed granuloma and vasculiticinfarcts. Focal neurological signs with cranial nerve palsies and abnormal CT brain findings are also far more commonly seen in chronic meningitis.[6] Gene X-pert (CB-NAAT) done on CSF of 90 patients, 56(62.2%) sample detected MTB and rest were found not detect MTB. With repeated sequential examination of CSF, Kennedy and Fallon reported tubercle bacilli in 87% of patients. In their study, AFB were 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.[9]The sensitivity of CSF PCR testing was only 60% in patients classified as having definite or probable TBM.[10] In another meta-analysis of PCR assay in TBM, the sensitivity was 56% and specificity was 98%.[11] In two

large community based series, hydrocephalus was seen in approximately 75% of patients, basilar meningeal enhancement in 38%, cerebral infarcts in 15% -30% and tuberculomas in 5-10%.[12,13] Out of total 90 patients, 16(18.75%) were suffered from viral meningitis. There were 3 cases who were succumbed to death. In this study 6(6.7%) patients had cryptococcal meningitis; out of which 5 patients had HIV infection and another one had no HIV infection. The patient without HIV infection, a diabetic, presented atypically with tiredness, lethargy, dullness, apathy, anorexia and intermittent confusion of one-week duration; Due to lack of headache and fever possibility of CNS infection was not considered in the initial few days. MRI brain revealed small basal ganglionic infarct. CSF analysis surprisingly revealed positive cryptococcal antigen in high titres. India ink stain was positive and he was started on amphotericin B and high dose IV fluconazole. Despite appropriate drug therapy, he rapidly deteriorated, comatosed and expired. The patient with HIV infection and cryptococcal meningitis recovered well with amphotericin. In this study, we came across an interesting and rare case of aspergillus meningitis. This 53 years old male developed right trigeminal neuropathy four years back. MRI brain showed small T2-hyperintense extra axial lesion in the right middle cranial fossa medial to right temporal lobe. The lesion was surgically removed and histopathology revealed aspergilloma. He continued antifungal therapy for 6months (Inj. Amphotericin B) and discontinued. Two years later, he developed recurrence of lesion in the similar site. He was started on oral voriconazole and the lesion disappeared with voriconazole. He discontinued the tablet one year later. After four years, at present he presented with one-month duration of daily, severe and persistent headache. He had mild neck stiffness and no neurological deficits. CT brain plain and contrast revealed hydrocephalus with dilatation of all 4 ventricles and there was no brain parenchyma or extra axial lesion. Due to the past history of intra cranial aspergilloma, possibility of aspergillus meningitis was strongly considered, CSF analysis showed elevated protein and elevated lymphocyte count. CSF PCR for aspergillus was positive. CSF TB PCR was negative and cryptococal antigen was negative. He was diagnosed as aspergillus meningitis and started on IV voriconazole. He was on regular oral voriconazole to prevent further relapse and he was asymptomatic at present. Aspergillus Meningitis is a rare entity and there are only few reported cases in the world literature. Aspergillus meningitis has been reported to be co-existent with active granulomatous or rhinocerebral lesion. Our patient was unique that he developed meningitis without co-existent intracranial aspergilloma. Though the number of deaths was highest in TB meningitis 7 (10.77%), the proportion of the mortality was highest in the case of viral meningitis (18.75%). There was a single death in case Cryptococcal meningitis in the study. A patient with pneumoncoccal meningitis and a patient with cryptococcal meningitis had rapidly progressive course and but they recovered after rigorous appropriate drug treatment.

## CONCLUSION

Chronic meningitisis an important neurological disease. This study documents the profile of chronic meningitis patients and highlights the modes of diagnosis and mortality. Although most patients requireclinical evaluation and CSF analysis, CT scan and Gene X-pert (CB-NAAT) study of CSF is also necessary to rule out structural intracranial lesions and tuberculous meningitis.

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Source of Support: None Declared
Conflict of Interest: None Declared