Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: www.saspublishers.com

OPEN ACCESS

Medicine

Clinical Profile of Adults with Tuberculous Meningitis

Dr. Naresh Chauhan, Dr. Balbir Singh Verma*, Dr. Dig Vijay Singh, Dr. Sudhir Sharma, Dr. Suresh Thakur

Department of Medicine, IGMC, Ridge Sanjauli Rd, Lakkar Bazar, Shimla, Himachal Pradesh 171001, India

DOI: 10.36347/sjams.2019.v07i12.050 | **Received:** 16.12.2019 | **Accepted:** 23.12.2019 | **Published:** 28.12.2019

***Corresponding author:** Dr. Balbir Singh Verma

Abstract **Original Research Article**

Aim and objective: To study clinical profile of adults with Tuberculous meningitis (TBM) admitted to Department of Medicine IGMC Shimla (H.P.). *Materials and Methods:* It was an observational hospital-based study, total of 40 adult cases were admitted and treated as TBM over a period of 1 year (August 2015 and July 2016), in Department of Medicine, IGMC Shimla. The data on demographic factors, clinical treatment, complications and laboratory findings, details of treatment and outcome were recorded and analyzed. ***Results****:* A total of 40 cases were admitted and treated as TBM over a period of 1 year. Majority of the patients, 21(52.5%) belonged to age group 18-39 years with male preponderance (M:F=2.6:1); 75% patients had duration of illness upto 14 days. Common symptoms were fever in 33 (82.5%), headache 26(65%) and altered sensorium 27(67.5%). AFB culture was positive in 10% cases. CSF staining for AFB was negative for all patients. The positive polymerase chain reaction of TB PCR in 42.5% and mean ADA value was 9.09±7. On neuroimaging, 20% cases had meningeal enhancement, 12.9% had hydrocephalus and 13.3% had ischemic lesions and tuberculomas in 13.8%. 32.5% patients were in stage I, 57.5% in stage II and 10% in stage III. At discharge 57.5% patients were asymptomatic, 37.5% were having some residual Deficit and 2(5.0%) died before discharge. ***Conclusion:*** A major problem in diagnosis of TBM was the absence of standardized diagnostic criteria, but now with advent of consensus case definition there is a better diagnostic clarity. With the advent and availability of PCR diagnostic modalities the diagnostic pickup of TBM has improved. The role of PCR in TBM diagnosis is still evolving and presents window of opportunity for early diagnosis, detecting resistance pattern and treatment.

Keywords: Central nervous system (CNS) tuberculosis, tuberculous meningitis, polymerase chain reaction (PCR).

INTRODUCTION

Tuberculosis has been a major cause of suffering and death since times immemorial [1]. The occurrence of extrapulmonary TB is directly proportional to the prevalence of TB infection [2]. Tuberculous meningitis (TBM) is one of the major manifestation of CNS tuberculosis (TB), account for 70 to 80% of total cases. The neurological sequelae in patients of TBM are common and the case fatality rate has been estimated to vary from 15% to 60% [1]. This sub acute form of meningitis is still an important public health problem in developing countries [3]. Early diagnosis and treatment with chemotherapy and active management of the complications are of great importance to prevent the irreversible neurologic sequelae and death. Delay in diagnosis and so in the start of effective treatment results in poor prognosis and sequelae in up to 25% of cases. Mycobacterial culture may take up to 6 weeks to yield results. Therefore, the diagnosis of tuberculous meningitis depends on the clinical manifestations of subacute to chronic meningitis with lymphocytic CSF and low CSF glucose levels. However, other forms of meningitis may mimic tuberculous meningitis. In many instances, the diagnosis and thereby the treatment of tuberculous meningitis is delayed owing to poor understanding of the disease pathogenesis and unavailability of rapid, sensitive, and affordable diagnostic tests [4]. Till date, all of the series of TBM reported in the literature stress the importance of early diagnosis and the prompt institution of chemotherapy [5]. The cornerstone of early diagnosis and initiation of appropriate treatment is solely based on higher degree of clinical suspicion. Hence, it is important to identify and understand the clinical pattern and disease spectrum of TBM to arrive at an early diagnosis [4]. Moreover, there are a few studies regarding the clinical profile of TBM. With these points in mind, the present study was conducted in the department of medicine IGMC Shimla to study the clinical profile of TBM.

MATERIALS AND METHODS

This was hospital based descriptive study, carried out in the department of medicine IGMC Shimla for a period of one year from 1st August 2015 to 31st July 2016. The study population comprised of all cases of suspected tubercular meningitis admitted to the department of medicine during the study period. This study included all subjects with age 18 years or above and having symptoms and signs of meningitis including one or more of the following; headache, irritability, vomiting, fever, neck stiffness, convulsions, focal neurological deficits, altered consciousness. The patients found to be non tuberculosis (non TBM) after investigation, with tuberculoma without evidence of meningeal involvement and who denied consent were excluded. The patients involved in the research project were adequately informed of the aims, methods, the anticipated benefits and potential risks of the study and the discomfort it may entail them and the remedies thereof. Written informed consent was obtained.

Table-1: Duration of illness

Characteristics		Total N=40
Duration of Presenting Complaint	≤5 Days	7(17.5%)
	6-10 days	17 (42.5%)
	11-14days	6 (15.0%)
	>2weeks	10 (25.0%)

TBM presented mostly with fever in 33 (82.5%). General constitutional symptoms were present in 21 (52.5%) only.

Table-2: General symptoms and signs

Characteristics	Total N=40
Fever	33(82.5%)
Constitutional Symptoms	21(52.5%)
Weight loss	10(25.0%)
Loss of Appetite	16(40.0%)

Among CNS manifestations headache was (65.0%) common presenting feature and on physical examination meningeal signs were present in 29 (72.5%) patients. On fundoscopy papilledema was present in two patients and both were females.

All patients were divided into definite, probable and possible cases as per diagnostic criteria. These diagnostic criteria were published in 'The Lancets Infectious Disease' (Volume 10, November 2010) [6]. The imaging of patients was done on 64 slice CT scanner (Model: VCT Xte; GE Healthcare) and 1.5 T Avanto system (Siemens, Erlangen, Germany) MRI machine. British Medical Research council grading system for staging was used. Data collected and entered in MS Excel 2007 and analysis done using epi info 3.4.3.

RESULTS

A total of 40 adult cases were admitted and treated as TBM over a period of 1 year. The mean age of the case series was 40.17 ± 16.26 years and majority belonged to age group 18-39 years. Majority of patients (72.5%) in this study were males. The duration of illness less than 10 days was observed in 60% patients and up to 14 days in 75% of patients. In maximum number of the patients (82.5%) duration of symptoms was more than 5 days.

Table-3: CNS manifestations of TBM

Characteristics	Total N=40
Headache	26(65.0%)
Vomiting	13(32.5%)
Photophobia	4(10.0%)
Convulsions	2(5.0%)
Meningeal Signs	29(72.5%)
Papilloedema	2(5.0%)

Altered level of consciousness was seen in 27 (67.5%) patients, most of the patients (57.5%) were in stage-2 as per British Medical Research council grading system.

Focal neurological deficit was present in 9(29.03%) patients. The cranial nerve palsies was present in 7 (17.5%) patients, 7 (17.5%) had hemiparesis and 1(2.5%) had paraparesis.

Table-4A: Focal Neurological Deficit

Characteristics	Total N=40	Male N=29	Female N=11
Focal Neurological Deficit	9(22.5%)	6(15%)	3(7.5%)

Table-4B

Characteristics	Number
Cranial Nerve Palsy	7
Hemeparesis	7
Paraparesis	1

CSF microbiological analysis revealed negative acid-fast stain in all patients, positive acid-fast bacillus (AFB) culture in 4(10%) patients and positive polymerase chain reaction of TB PCR in 17(42.5%). All the gene x-pert cases were rifampicin sensitive. ADA was done in 30 cases. Mean value of ADA was 9.09±7.97. Probability of a definite case increased as the value of ADA increased, but low value could not exclude a definite case.

Table-5: ADA (adenosine deaminase)

ADA (u/l) N=30	No. of patients	Definite cases	Probable cases	Possible cases
0-5	9 (30.0%)	3	0	6
5.1-10	13 (43.3%)	6	2	5
>10	8 (26.7%)	6	0	2

Brain imaging was performed in 31(77.5%) patients either plain CT or MRI with contrast. It was normal in 24 (60%). There was hydrocephalus in 4 (13.8%), ischaemic lesions in 4 (13.8%), meningeal enhancement in 6 (20.7%), and tuberculomas in 4 (13.8%).

Table-6: Brain Imaging

Characteristics		Total N=40	Male N=29	Female N=11	Stage of Disease		
					Stage I	Stage II	Stage III
Brain imaging	Not Done	9(22.5%)	7(17.5%)	2(5%)			
	Done	31(77.5%)	22(55%)	9(22.5%)			
Basal meningeal Enhancement	Present	6(19.4%)	3(9.7%)	3(9.7%)	0	4	2
Infarction	Present	4(12.9%)	2(6.5%)	2(6.5%)	0	3	1
Tuberculoma	Present	4(12.9%)	2(6.5%)	2(6.5%)	2	1	1
Hydrocephalus	Present	4(12.9%)	3(9.7%)	1(3.2%)	0	3	1

Out of 40 cases, there were 20(50%) definitive cases, 6(15%) probable cases and 14(35%) possible TBM cases as per the established diagnostic criteria. Majority belongs to definitive category. Drug resistance was not found in any case.

Table-7: Diagnostic category

Category	Number	Male	Female
Definite Case	20 (50%)	14	6
Probable Case	6 (15%)	4	2
Possible Case	14 (35%)	11	3

Maximum number of patients was treated with category 1 ATT along with steroids. Only 2 patients died out of 40.

Table-8: Outcome at Discharge

Outcome at Discharge	Number	Male	Female
A symptomatic	26 (65.0%)	20	6
Some Residual Deficit	12 (30.0%)	8	4
Death	2 (5.0%)	1	1

DISCUSSION

TBM is a common infectious disease with a grave outcome especially in developing countries like India. In comparison to total number of cases in Himachal Pradesh, the number of cases admitted to IGMC may be less. This could be explained by the fact that some cases of TBM are also referred and treated in other Medical Colleges, District and private Hospitals.

In our study, majority of the patients 21 (52.5%) belonged to age group 18-39 years. Mean age was 40.17 ± 16.26 years as compared to the study done in PGI Chandigarh where mean age of TBM patients was 36.42±16.20 yrs [7]. In the study done at S.K. Institute of Medical Sciences, Srinagar; most common age group of 20 to 39 years was observed [8]. In prospective analysis of all adult cases of TBM in Neurology unit of National Hospital of Sri Lanka, mean age of the series was 44 years [4]. Likewise other studies, our study also revealed that TBM is common in second and third decade of life. In our study, 72.5% were males and 27.5% were females diagnosed to have TBM which was quite similar to the study done at PGI Chandigarh, 61.8% patients were males and 38.2% were females [7]. Like other studies, we can say that TBM is more common among males.

In our study, in majority of patients, 33 (82.5%), duration of symptoms was more than 5 days. In Australian, the duration of presenting symptoms varied from 1 day to 9 months, although 55% presented with less than 2 weeks of symptoms [5]. In the study of N. E. Anderson et al the duration of symptoms before presentation was 1day–12 months [9]. In concordance with the study of N. E. Anderson *et al.*, and Australian series, we could say that duration of illness could be less than even 5 days [5, 9]. In our study, TBM presented with fever in 33 (82.5%) and general constitutional symptoms in 21 (52.5%) cases. In comparison to this in PGI study [7] and study done at Dhaka [10], fever was present in 90.9% and 91.7% cases respectively. However, the study done in Neurology unit of National Hospital of Sri Lanka [4], fever presented in 64 (71%) and general constitutional

symptoms in 61 (68%) cases. It is evident from above studies that fever is the common presentation in TBM; however prevalence was highest in Dhaka study and lowest in study done in Sri-Lanka [4, 10].

In our study, headache was present in (65.0%), vomiting in (32.5%) cases and on physical examination meningeal signs were present in (72.5%). However, in PGI study presentation was: headache (72.7%), neck rigidity (67.3%), vomiting (54.5%) and altered sensorium (65.5%). Most of the patients, 57.5% were in stage-II and only 10% patients in stage III. Similarly, in PGI study higher number of patients (50.9%) was belonged to the stage II while 36.4% were in stage III followed by 12.7% patients who were in stage I. As far as CNS features concerned, our study was comparable with other studies [4, 8, 10]. Headache and altered sensorium were common presentation in TBM; however, headache ranked second in our study with some difference. Neck rigidity was the most common presenting sign. The papilledema was present in 5.0% cases similar to Srinagar study [8], papilledema was also present in some patients.

The focal Neurological Deficit was seen in 22.5% patients in this study. Whereas, the study done in French intensive care unit [11], showed 52% cases of focal neurological deficit. Results of study done in Sri-Lanka [4] showed cranial nerve palsies in 23 (26%) patients, in comparison to this lower incidence of cranial nerve palsies were observed in 7 (17.5%) patients in present study. The sixth nerve palsy (5%) was most commonly involved cranial nerve which is similar to the PGI study [7], where 6th nerve involvement was 9.1%. In the Dhaka study 10.0% had cranial nerve palsy and 20.0% had long tract sign [10]. Our study was comparable to Dhaka study in respect to focal neurological deficit but differ from French study [10, 11]. This may be due to high prevalence of TB in Asian countries and more emphasis on clinical suspicion, hence patients treated in early stages, so lesser number of patients with neurological deficit.

CSF microbiological analysis in our study revealed negative AFB stain in all patients, positive AFB culture in 4(10.0%) patients. However, in the study of PGI Chandigarh [7], 2 were positive for AFB stain and 12 (21.8%) were positive for culture. Moreover, in PGI study [7] PCR showed high sensitivity of 81.81% as compared to 45.5% positivity in present study. In comparison to this, study done by N. E. Anderson *et al.*, [9], AFB stain positive in17% patients and PCR assay was positive in 77% patients. The factors attributed to low sensitivity of PCR in our study are probably low volume of sample sent for investigation, and many patients presented to institution after taking antibiotics. Mean ADA in our study was 9.09±7.97. Our study also concluded that number of definite cases increased as its value increased. PGI study [7] concluded that A cut-off value of 9.5 IU/L showed 83.3% sensitivity and 99.98% specificity.

In our study, brain imaging was performed in 31(77.5%) patients and found hydrocephalus in 3 (12.9%), ischemic lesions in 4 (13.3%), meningeal enhancement in 5(20%), tuberculomas in 4 (13.3%). In the study in Sri Lanka [4] neuroimaging showed normal study in 13 (15%), hydrocephalus in 16 (18%), meningeal enhancement in 73 (82%), enhancing lesions in 14 (16%) and ischemic lesions in 15 (17%). According to the consensus diagnostic criteria, in our study there were 50% definitive cases, 15% probable cases and 35% possible TBM cases. In PGI study [7], there were 9 confirmed and 46 suspected cases. In Sri-Lankan study [4], there were 22 (24.71%) definitive, 46 probable and 21 possible cases. In the study done by N. E. Anderson *et al*., there was 71 (68%) definitive cases and 33 (32%), probable cases [9].

In our study, patients in stage I were put on ATT either category I or category II depending on previous history. Patients in stage II or III were put on steroids along with ATT. This observation was in concordance with the literature as well as study done in Kashmir which observed that ATT and steroid in stage II and III are the best therapeutic modality with more than 90% survival [8].

In our study, at the time of discharge 57.5% patients were asymptomatic, 37.5% patients were have residual Deficit and 5.0% died before discharge. In comparison to this, the study done in Sri-Lanka [4] 49% had residual sequelae and 27% died during hospitalisation.The study done at PGI Chandigarh reported overall mortality of 43.63% [7]. Mortality in our study is low because of early presentation of patients and early diagnosis. 42.5% of total patients presented within 10 days of onset of illness as compared to PGI study in which all the patients had duration of illness more than 14 days.

CONCLUSION

TBM is a sub acute infection and the challenge is early diagnosis and treatment. A major problem in diagnosis of TBM was the absence of standardized diagnostic criteria, but now with advent of consensus case definition there is a better diagnostic clarity. With the advent and availability of PCR diagnostic modalities the diagnostic pickup of TBM has improved. Rapid and early diagnosis by positive CSF PCR and CT/MRI findings should replace CSF AFB staining and culture in future for the diagnosis of CNS TB [12]. PCR has a good sensitivity but specificity depends on stringent laboratory procedures, especially to avoid DNA contamination.

REFERENCES

1. Mathuranath PS, Radhakrishnan K, Sharma SK, Tuberculosis, second edition;Jaypee Brothers Medical Publishers Ltd.; chapter 21, Neurological Tuberculosis; 2009:304-329.
2. Garg RK. Tuberculosis of the central nervous system. Postgrad Med Journal. 1999;75:133-140.
3. Roos KL, Tyler KL. Harrison' s Principles of Internal Medicine. Volume II 19th edition; McGraw Hill Education; chapter 164, Meningitis, encephalitis, brain abscess, and empyema; 2015;898-899.
4. Gunawardhana SA, Somaratne SC, Fernando MA, Gunaratne PS. Tuberculous meningitis in adults: a prospective study at a tertiary referral centre in Sri Lanka. The Ceylon medical journal. 2013 Mar;58(1):21-5.
5. Thwaites G, Chau TT, Mai NT, Drobniewski F, McAdam K, Farrar J. Tuberculous meningitis. Journal of Neurology, Neurosurgery & Psychiatry. 2000 Mar 1;68(3):289-99.
6. Marais S, Thwaites G, Schoeman JF, Török ME, Misra UK, Prasad K, Donald PR, Wilkinson RJ, Marais BJ. Tuberculous meningitis: a uniform case definition for use in clinical research. The Lancet infectious diseases. 2010 Nov 1;10(11):803-12.
7. Kaur H. Analysis of Tuberculous Meningitis Patients, Journal of Clinical and Diagnostic Research. 2015 Jan, 9(1):DC15-DC19.
8. Saleem SM, Shaw JA, Lone MA. Clinical profile of tuberculous meningitis in Kashmir. Volume11, JK Practionars, 2004;11(3):178-181.
9. Anderson NE, Somaratne J, Mason DF, Holland D, Thomas MG. A review of tuberculous meningitis at Auckland City Hospital, New Zealand. Journal of Clinical Neuroscience. 2010 Aug 1;17(8):1018-22.
10. Sarkar DN, Hossain MI, Shoab AK, Quraishi FA. Presentation of Tuberculous Meningitis Patients: Study of 30 Cases. Medicine Today. 2013 Aug 4;25(1):32-5.
11. Zuger A. Tuberculosis. In: Scheld WM, Whitley RJ, Marra CM, editors. Infection of the central nervous system, 3rd edition. Lippincot Williams and Williams. 2004;441-460.
12. Aher A, Paithankar M, Bhurke B. Study of central nervous system tuberculosis. Journal Assoc Physician India. 2018 Jan;66(1):41-4.