

CLINICAL SPECTRUM AND OUTCOME OF PATIENTS WITH TUBERCULOUS MENINGITIS AT A TERTIARY CARE HOSPITAL OF PAKISTAN

Atifa Gilani, Zahid Hassan, Khurram haq Nawaz, Muhammad Babar Khan*, Saeed Arif, Sakhawat Kazmi

Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Combined Military Hospital Lahore/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To assess the clinical profile and outcome of patients admitted with the diagnosis of tuberculous meningitis (TBM) at neurology unit of a tertiary care teaching hospital of Pakistan.

Study Design: Cross-sectional study.

Place and Duration of Study: Neurology department, Pak Emirates Military Hospital Rawalpindi, from Dec 2018 to Jun 2019.

Methodology: This study was conducted on 69 patients of tuberculous meningitis admitted. Demographic profile included age, gender, and the symptoms with which the patient presented. Neurological complications were also documented among the target population. Outcomes included recovery, shifting to intensive care unit and death.

Results: A total of 69 patients admitted in neurology ward diagnosed and managed as tuberculous meningitis in the study duration time. Male to female ratio was 1.4:1. Mean age of patients diagnosed with tuberculous meningitis in our study was 34.23 ± 3.915 years. Most of the patients presented with the fever followed by headache. Out of 69 patients, 41 (59.4%) recovered, 22 (31.9%) were shifted to the intensive care unit and 6 (8.7%) died. Seizures were the commonest neurological complication faced by the patients followed by cranial nerve palsies.

Conclusion: Fever and headache were common symptoms with which patients of tuberculous meningitis presented in our study population. Most of the patients recovered in the ward but a high percentage required intensive care unit admission as well. Seizures and cranial nerve palsies were commonly experienced complication by patients included in our study.

Keywords: Neurology, Outcome, Tuberculous meningitis.

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INTRODUCTION

Tuberculosis is an infection living for a long time with the human beings in various forms. Both eastern and western countries have been threatened with this infection and millions of deaths worldwide have been attributed to this lethal pathogen¹. Even in twenty first century infectious disease scientist are trying to fight with this bacteria but still their success has not been able to make the world tuberculosis free. Tuberculosis can present in various forms and almost all the organs of body can fall prey to this virulent organism². It may lead to serious complications an when involve the vital organs like brain may lead to permanent disabilities or even death.

Neurology is an emerging specialty in our part of the world with <200 qualified neurologist available to counter the burden of neurological illnesses in our population³. On the other hand neurological manifestation of tuberculosis including tuberculous meningitis is a fairly common clinical condition in the neurology setting of both developed and underdeveloped countries^{4,5}, tuberculous meningitis (TBM) behaves very differently from ordinary pulmonary TB so exact diag-

nosis and a specially tailored management plan is required to save the patient from death or other untoward complications.

A lot of work has been done all over the world on accurate diagnosis and management of TBM in all parts of the world. Lee *et al*, contributed in this aspect by designing a score to differentiate TBM from viral meningitis⁶. Even in a developed country like France, TBM patients in ICU showed poor prognosis emphasizing the importance of early recognition and management preventing the requirement of ICU admission⁷. Patients in China showed mixed pattern and around 20 percent of the treatment resistant patients died even at the tertiary care setting. Timely start of management based on international guidelines was associated with good outcome among these patients⁸. A similar study conducted in our neighboring country India revealed that fever and headache were the common presentations among the patients of this lethal condition and neurological complications were also common⁹.

Considering TB a common diagnosis in our population, this topic was of utmost important and the results may be generalizable to all the third world countries. Early recognition and management not only reduce the mortality but also limit the ICU admission and disability in the patient. Statistics from Pakistan

Correspondence: Dr Atifa Gilani, Saifullah Street, Gulberg Colony, Behind Sitara Market Mandian, Abbottabad Pakistan

Received: 25 Jul 2019; revised received: 10 Apr 2020; accepted: 28 Apr 2020

were really limited in this regard and those available are also from children population or regarding comparison of fungal and tuberculous meningitis at a private hospital of Karachi¹⁰, but neurological manifestations have been least discussed. We therefore planned this study with the objective to look for the neurological manifestations of this bacterial infection.

METHODOLOGY

This cross-sectional study was conducted at the Neurology Unit of Pak Emirates Military Hospital (PEMH) Rawalpindi, from December 2018 to June 2019. Sample was gathered by using the non-probability consecutive sampling technique. Sample size was calculated by using the WHO sample size calculator and using population prevalence proportion of 2.7%^{11,12}. All patients between the age of 12-65 years admitted in the neurology department and diagnosed as TBM by the consultant neurophysician were included in the study. Patients who were referred from other military, public sector and private hospitals with the same diagnosis were also included in the analysis in addition to the referrals from the other wards of own hospital. Infectious diseases is even a lesser developed specialty in our set up and no in-patient designated ward exists in our hospital, therefore most of the TBM patients are treated at the neurology unit in liaison with the infectious diseases expert if available. Marais *et al* devised a definition for the diagnosis of tuberculosis which we used in our study¹². Thereby, patients were considered as having a definite TBM if evidence of Mycobacterium tuberculosis (MTB) is found in the cerebrospinal fluid (CSF) either by detection of acid-fast bacilli (AFB) on microscopy or by culture or by molecular technique such as nucleic acid amplification (NAA) test. Radiological investigation of choice was magnetic resonance imaging which was performed in all the participants and reported by the consultant radiologist. Exclusion criteria were the patients with unclear medical diagnosis. Pregnant patients or those with CSF India ink stain positive for the fungal growth were also not included in the study. Patients with post traumatic meningitis were also the part of exclusion criteria.

Planning of study and inclusion/exclusion criteria was finalized prior to the application of ethics approval letter no. A/28/Nov/2018) to the intuitional review board committee of PEMH Rawalpindi. This tertiary care hospital 120 bed facility with 4 consultants and around 10 residents. Outcomes included recovery, shift to intensive care unit and death. A specialized

proforma was designed for the study filled by the neurophysician after interviewing the patient and seeing the medical records.

Descriptive statistics were used to describe the results of this study. SPSS version 23 was used for this purpose. Mean and standard deviation for the age of study participants was calculated. Frequency and percentages for gender, symptoms with which the patient presented, neurological complications and outcome were calculated and tabulated.

RESULTS

A total of 79 patients admitted in the neurology unit with confirmed diagnosis of TBM were initially approached to get them included in the analysis. Two were pregnant, two were either over or under age, three had no clear diagnosis of the underlying medical condition three patients did not give consent to include them in the study. Out of 69 patients included in the final analysis 41 were male and 28 were female. Male to female ratio was 1.4:1. Mean age of patients diagnosed with TBM in our study was 34.23 ± 3.915 years.

Table-I: Characteristics of patients admitted with tuberculous meningitis (n=69).

Age (years)	
Mean ± SD	34.23 ± 3.915
Range (min-max)	12-59 years
Gender	
Male	41 (59.4%)
Female	28 (40.6%)
Clinical Features at Presentation	
Fever	19 (27.5%)
Headache	12 (17.4%)
Vomiting	10 (14.4%)
Weight loss	10 (14.4%)
Seizures	06 (8.6%)
Cranial nerve palsy	05 (2.2%)
Confusion	04 (5.7%)
Others	03 (4.3%)

Table-II. Neurological complications among the patients admitted with tuberculous meningitis (n=69).

Medical Conditions	n (%)
Motor Deficit	08 (11.6%)
Cranial Nerve Palsies	09 (13.1%)
Seizures	12 (17.4%)
Optic Atrophy	01 (1.4%)
Coma	01 (1.4%)
Others	01 (1.4%)

Table-III: Outcome of patients diagnosed and treated as tuberculous meningitis.

Total	Recovery	Shifted to ICU	Death
69	41 (43.3%)	22 (15%)	06 (28.3%)

Other characteristics of study population have been summarized in table-I. Most of the patients presented with the fever 19 (27.5%) followed by headache 12 (17.4%). Seizures 12 (17.4%) were the commonest neurological complication faced by the patients followed by cranial nerve palsies 9 (13.1%) (table-II). Out of 69 patients, 41 (59.4%) recovered, 22 (31.9%) were shifted to the intensive care unit and 6 (8.7%) died (table-III).

DISCUSSION

Pakistan is the country with high prevalence of communicable and infectious diseases including the Tuberculosis¹³. Thousands of deaths in this region have been attributed to this treatable and preventable disease¹⁴. TBM has been the most common causes of mortality and morbidity among the patients suffering from TB all over the world especially the developing countries¹⁵. Patients can present with variety of symptoms initially as shown in our study so accurate knowledge of this problem among the primary care physicians, infectious diseases specialist and neurologist can enable them to suspect and diagnose this illness timely.

Paul *et al*, and Anjum *et al*, in their studies in 2017 and 2018 have concluded that TBM have been more commonly diagnosed in male population^{9,16}. Our results were also similar and neurological manifestations of TB were ore observed in the male population as compared to the female population. Multiple reasons could be given for this finding. Either males have really more chance to acquire this infection or they have more chances of developing serious complications like TBM. We conducted this study in a hospital where mostly military personals are managed so recruitment chance of male patients increases automatically giving rise to selection bias.

Our study population reported fever as the commonest presenting feature followed by headache. Similar results have been reported in the studies done in the past by Paul *et al*, in 2017 and Luo *et al*, in 2018 on similar subject^{9,17}. These two symptoms are the common finding among the patients of various outpatient departments (OPD) including the general practitioner and medical OPD. Accurate history, general physical and systemic examination, relevant laboratory and radiological investigations can give these symptoms a definite shape and enable the physician to reach the diagnosis. Sharing of experience of various local settings can help the neurologist and infectious disease specialist to develop our own protocol for diagnosing TBM is suspected cases.

Seizure was the commonest neurological complication these patients reported in our analysis followed by the cranial nerve palsies. These complications have been seen among the patients of TBM in other settings as well in studies done by Cantier *et al*, in 2018 and Merkler *et al*, in 2017^{7,18}. Sometimes a patient from remote area with poor primary medical services may present with these complications as first presentation. Country like ours where TB is highly prevalent, TBM should be considered a possibility if patient presents with any neurological signs.

Outcome was variable in our analysis. Six patients out of 69 died. This finding is in accordance with the existing literatures as TBM has been considered a life threatening illness worldwide supported by results of studies done by Zhang *et al*, in 2016 and Merkler *et al*, in 2017^{8,19}. An interesting finding was the number of patients which required shifting to the intensive care unit. This raises a major question on the cost and disability associated with management of this illness. A large number of patients requiring ICU means that liaison with an ICU setting is required for neurologist and infectious diseases specialist in order to manage all the cases of TBM. This finding also highlights the importance of early diagnosis and treatment of TBM and avoiding the possibility of shifting to ICU and minimize the disability. Hey *et al*, in 2017 and Hagan *et al*, in 2013 have also shown that patients of TBM managed in the general ward have better outcome than the patients managed in the critical care settings¹⁹⁻²¹. Large number of patients recovered with minimum disability in our analysis which highlights the importance of effective management plan among these patients.

LIMITATION OF STUDY

Selection bias was the major limitation of our study. Sample from multiple or public sector hospitals would have been more representative of the general population instead of recruiting the patients from a military setting only. Studies addressing this limitation may generate better quality results which could be generalizable to general population.

CONCLUSION

Fever and headache were common symptoms with which patients of tuberculous meningitis presented in our study population. Most of the patients recovered in the ward but a high percentage required ICU admission as well. Seizures and cranial nerve palsies were commonly experienced complication by patients included in our study.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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