

Clinical and Radiological features and Outcome of hospitalized patients with CNS tuberculosis: A prospective observational study in a tertiary care centre, Mumbai

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Abstract

Background: Tuberculosis (TB) is a major public health problem in India. Ten percent of all patients with TB have CNS involvement. Delayed diagnosis of this disease is associated with increased mortality. This study assesses the clinico-radiological features as well as outcomes in patients with various forms of CNS TB.

Methods: A prospective observational study conducted at tertiary care centre Mumbai between January 2020- July 2022. Each patient was assessed from admission to 3- month follow up. Detailed clinical examination including lab examination was done. All patients were divided into different categories based on Singhal

staging and Modified MRC grading for TBM. APACHE 2 score was evaluated for severity of illness. Outcome was measured in terms of mortality and morbidity.

Results: Our study had 70 patients with a mean age of 38.94 ± 20.75 years. Fever was the most common symptom in patients with TBM (98.57%). Of total 70 enrolled cases it was found that 57(81.43%) patients survived whereas 13(18.57%) were expired. Co infection with HIV, HBV as well as basal exudate, hydrocephalus, infarct and tuberculoma on CT were significant predictor for mortality in CNS TB.

Conclusions: Mortality rate in CNS TB is high with optimal medical management and timely surgical interventions like Ventriculoperitoneal shunt, External Ventricular Drain (EVD), Decompression Craniotomy many lives can be saved.

Keywords: Outcome in CNS TB, clinical features of CNS TB, Radiological findings of CNS TB,

Introduction

Tuberculosis (TB) currently ranks as the second most frequent infectious agent-related cause of mortality in adults globally next only to COVID19 [1]. Due to the continued pandemic, there were fewer new detections of TB in 2020, which increased death and burden, particularly in developing countries [2]. The World Health Organization (WHO) put into action the End TB Strategy in 2015, with the primary goals of lowering the incidence and mortality rates of TB by 20% and 35%, respectively, between 2015 and 2020 [3].

Although pulmonary symptoms are the most common TB presentation, extrapulmonary TB (EPTB) cases are not uncommon, accounting for 15% of all TB recorded cases [4]. One of the most difficult clinical diagnosis and with a high morbidity and death rate is central nervous system TB (CNS-TB). Children under the age of five

and immunocompromised people have a significant risk of developing CNS-TB [5,6]. TB meningitis, the most prevalent manifestation of CNS-TB, is classified according to its anatomical localization (intracranial and spinal) [7,8].

Early identification of risk factors and appropriate treatment can prevent the mortality in CNS TB. Thus this study was conducted with the following

Objectives

- 1) To study clinical features, comorbidities, CSF analysis and radiological feature of these patients.
- 2) To study demographic profile and risk factors for development of CNS tuberculosis.
- 3) To study treatment received including anti tubercular drugs, ancillary therapy, steroids, surgical intervention, and outcome in form of mortality and morbidity.

Materials and Methods

This prospective cross sectional observational study was conducted in a tertiary care public hospital of Mumbai from January 2020- July 2022. All the patients newly diagnosed with CNS Tuberculosis during that period were included in the study. Diagnostic criteria for CNS TB were; history symptoms of more than 7 days duration (fever, headache, vomiting, convulsion, focal deficit); CSF finding suggestive of TB on routine examination and biochemistry with or without confirmation by PCR/ culture OR radiological evidence of CNS TB. Patients subsequently proven to have alternate etiologies like bacterial meningitis, fungal meningitis confirm by microbiological test or non-infective disease like brain tumor by neuroimaging or by biopsy were excluded from the study.

Approval from Institutional ethics committee was obtained. Informed consent was taken from study subjects or their relatives after explaining them the

purpose of the study.

Data were collected by using predesigned, pretested questionnaire including sociodemographic details and symptomatology. Detailed Clinical examination was done including general examination, CNS examination (GCS, focal deficit, meningeal irritation signs). All patients underwent biochemical lab tests. X-ray chest (PA view) and relevant neuroimaging as per discretion of treating physician.

CSF Examination (if not contraindicated) was done for routine microscopy, ADA (Adenosine Deaminase), and MGIT (Mycobacteria Growth Indicator Tube). CSF PCR and culture for mycobacterium TB were done when relevant. Other tests like Bacterial /Fungal Culture and sensitivity done as of when required.

CT Brain with contrast was done in all cases unless contra-indicated or not feasible. Neuroimaging was repeated as and when indicated as per discretion of treating physician. Note was made of radio imaging finding like normal, exudates, hydrocephalus, vasculitis, and tuberculoma.

All patients were divided into different categories based on **Singhal staging** and **Modified MRC grading** for TBM. **APACHE 2** score was evaluated for severity of illness. Patients were treated according to guidelines of RNTCP. Follow up was done daily at time of admission in hospital, on the day of discharge and at 3 months.

Statistical analysis:

Data were analyzed using IBM SPSS Statistics Version 23. Descriptive statistics such as mean (standard deviation) and percentages were used to summarize the data. Chi-square test was used for testing the significance between categorical variables. Student t test was used to see the difference between continuous variables. Significance level was kept at 0.05.

Results

Out of total 70 cases diagnosed with CNS TB during the study period, 27(38.57%) were males and 43(61.43%) were females. Mean age was 38.94 ± 20.75 years.

In present study, patient presented with chief complaints of 98.57% patients with fever, 81.43 % with headache, 64.29% with vomiting, 55.71 % with alter sensorium and 38.57 % patients with convulsion (Table1). In present study 20 patient had history of tuberculosis. In our study cranial nerve involvement seen in 10 % patients. Which include cranial nerve 2, 3 and 7 and GCS score = 7- 15, GCS score was less than 10 in 18 (25.71%) patients , while GCS was more than 10 in 52 (74.29%) patients.

Table 1: Distribution of study subjects according to presenting complaints

Presenting complaints	Number	Percentage
Fever	69	98.57
Headache	57	81.43
Convulsion	27	38.57
Vomiting	45	64.29
Altered sensorium	39	55.71

Of total 70 enrolled cases it was found that 57(81.43%) patients survived whereas 13(18.57%) were expired (Figure 1). Out of 13 expired patients, 11 patients died in hospital during indoor period. 7 died of raised intracranial pressure, 3 due to septic shock, 1 patient due septic ARDS and 1 due cardiac arrest. 2 patients died after discharge from hospital.

These deaths noted on telephonic conversation and exact cause of death is not known. In present study Residual neurological disability was reported in terms of cranial nerve involvements, focal neurological deficit. In this 13 patients have hemiparesis with facial nerve involvement,

7 patients have cranial nerve involvement, out of which 3 have CN 2 and 2 have CN3 and 2 have CN 6 involvement.

Figure 1: Distribution of study subjects according to Mortality

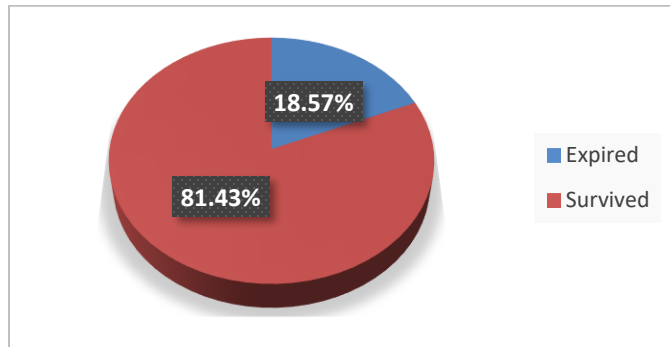


Table 2: Association of Co-morbidities with mortality in CNS TB

Co-morbidities	n	Expired N(%)	Survived N(%)	P value
DM	10	3(30)	7(70)	0.31
HTN	7	1(14.29)	6(85.71)	0.75
HIV	6	3(50)	3(50)	0.03*
HBV	1	1(100)	0(00)	0.03*
IHD	2	1(50)	1(50)	0.24
Obesity	2	1(50)	1(50)	0.24
Malnutrition	5	1(20)	4(80)	0.93

*Significant

Mortality rate was significantly higher in those presented with fever, neurological deficit & involvement of cranial nerves. Out of 6 CNS TB patients having HIV 3(50 %) died and 3(50%) survived whereas the one patient of CNS TB with positive HBV status died. HIV and HBV infection was significantly associated with mortality in CNS TB. Other comorbidities like Diabetes, Hypertension, Ischemic heart disease, Obesity and malnutrition were not significantly associated with mortality (Table 2).

Table 3: Association of CSF examination findings with mortality in CNS TB

CSF examination	Expired Mean(SD)	Survived Mean(SD)	P value
Cells	48.53(32.08)	54.28(56.36)	0.72
Polymorphs	9.53(6.75)	11.11(17.80)	0.75
lymphocytes	39.76(28.13)	42.30(48.03)	0.85
Protein	83.16(49.66)	80.45(37.81)	0.82
Sugar	41(10.80)	41.67(12.83)	0.86
ADA	18.72(10.96)	17.10(9.78)	0.59

On CSF examination Mean of cells among those who expired was 48.53 ± 32.08 cells/mm³ and those who survived 54.28 ± 56.36 cells/mm³. Mean of Polymorphs among those who expired was 9.53 ± 6.75 cells/mm³ and those who survived was 11.11 ± 17.80 cells/mm³. Mean of lymphocytes among those who expired was 39.76 ± 28.13 cells/mm³ and those who survived was 42.30 ± 48.03 cells/mm³. Mean CSF Protein value among those who expired was 83.16 ± 49.66 mg/dL and those who survived was 80.45 ± 37.81 mg/Dl. Mean CSF sugar value among those who expired was 41 ± 10.80 mg/dL and those who survived was 41.67 ± 12.83 mg/dL. Mean CSF ADA value among those who expired was 18.72 ± 10.96 (IU/L) and those who survived was 17.10 ± 9.78 (IU/L). None of these CSF analysis parameters were significantly associated with outcome (Table 3). On CSF examination 2 patients were found positive for CNS TB by gene xpert.

Table 4: Association of CT findings with mortality in CNS TB

CT findings	Total N	Expired N(%)	Survived N(%)	P value
Meningeal enhancement	45	10(22.22)	35(77.77)	0.29
Basal exudate	22	8(36.36)	14(63.63)	0.009*
Hydrocephalus	16	9(56.5)	7(43.75)	0.00*
Infarcts	15	6(40)	9(60)	0.01*
Tuberculoma	30	9(30)	21(70)	0.03*

*Significant

CT findings CNS TB patients show that Meningeal enhancement was found in 45 cases, Basal exudate in 22 cases, hydrocephalus in 16 cases, infarct in 15 cases and tuberculoma in 30 cases. Basal exudate, hydrocephalus, infarct and tuberculoma were significant risk factor for mortality in CNS TB (Table 4).

Table 5: Association of Singhal stage, MRC grade and APACHE 2 score with mortality in CNS TB

	Total N	Expired N (%)	Survived N (%)	P value
Singhal stage	N	N (%)	N (%)	
1	15	1(6.67)	14(93.33)	0.42
2	15	2(13.33)	13(86.67)	
3	19	5(26.32)	14(73.68)	
4	21	5(23.81)	16(76.19)	
MRC grading	N	N(%)	N(%)	
Grade 1	30	5(16.67)	25(83.33)	0.89
Grade 2	22	4(18.18)	18(81.82)	
Grade 3	18	4(22.22)	14(77.78)	
Apache 2 score		Mean(SD)	Mean(SD)	
	70	11.53(7.28)	9.40(5.62)	0.24

In the present study out of those who need interventions 66.67% expired an 33.33% survived and correlation between need of interventions and outcome was found to be statistically significant.

In these study all patients received standard weight base AKT regimen according to RNTCP guidelines and received ancillary treatment like mannitol and inj. dexamethasone (0.4 mg/kg) followed by oral prednisolone for duration of 1 month to 2 month. Duration of steroid were based on clinical examination. Despite above medical treatment some patients required surgical interventions include VP shunt (33.33%), EVD (external ventricular drain) (44.44%) and decompression craniotomy (22.22%). Most of these surgical interventions were needed in first week of admission in hospital. 20 patients have permanent disability.

Discussion

One of the most feared complications of TB is tuberculosis of the central nervous system due to the higher mortality rates and the disabling neurological sequelae [9]. In the present study mortality rate was 18.57%. Similarly Mortality rate reported in other study was 37.5% [10].

In the present study HIV & HBV infection was significantly associated with mortality. Study done by El Sahly HM et al [11] reported that HIV infection was not significantly associated with mortality. In the present study majority (98.57%) were presented with fever, followed by headache(81.43%),vomiting(64.29%),altered sensorium(55.71%),convulsion(38.57%). Similar findings were observed in othe studies[12,13].

In the present study Basal exudate, hydrocephalus, infarct and tuberculoma were significant risk factor for mortality in CNS TB .Study done by Goyal V et al[14] found that on CT findings that meningeal enhancement and basal exudates and tuberculoma were not significantly associated with mortality but association of

hydrocephalus & infarct with mortality was found to be statistically significant.

In this study APACHE 2 score was not significantly associated with mortality. Study done by C-H. Chou et al [15] found that those who expired had low APACHE 2 score whereas those who Survived had high APACHE 2 score and this difference was found to be statistically significant. In the present study maximum deaths were observed in those with Singhal stage 3 and 4 but Singhal staging was not significantly associated with outcome. Akdemir Kalkan et al [10] in their study found that four of the 5 (80%) patients who were at Stage 3 upon admission died, and the highest mortality rate was observed in this group whereas 50% of patients at Stage 2 upon admission died. In the present study those with MRC grade 3, 22.22% expired, those with MRC grade 2, 18.18% expired and those with MRC grade 1, 16.67% expired. Survival was high in MRC grade 1 however, was not significantly associated with outcome. Study done by Goyal V et al [14] found that those with MRC grade 3, 56% expired, those with MRC grade 2, 44% expired and those with MRC grade 1, no one was expired.

Conclusion

CNS TB continue to be common clinical problem require hospital admission and present with high mortality. These are the common complains Fever, headache vomiting, alter consciousness and convulsion in decreasing order. Co infection with HIV and HBV found to be significant risk factors for mortality. Radio-imaging is continue to be important modality Presence of basal exudate, hydrocephalus, infarct, tuberculoma on CT are the significant risk factors for mortality. With optimal medical management and timely surgical interventions like Ventriculoperitoneal shunt, External

Ventricular Drain (EVD), Decompression Craniotomy many lives can be saved.

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