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CLINICAL PROFILE OF PATIENTS WITH TUBERCULOUS MENINGITIS

General Medicine

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ABSTRACT

Background: Tuberculosis remains a major global health problem. An estimated 10.4 million new cases of TB occurred worldwide. Early diagnosis of tuberculous meningitis (TBM) plays a crucial role in saving lives and reducing disability. There have been many studies conducted on the clinical symptomatology of TBM in children, but fewer studies on adults. With this background, we conducted this study find out various laboratory and radiological parameters and short term outcomes in TBM patients.

Methodology: The present cross sectional study was conducted on 60 patients with TBM based on the CSF analysis and or radiological diagnosis. The detailed history and examinations were done. Relevant investigations like complete blood count, chest X ray, sputum microscopy, CSF examination, CBNAAT, CT or MRI were done. Detailed Neurological examination was done to assess condition of the patient, meningeal signs and focal neurological deficit. The data was analysed using Epi info version 7.2. The significance level was set at 0.05.

Results: The mean age of the study subjects was 38.33 ± 13.46 years with male preponderance (68.33%). The most common chief compliant was fever (80%) followed headache (75%). The most common sign was altered mental status (53.33%) and focal neurological signs (40%). 20% cases had active pulmonary TB, 16.67% had history of HIV and 13.33% had past history of TB. 45% of the patients were BMC grade III. 83.33% of the CSF had high total counts and 43.33% had high protein levels. 53.33% had abnormal MRI and 31.67% abnormal Chest X ray. Mortality was seen in 25% of the patients. Presence of HIV was the only factor which influenced the outcome.

Conclusion: TBM cases are more common in middle age males. Fever and vomiting are common symptoms but chances of cranial nerve palsy should also be kept in mind while diagnosis. The presence of HIV affects the outcome significantly.

KEYWORDS

Tuberculous meningitis, BMC Grade, Focal neurological signs

INTRODUCTION:

Tuberculosis remains a major global health problem. An estimated 10.4 million new cases of TB occurred worldwide. The World Health Organization's 'End TB Strategy' calls for a 90% reduction in TB deaths and 80% reduction in TB incidence rate by 2030. The rate of reduction in yearly incidence was 1.5%, which falls below the required target of 4–5%. These figures reflect the ongoing evolving challenges faced in the prevention and treatment of tuberculosis[1]. The mortality due to tuberculous meningitis (TBM) in India is 1.5 per 100,000 populations[2,3].

Despite being an TB endemic country, data regarding clinical, radiological, laboratory parameters and final outcome of adult TBM patients is sparse in India. Analysis of such variables in various countries has shown association of various factors with the prognosis of the disease[2,3,4].

Vague and varied clinical symptomatology, poorly sensitive diagnostic laboratory tests, problem of multi drug resistant tuberculosis and duration of tuberculosis and difficult treatment options for the complications of TBM makes it a difficult task for a clinician in controlling the ill effects of the disease[5,6].

Early diagnosis of TBM plays a crucial role in saving lives and reducing disability because the prognosis is dependent on the patient's severity at the time that effective antibiotics and steroids are started[9,10]. There have been many studies conducted across the world on the clinical symptomatology of TBM in children, but very few studies on adult patients. With this background, we conducted a study to address the following objectives.

OBJECTIVES: 1. To study various laboratory parameters and radiological parameters in TBM. 2. To study short term outcome in TBM patients

MATERIAL AND METHODS

The present cross sectional study was conducted on 60 patients with TBM based on the CSF analysis and or radiological diagnosis and with age more than 12 years, admitted under Medicine wards and ICU in CPR Hospital, Kolhapur, Maharashtra. Patients who do not give consent for the study, cases having post TBM, CSF staining or culture reveals pyogenic organisms or positive fungal growth in CSF, were excluded.

After taking informed consent from the patient or the relative the detailed history and examination was done and were noted down in the pretested case record form. Detailed Neurological examination was done to assess condition of the patient, meningeal signs and focal neurological deficit.

Relevant investigations like complete blood count, chest X ray, sputum microscopy, CSF examination and CT or MRI were done. CSF examination was done including the microscopy, sugar, cells, proteins, gram staining and ZN staining, ADA levels and CBNAAT was also done. An ethical committee of the institute permission was taken before the start of the study.

Data was entered in Microsoft Excel and analysed using Epi info version 7.2. The qualitative data was expressed in percentages. To test the difference between 2 proportions chi square or fisher's exact test was used. The quantitative data was expressed in terms of mean and standard deviation. To test the difference between the two means student t test was used. The significance level was set at 0.05.

RESULTS:

We included 60 cases in our study. The mean age of the study subjects was 38.33 ± 13.46 years with minimum of 18 years and 72 years maximum. The most common age group was 41 to 50 years followed by 21 to 30 years. Majority of the study subjects were males.

Table 1: Presenting symptoms, signs and other relevant history (n=60)

Symptoms/Signs		Frequency	Percentage
Symptoms	Cough >2 weeks	19	31.67
	Fever	48	80.00
	Headache	45	75.00
	Photophobia	7	11.67
	Seizures	17	28.33
	Vomiting	28	46.67
	Weight loss	16	26.67
Signs	Altered mental status	32	53.33
	Cranial nerve palsy	5	8.33
	Focal neurological signs	24	40.00
	Neck stiffness	8	13.33
	Brudzinski's sign	11	18.33
	Kernig's sign	9	15.00
Other relevant history	Active pulmonary TB	12	20.00
	BCG vaccination	16	26.67
	HIV	10	16.67
	Other associated diseases	12	20.00
	Past history of TB	8	13.33

The most common chief compliant was fever followed headache and vomiting. The most common sign was altered mental status and focal neurological signs. About 20% cases had active pulmonary TB, 20% had other associated diseases, 26.67% had their BCG vaccination done, 16.67% had history of HIV and 13.33% had past history of tuberculosis. (Table 1). 45% patients were BMC grade 3 and 38.33% were Grade 2. (Chart 1) Based on GCS, 26.67% were in minor category, 43.33% had moderate GCS and 30% had severe GCS in the present study.

Chart 1: Distribution of the study based on BMC grade

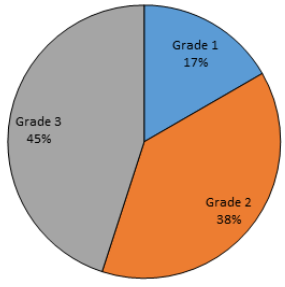


Table 2: Distribution of the study based on the CSF parameters:

CSF parameters		Frequency	Percentage
Total count	High	50	83.33
Glucose	Low	13	21.67
Proteins	High	26	43.33
ADA	High	45	75.00
CBNAAT	Positive	50	83.33
Radiological parameters			
MRI	Abnormal	32	53.33
Chest X ray	Abnormal	19	31.67

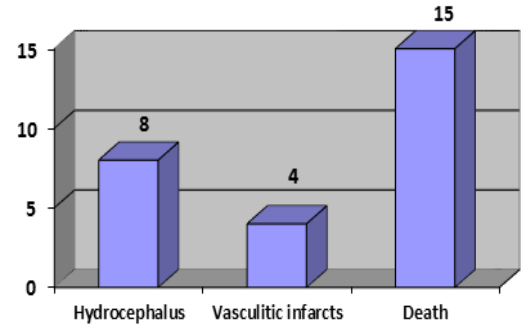
About 83.33% of the CSF had high total counts, 21.67% had low glucose levels and 43.33% had high protein levels. 75% of the cases had ADA levels more than 10IU/dl and 83.33% had CBNAAT positive. About 53.33% had abnormal MRI and 31.67% had abnormal Chest X ray. (Table 2)

13.33% had hydrocephalus, 6.67% had Vasculitic infarcts and 25% of the patients succumbed to death. History of presence of HIV was the only factor which influenced the outcome of the patients. Other factors were not significantly associated with outcome.

Table 4: Distribution Of The Various Parameters Based On The Outcome

Parameters	Alive	Dead	P value
	No./mean (%/SD)	No./mean (%/SD)	
Mean Age (Years)	37.80 (14.12)	39.93 (11.53)	0.5992
Male	30 (66.67)	11 (73.33)	0.6307
Cough >2 weeks	14 (31.11)	5 (33.33)	0.8231
Fever	38 (84.44)	10 (66.67)	0.1365
Headache	33 (73.33)	12 (80.00)	0.6051
Photophobia	5 (11.11)	2 (13.33)	0.8165
Seizures	14 (31.11)	3 (20.00)	0.4081
Vomiting	21 (46.67)	7 (46.67)	1.000
Weight loss	14 (31.11)	2 (13.33)	0.1775
Altered mental status	22 (48.89)	10 (66.67)	0.2310
Cranial nerve palsy	4 (8.89)	1 (6.67)	0.7874
Focal neurological signs	16 (35.56)	8 (53.33)	0.2335
Neck stiffness	8 (17.78)	3 (20.00)	0.8472
Active pulmonary TB	10 (22.22)	2 (13.33)	0.4560
BCG vaccination	14 (31.11)	2 (13.33)	0.1775
HIV	4 (8.89)	6 (40.00)	0.0051
Other associated diseases	8 (17.78)	4 (26.67)	0.4560
Past history of TB	6 (13.33)	2 (13.33)	1.000

Chart 3. Complications among the Patients



DISCUSSION:

TB meningitis can initially display vague symptoms and these symptoms can last for several weeks before more specific symptoms of meningitis, such as severe headache, dislike of bright lights and neck stiffness occur. With this background, we conducted a cross sectional study to understand the clinical profile of the patients with TBM in our hospital.

In our study, the mean age of subjects was 38.33 ± 13.46 years (18 to 72 years). **Modi M. et al**[9] found that the mean age was 30.4 ± 13.8 years (range = 13–69 years). In a study by **Sanjeev Kumar et al**[10] and **Kaur H et al**[11] the mean age was similar to our study. We found majority of the study subjects were males (68.33%). Male to Female ratio was 2.15 : 1. **Kaur H et al**[11] studied 61.8% patients were males and 38.2% were females. **Paul SA et al**[12] and **Fan HW et al**[13] had findings similar to our study. **Sanjeev Kumar et al**10 inferred that in their study the male: female ratio was 0.8.

Our study shows the most common compliant was fever (80%), headache (75%) and vomiting (46.67%). The most common sign was altered mental status (53.33%) and focal neurological signs (40%). **Hsu PC et al**[14] revealed that the common presenting symptoms and signs were fever (81.5%), consciousness disturbance (63.0%), headache (60.2%) and neck stiffness (54.6%). **Sutlas PN et al**[15] inferred that the most frequent presenting signs were alterations in consciousness and focal neurological signs. Behavioral changes were present in 39.3% of patients. Similar observations were seen in a study by **Paul SA et al**[12]. If a patients with altered sensorium, headache and vomiting with fever TBM has to be kept as one of the important differential diagnosis.

In the present study, 20% cases had active pulmonary TB, 20% had other associated diseases, 16.67% had history of HIV and 13.33% had past history of tuberculosis. **Fan HW et al**[13] inferred that 35 cases were accompanied with active pulmonary tuberculosis. **Enberg MG et al**[16] inferred that in 9 (17%) patients there was a remote history of TB and 13 (25%) had co-infection with HIV. We observed about 45% of the patients were BMC grade 3. 44% were in stage II and 56% were in stage III in a study conducted by **Sutlas PN et al**[15]. In a study by **Hsu PC et al**[14] and **Enberg MG et al**[16] findings were similar to our study.

Regarding CSF analysis, similar to our study findings, **Enberg MG et al**[16] inferred that 68% of patients had in the CSF of 1.1 g / L, 80%, glucose <0.4 g/L, in 93% the count of leukocytes were <500/mm^3, with predominance of mononuclear cells in 72% of the cases. The CSF Koch culture was positive in 45% of the patients and the smear in CSF was negative in 100%.

53.33% had abnormal MRI and 31.67% had abnormal Chest X ray in our study. **Modi M. et al**[9] had abnormal MRI in 96.7% patients. Hydrocephalus was seen in 109 (52.1%) patients. **Sutlas PN et al**[15] had Hydrocephalus was demonstrated in 14 (23%) patients; Tuberculomas were seen in 21 (34%) patients. We observed that 25% of the patients succumbed to death. **Kaur H et al**[11] showed that mortality was highest in confirmed cases (66.67%) and there was increase in mortality as the stage of disease increased. **Sanjeev Kumar et al**[10] inferred that 15.8% patients died by 6 months follow up in their study.

We observed, presence of HIV was the only factor which influenced the outcome of the patients. Other factors were not significantly associated. **Kaur H et al**[11] studied, 24 patients died due to the disease which included all HIV positive cases. Multinomial logistic regression of the factors revealed age ≥ 40 year, past history of TB, presence of basal exudates and hydrocephalus in neuroimaging as significant risk factors for mortality in TBM patients. In a study conducted by **Modi M. et al**[9], when poor outcome was defined by death, clinical parameters associated with high risk of death included higher age, longer duration of illness presence of altered sensorium, lower GCS score and stage 3 TBM. The logistic regression analysis showed altered sensorium, motor deficit, seizures and isolation of multi-drug resistant (MDR) M. Tuberculosis were independent predictors of death as compared to recovery in study conducted by **Gupta R et al**[17].

CONCLUSION:

To conclude, the TBM cases were more common in middle age groups (21 to 50 years) and among males (68.33%). Fever, vomiting and headache were the common symptoms but chances of cranial nerve palsy should also be kept in mind when diagnosis is made. CSF showed high total counts, low glucose and high protein levels among our subjects. The presence of HIV affects the outcome significantly.

LIMITATIONS:

It was a cross sectional study and single center study. Prospective cohort studies conducted would have yielded better association between the short term and long term outcome.

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