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Original Research Article

Clinical presentations among adult patients with tuberculous meningitis

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ABSTRACT

Background: Bangladesh is a country with a high burden of pulmonary as well as extrapulmonary tuberculosis. TBM is a particularly important public health issue in our country. Identifying prognostic predictors would improve the quality of management and ultimately will prevent long-term mortality and morbidity. The aim of the study was to observe and identify the most common clinical presentations among patients with tuberculous meningitis.
Methods: This hospital-based prospective cohort study was carried out at the in-patient Department of Clinical Neurology at the National Institute of Neurosciences and Hospital (NINS and H), Dhaka, Bangladesh from October 2016 to September 2017, 1 year. A total of 54 patients admitted to the hospital with features of tuberculous meningitis (TBM) were selected for the study following inclusion and exclusion criteria.
Results: Over 70% of patients were adolescents or young adults with a mean age of 28.2±12.3 years. The majority (48.2%) of the participants were from TBM stage II, while 37% were from stage III of TBM. Fever, headache, and systematic symptoms were the most frequent clinical presentations. The median delay in treatment was 30 days. Interruption in anti-TB treatment was reported in 3 (9.3%) cases.
Conclusions: The study found that among possible TBM cases, the most frequent clinical features were fever, headache, and systematic symptoms. Focal neurological deficit and cerebral nerve palsy also had a high prevalence among the participants. The majority of the participants were young adults and female prevalence was high in the present study. The majority were from stage II TB among the study participants.

Keywords: Clinical presentations, Meningitis, Respiratory, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is a global pandemic and is caused by the Mycobacterium tuberculosis complex.[1] It causes ill health for approximately 10 million people each year and is one of the top ten causes of death worldwide and the second leading cause of death from an infectious disease after HIV.[2,3] According to recent data, the disease causes approximately 9 million new cases and 1.5 million deaths each year.[1] TBM (tuberculous meningitis) is a particularly important public health issue in our country. Bangladesh is a country with a high burden of pulmonary as well as extrapulmonary tuberculosis. TB can affect various organs of the body, but it most commonly affects the lungs and is known as pulmonary TB. When TB affects other organs, it is recognized as extra-pulmonary TB. The majority of the pulmonary cases are pulmonary TB, while only 15-20% of cases are extrapulmonary

TB.[4,5] TBM is the most common and severe form of CNS tuberculosis.[6] The relative incidence of this disease is 0.4-1% of all cases of TB.[7-9] It affects all age groups, however, recent data suggest that individuals aged 15 and above accounted for 88% of all patients.[10] Because of the deadly consequences of this disease, early diagnosis is an essential component in the management of tuberculous meningitis.[5] However, prediction of the outcome of this devastating condition is difficult due to its protracted course, the virulence of the infecting agent, unknown underlying pathological mechanisms, variations in host immunity, and CSF penetration for ATT.[11,12] CM and TBM are the two most common types of chronic infectious meningitis, especially in developing countries, and may have similar clinical manifestations and cerebrospinal fluid (CSF) findings.[13,14]

Although mortality has decreased significantly in recent years, with the advent of new antimicrobial drugs, diagnostic techniques, and treatment strategies, it remains high. CM and TBM are easily misdiagnosed due to vague clinical syndromes associated with these conditions.[13,15]

The present study was conducted to better identify the clinical presentations of TBM patients so that it can better help in identifying TBM cases with more accuracy.

METHODS

This hospital-based prospective cohort study was carried out at the Inpatient Department of Clinical Neurology at the National Institute of Neurosciences and Hospital (NINS and H), Dhaka, Bangladesh from October 2016 to September 2017, 1 year. Patients admitted to the hospital with features of Tuberculous Meningitis (TBM) were selected for the study. A consecutive sampling method was used to select a total of 54 patients following the inclusion and exclusion criteria. Informed written consent was obtained from each of the participants, and ethical approval was also obtained from the ethical review committee of the study hospital. Data was collected through a pre-prepared questionnaire given to the participants, and medical data were collected from hospital records. The study used SPSS version 25.0 for statistical analysis and presented results in tables and figures. The confidence interval was set at 95%. The chi-square test was used to compare qualitative variables and paired t-test for quantitative variables. A p-value of less than 0.05 was considered statistically significant. Descriptive statistics were used to describe the population by age, gender, marital, education, and socioeconomic status. Univariate analysis was conducted using the Chi-square test and Fisher's Exact Test to determine the association of different variables on outcome. Logistic regression analysis was used to identify independent predictors of mortality. Variables with p-values less than or equal to 0.05 by univariate analysis were entered into a multivariate logistic regression model for further assessment to eliminate confounding factors.

Inclusion criteria

Features of tuberculous meningitis (TBM, age ≥18 years and patients who had given consent to participate in the study were included.

Exclusion criteria

Positive CSF Gram or India ink stain, bacterial brain abscess (space-occupying lesion on cerebral imaging), known pregnancy, diagnosis of multi drug-resistant TBM and lack of consent were excluded.

RESULTS

Over 70% of patients were adolescent or young adults with a mean age of 28.2±12.3 years. A majority (48.2%) of the participants were from TBM stage II, while 37% were from stage III of TBM. Fever, headache, and systematic symptoms were the most frequent clinical presentations. The median delay in treatment was 30 days. Interruption in anti-TB treatment was reported in 3 (9.3%) cases (Table 1).

Table 1: Distribution of patients by their demographic characteristics (n=54).

Demography	Frequency	Percentage
Age* (Years)		
< 30	38	70.4
30-40	5	9.3
40-50	7	13.0
≥ 50	4	7.3
Mean±SD	28.2±12.3	
Age range	13-70	
Sex		
Male	20	37.0
Female	34	63.0
Marital status		
Married	32	59.3
Unmarried	22	40.7
Educational status		
Below SSC	29	53.7
Above SSC	25	46.3
Socioeconomic status		
Lower class	18	33.3
Middle class	35	64.8
Upper class	1	1.9

Over 70% of the patients were adolescents or young adults (<30 years old) with the mean age of the patients being 28.2±12.3 years. A female predominance (63%) was observed in the series. Nearly 60% were married, over half (53.7%) were below SSC level educated and 65% were from middle-class families.

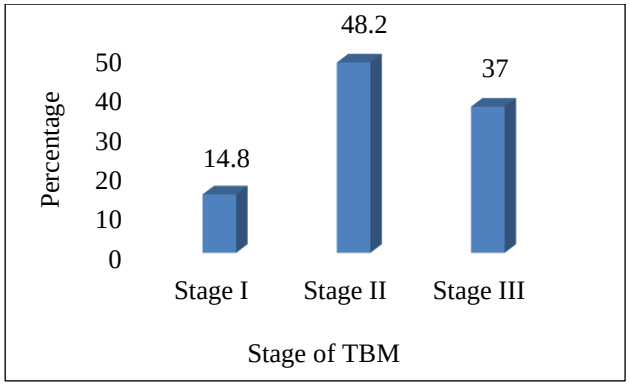

Figure 1: Distribution of TBM patients by the stage of the disease (n=54).

The majority (48.2%) of the participants were from TBM stage II, while 37% were from stage III of TBM. Only the remaining 14.8% were from stage I of TBM (Figure 1).

Table 2: Distribution of patients by their clinical features (n=54).

Clinical features	Frequency	Percentage
Duration of illness >45 (days)*	24	44.4
Clinical presentations		
Fever	53	98.1
Headache	49	90.7
Vomiting	32	59.3
Convulsion	19	35.2
Altered sensorium	20	37.0
Systemic symptoms	36	66.7
H/o recent contact with TB Pt.	18	33.3
Focal neurological deficit	32	59.3
Hemiplegia	8	14.8
Paraplegia	6	11.1
Cranial nerves palsy	26	48.1
Visual impairment	9	16.7
Optic neuritis	9	16.7
Papilledema	5	9.3
Extra CNS TB	10	18.5

Table 3: Distribution of patients by treatment-related factors (n=54).

Treatment-related factors	Frequency	%	Median (range)
Treatment delay (days)	-	-	30 (15-90)
Interruption anti-TB treatment	3	5.6	-
CSF diversion (VP shunt)	5	9.3	-
Paradox	5	9.3	-

Approximately 45% of the TBM patients had greater than 45 (range: 15-90) days of illness at the time of admission. The patients invariably presented with fever (98.1%) followed by headache (90.7%), systemic symptoms (66.7%), vomiting (59.3%), and focal neurological deficit (59.3%). Other less common symptoms were cranial nerve palsy (48.1%), altered sensorium (37%), and convulsion (35.2%). Hemiplegia (14.8%), paraplegia (11.1%), visual impairment and optic neuritis (16.7%) and papilledema (9.3%) were even less common presentations (Table 2).

The median delay in treatment was 30 days. Interruption in anti-TB treatment was reported in 3 (9.3%) cases. CSF diversion (VP shunt) was done in 5 (9.3%) cases.

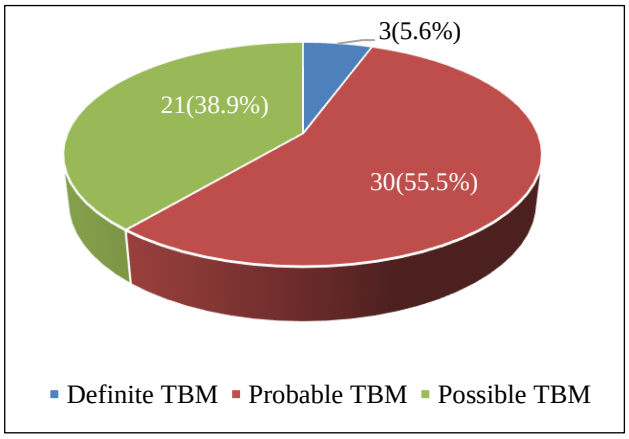

Figure 2: Distribution of patients by their final diagnosis.

Final diagnosis established 3 (5.6%) cases as definite TBM, 30 (55.6%) as probable TBM and 21 (38.9%) as possible TBM (Figure 2).

DISCUSSION

Tuberculosis is an endemic disease in Bangladesh and Tuberculous Meningitis (TBM) is the most severe life-threatening form of TB. Although TB has some common clinical factors, those can often be misdiagnosed as cryptococcal meningitis or CM. The present study was conducted with only the participants who had presented features of TBM. The aim of the study was to observe the prevalence of different clinical presentations among TBM suspect cases to determine the relation between TBM and such clinical features. In the present study, over 70% of the participants were adolescents or young adults, under the age of 30 years. This high prevalence of young adults among TBM patients was also observed in another Bangladeshi study, where 53.3% had been between the age of 20-39 years.[16] The study also showed a female predominance among the participants, which was similar to the findings of another Asian study.[17] The majority of the participants were from the middle socio-economic class, and 53.7% had education below SSC levels. Among the 54 participants, 48.2% were at stage II of

TBM, while 37% were at stage III. At the time of the admission, almost half (44.4%) of the participants had been suffering from TBM illness for over 45 days, and the overall range of the participants suffering from TBM features was from 15 days to 90 days. Among the clinical presentations, almost everyone had a fever and headache, while over half (59.3%) had vomiting as a symptom. Focal neurological deficit and cranial nerve palsy also had a high prevalence among the participants. A total of 66.7% of the participants had shown systemic symptoms. Conversion and alerted sensorium also had a high prevalence of over 30%. 33.3% of the participants also had a history of recent contact with TB patients. These clinical factors seem to be the most influential among TBM patients, and this statement is also supported by findings of other similar studies.[16,18,19] Other than these prominent features, some other symptoms like hemiplegia, paraplegia, visual impairment, optic neuritis, papilledema, etc. were also observed among the participants of the present study. Observing the treatment-related factors of the participants, the median treatment delay of the participants was 30 days. The majority of the participants faced no major problems during the treatment period, while 5.6% had interruption during their anti-TB treatment, 9.3% had CSF diversion, and another 9.3% had faced paradoxical reactions during their TB treatment. The final diagnosis of the participants revealed that out of the 54 participants, only 5.6% had definite TBM, 55.5% had probable TBM and the remaining 38.9% had definite TBM. The incidence of definite TBM was extremely low in our study compared to other studies with a much higher incidence of definite TBM.[8] In the present series, the causes of less number of definite TBM may be due to the volume of CSF submitted, repetition of LPs, and the capacity of laboratories and technicians' experience, as observed in some other studies.[20-22] However, a study by Kalita et al also had a low amount of TBM definite cases similar to our studies.[23]

This study has few limitations. The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. The number of definite TBM cases was very low.

CONCLUSION

The study found that among possible TBM cases, the most frequent clinical features were fever, headache, and systematic symptoms. Focal neurological deficit and cerebral nerve palsy also had a high prevalence among the participants. The majority of the participants were young adults and female prevalence was high in the present study. The majority were from stage II of TB among the study participants.

Recommendations

The lack of TBM definite cases greatly impacted the goal of the study. A larger study with much larger sample size and longer duration could help in better understanding the common clinical features of TBM.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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