Predictors Modifying the Outcome of Tuberculous Meningitis (TBM) in Adults: A Hospital Based Study in Bangladesh

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Abstract

Background: Outcome of TBM can be modified by several predictors. Objective: This study was undertaken to evaluate the predictors of outcome of tuberculous meningitis (TBM) at 6 and 9 months. Methodology: This hospital based prospective cohort study was carried out from October, 2016 to September, 2017 (1 year) in the in-patient Department of Neurology at the National Institute of Neurosciences & Hospital (NINS & H), Dhaka, Bangladesh. All the patients with age 18 years or more of both sexes with features of TBM fulfilling the case definition criteria was included as the study population. The outcome was measured at 6 and 9 months by modified Rankin Scale (mRS) with no disability (score=0), mild disability (score = 2), moderate disability (score=3-4), severe disability (score=5) and dead (score=6). For statistical analysis outcome was classified as death and survival group. A number of clinical, laboratory and radiological parameters were evaluated initially by univariate and finally multiple regression analysis. Results: A total 54 TBM patients were included in this study. Over 70% of the patients were adolescent or young adult (< 30 years) with mean age of 28.2 ± 12.3 years and 63% were female. Staging of the TBM showed that nearly half (48.1%) were at stage II and 37% cases were in stage III disease. Baseline imaging (CT-scan and MRI) showed basal meningeal enhancement in 40.7% cases, hydrocephalus in 40.7%, infarction 46.3% and tuberculoma in 29.6% cases. Final diagnosis was established as definite TBM in 3(5.6%) cases, probable TBM 30(55.6%) and possible TBM in 21(38.9%) cases. In terms of 6-months outcome, 16(29.6%) cases died and 10(18.5%) had recovered without any neurological sequelae; however, mild, moderate and severe disability were in 11.1%, 27.8% and 13% cases respectively. At the 9 months of evaluation 13 (24.0%) had complete recovery without any neurological sequelae, 22 (40.9%) patients survived with various degree of disabilities like visual impairment, hemi or paraplegia, cognitive impairment, rest or died with a total mortality of 19(35.1%). In univariate analysis, age >50 years (p=0.019), duration of illness before initiation of treatment (>45 d) (p = 0.041), convulsion (p = 0.010), altered sensorium (p<0.001), delayed initiation of treatment >1 month (p=0.041) and stage III TBM (p<0.001) were significantly associated with mortality. In multivariate analyses stage III TBM (p=0.004), altered sensorium (p=0.036), delayed initiation of treatment >1 month (p=0.043) emerged as independent predictors of mortality. Conclusions: In conclusion stage III TBM, altered sensorium and delayed initiation of treatment more than 1 month are the independent predictors of mortality in TBM patients. [Journal of National Institute of Neurosciences Bangladesh, January 2021;7(1): 14-19]

Keywords: Predictors; Outcome; Tuberculous Meningitis; TBM

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Introduction
Tuberculosis (TB) is a global pandemic and is caused by the Mycobacterium tuberculosis complex. It causes ill-health for approximately 10 million people each year and is one of the top ten causes of death worldwide and second leading causes of death from an infectious disease after HIV. Bangladesh is one of the high burden countries (HBCs) among 30 for tuberculosis reported by WHO with the incidence of 221/100000 and mortality 40/100000 annually.

TB most commonly affects the lungs (pulmonary TB), although it can also affect other organs and systems (extra pulmonary TB). About 15.0% to 20.0% of TB cases are extra pulmonary. The World Health Organization (WHO) reported 0.8 million extra pulmonary TB cases worldwide in 2013. TBM is the severe form of CNS tuberculosis. The relative incidence of this disease is 0.4% to 1.0% of all cases of TB. The disease affects all the age groups. However recent data suggests that 15 years or more age group comprises about 88.0% of all patients. The actual incidence and prevalence of TBM is not yet clearly defined in our country. The worldwide mortality rate of this disease is 20.0% to 69.0% and about half of the survivors developed neurological sequelae like visual loss, motor and cognitive deficits. Early diagnosis is an essential component in management of tuberculous meningitis to prevent mortality and morbidity. However prediction of ultimate outcome of this condition is difficult due to its prolonged course, the virulence of the infecting agent, non specific pathological mechanisms, difference in host immunity and CSF penetration for ATT.

Many prognostic predictors have been studied globally to predict the outcome of these serious disorders. Among them important are the stage of the disease (stage I, II, III), age, sex, seizure, H/O close contact with tuberculous patient, underlying co morbidities, duration of illness, fever, headache, visual impairment, alteration of consciousness, mental status abnormalities, neck stiffness, cranial nerve palsy, changes in fundus, focal neurological deficit, extra meningeal tuberculosis, CSF cell (TC of WBC), protein, glucose, image (hydrocephalus, infarction, basal meningeal enhancement, tuberculoma), timing of initiation of anti-TB drugs, treatment with corticosteroid, drug toxicity, shunt surgery and neurophysiological findings (EEG, motor and somatosensory evoked potentials).

Outcome of TBM depend on more than one variable, in that circumstances multivariate analysis is a useful method for it's benefit of determining the effect of each variable while controlling the influence of the others. As evidence suggest that neurological status in TBM patient changes at 6 and 9 months. The purpose of the present study was to identify the prognostic predictors of outcome in adult of TB meningitis in Bangladesh at 6 and 9 months.

Methodology
This present study was designed as hospital-based...
prospective cohort study conducted in the inpatient Department of Neurology at the National Institute of Neurosciences & Hospital (NINS & H), Dhaka, Bangladesh. The patients with features of TBM fulfilling the ‘consensus case definition criteria for TBM’\textsuperscript{18} were included as the study population. According to the consensus case definition the cases were categorized as definite, probable, possible and not TBM group. Not TBM patients were excluded from the study. After the enrollment, necessary investigation including CSF study and neuroimaging like MRI of brain with contrast were performed. Inclusion criteria were patients of 18 years or more of both sex categorized as definite, probable and possible Tuberculous Meningitis. Exclusion criteria were positive CSF for Gram or India Ink stain, ICSOL, serum bilirubin > 2.5 x ULN, ALT >5 x ULN, S. Creatinine >3 x ULN, pregnancy. All the patients were treated initially (intensive phase) for 2 months and then a maintenance phase for 10 months with standard anti TB four drugs regimen according to weight based NTP schedule under DOTS along with corticosteroid coverage\textsuperscript{3,17,19}. CSF diversion surgery was considered in selective cases of hydrocephalus. Pyridoxine was given with isoniazid therapy throughout the treatment. Paradoxical response was managed with short course of corticosteroid in standard dose and duration\textsuperscript{10-21}. Second line antituberculous therapy was used in resistance cases of first line drug according to the standard protocol\textsuperscript{13,17}. Follow-up was done at OPD of NINS&H at 6 and 9 months. The outcome was measured at 6 and 9 months by modified Rankin Scale (mRS) with no disability (score=0-1), mild disability (score=2), moderate disability (score=3-4), severe disability (score=5) and dead (score=6)\textsuperscript{23}. For statistical analysis outcome was classified as death and survival group. A number of clinical, laboratory and radiological parameters were evaluated initially by univariate and finally by multiple regression analysis.

**Statistical Analysis:** Statistical analysis of the study was done by SPSS version 25.0. Confidence interval was considered at 95.0% level. Less than 0.05 was taken as statistically significant. Univariate analysis was conducted first using Chi-square test and Fisher’s Exact Test to determine association of different variables on outcome. Then independent predictor was determined on mortality using logistic regression analysis. To eliminate confounding factors in predicting the risk for mortality, variables with p value ≤0.05 by univariate analysis were entered into a multivariate logistic regression model for further assessment.

**Results**
A total 54 TBM patients were included in this study. Over 70.0% patients were adolescent or young adult (more than 30 years) with mean age of 28.2 ± 12.3 years with a female preponderance (63%) (Table 1).

| Demography | Frequency | Percent |
|------------|-----------|---------|
| Age (Years) |           |         |
| < 30       | 38        | 70.4    |
| 30 – 40    | 5         | 9.3     |
| 40 – 50    | 7         | 13.0    |
| ≥ 50       | 4         | 7.3     |
| Sex        |           |         |
| Male       | 20        | 37.0    |
| Female     | 34        | 63.0    |

At admission nearly half (48.1%) were at stage II and 37% cases were in stage III disease (Table 2).

| Stages of TBM | Frequency | Percent |
|---------------|-----------|---------|
| I             | 8         | 14.8    |
| II            | 26        | 48.1    |
| III           | 20        | 37.0    |
| Total         | 54        | 100     |

Baseline imaging (CT-scan and MRI) showed basal meningeal enhancement and hydrocephalus in equal number of patients (40.7%), infarction in 46.3% and tuberculoma in 29.6% cases [Figure 1].

**Table 1:** Distribution of Patients by their Demographic Characteristics (n=54)

**Table 2:** Categorization of Patients according to the Stages (n=54)

**Figure 1:** Categories for patients with suspected tuberculous meningitis\textsuperscript{23}

Table 3 shows in terms of 6-months outcome, 10(18.5%) came round without any sequelae, over one-quarter (38.8%) had mild to moderate disability. 13% had severe disability. In this period 16(29.6%) patients died due to disease process.
Final diagnosis was established as definite TBM in 3(5.6%) cases, probable TBM 30(55.6%) and possible TBM in 21(38.9%) cases. In terms of 6-months outcome, 16(29.6%) cases died while 10(18.5%) had recovered without any neurological sequelae; however, mild, moderate and severe disability were observed in 11.1%, 27.8% and 13% cases respectively (Table 3).

Table 3: Distribution of patients by their outcome at 6 months (n=54)

| Outcome at 6 months | Frequency | Percent |
|---------------------|-----------|---------|
| No disability (good outcomes) | 10 | 18.5 |
| Mild / Moderate Disability (intermediate outcomes) | 21 | 38.8 |
| Severe disability (Poor outcome) | 7 | 13.0 |
| Death | 16 | 29.6 |
| Total | 54 | 100 |

Figure II: Pie diagram showing final diagnosis in 54 cases

At the 9 months of evaluation 13 (24.0%) had complete recovery without any neurological sequelae, 22 (40.9%) patients survived with various degree of disabilities like visual impairment, hemi or paraplegia, cognitive impairment and rest of the patients died 19(35.1%) (Table 4; Figure III).

Table 4: Distribution of patients by their outcome at 9 months (n=38)

| Outcome at 9 months | Frequency | Percent |
|---------------------|-----------|---------|
| No disability (good outcomes) | 13 | 34.2 |
| Mild / Moderate Disability (intermediate outcomes) | 19 | 50 |
| Severe disability (Poor outcome) | 3 | 7.9 |
| Death | 3 | 7.9 |
| Total | 38 | 100 |

16 patient were died at 6 month follow up were excluded from the analysis.

Table 5: Univariate analysis of predictors of mortality related to clinical, CSF and diagnostic findings

| Risk Factors | Group | P value | Relative Risk (95% CI of RR) |
|--------------|-------|---------|-----------------------------|
| Age >50 years | Dead (n = 19) | 3(15.8) | 1(2.9) | 0.019 | 2.3(1.1 – 4.7) |
| Sex (Male) | 8(42.1) | 12(34.3) | 0.570 | Not computed |
| Duration of illness (> 45 d) | 12(63.2) | 12(34.3) | 0.041 | 2.1(1.0 – 4.6) |
| Convulsion | 11(57.9) | 8(22.9) | 0.010 | 2.5(1.2 – 5.2) |
| Altered sensorium | 13(68.4) | 7(20.0) | <0.001 | 3.6(1.6 – 8.1) |
| Focal neurological deficit | 8(42.1) | 24(68.6) | 0.059 | Not computed |
| Hemiplegia/paraplegia | 4(21.1) | 4(11.4) | 0.583 | Not computed |
| Cranial nerve palsy | 7(36.8) | 19(54.3) | 0.221 | Not computed |
| Optic neuritis | 2(10.5) | 7(20.0) | 0.610 | Not computed |
| Papilloedema | 1(5.3) | 4(11.4) | 0.417 | Not computed |
| Extra-meningeal TB | 1(5.3) | 9(25.7) | 0.064 | Not computed |
| Comorbidities | 4(21.1) | 9(25.7) | 0.951 | Not computed |
| Raised CSF protein | 10(52.6) | 17(48.6) | 0.776 | Not computed |
| Low glucose | 13(68.4) | 22(62.9) | 0.683 | Not computed |
| Delayed initiation of Rx > 1 month | 12(63.2) | 14(40.0) | 0.041 | 1.8(0.8 – 3.9) |
| WBC > 11000 (cu-mm) | 11(57.9) | 16(45.7) | 0.393 | Not computed |
| Definite & probable TBM | 10(52.6) | 23(65.7) | 0.346 | Not computed |
| Stage III TBM | 14(73.7) | 6(17.1) | <0.001 | 4.7(2.0 – 11.2) |
| CSF diversion (VP shunt) | 2(10.5) | 3(8.6) | 0.583 | Not computed |
| Paradoxical response | 0(0.0) | 5(14.3) | 0.103 | Not computed |
In univariate analysis, age >50 years (p=0.019), duration of illness before initiation of treatment (>45 d) (p = 0.041), convulsion (p = 0.010), altered sensorium (p<0.001), delayed initiation of treatment >1 month (p=0.041) and stage III TBM (p=0.001) were significantly associated with mortality (Table 5).

In multivariate analyses stage III TBM (p=0.004), altered sensorium (p=0.036), delayed initiation of treatment >1 month (p=0.043) emerged as independent predictors of mortality (Table 6).

Table 6: Multivariate Logistic Regression Analysis Showing Predictors of Outcome in TBM

| Variables of interest | Univariate analysis | Multivariate analysis |
|-----------------------|---------------------|----------------------|
|                       | (p-value)           | Relative Risk (95% CI of RR) | P value |
| Age >50 years         | 0.019               | 0.9(0.09 – 2.5)        | 0.488 |
| Duration of illness   |                     |                      |       |
| (> 45 d)              | 0.041               | 0.3(0.05 – 3.8)        | 0.244 |
| Convulsion            | 0.010               | 2.2(1.0 – 5.4)         | 0.051 |
| Altered sensorium    | < 0.001             | 2.3(1.4 – 6.7)         | 0.036 |
| Delayed initiation of |                     |                      |       |
| Rx > 1 month          | 0.041               | 1.3(0.7 – 4.4)         | 0.043 |
| Stage III TBM         | < 0.001             | 3.6(1.5 – 8.5)         | 0.004 |

Discussion
Among the 54 TBM patients most (70.0%) were adolescent and young adults (<30 years) with a female preponderance (63.0%). An Indian study also found a female predominance20. Most of the patients presented at stage II (48.1%) and stage III (37.0%) on admission. Yasar et al12 in their study also found maximum patients at stage II on presentation.

In this series only 3 cases (5.6%) were GeneXpert positive and classified as definite TBM. AFB was not found in any of the cases. Sensitivity of AFB stain and GeneXpert in TBM is 37.0% and 59.0% respectively, depending on the procedure, volume of CSF submitted, repetition of LPs and the capacity of laboratories and technician’s experience18,22. Kalita and Misra16 also found a very low sensitivity of AFB in CSF during evaluation of 58 TBM cases.

Baseline imaging (CT scan and MRI) findings in the present series revealed that infarction was the commonest (46.3%) finding followed by basal meningeal enhancement and hydrocephalus in equal number of patients (40.7%). Tuberculoma was present in 29.6% cases. However the imaging in 11(20.37%) patients revealed no abnormality. Almost similar findings were observed by Hsu et al13 during evaluation of 95 TBM patients except a lower frequency of tuberculoma in their study. On the other hand tuberculosis was found to be present in more than half of patients of TBM in study by Tai et al4.

In the present study definite diagnosis of TBM (Definite TBM) was established only in 3(5.6%) cases which is near (5.2%) to the study by Kalita and Misra16. The rest were probable [30(55.6%)] and possible [21(38.9%)]. The rate of definite TBM was more in the series by Lau et al8 involving 166 patients. In the present series the possible explanation for less number of definite TBM may be submission of conventional volume of CSF (where higher CSF volume could have yielded better), non-repetition of LPs and finally limitation of the laboratories and technician’s experience.

The 6- and 9-month mortality rate in this study was 29.6% (16/54) and 35.2% (19/54) respectively which is almost similar to the mortality rate reported by Hsu et al13. Other literature also revealed similar findings11. In univariate analysis six variables [age more than 50 years, duration of illness before initiation of treatment (more than 45 d), convulsion, altered sensorium, delayed initiation of treatment more than 1 month and stage III TBM] were found to be significantly associated with mortality. Among them stage III TBM, altered sensorium, delayed initiation of treatment more than 1 month emerged as independent predictors of mortality.

In conclusion, stage III TBM, altered sensorium and delay (more than 1 month) in initiation of treatment are independent predictors of mortality in TBM patient.

References
1. Gallardo CR, Rigau-Comas D, Valderrama Rodriguez A, Roqué i Figuls M, Parker LA, Caylà J, et al. Fixed-dose combinations of drugs versus single-drug formulations for treating pulmonary tuberculosis. The Cochrane Library. 2016 Jan 1.
2. World Health Organization (WHO). Global tuberculosis report 2017. 2018. [Available at:http://www.who.int/tb/publications/global_report/gtr2017_main_text.pdf. accessed on: 2/10/18]
3. National Tuberculosis Control Programme (NTP). National Guidelines and Operational Manual for Tuberculosis Control. 2013. 5th ed. DGHS, Dhaka.
The prediction of ultimate outcome of this condition is crucial. It is important to note that in cases of extra pulmonary TB, the World Health Organization (WHO) most commonly affects the lungs (pulmonary TB). TB is a global pandemic and is caused by Mycobacterium tuberculosis. The incidence of TB is reported to be 221/100000 and mortality rates in high burden countries (HBCs) among 30 for tuberculosis. Developed neurological sequelae like visual loss, motor weakness, and cognitive deficits are often observed. Early diagnosis is essential to prevent development of neurological sequelae. Neurological symptoms such as changes in level of consciousness, mental status abnormalities, neck stiffness, cranial nerve palsy, changes in fundus, focal weakness, and papilledema are common. Among patients with tuberculosis meningitis, predictors of mortality include age, sex, seizure, history of close contact with tuberculous patients, and delay in initiation of anti-TB therapy. Posterior reversible encephalopathy syndrome (PRES) is another important clinical condition that can occur in patients with tuberculosis meningitis.

Methodology

The aim of this study was to evaluate predictors of outcome in adult patients with tuberculous meningitis (TBM) in Bangladesh. The study excluded pregnant patients. Tuberculous meningitis was defined according to the World Health Organization (WHO) criteria. Laboratory investigations, including tuberculin skin test, cerebrospinal fluid (CSF) examination, and imaging studies were performed. CSF samples were submitted to a laboratory technician. The purpose of this study was to evaluate the predictive value of different variables on the outcome of adult TBM.

Results

Among 58 patients with TBM, 40(68.9%) had mild disability (score=2), 10(18.5%) came round without any sequelae, and 8(13.8%) had severe disability (Table 3). In this period, mild, moderate, and severe disability were observed in 11.1%, 27.8%, and 13% cases, respectively (Table 4; Figure III).

Conclusions

The study suggests that 15 years or more age group comprises the most number of patients (40.7%). Tuberculoma was present at stage II (48.1%) and stage III (37.0%) on admission. Female predominance was observed (63.0%). An Indian study also found a female predominance. Most of the patients presented with isoniazid therapy throughout the treatment. Corticosteroid in standard dose and duration was treated initially (intensive phase) for 2 months and then continued for 3 to 6 months (extension phase). The number of patients (30.8%) with a positive CSF for Gram or India Ink stain, ICSOL, or positive AFB smear were evaluated.


case-control study. The Lancet Infectious Diseases. 1999;3(3):261-5.
17. Centers for Disease Control and Prevention. Treatment of tuberculosis, American Thoracic society, CDC, and Infection Diseases Society of America: Treatment of Tuberculosis. The Morbidity and Mortality Weekly Report (MMWR). 2003;52:1-77.
18. Marais S, Thwaites G, Schoeman JF, Török ME, Misra UK, Prasad K, et al. Tuberculous meningitis: a uniform case definition for use in clinical research. The Lancet Infectious Diseases. 2010;10(11):803-12.
19. Joint Tuberculosis Committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. Thorax. 1998;53(7):536-48.
20. Gupta M, Bajaj BK, Khwaja G. Paradoxical response in patients with CNS tuberculosis. Journal Association of Physicians of India. 2003;51:257-60.
21. Lanzafame M, Vent S. Tuberculosis-immune reconstitution inflammatory syndrome. Journal of Clinical Tuberculosis and Other Mycobacterial Diseases. 2016;3:6-9.
22. Nhu NT, Heemskerk D, Chau TT, Mai NT, Nghia HD, Loc PP, et al. Evaluation of GeneXpert MTB/RIF for diagnosis of tuberculosis meningitis. Journal Clinical Microbiology. 2014;52(1):226-33
23. George EL, Iype T, Cherian A, Chandy S, Kumar A, Balakrishnan A, et al. Predictors of mortality in patients with meningeal tuberculosis. Neurology India 2012;60(1):18

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4. Tai ML, Mohd-Nor H, Rahmat K, Viswanathan S, Abdul Kadir KA, Ramli N, et al. Neuroimaging findings are sensitive and specific in diagnosis of tuberculous meningitis. Neurology Asia. 2017;22(1)
5. Pai M, Flores LL, Pai N, Hubbard A, Riley LW, Colford Jr JM. Diagnostic accuracy of nucleic acid amplification tests for tuberculosis meningitis: a systematic review and meta-analysis. The Lancet Infectious Diseases. 2003;3(10):633-43.
6. Prasad K, Singh MB. Corticosteroids for managing tuberculous meningitis. Cochrane Database of Systematic Reviews. 2016(1).
7. Erdem H, Ozturk-Engin D, Tireli H, Kilicoglu G, Defes S, Gulsun S, et al. Hamisi scoring in the prediction of unfavorable outcomes from tuberculous meningitis: results of Haydarpaşa-II study. Journal of Neurology. 2015;262(4):890-8.
8. Lau KK, Yu I, Chan A, Wong L, Tam CM, Sheng B, Li HL, Hong Kong Tuberculous Meningitis Study Group. A registry of tuberculous meningitis in Hong Kong. The International Journal of Tuberculosis and Lung Disease. 2005;9(12):1391-7.
9. Thwaites G, Fisher M, Hemingway C, Scott G, Solomon T, Innes J. British Infection Society guidelines for the diagnosis and treatment of tuberculous meningitis in adults and children. Journal of Infection 2009;59(3):167-87.
10. Erdem H, Ozturk-Engin D, Elaldi N, Gulsun S, Sengo G, Crisan A, et al. The microbiological diagnosis of tuberculous meningitis: results of H aydarpasa-i study. Clinical Microbiology and Infection. 2014;20(10):600-8
11. Thwaites GE, Bang ND, Dung NH, Quy HT, Oanh DT, Thoa NT, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. New England Journal of Medicine. 2004;351(17):1741-51
12. Yasar KK, Pehlivanoglu F, Sengo G. Predictors of mortality in tuberculous meningitis: a multivariate analysis of 160 cases. The International Journal of Tuberculosis and Lung Disease. 2010;14(10):1330-5
13. Hsu PC, Yang CC, Ye JJ, Huang PY, Chiang PC, Lee MH. Prognostic factors of tuberculous meningitis in adults: a 6-year retrospective study at a tertiary hospital in northern Taiwan. Journal of Microbiology, Immunology and Infection. 2010;43(2):111-8
14. Misra UK, Kalita J, Roy AK, Mandal SK, Srivastava M. Role of clinical, radiological, and neurophysiological changes in predicting the outcome of tuberculous meningitis: a multivariable analysis. Journal of Neurology, Neurosurgery & Psychiatry. 2000;68(3):300-3
15. Van-Well GT, Paes BF, Terwee CB, Springer P, Roord JJ, Donald PR, et al. Twenty years of pediatric tuberculous meningitis: a retrospective cohort study in the western cape of South Africa. Pediatrics 2009;123(1):e1-8
16. Kalita J, Misra UK. Outcome of tuberculous meningitis at 6 and 12 months: a multiple regression analysis. The International Journal of Tuberculosis and Lung Disease. 1999;3(3):261-5.