Bangladesh Journal of Neuroscience 2023; Vol. 39 (1): 22-30

Evaluation of Factors Affecting Short-Term Clinical Outcome in Adult Patients with Tuberculous Meningitis

ADNAN SM[1], AZAM A[2], HASSAN K[3], TAPU SD[4], CHOWDHURY MMH[5], DAS A[6], HASSANUZZAMAN M[7], RASHID MM[8], HAQUE A[9]

Abstract:

Background: *Tuberculous meningitis (TBM) is the most devastating form of Tuberculosis (TB) and is associated with high mortality.* ***Objective:*** *This study aimed to investigate the factors associated with short-term poor outcomes of TBM in patients admitted to a tertiary care hospital in Bangladesh.* ***Methodology:*** *This prospective analytical study included 42 patients with features of TBM, fulfilling the case definition criteria from the Department of Neurology and the Department of Medicine of Chattogram Medical College Hospital. The demographic, clinical, biochemical, and radiological data at baseline were collected, and clinical outcomes of patients were assessed by a modified Rankin Scale (MRS) and 'two simple questions' score at the time of discharge and three months from the time of diagnosis and initiation of treatment. The outcome was classified as good (survived and had modified mRS score of 0-2 and good or intermediate score in 'two simple questions' score) and poor (died or had mRS score> two and poor score in 'two simple questions' score).* ***Results:*** *The patients' median (range) age was 37.5 (18-75) years, and 50% were male. Three months of mortality and poor outcome were observed in 19% and 40.5% of the patients. In univariate analysis, not vaccinated with Bacille Calmette Guerin (BCG) (p=0.019), lower GCS (p<0.001), altered sensorium (p=0.013), meningeal irritation signs (p=0.03), presence of hydrocephalus on brain imaging (p=0.047), low cerebrospinal fluid (CSF) glucose (p=0.016), increased CSF protein (p=0.023), and CSF pleocytosis (p=0.005), ESR (p=0.001), hyponatremia (p=0.015), definite TBM (P<0.001), and Stage III TBM (p=0.001) were significantly associated with short term poor outcome. On multivariate analysis, altered sensorium (p=0.032) and Stage III TBM (p=0.017) were independent predictors of short-term poor outcomes.* ***Conclusions:*** *TBM patients with poor outcomes were more likely to have altered mental status on admission and stage III disease than TBM patients with good outcomes.*

Keywords: T*ubercular meningitis; Outcome; Bangladesh, TB*

Introduction

Tuberculous meningitis (TBM), the fatal form of TB, occurs in 1–5% of those with tuberculosis (TB).[1] In the developed world, where there is a lower prevalence of TB in the population, estimates are that TBM accounts for 6% of all causes of meningitis. In locations with a higher prevalence of Mycobacterium tuberculosis (MTB) in the

1. Dr. Samee M Adnan, Registrar, Department of Neurology, Chittagong Medical College Hospital, Chattogram, Bangladesh.
2. Dr. Akramul Azam, Assistant Professor, Department of Neurology, Chattogram Medical College & Hospital, Chattogram, Bangladesh.
3. Dr. Kamrul Hassan, Medical Officer, Satkania Upazila Health Complex, Chattogram, Bangladesh
4. Dr. Shagor Deb Tapu, Medical Officer, Khagrachhari Modernized Sadar Hospital, Khagrachhari. Bangladesh.
5. Dr. Md. Mubinul Huq Chowdhury, Emergency Medical Officer, Khagrachhari Modernized Sadar Hospital, Khagrachhari, Bangladesh.
6. Dr. Aditi Das, Indoor Medical Officer, Department of Neurology, Chittagong Medical College Hospital, Chattogram, Bangladesh.
7. Professor Dr. Md. Hassanuzzaman, Professor and Head, Department of Neurology, Chattogram Medical College & Hospital, Chattogram, Bangladesh
8. Dr. Md Mamunur Rashid, Associate Professor & Head, Department of Clinical Tropical Medicine, Bangladesh Institute of Tropical and Infectious Disease (BITID), Faujderhat, Chattogram.
9. Dr. Anika Haque, MD (Internal Medicine), Phase B Resident, Chittagong Medical College, Chattogram, Bangladesh.

Corresponding Author: Dr. Samee M Adnan, Registrar, Department of Neurology, Chittagong Medical College Hospital, Chattogram, Bangladesh. Mobile: 01611-428683, Email: sameecomc@gmail.com

population, estimates are that TBM accounts for up to one-third to one-half of all bacterial meningitis.2 Patients at extremes of age and with HIV co-infection carry the highest mortality.3,4 In general, the prognosis of TBM depends on the patient's neurologic status at the time of initial presentation and the timeliness of the initiation of anti-tuberculous agents.[5]

Recognition and diagnosis of TBM are difficult, given the variability in clinical presentation. The additional diagnostic difficulty is that the symptoms can be present anywhere from a few days to six months.[5] Confirming the diagnosis of TB is a difficult diagnostic dilemma, which is especially true in resource-poor areas. Definitive diagnosis results from identifying MTB in the CSF. Low bacterial numbers in CSF lead to challenges in MTB detection and diagnostic confirmation of TBM. Polymerase chain reaction (PCR) has a moderate sensitivity in the diagnosis, and a similar result was reported when CSF GeneXpert was applied6,7; metagenomic next-generation sequencing is also tested in the diagnosis of TBM and presented with moderate diagnostic performance.[8] Hence, diagnosis usually relies on clinical evidence, which combines supportive clinical, laboratory, and radiological findings. Standardized diagnostic criteria for TBM have yet to be established, and most reports have used different case definitions.[9,10] To address these issues, an "International Tuberculous Meningitis workshop" took place in Cape Town, South Africa, in May 2009 to establish a "Consensus Case Definition" for TBM to be used in future clinical research which should be uniformly applicable, irrespective of the patient's age or HIV infection status or the resources available in the research setting with the attendance of 41 participants from seven countries with 13 international TBM experts.[10] The diagnosis remains a clinical challenge, which would contribute to a significant delay in the initiation of anti-TB therapy, which may affectthe outcome. Hence, characterizing the risk factors associated with a poor outcome may improve the present situation in the management of TBM.

From time to time, several researchers have tried to predict the outcome of TBM based on clinical, radiological, and CSF parameters. Determination of the possible factors for short-term outcomes could be effective in the early detection of high-risk patients. This can allow the clinician to carefully monitor the patients during their hospital stay to improve their functional outcomes and minimize mortality. A better comprehension of the prognostic factors can offer more realistic expectations for patients and their families. It can provide useful information regarding management purposes with speculation of time needed for patients' clinical improvement. Clinical indices such as age, no BCG vaccination, underlying comorbidities, stage of meningitis, progression of stages, cranial nerve palsy, focal weakness, seizures or coma on admission, and radiological signs such as hydrocephalus, infarct, and tuberculoma have been assessed as predictors of mortality and neurological sequelae of TBM in previous studies.[4,11-14] It is to be noted that studies that address the factors associated with the outcome of TBM in the Bangladeshi population are in extremely short supply.

In this background, this study aimed to examine whether different clinical, CSF, and radiological parameters, as observed in the literature from other regional and international data, are similar to our setting. The results may clarify the clinical characteristics with factors affecting the short-term outcome of TBM patients in our setting and may improve the management of the disease.

Materials and Methods

This prospective observational study was carried out in the Department of Neurology and Department of Medicine of Chattogram Medical College Hospital, Chattogram, Bangladesh from September 2021 to August 2022. The study protocol was approved by the Ethical and Review Committee of Chittagong Medical College Hospital. Informed written consent was obtained from the legal guardian or caregiver of the patients.

Patients aged 18 years or more, admitted in the Department of Neurology and Medicine of CMCH with a diagnosis of suspected TBM [Patients presenting with symptoms consistent with clinical entry criteria which have a duration of more than 5

days (one or more of the following: headache, irritability, vomiting, fever, neck stiffness, convulsions, focal neurological deficits, altered consciousness, or lethargy)]9,10 were included in the study. Exclusion criteria were pregnant patients or patients with any other contraindications to neuroimaging or neuroimaging with contrast, patients who had already received ant-TB therapy for the ongoing illness, patients, or nearest relatives' unwillingness to participate in the study, and CSF stain, culture, and/or genotypic test showing microorganism other than acid-fast bacilli.

Relevant demographic, clinical, biochemical, and imaging data were collected by interviewing, detailed physical examination, and reviewing the investigational reports. The patients' neurologic statuses at admission were classified as stage I to stage III according to the staging established by the Medical Research Council (1984). All patients were graded for severity at study entry. TBM cases were categorized as probable, possible, and definite TBM as per the diagnostic criteria.[10]

Patients were monitored closely for death, neurological deterioration (onset of new focal neurological signs or fall in GCS), and drug-related adverse events. A follow-up visit was scheduled three months after the diagnosis and initiation of anti-TB treatment to assess the outcome. The short term was defined as the end of intensive phase of treatment, meaning 3 months after diagnosis and initiation of treatment. Outcome was evaluated by the "simple questions" score15 and mRs at the time of discharge and at 3 months after diagnosis and initiation of treatment: Favorable outcome means mRs score 0-2, and poor outcome means mRs score 3-6.

Data analysis was done by using SPSS-23. Patients were categorized as favorable or poor according to their 03-month outcome. Continuous data were expressed as mean ± standard deviation (SD) for normally distributed data or median and

25%–75% interquartile range for non-normally distributed data. Categorical variables were presented as frequency (percentages) or proportions. Student's t-tests were used to analyze normally distributed continuous variables, while the Mann–Whitney U-tests were used for non-normally distributed continuous variables. Categorical variables were compared using the Chi-square test or Fisher's exact test. Multivariate regression analysis was used to identify significant factors influencing time to death. To eliminate confounding factors in predicting the risk for mortality, variables with p-value d"0.05 by univariate analysis were entered into a multivariate logistic regression model for further assessment. The effect size was described as relative risk (RR) with a 95% confidence interval (CI) for the RR.

Results

Initially, a total of 52 clinically suspected TBM cases were screed for eligibility in the present study. Out of them, 49 were eligible and enrolled for follow-up for three months. At the end of three-month follow-up, complete data were available for 42 patients which were included in the final analysis. Overall, the median (IQR) age was 37.5 (23.5-64.3) years. According to the classification criteria, 20 (47.6%), 16 (38.1%), and 6 (14.3%) of the patients were classified as probable, definite, and TBM cases. Out of 42 patients, 4 patients died in-hospital, giving an in-hospital mortality rate of 9.5%. in total, 8 (19%) patients expired within three months of follow-up (Figure 1). Out of 42 patients at the end of three months, 25 patients (59.5%) had good outcomes (mRS score ≤2). Other 17 (40.5%) patients had poor outcomes (at 90-days: expired or had mRS score was ≥3) (Figure 2).

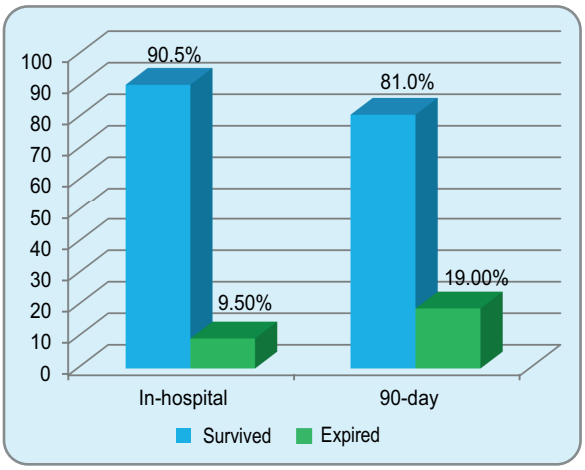

Figure 1: *Bar diagram showing in-hospital and 90-day mortality rates of patients (n=42).*

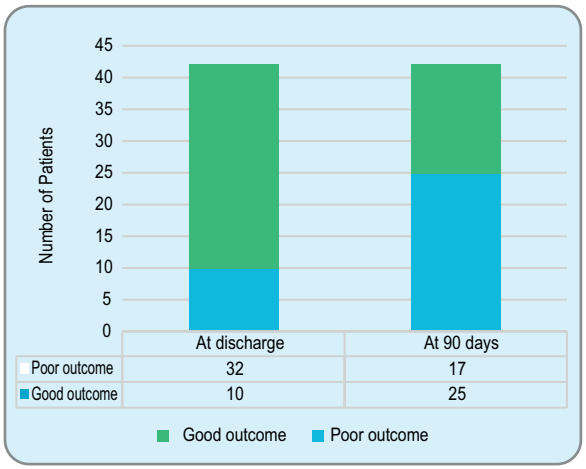

Figure 2: .....

Table I depicted that, among different demographic and TB-related medical characteristics, only BCG vaccination status was significantly associated with outcome- unvaccinated patients were more likely to have poor outcomes than their counterparts (p=0.019).

Table II shows that, confusion, unconsciousness, lower GCS, presence of altered sensorium, and meningeal irritation signs at presentation were significantly associated with three- month outcome. Table III shows that the most frequent findings in cranial CT/MRI were hydrocephalus (71.4%), followed by infarct (66.7%), exudates at any site (33.3%), and tuberculoma (31%). A higher proportion of patients with hydrocephalus had poor outcomes than their counterparts. Signs of active TB on chest X-rays were seen in 23.8% of the cases. The commonest site of the exudates was basal cisterns (33.3%). CSF GeneXpert provides the highest diagnostic yield, positive in 15 CSF (35.7%) sam- ples. None of the samples was

Table I

Association of demographics and TB-related characteristics with outcome (n=42)

	90-day outcome		
Characteristics	Good (n=25)	Poor (n=17)	P value
Age group, years	35.0 (23.0-63.0)	45.0 (27.0-65.0)	0.564‡
Sex			
Female	13 (61.9)	8 (38.1)	
Male	12 (57.1)	9 (42.9)	0.753*
BCG unvaccinated	2 (22.7)	7 (77.8)	0.019**
Contact history of TB	9 (50.0)	9 (50.0)	0.348*
Comorbidity	8 (72.7)	3 (27.3)	0.477*
Smoking history	12 (60.0)	8 (40.0)	0.952*
Past H/O TB	4 (100.0)	0 (0)	0.134**
H/O TB treatment	3 (100.0)	0 (0)	0.260**
Interval[a] , days	30.0 (21.5-47.5)	30.0 (18.5-45.0)	0.887‡
Interval[b] , days	3.0 (3.0-5.5)	3.0 (2.0-5.5)	0.810‡

Data were expressed as frequency (%) or Median (IQR). % indicates row total *Chi-square test; ‡Mann-Whitney
U test; **Fisher's exact test;. IQR: Interquartile range.
aInterval from symptom onset to admission; bInterval from admission to treatment.

positive for AFB and only one sample was culture positive. The median CSF glucose and CSF/blood glucose ratio was significantly lower in patients with poor outcomes than the patients with good outcomes. On the other hand, the inverse trend was observed regarding CSF protein and cell count. Significant portions of a patient with poor outcomes had GeneXpert positive in their CSF. Regarding the biochemical parameters, median ESR was significantly higher and serum Na concentration was significantly lower in patients with poor outcomes than their counterparts.

Most of the patients with probable (90%) and possible (100%) TBM had good outcomes, compared to only 6.3% of the patients with definite TBM (p<0.001, Chi-square test). The proportion of poor outcomes increased as the stage of TBM at the initiation of treatment increased and the association was significant statistically (Table IV).

In multivariate analyses, stage III TBM (p=0.017) and altered sensorium (p=0.032) emerged as independent predictors of short-term poor outcome (Table V).

Table-II

Association between presenting sign and symptom with outcome

Symptom and sign	90-day outcome		P value
	Good (n=25)	Poor (n=17)	
Fever	25 (100.0)	17 (100.0)	—-
Night sweat	19 (76.0)	15 (88.2)	0.439**
Weight loss	22 (88.0)	13 (76.5)	0.413**
Anorexia	24 (96.0)	17 (100.0)	1.0**
Persistent cough	9 (36.0)	6 (35.3)	1.0*
Headache	24 (96.0)	17 (100.0)	1.0**
Vomiting	20 (80.0)	17 (100.0)	0.070**
Seizure	5 (20.0)	5 (29.4)	0.714**
Confusion	12 (48.0)	16 (94.1)	0.002*
Unconsciousness	6 (24.0)	12 (70.6)	0.003*
Hemiparesis	12 (48.0)	8 (47.1)	0.952*
Dysarthria/aphasia	8 (32.0)	7 (41.2)	0.774*
Visual disturbance	15 (60.0)	6 (35.5)	0.208*
GCS	11 (13-15)	8 (7-10)	<0.001‡
Altered sensorium	11 (44.0)	14 (82.4)	0.013*
Meningeal irritation signs	18 (72.0)	17 (100.0)	0.030**
Papilledema	13 (52.0)	11 (64.7)	0.530**
Cranial nerve palsy	14 (56.0)	9 (52.9)	1.0*

Data were expressed as frequency (%) or median (IQR) as appropriate. *Chi-square test; ‡Mann-Whitney U test. **Fisher's exact test

Table-III

Baseline radiological, CSF and other biochemical characteristics of the cohort (n=42) and their association with outcome.

Variables	Frequency (%)/ Median (IQR)	90-day outcome		P value
		Good (n=25)	Poor (n=17)	
Cranial CT/MRI features				
Hydrocephalus	30 (71.4)	15 (60.0)	15(88.2)	**0.047***
Exudates at any site	15 (35.7)	6 (24.0)	9 (52.9)	0.055*
Basal exudates	14 (33 3)	6 (24 0)	8 (47 1)**\^ i i % % i y**	0 120*
Sylvian exudates	4 (9.5)	2 (8.0)	2 (11.8)	1.0"
Optochiasmatic exudates	1 (2.4)	1 (4.0)	0(0)	1.0"
Tuberculomas	13(31.0)	9 (36.0)	4 (23.5)	0.391*
Infarcts	28 (66.7)	16(64.0)	12(70.6)	0.657*
Chest x-ray features				
Signs of active TB	10(23.8)	6 (24.0)	4 (23.5)	1.0*
CSF parameters				
Glucose, mg/dl	38.5 (30.3-46.5)	42.0 (35.5-47.9)	31.0 (25.0-44.5)	**0.016***
CSF/blood glucose	0.33 (0.24-0.39)	0.35 (0.29-0.41)	0.26 (0.22-0.35)	**0.023***
Protein, mg/dl	116.5 (86.0-190.3)	110(86-128)	206 (95-298)	**0.023***
Cell count	75.0 (23.8-120.0)	50.0(19.0-90.0)	120 (70-200)	**0.005***
Lymphocyte, %	100.0 (88.8-100.0)	100 (87.5-100)	100 (87.5-100)	0.923*
AFB negative	42(100)	25(100)	17(100)	
GeneXpert positive	15 (35.7)	1 (4.0)	14(82.4)	**<0.001***
Culture positive	1 (2.4)	0(0)	1 (5.9)	**1.0
Other biochemical parameters				
ESR, mm	65 (52-86)	60 (48-76)	95 (63-112)	**0.001***
Serum Na, mmol/l	126(114-133)	130(123-135)	116(111-128)	**0.015***
Serum K, mmol/l	3.6 (3.3-3.9)	3.7 (3.4-3.9)	3.5 (3.2-4.3)	0.441*
Serum ALT, IU/L	42 (35-48)	22 (20-24)	21 (19-23)	0.714*
Serum creatinine	1.0 (0.7-1.2)	1.0 (0.7-1.3)	1.0 (.08-1.3)	0.536*
Positive MT test	37 (88.1)	20 (80.0)	17(100.0)	**0.070
Positive HIV	1 (2.5)	0(0)	1 (5.9)	**0.405
Cranial CT/MRI features				

Data were expressed as frequency (%) or median (IQR) as appropriate. *Chi-square test; ‡Mann-Whitney U test. **Fisher's exact test.

Table-IV

Distribution of the patients according to their TBM staging and classification

Variables	90-day outcome		
	Good (n=25)	Poor (n=17)	P value*
TBM classification			
Probable TBM	18 (72.0)	2 (11.8)	
Possible TBM	6 (24.0)	0 (0)	<0.001
Definite TBM	1 (4.0)	15 (88.2)	
TBM staging At admissionStage I	1 (4.0)	0 (0)	
Stage II	19 (76.0)	4 (23.5)	0.001
Stage III	5 (20.0)	13 (76.5)	
TBM staging Beginning of anti-TB treatment			
Stage I	1 (4.0)	0 (0)	
Stage II	19 (76.0)	4 (23.5)	0.001
Stage III	5 (20.0)	13 (76.5)	

Data were expressed as frequency (%).*Chi-square test;

Table-V

Multivariate Logistic Regression analysis showing predictors of outcome in TBM

Variables	RR (95% CI)	P value
BCG unvaccinated	8.05 (0.89-45.77)	0.112
Altered sensorium	2.15 (1.02-44.14)	0.032
Meningeal irritation signs	1.03 (0.78-2.12)	0.142
Hydrocephalous	2.33 (0.93-84.12)	0.078
CSF/blood glucose	0.58 (0.01-1.98)	0.112
CSF protein, mg/dl	1.01 (0.35-2.11)	0.339
CSF cell count	1.01 (0.45-1.97)	0.097
ESR, mm 1st hour	1.01 (0.88-2.10)	0.119
Serum Na, mmol/l	0.98 (0.80-1.05)	0.281
Definite TBM	2.3 (0.15-21.24)	0.087
Stage III TBM	9.00 (2.93-17.61)	0.017

RR: Relative risk; CI: Confidence interval

Discussion

There is still no consensus on predictors of poor outcomes in TBM. Few studies addressed the factors associated with the outcome of TBM in the Bangladeshi population.14,16-18 The present prospective observational study was conducted in a tertiary care hospital in Chattogram, Bangladesh, to provide insight into this issue.

In the present study, BCG vaccination status was significantly associated with outcomes in the present study in univariate analysis. Unvaccinated patients were more likely to have poor outcomes than their counterparts. The protective effect of BCG against TBM and miliary TB was well-established.19 A delay in treating TBM was an important predictor of death in previous studies.11,12,16 However, factors delaying the initiation of treatment were not revealed as significant for poor outcomes in the present study. Among the clinical features, in univariate analysis, confusion, unconsciousness, lower GCS, presence of altered sensorium and meningeal irritation signs were significantly associated with three-month outcomes in the present study.

Among the radiological features, the presence of hydrocephalous on the cranial CT/MRI was found to have a significant association with outcome. The higher proportion of patients with the radiological feature of hydrocephalous had poor outcomes than their counterparts. The median CSF glucose and CSF/blood glucose ratio was significantly lower in patients with poor outcomes than the patients with good outcomes. On the other hand, an inverse trend was observed regarding CSF protein and cell count. Regarding the biochemical parameters, median ESR was significantly higher and serum sodium concentration was significantly lower in patients with poor outcomes than their counterparts. Most of the patients with probable (90%) and possible (100%) TBM had good outcomes, compared to only 6.3% of the patients with definite TBM. The proportion of poor outcomes increased as the stage of TBM at the initiation of treatment increased and the association was significant statistically. A previous study observed that; age more than 50 years, duration of illness before initiation of treatment (more than 45 day), convulsion, altered sensorium, delayed initiation of treatment more than one month and stage III TBM were found to be significantly associated with mortality.[16] Stage III TBM and altered sensorium were reported as independent predictor of mortality in TBM in several studies.[13,16,20,21]

Outcome of TBM depends on more than one variable, in those circumstances multivariate analysis is a useful method for its benefit of determining the effect of each variable while controlling the influence of the others.21 Among the variables found to have a significant association in univariate analysis, in multivariate analyses stage III TBM and altered sensorium emerged as independent predictors of three-months poor outcome. Stage III TBM and altered sensorium were reported as independent predictor of mortality in TBM in several studies.[13,16,21] In the present study, CSF glucose and protein levels which was found to be significantly associated with poor outcome in univariate analysis, failed to retain their association in multivariate analysis, which was similar to other studies.[4,13]

Conclusion

This study demonstrated that TBM patients who have altered mental status on admission and stage III disease are more likely to have poorer outcome. So, there should be no delay in the initiation of anti-TB therapy when suspected.

References

1. Donovan J, Thwaites GE, Huynh J. Tuberculous meningitis: where to from here? Current Opinion in Infectious Diseases.2020;33(3):259-66.
2. Lee SA, Kim SW, Chang HH, Jung H, Kim Y, Hwang S, et al. A new scoring system for the differential diagnosis between tuberculous meningitis and viral meningitis. Journal of Korean Medical Science. 2018;33(31):e201.
3. Davis A, Meintjes G, Wilkinson RJ. Treatment of tuberculous meningitis and its complications in adults. Current treatment options in neurology. 2018;20(3):1-5.
4. 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.
5. Soria J, Metcalf T, Mori N, Newby RE, Montano SM, Huaroto L, et al. Mortality in hospitalized patients with tuberculous meningitis. BMC infectious diseases. 2019;19(1):1-7.
6. Sun L, Yao L, Fu G, Lin L, Zhu E, Huang J. A comparison of the accuracy of the CapitalBio Mycobacterium real-time polymerase chain reaction and the Xpert MTB/RIF assay for the diagnosis of tuberculous meningitis. International Journal of Infectious Diseases. 2021;104:92-6.
7. Ratageri VH, Illalu S, Fattepur SR, Wari PK. The utility of CSF Xpert MTB/RIF in diagnosis of tubercular meningitis in children. The Indian Journal of Pediatrics. 2019;86(12):1089-93.
8. Wang S, Chen Y, Wang D, Wu Y, Zhao D, Zhang J, et al. The feasibility of metagenomic

next-generation sequencing to identify pathogens causing tuberculous meningitis in cerebrospinal fluid. Frontiers in microbiology. 2019;10:1993.

9. Thwaites G, Fisher M, Hemingway C, Scott G, Solomon T, Innes J. British Infection Society British Infection Society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. J Infect. 2009;59(3):167-87.

10. 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.

11. Hosoglu S, Geyik M F, Balik I, Aygen B, Erol S, Aygencel T G, et al. Predictors of outcome in patients with tuberculous meningitis. The International Journal of Tuberculosis and Lung Disease. 2002;6(1):64-70.

12. Sheu JJ, Yuan RY, Yang CC. Predictors for outcome and treatment delay in patients with tuberculous meningitis. The American journal of the medical sciences. 2009;338(2):134-9.

13. Yasar KK, Pehlivanoglu F, Sengoz 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.

14. Modi M, Sharma K, Prabhakar S, Goyal MK, Takkar A, Sharma N, et al. Clinical and radiological predictors of outcome in tubercular meningitis: a prospective study of 209 patients. Clinical Neurology and Neurosurgery. 2017;161:29-34.

15. Ahmed K, Hussain ME, Hoque MA, Saha UK, Chowdhury RN, Islam R, et al. Predictors Modifying the Outcome of Tuberculous Meningitis (TBM) in Adults: A Hospital Based Study in Bangladesh. Journal of National Institute of Neurosciences Bangladesh. 2021;7(1):14-9.

16. Ahmadinejad Z, Ziaee V, Aghsaeifar M, Reiskarami SR. The prognostic factors of tuberculous meningitis. International Journal of Infectious Diseases. 2003;3(1):1-7.

17. Wang MS, Zhao M, Liu XJ. Risk factors for poor outcome in childhood tuberculous meningitis. Scientific reports. 2021;11(1):1-5.

18. Rodrigues LC, Diwan VK, Wheeler JG. Protective effect of BCG against tuberculous meningitis and miliary tuberculosis: a meta-analysis. International journal of epidemiology. 1993;22(6):1154-8.

19. Misra UK, Kalita J, Kumar M, Tripathi A, Mishra P. Complications of tuberculous meningitis and their effect on outcome in a tertiary care cohort. The International Journal of Tuberculosis and Lung Disease. 2020;24(11):1194-9.

20. 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.

21. Dorman P, Dennis M, Sandercock P. Are the modified “simple questions” a valid and reliable measure of health related quality of life after stroke?. Journal of Neurology, Neurosurgery & Psychiatry. 2000 Oct 1;69(4):487-93.