

Frequency of functional outcome and predictors of mortality in patients with tuberculous meningitis at tertiary care hospital Karachi

Hafiza Neelam Zulfiqar Lakhani, Khalid Sher, Barkha, Munir Afzal, Muhammad Nawaz, Yumna Aijaz

Jinnah Postgraduate Medical Centre, Karachi Pakistan

ABSTRACT

Background: Tuberculous meningitis is a severe form of extrapulmonary tuberculosis associated with significant neurological disability and mortality. To determine the frequency of functional outcome and predictors of mortality in patients presenting with tuberculous meningitis at Tertiary Care Hospital, Karachi.

Material and Methods: This descriptive, longitudinal study was carried out in the Department of Neurology, Jinnah Postgraduate Medical Centre (JPMC), Karachi from 1st February 2026 to 30th July 2026. All patients with tuberculous meningitis were recruited using a non-probability consecutive sampling method. Functional outcomes were evaluated after admission at 90 days with the modified Rankin Scale [mRS] of which good functional outcome was considered as mRS ≤ 2 and poor functional outcome as mRS 3–6. British Medical Research Council (BMRC) staging system was used. A p-value ≤ 0.05 was considered statistically significant.

Results: Among 147 patients with tuberculous meningitis, the median age was 41.0 years (IQR: 31.0–55.0), and 89 (60.5%) were male. Mortality was significantly higher among patients with BMRC Stage III disease than among those with Stage I/II disease (60.9% vs. 22.8%, $p < 0.001$). On multivariable logistic regression analysis, mechanical ventilation (adjusted odds ratio [AOR]=6.92, 95% CI: 2.41–19.84, $p < 0.001$), BMRC Stage III disease (AOR=4.58, 95% CI: 2.01–10.42, $p < 0.001$), hydrocephalus (AOR=3.37, 95% CI: 1.42–7.98, $p = 0.006$), and serum sodium ≤ 125 mmol/L (AOR=2.76, 95% CI: 1.12–6.79, $p = 0.027$) were independently associated with increased odds of mortality.

Conclusions: Despite treatment, tuberculous meningitis was found to be associated with significant mortality and functional disability.

Keywords: Tuberculous meningitis, Functional outcome, Modified Rankin Scale, Prognostic factors.

BACKGROUND

Tuberculous meningitis (TBM) is one of the most severe extrapulmonary tuberculosis (EPTB) forms, causing high mortality rates and long-term neurological disability in the survivors. Even with improvements in TB control and antimicrobial treatment, TBM is still a significant clinical challenge, especially in high TB burden countries where delayed diagnosis and treatment initiation are associated with morbidity and mortality.¹ While microbiological confirmation is the gold standard for diagnosis, conventional cerebrospinal fluid (CSF) smear microscopy and culture have limited sensitivity,

and may delay treatment decisions in TBM.² A new approach, such as molecular diagnostic tools, biomarkers and predictive models, are thus being investigated to enhance early diagnosis and risk stratification.³

Even with proper treatment, TBM is often accompanied by death and permanent functional deficits. Factors including advanced disease stage, neurologic complications and immunosuppression including human immunodeficiency virus (HIV) infection have been shown to have significant effects on mortality and clinical outcomes.^{4,5} The complex interaction between host immune response and central nervous system involvement can lead to disease progression through inflammatory mediated neuronal injury, hydrocephalus and other neurologic complications.⁶

While guidelines for standardized treatment indicate a combination of antimicrobial treatment, the use of adjunctive corticosteroids, and prompt identification of complications, there are significant variations in outcomes, especially in resource-poor environments. Variations in access to care, diagnostic testing, treatment delay, and clinical care can impact survival and functional recovery.^{7,8}

Correspondence: Dr. Hafiza Neelam Zulfiqar Lakhani, Postgraduate Trainee, Department of Neurology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan

Email: mneelum@yahoo.com

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There is still limited data on functional outcome and mortality determinants of patients with TBM in Pakistan, especially from tertiary care centers. Although some prognostic factors have been identified in previous studies (such as neurological status on admission, severity of illness and clinical complications), locally relevant data is needed to better understand the prognostic factors in the specific healthcare environment.^{9,10}

Therefore, this study was conducted to determine functional outcomes and identify predictors of mortality among patients with tuberculous meningitis admitted to a tertiary care hospital in Karachi. The study will aim to describe the clinical features, treatment outcomes and factors associated with mortality to enhance prognosis and clinical decisions in TBM patients.

MATERIAL AND METHODS

This was a descriptive longitudinal study carried out in the Department of Neurology, Jinnah Postgraduate Medical Centre, Karachi. The study was conducted from 1st February 2026 to 30th July 2026 after receiving institutional approval from the Institutional Review Board (IRB) committee at Jinnah Postgraduate Medical Centre (JPMC), Karachi (Reference No. F.2-81/2026-GENL/12/JPMC dated 26th January 2026).

Sample size was determined by the WHO recommended method for the estimation of a single population proportion. The sample size for a tuberculous meningitis study using a 95% confidence interval and 8% margin of error and an expected mortality proportion of 43% as reported in the previous study by Thwaites *et al.*,¹ was calculated to be 147 patients. Patients were recruited using a nonprobability consecutive sampling technique in the study period.

Tuberculous meningitis was diagnosed when at least two of the following clinical features for > 1 week and at least one of the following laboratory findings was present. Clinical parameters were either fever of $\geq 99^{\circ}\text{F}$, dull continuous headache with a Visual Analogue Scale (VAS) score ≥ 6 for >1-week, recurrent vomiting (3 episodes/day for 3 consecutive days), or house hold/community contact with a TB patient in the last 2 years. Laboratory findings was defined as a positive CSF acid-fast bacilli (AFB) smear (by fluorescence staining), growth of *Mycobacterium tuberculosis* in culture or characteristic CSF abnormalities defined as lymphocytic pleocytosis (20-500 cells/mm³), CSF

protein concentration $\geq 100\text{mg/dl}$, CSF glucose concentration $\leq 60\%$ of simultaneous plasma glucose concentration.

The study involved patients between the age of 20 and 70 years. Patients with central nervous system malignancy, viral meningoencephalitis, history of head trauma, congestive cardiac failure, chronic obstructive pulmonary disease, chronic renal failure and previous stroke were excluded.

The modified Rankin Scale (mRS) was used to assess functional outcome at 90 days after admission. The mRS is a 7-point scale (0–6) used to measure disability and dependence in daily activities after neurological disorders, with higher scores indicating greater disability. A good functional outcome was defined as mRS ≤ 2 (functional independence), while poor functional outcome was defined as mRS 3–6 (moderate to severe disability, dependency, or death). Mortality was recorded during follow-up, and potential predictors were assessed. The functional status of patients was divided in two groups according to outcome. Good functional outcome was defined as mRS score of 2 or less, functional independence and being able to carry out daily activities without much assistance. A poor functional outcome was considered to be an mRS score of 3 – 6, which indicates moderate to severe disability, dependency, or death. Mortality was reported throughout follow-up and potential predictors of mortality were evaluated. These were age >60 years, serum sodium level $\leq 125\text{ mmol/L}$, need for mechanical ventilation, TLC >9000 cells/mm³, BMRC stage III disease and the presence of hydrocephalus on neuroimaging.

Information was gathered by direct interviews and by reviewing patients hospital medical records with a data collection proforma. Basic demographic data such as age, sex, socio-economic and educational status, and occupation was obtained. The clinical parameters such as presenting symptoms, duration of illness, BMRC stage, neurological examination findings, laboratory parameters and radiological findings were recorded. The British Medical Research Council (BMRC) staging was used for assessing the clinical severity of tuberculous meningitis. Stage I BMRC suggests the presence of non-specific symptoms but no neurologic deficits, stage II BMRC suggests neurologic signs are present but are not severe, and stage III BMRC suggests severe neurologic impairment, altered consciousness, or major

complications. Appropriate treatment information and clinical course were monitored during the course of the study. Patients were followed up in a prospective fashion, and functional outcome and the death rate were recorded at the 90-day follow-up.

Data analysis was done by Statistical Package for Social Sciences (SPSS) version 24. Normality of continuous variables was tested by Kolmogorov–Smirnov test. Age was not Normally distributed and were expressed median and interquartile range (IQR). The data of the categorical variables were presented as frequencies and percentages. Chi-square or Fisher's exact test was used to analyze the relationships between categorical variables and death or functional outcome as appropriated. Univariate analyses were done first to look for factors that may be associated with death. Variables that were found to be significantly associated in the preliminary analysis were subsequently analyzed by univariate logistic regression analysis to obtain unadjusted odds ratios (UORs) and 95% confidence intervals (CIs). For inclusion in the multivariable logistic regression model, variables were selected as having a p-value of ≤ 0.25 by the univariate logistic regression. To identify independent predictors of mortality they were adjusted for potential confounding factors by multivariable logistic regression analysis. For each of these predictors, adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were computed. Model assumptions were evaluated prior to model interpretation, such as multicollinearity among independent variables and overall model adequacy. Statistically significant results were defined as p-value ≤ 0.05 .

RESULTS

During the study period, 147 cases of tuberculous meningitis were included and followed-up for 90 days. The median age of the study group was 41.0 (55.0 – 31.0) years. Among the enrolled patients, 89 (60.5%) were males and 58 (39.5%) were females. The majority of patients belonged to the age group of 41–50 years ($n=39$, 26.5%), followed by 31–40 years ($n=38$, 25.9%). In terms of admission disease severity, the most common was BMRC stage II ($n=68$, 46.3%), followed by stage III ($n=51$, 34.7%) and stage I ($n=28$, 19.0%). Thirty-eight patients (25.9%) had hydrocephalus and 19 (12.9%) needed mechanical ventilation during hospital

stay. Forty-six (31.3%) patients died during the 90-day follow-up period (Table-I).

Demographic, clinical, laboratory and radiological features of the study population are shown in Table II. Most frequent presenting symptoms were persistent fever ($n=132$; 89.8%) and headache (VAS ≥ 6) ($n=126$; 85.7%). Of the CSF parameters, lymphocytic pleocytosis was seen in 139 (94.6%) patients, CSF protein concentration was elevated in 134 (91.2%) patients and CSF glucose concentration was decreased in 121 (82.3%) patients. AFB smear positivity was seen in CSF of 18 (12.2%) patients while CSF culture positivity was seen in CSF of 29 (19.7%) patients. Thirty-one (21.1%) patients had severe hyponatremia (serum sodium ≤ 125 mmol/L) and 82 (55.8%) patients had elevated TLC (>9000 cells/mm³).

Seventy-nine (53.7%) patients achieved a good functional outcome (mRS ≤ 2) at 90-days follow-up while 68 (46.3%) had poor functional outcome (mRS 3–6). Patients with more severe disease and clinical complications had significantly higher mortality rates. The BMRC stage III group, mechanical ventilation group, hydrocephalus group, severe hyponatremia group and >60 years-old group had significantly higher mortality than their respective comparison groups (Table-III). On univariate analysis, age >60 years, serum sodium ≤ 125 mmol/L, TLC >9000 cells/mm³, mechanical ventilation, BMRC Stage III, and hydrocephalus were significantly associated with increased odds of mortality. On multivariate analysis, serum sodium ≤ 125 mmol/L, mechanical ventilation, BMRC Stage III, and hydrocephalus remained significant independent predictors of mortality. Patients with serum sodium ≤ 125 mmol/L had 2.76 times higher odds of mortality (95% CI: 1.12–6.79; $p=0.027$). Mechanical ventilation was associated with 6.92 times higher odds of mortality (95% CI: 2.41–19.84; $p<0.001$). Patients with BMRC Stage III had 4.58 times higher odds of mortality compared with Stage I/II (95% CI: 2.01–10.42; $p<0.001$). Similarly, patients with hydrocephalus had 3.37 times higher odds of mortality (95% CI: 1.334–8.823; $p=0.006$). Age >60 years and TLC >9000 cells/mm³ were significant in univariate analysis but were not independently associated with mortality after multivariate adjustment ($p=0.078$ and $p=0.139$, respectively) Shown in Table-IV.

Table-I: Baseline demographic and clinical characteristics of patients with tuberculous meningitis (n=147).

Variables	n (%)
Age group (years)	
20–30	28 (19.0)
31–40	38 (25.9)
41–50	39 (26.5)
51–60	25 (17.0)
>60	17 (11.6)
Median Age (years)	41 (55.0 – 31.0)
Gender	
Male	89 (60.5)
Female	58 (39.5)
BMRC stage at presentation	
Stage I	28 (19.0)
Stage II	68 (46.3)
Stage III	51 (34.7)
Hydrocephalus	38 (25.9)
Mechanical ventilation	19 (12.9)
Mortality	46 (31.3)

Table-II: Clinical, laboratory, and radiological characteristics of enrolled patients (n=147).

Variables	n (%)
Persistent fever	132 (89.8)
Headache (VAS ≥6)	126 (85.7)
Recurrent vomiting	74 (50.3)
History of TB exposure	61 (41.5)
CSF findings	
Lymphocytic pleocytosis	139 (94.6)
Elevated CSF protein ≥100 mg/dL	134 (91.2)
Reduced CSF glucose	121 (82.3)
CSF AFB smear positive	18 (12.2)
CSF AFB culture positive	29 (19.7)
Clinical predictors	
Age >60 years	17 (11.6)
Serum sodium ≤125 mmol/L	31 (21.1)
TLC >9000 cells/mm ³	82 (55.8)
Mechanical ventilation required	19 (12.9)
Hydrocephalus	38 (25.9)

Table-III. Association of clinical predictors with mortality among patients with tuberculous meningitis (n=147).

Variables	Categories	Mortality		p value
		Died (n=46) n (%)	Survived (n=101) n (%)	
Age	≤60 years	36 (78.3)	94 (93.1)	0.012
	>60 years	10 (21.7)	7 (6.9)	
Serum sodium	>125 mmol/L	29 (63.0)	87 (86.1)	0.002
	≤125 mmol/L	17 (37.0)	14 (13.9)	
TLC	≤9000 cells/mm ³	13 (28.3)	52 (51.5)	0.012
	>9000 cells/mm ³	33 (71.7)	49 (48.5)	
Mechanical ventilation	No	32 (69.6)	96 (95.0)	<0.001
	Yes	14 (30.4)	5 (5.0)	
BMRC stage	Stage I/II	18 (39.1)	78 (77.2)	<0.001
	Stage III	28 (60.9)	23 (22.8)	
Hydrocephalus	No	26 (56.5)	83 (82.2)	0.001
	Yes	20 (43.5)	18 (17.8)	

Table-IV: Factors associated with mortality among Patients with tuberculous meningitis (n=147).

Factors	Study Parameter	Univariate logistic regression		Multivariate logistic regression	
		p-value	OR 95% CI	p-value	OR 95%
Age	≤60 years		Reference		Reference

	>60 years	0.013	3.73	1.319 – 10.584	0.078	2.417	0.91–6.39
Serum sodium	>125 mmol/L		Reference			Reference	
	≤125 mmol/L	0.002	3.64	1.600–8.294	0.027	2.76	1.12–6.79
TLC	≤9000 cells/mm ³		Reference			Reference	
	>9000 cells/mm ³	0.010	2.69	1.271–5.97	0.139	1.84	0.82–4.11
Mechanical ventilation	No		Reference			Reference	
	Yes	<0.001	8.40	2.805–25.152	<0.001	6.92	2.41–19.84
BMRC stage	Stage I/II		Reference			Reference	
	Stage III	<0.001	5.27	2.485–11.201	<0.001	4.58	2.01–10.42
Hydrocephalus	No		Reference			Reference	
	Yes	0.001	3.547	1.635 – 7.694	0.006	3.37	1.334 – 8.823

TLC: Total Leukocyte Count; BMRC: British Medical Research Council.

DISCUSSION

One of the most severe forms of tuberculosis – tuberculous meningitis (TBM) – continues to have a high mortality rate and risk of permanent neurologic disability. In this study, 147 patients were followed for 90 days and 31.3% died and 46.3% of those who survived had poor functional outcome (mRS 3–6). These results confirm that TBM, even when treated, causes significant clinical disease burden. Maleki Rad *et al.* also found high mortality rates in adults with TBM especially when the diagnosis was delayed, disease was more advanced and clinical complications were present.¹¹ Wang *et al.* also reported that neurological severity at presentation was associated with higher long-term mortality with stage II and III disease.¹²

This study found severe hyponatremia to be an independent risk factor for death. Patients with serum sodium ≤125 mmol/L had approximately 2.8-fold higher adjusted odds of death. This discovery suggests that significant sodium disturbance may help identify patients with more systemic and/or neurologic involvement who should be closely monitored. Inflammatory and physiological disturbances may also affect prognosis as systemic immune abnormalities such as low serum complement levels have been reported to be associated with increased mortality in TBM.¹³

Mechanical ventilation was the most significantly independently associated with mortality. The need for ventilation is a sign of significant neurological deterioration and/or loss of consciousness, respiratory compromise, or late intracranial complications. Metabolic signatures of disease severity were linked to adverse outcomes in TBM as shown by Ardiansyah *et al.*¹⁴ Hydrocephalus was also an independent predictor of death. This association might be explained by raised ICP, impaired cerebral perfusion and secondary brain injury. Canas *et al.* demonstrated that imaging and

clinical parameters added to the prognostic evaluation in TBM.¹⁵

When considered independently, BMRC stage III disease increased the risk of death by over 4 times. This confirms the value of neurological stage at admission as a prognostic marker. Nacarapa *et al.* also found that advanced clinical presentation was another mortality predictor for patients with HIV-associated TBM [16]. Enhanced CSF lactate levels were associated with poor outcome in TBM¹⁸ and Li *et al.* showed the potential of the machine-learning models for identification of prognostic factors in TBM.¹⁷

LIMITATIONS

The strengths of the study were prospective follow-up, consecutive recruitment, standardised 90-day outcome assessment and the use of multivariable analysis. These limitations were its single-centre design and lack of advanced biomarkers including CSF lactate, inflammatory cytokines and molecular prognostic markers. These predictors should be validated and locally applicable risk models developed in future multicentre studies. Mechanical ventilation, BMRC stage III disease, hydrocephalus and severe hyponatremia were the main independent factors for death and are important to identify early to facilitate more intensive monitoring and prompt escalation of care.

CONCLUSION

Despite the treatment strategies, tuberculous meningitis continued to have significant mortality and functional disability. Nearly one third of patients died during 90-day follow-up and almost half had poor functional outcome in this study. Mechanical ventilation, hydrocephalus, and severe hyponatremia were significant risk factors for poor

outcome in advanced BMRC stage. Early identification of these predictors could make timely intervention, stricter monitoring and targeted management strategies possible to decrease the mortality and neurological disability that is associated with tuberculous meningitis.

DISCLOSURES

None

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Hafiza Neelam Zulfiqar Lakhani: Study conception, data acquisition, manuscript drafting, final approval, accountable for all aspects of publication

Khalid Sher: Study conception and design, supervision, critical review for important intellectual content, final approval, accountable for all aspects of publication

Barkha: Data collection, literature review, manuscript drafting, final approval, accountable for all aspects of publication

Munir Afzal: Data analysis and interpretation, critical manuscript review, final approval, accountable for all aspects of publication

Muhammad Nawaz: Data acquisition, clinical interpretation, manuscript revision, final approval, accountable for all aspects of publication

Yumna Aijaz: Data analysis and interpretation, literature review, manuscript revision, final approval, accountable for all aspects of publication

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