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Analysis of risk factors for long-term mortality in patients with stage II and III tuberculous meningitis

Ling Wang^{1,2,3}, Zhihan Gu⁴, Xiaoli Chen^{1,2,3}, Xiaomin Yu^{1,2,3} and Xiandong Meng^{5*}

Abstract

Objective To investigate risk factors associated with long-term mortality in patients with stage II and III tuberculous meningitis (TBM).

Methods This retrospective analysis examined patients who were first diagnosed with stage II and III TBM at West China Hospital of Sichuan University between January 1, 2018 and October 1, 2019. Patients were followed via telephone and categorized into survival and mortality groups based on 4-year outcomes. Multivariate logistic regression identified independent risk factors for long-term mortality in stage II and III TBM.

Results In total, 178 patients were included, comprising 108 (60.7%) males and 36 (20.2%) non-survivors. Mean age was 36 ± 17 years. Compared to survivors, non-survivors demonstrated significantly higher age, heart rate, diastolic blood pressure, blood glucose, rates of headache, neurological deficits, cognitive dysfunction, impaired consciousness, hydrocephalus, and basal meningeal inflammation. This group also exhibited significantly lower Glasgow Coma Scale (GCS) scores, blood potassium, albumin, and cerebrospinal fluid chloride. Multivariate analysis revealed age (OR 1.042; 95% CI 1.015–1.070; $P=0.002$), GCS score (OR 0.693; 95% CI 0.589–0.814; $P<0.001$), neurological deficits (OR 5.204; 95% CI 2.056–13.174; $P<0.001$), and hydrocephalus (OR 2.680; 95% CI 1.081–6.643; $P=0.033$) as independent mortality risk factors. The ROC curve area under age was 0.613 (95% CI 0.506–0.720; $P=0.036$) and 0.721 (95% CI 0.615–0.826; $P<0.001$) under GCS score.

Conclusion Advanced age, reduced GCS scores, neurological deficits, and hydrocephalus were identified as independent risk factors for mortality in stage II and III TBM patients.

Keywords Tuberculous meningitis (TBM), BMRC, Mortality

*Correspondence:

Xiandong Meng
wchmcmxd@163.com

¹Department of Emergency Medicine, West China Hospital, Sichuan University/ West China School of Nursing, Sichuan University, Chengdu, China

²Disaster Medical Center, Sichuan University, Chengdu, China

³Nursing Key Laboratory of Sichuan Province, Chengdu 610041, China

⁴Department of Emergency Medicine, Laboratory of Emergency Medicine, School of Medicine, West China Hospital, Sichuan University, Chengdu, China

⁵Mental Health Center, West China Hospital, Sichuan University/West China School of Nursing, Sichuan University, Chengdu, Sichuan 610041, China



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Introduction

Tuberculosis (TB) represents a leading cause of infectious disease related deaths globally. TB mortality continues to rise, with untreated cases resulting in up to 50% fatalities [1]. Per the WHO, over 100,000 individuals develop tuberculous meningitis (TBM) annually [2]. As the most severe manifestation of TB, TBM confers substantial neurological morbidity and high mortality. Approximately 80,000 adults were estimated to die from TBM in 2019, with around 30% average mortality [3, 4]. Overall mortality risk reaches 23% by 3 months and 25% by 12 months post-diagnosis [5], with associated disability or death approaching 50% [6–9]. This confers tremendous personal and public health burden.

Due to ambiguous initial presentation and diagnostic challenges, most TBM patients fail to receive timely intervention [10, 11]. Moreover, many present at later stages of illness (stage II/III) [12, 13]. Disease severity per the British Medical Research Council (BMRC) stratification correlates with outcomes; higher classification indicates greater mortality risk [14]. A prior meta-analysis found ~70% of TBM patients to have stage II/III disease [5]. Another systematic review and meta-analysis found that patients with stage II (28.5%) and stage III (64.8%) tuberculous meningitis have a significantly higher risk of death than stage I (17.5%) [9], but clear factors for death have not been identified. Such advanced disease denotes critical status with generally poor prognosis despite treatment. While some analyses have evaluated prognostic variables in stage I-III TBM [15–17], few studies have exclusively focused on delineating long-term risk factors for mortality in stage II and III patients. As outcome heavily relies on accurate diagnosis and effective therapy [15], this study aimed to identify prognostic indicators in advanced TBM as early as possible. Timely targeted treatment and nursing care may improve outcomes. We examined risk factors for long-term mortality in stage II and III TBM.

Information and methodology

Study subjects

This retrospective study examined adult patients (≥ 18 years) who were first diagnosed with stage II or III TBM at West China Hospital of Sichuan University between January 1st, 2018 and October 1st, 2019. Patients were included in the study according to the standard TBM case definition proposed by Marais, which included clinical criteria, cerebrospinal fluid criteria, brain imaging criteria, evidence of tuberculosis elsewhere, and excluded other diagnoses. Obtain: Alternative diagnoses must be confirmed microbiologically, serologically, or histopathologically [18]. TBM severity was stratified based on the 2010 International Consensus [18] and British Medical Research Council (BMRC) criteria (grade I (GCS 15;

no focal neurological signs), grade II (GCS 11–14, or 15 with focal neurological signs), and grade III (GCS ≤ 10) [19]. Exclusion criteria comprised insufficient clinical data, incomplete lab or imaging tests, pregnancy/lactation, prior neuropsychiatric disorders, sequelae of stroke/brain tumors/trauma, and malignant tumors.

Research method

Data was extracted from the hospital electronic medical record system. We collected the following data from patients at the time of admission. Collected information included demographics (age, sex, extraskelatal TB), vital signs, symptoms (fever, night sweats, cough, headache, meningeal irritation, neck stiffness, neurological deficits, cognitive impairment, altered consciousness, cranial nerve palsies, weight loss, nausea/vomiting, Glasgow Coma Scale [GCS] score), lab tests (platelet count, electrolytes, blood glucose, albumin, cerebrospinal fluid analysis), and brain imaging findings (hydrocephalus, infarction, basal enhancement/exudates, meningeal inflammation).

Management

Patients received two months of intensive treatment (isoniazid (10–20 mg/kg/day; up to 1200 mg/day), rifampicin (10–20 mg/kg/day; up to 600 mg/day), pyrazinamide (20–30 mg/kg/day; up to 1500 mg/day), ethambutol (15–20 mg/kg/day; up to 750 mg/day), and dexamethasone (0.4 mg/kg/day; up to 16 mg/day) and ten months of continuous treatment (isoniazid (10–20 mg/kg/day, up to 1200 mg/day), rifampicin (10–20 mg/kg/day, up to 600 mg/day).

Follow-up and outcome indicators

Inpatients were followed via electronic medical records. Discharged patients were contacted by phone. Cases lost to follow-up after three unsuccessful contact attempts were excluded. The primary outcome was all-cause mortality within four years of TBM diagnosis.

Statistical analysis

Statistical analyses were conducted using SPSS version 22.0 (USA, IBM analytics). Normal continuous measurements are presented as means \pm standard deviations. Groups were compared via independent samples t-tests, while count data were analyzed using χ^2 tests. Variables with $p < 0.05$ on univariate testing were entered into a multivariate logistic regression model. Multivariate binary logistic regression identified factors independently predictive of 4-year mortality in stage II and III TBM. Results were expressed as odds ratios with 95% confidence intervals. Model adequacy was evaluated through Hosmer-Lemeshow testing. The significance level α was defined as 0.05. Receiver operating characteristic (ROC)

Table 1 General analysis of patients in the survival and mortality with stage II and III TBM¹

Variable	Survival (n = 142)	Mortality (n = 36)	P
Male, n,(%)	90 (63.4%)	18 (50%)	0.142
Age, years, mean ± sd	35 ± 16	43 ± 20	0.014
Combined tuberculosis mycobacterial infection at other sites, n,%	15 (10.6%)	7 (19.4%)	0.148
clinical stage			< 0.001
Stage II	131 (86.8%)	20 (13.2%)	
Stage III	11 (40.7%)	16 (59.3%)	
admission vital signs			
Body temperature (°C), mean ± sd	37.09 ± 0.91	37.24 ± 0.88	0.352
Heart rate (beats/min), mean ± sd	83.37 ± 19.10	93.44 ± 18.06	0.046
Respiration (breaths/min), mean ± sd	20.45 ± 2.40	21.28 ± 3.38	0.093
SBP ^a (mmHg), mean ± sd	123.61 ± 54.66	126.58 ± 21.28	0.750
DBP ^b (mmHg), mean ± sd	72.32 ± 15.30	80.03 ± 14.24	0.007

Note:¹TBM: Tuberculosis meningitis;^aSBP: Systolic blood pressure;^bDBP: Diastolic blood pressure

Table 2 Analysis of clinical symptoms in patients with stage II and III TBM¹ in the survival and mortality

Variable	Survival	Mortality	P
Fever (> 37.5 °C)>5 days, n,(%)	120 (84.5%)	26 (72.2%)	0.086
Night sweats, n,(%)	37 (26.1%)	8 (22.2%)	0.636
Cough > 2 weeks, n,(%)	37 (26.1%)	9 (25.0%)	0.897
Headache, n,(%)	133 (93.7%)	28 (77.8%)	0.004
Neck stiffness, n,(%)	104 (73.2%)	29 (80.6%)	0.367
Peripheral nerve dysfunction, n,(%)	41 (28.9%)	23 (63.9%)	< 0.001
Cognitive dysfunction, n,(%)	29 (20.4%)	14 (38.9%)	0.021
Altered consciousness, n,(%)	77 (54.2%)	29 (80.6%)	0.004
Cranial nerve palsy, n,(%)	44 (31.0%)	11 (30.6%)	0.960
Weight loss, n,(%)	55 (39%)	11 (30.6%)	0.349
Vomiting, n,(%)	95 (66.9%)	19 (52.8%)	0.115
Nausea, n,(%)	82 (57.7%)	17 (47.2%)	0.256
GCS score	13 ± 2	11 ± 3	< 0.001

Note:¹TBM: Tuberculosis meningitis

curves assessed the predictive utility of age and GCS scores for long-term prognosis.

Results

Demographics and clinical features

In total, 178 eligible patients were analyzed, including 108 (60.7%) males and 36 (20.2%) non-survivors. Mean age was 36 ± 17 years. Stage III patients showed markedly higher long-term mortality versus stage II (59.3% vs. 13.2%, $p < 0.001$). Compared to survivors, non-survivors demonstrated significantly older age ($p = 0.014$); faster admission heart rate ($p = 0.046$) and diastolic blood pressure ($p = 0.046$); and higher rates of headache ($p = 0.004$), neurological deficits ($p < 0.001$), cognitive dysfunction

Table 3 Comparison of laboratory and radiologic features at admission between TBM stage II/III survival and mortality

Variable	Survival	Mortality	p
Laboratory data			
Platelets, 10 ⁹ /L, mean ± sd	233.46 ± 89.45	221.25 ± 80.82	0.457
Blood potassium, mmol/L, mean ± sd	3.68 ± 0.48	3.44 ± 0.49	0.009
Blood leukocyte count, 10 ⁹ /L, mean ± sd	7.92 ± 3.13	8.24 ± 4.35	0.611
Blood glucose, mmol/L, mean ± sd	6.07 ± 1.36	6.72 ± 1.61	0.014
Blood sodium, mmol/L, mean ± sd	131.70 ± 7.62	132.34 ± 6.78	0.646
Human blood albumin, g/L, mean ± sd	38.76 ± 4.71	35.89 ± 6.18	0.003
CSF ^a blood glucose, mmol/L, mean ± sd	1.91 ± 0.97	2.16 ± 1.18	0.179
CSF ^a protein, g/L, mean ± sd	3.08 ± 6.57	3.95 ± 4.77	0.453
CSF ^a chloride, mmol/L, mean ± sd	113.74 ± 7.52	110.71 ± 9.08	0.040
Imaging			
Hydrocephalus, n,(%)	42 (29.6%)	22 (61.1%)	< 0.001
Cerebral infarction, n,(%)	60 (42.3%)	21 (58.3%)	0.084
Basement membrane exudate, n,(%)	8 (5.6%)	6 (16.7%)	0.028
Meningeal enhancement, n,(%)	42 (29.6%)	13 (36.1%)	0.449

Note:¹TBM: Tuberculosis meningitis;^aCSF: Cerebrospinal fluid

($p = 0.021$), and impaired consciousness ($p = 0.004$). Non-survivors also exhibited lower GCS scores ($p < 0.001$). No other univariate differences reached statistical significance ($p > 0.05$) (Tables 1 and 2).

Comparison of auxiliary examination results

Compared to survivors, non-survivors showed significantly higher blood glucose ($P = 0.014$), increased hydrocephalus ($P < 0.001$), and greater basal meningeal inflammation ($P = 0.028$). Conversely, non-survivors demonstrated significantly lower blood potassium ($P = 0.009$), serum albumin ($P = 0.003$), and cerebrospinal fluid chloride ($P = 0.040$). No other between-group differences in lab or imaging findings reached statistical significance ($P > 0.05$) (Table 3).

Results of multifactorial analysis

A multivariate logistic regression analysis evaluated associations between candidate risk factors (age, admission vital signs, presenting symptoms, GCS, lab values, imaging findings) and 4-year mortality in TBM. Results identified advanced age (OR 1.042; 95% CI 1.015–1.070; $P = 0.002$), lower GCS scores (OR 0.693; 95% CI 0.589–0.814; $P < 0.001$), neurological deficits (OR 5.204; 95% CI 2.056–13.174; $P < 0.001$), and hydrocephalus (OR 2.680; 95% CI 1.081–6.643; $P = 0.033$) as significant independent predictors of long-term mortality (Table 4). The

Table 4 Analysis of independent factors for long-term mortality in stage II and III TBM¹

Variable	P	OR ^a	95% CI ^b
Age	0.002	1.042	1.015, 1.070
GCS score	<0.001	0.693	0.589,0.814
Peripheral nerve dysfunction	<0.001	5.204	2.056,13.174
Hydrocephalus	0.033	2.680	1.081,6.643

Note:¹TBM: Tuberculosis meningitis;^aOR: Odds ratio;^bCI: Confidence interval

Hosmer-Lemeshow test produced $\chi^2=7.391$, $P=0.495$, supporting adequate model fit.

Predictive value of age and GCS score

ROC analysis examined the utility of age and admission GCS scores to prognosticate long-term mortality in stage II/III TBM (Fig. 1). For age, the area under the curve measured 0.613 (95% CI 0.506–0.720; $P=0.036$), with an optimal cut-off of 44.5 years, 47.2% sensitivity, and 73.2% specificity. The GCS ROC area was 0.721 (95% CI 0.615–0.826; $P<0.001$), with an optimal cut-point of 11, conferring 52.8% sensitivity and 86.6% specificity (Table 5).

Discussion

Previous studies have highlighted the association between the severity Tuberculous Meningitis (TBM) and negative clinical outcomes [20, 21]. Increased mortality rates have been linked to higher Medical Research Council (RC) classification scores [22], and more advanced stages of TBM have been associated with a six-fold

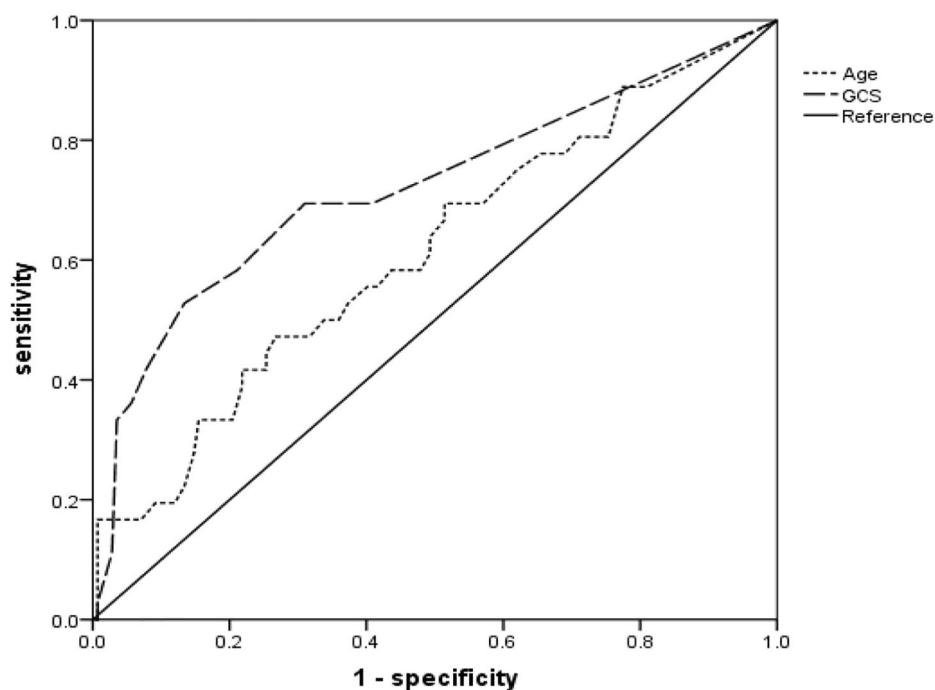
Table 5 Predictive accuracy of age and GCS score for long-term mortality in stage II/III TBM patients

Variable	AUC	p	95% CI
Age	0.613	0.036	0.506, 0.720
GCS	0.721	<0.001	0.615, 0.826

Note:¹TBM: Tuberculosis meningitis

increase in the risk of death in patients [15]. Our study reaffirms these findings, showing that the mortality rate in stage III patients is nearly four times higher than in those at stage II. Thus, it is critical to identify and monitor the factors influencing long-term mortality in patients with advanced TBM to improve their overall health.

In our study, we found that TBM predominantly affects younger adults, with the average age of stage II and III patients being approximately 36 ± 17 years. This is consistent with the findings of a previous study by Gu J [13]. The long-term mortality rate in our sample was 20.2%, which aligns with previous research [15, 23]. We observed that the age of patients in the deceased group was significantly higher than that of the survivors. Moreover, the majority of older patients were at stage II or III of the disease [24]. Gu J et al. [13] reported that 63.3% of TBM patients with poor prognoses were above 60 years of age. However, sample primarily consisted of young and middle-aged stage II patients, resulting in some inconsistencies. We identified a cut-off age of 44.5 (sensitivity 47.2%, specificity 73.2%, $P=0.036$), suggesting that the risk of mortality increases with age. This could

**Fig. 1** The ROC curves of age and GCS in predicting long-term prognosis in patients with Stage II and III TBM

be attributed to the presence of multiple comorbidities in older individuals, weakened immune defense mechanisms, and suboptimal immune responses to mycobacterium infection [24].

In our study, the Glasgow Coma Scale (GCS) emerged as an independent predictor of long-term mortality in patients with Stage II and III TBM, corroborating previous studies that highlighted an association between low GCS scores and unfavorable outcomes [12, 13, 21, 25]. The strength of our study lies in its extended follow-up period, allowing us to gain a comprehensive understanding of the long-term survival prospects of TBM patients. The GCS is a widely used and reliable tool that assesses consciousness impairment in TBM patients by evaluating eye opening, verbal, and motor responses. It can also predict cognitive function and motor-related sequelae [26]. In our cohort, patients with lower GCS scores exhibited higher levels of consciousness impairment. We found that mortality rates significantly increased when GCS scores were 11 (sensitivity 52.8%, specificity 86.6%, $P < 0.001$). Therefore, healthcare professionals should accurately assess and closely monitor changes in patients' level of consciousness, pupil dilation, and other relevant indicators. Timely evaluation is essential for developing an individualized, evidence-based management plan.

Our multivariate analysis identified peripheral neurological dysfunction as an independent risk factor for long-term mortality in Stage II and III TBM patients. In TBM, mycobacterium tuberculosis invades the meninges and brain parenchyma, activating and penetrating the subarachnoid space with tubercle bacilli, which then disseminate with the cerebrospinal fluid (CSF). This can result in neurological dysfunction in various segments of the spinal cord [26]. Peripheral neurological deficits may manifest as hemiplegia, vision or hearing loss, ataxia, unresponsiveness, among others [27, 28]. In our study, 63.9% of long-term deceased patients presented with peripheral neurological symptoms, such as numbness, facial asymmetry, limb weakness, fine motor dysfunction, and urinary and fecal incontinence. These symptoms significantly impaired the patients' self-care ability and negatively impacted their quality of life, leading to feelings of inferiority, guilt, and loneliness [29]. Quality of life and mental well-being significantly influence disease progression, and strong familial and social support are crucial in enhancing treatment adherence [30]. Therefore, it is essential to mobilize resources for patients diagnosed with advanced TBM to provide psychological support, alleviate negative emotions, and improve their motivation and confidence in adhering to their treatment regimen.

Existing literature suggests a strong association between hydrocephalus and adverse outcomes, including mortality, in TBM patients [31–33], particularly those

with higher MRC classification. Our study reaffirms these findings. The inflammatory response elicited by mycobacterium tuberculosis infection in the subarachnoid space can lead to a viscous exudate obstructing the subarachnoid space at the brain base, causing hydrocephalus [21]. This common intracranial complication can occur at any stage of TBM and often results in increased intracranial pressure [34]. This may be a primary contributor to elevated intracranial pressure in TBM patients, leading to functional impairments affecting learning, memory, and movement [35], and in severe cases, coma, brain herniation, or death. Head CT/MRI is a reliable tool for diagnosing and assessing the severity of hydrocephalus in TBM patients [36, 37]. Medical professionals should closely monitor imaging results, especially signs of hydrocephalus, in Stage II/III TBM patients. Prompt review of CT or MRI scans is crucial if changes in consciousness level or pupils are observed.

Limitations

The present study has several limitations, including its retrospective design, single-site sampling, reliance on our hospital's patient records, and relatively small sample size. Future investigations would benefit from a larger sample size and a multi-center, prospective study design.

Conclusions

Age, GCS score, peripheral neurological dysfunction, and hydrocephalus are independent predictors of long-term mortality in advanced TBM patients. Therefore, healthcare professionals should pay close attention to these clinical manifestations, enhance assessment procedures, and provide timely intervention.

Abbreviations

BMRC	British Medical Research Council
TB	Tuberculosis
TBM	Tuberculosis meningitis
GCS	Glasgow Coma Scale
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
CSF	Cerebrospinal fluid
OR	Odds ratio
CI	Confidence interval
ROC	Receiver Operating Characteristic

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Author contributions

Ling Wang conceptualized the study, drafted the manuscript, analyzed the data, and critically revised the manuscript for important intellectual content. Zhihan Gu and Xiaoli Chen contributed to data analysis. Xiaomin Yu was involved in the diagnosis and confirmation of tuberculosis meningitis patients. The corresponding author was responsible for study concept design, data analysis and interpretation, manuscript preparation, and intellectual content review. All authors read and approved the final.

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Data availability

All data generated or analyzed during this study are included in this article.

Declarations

Ethics approval and consent to participate

This study was by the Human Ethics Committee of West China Hospital of Sichuan University (Ethics No.: 2018–598) and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants and/or their legal guardian(s). All methods were carried out following the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Geneva, World Health organization. ; 2022. licence: cc BY-NC-SA 3.0 iGo.Global tuberculosis report 2022[EB/OL]. (2022-10-27)[2023-09-20]. <https://iris.who.int/bitstream/handle/10665/363752/9789240061729-eng.pdf?sequence=1>.
2. Seddon JA, Tugume L, Solomons R, Prasad K, Bahr NC, Tuberculous Meningitis International Research Consortium. The current global situation for tuberculous meningitis: epidemiology, diagnostics, treatment and outcomes. *Wellcome Open Res.* 2019;4:167. 10.12688/wellcomeopenres.15535.1. PMID: 32118118; PMCID: PMC7029758.
3. Dodd PJ, Osman M, Cresswell FV, Stadelman AM, Lan NH, Thuong NTT et al. The global burden of tuberculous meningitis in adults: a modelling study. *plos glob Public Health* 2021;1(12).
4. Cantier M, Morisot A, Guérot E, et al. Functional outcomes in adults with tuberculous meningitis admitted to the ICU: a multicenter cohort study. *crit Care.* 2018;22(1):1–8.
5. Stadelman AM, Ellis J, Samuels THA, Mutengesha E, Dobbin J, Ssebambulidde K, Rutakingirwa MK, Tugume L, Boulware DR, Grint D, Cresswell FV. Treatment outcomes in adult tuberculous meningitis: a systematic review and Meta-analysis. *Open Forum Infect Dis.* 2020;7(8):ofaa257. <https://doi.org/10.1093/ofid/>. PMID: 32818138; PMCID: PMC7423296.
6. Dian S, Ganiem AR, van Laarhoven A. Central nervous system tuberculosis. *Curr Opin Neurol.* 2021;34(3):396–402. doi: 10.1097/WCO.0000000000000920. PMID: 33661159; PMCID: PMC8283909.
7. Donovan J, Thwaites GE, Huynh J. Tuberculous meningitis: where to from here? *Curr Opin Infect Dis.* 2020;33(3):259–66. doi: 10.1097/QCO.0000000000000648. PMID: 32324614; PMCID: PMC7259381.
8. Ahlawat S, Chaudhary R, Dangi M, Bala K, Singh M, Chhillar AK. Advances in tuberculous meningitis diagnosis. *Expert Rev Mol Diagn.* 2020;20(12):1229–41. Epub 2020 Dec 21. PMID: 33259249.
9. Wang MG, Luo L, Zhang Y, et al. Treatment outcomes of tuberculous meningitis in adults: a systematic review and meta-analysis[J]. *BMC Pulm Med.* 2019;19:1–11.
10. Ssebambulidde K, Gakuru J, Ellis J, Cresswell FV, Bahr NC. Improving technology to diagnose tuberculous meningitis: are we there yet? *Front Neurol.* 2022;13:892224. <https://doi.org/10.3389/fneur.2022.892224>. PMID: 35711276; PMCID: PMC9195574.
11. Foppiano Palacios C, Saleeb P. Challenges in the diagnosis of tuberculous meningitis. *J Clin Tuberc Other Mycobact Dis.* 2020;20:100164. <https://doi.org/10.1016/j.jctube.2020.100164>. Erratum in: *J Clin Tuberc Other Mycobact Dis.* 2020;21:100177. PMID: PMC7240715.
12. Li K, Tang H, Yang Y, Li Q, Zhou Y, Ren M, Long X, Shen W, Hu R, Wang X, Zeng K. Clinical features, long-term clinical outcomes, and prognostic factors of tuberculous meningitis in West China: a multivariate analysis of 154 adults. *Expert Rev Anti Infect Ther.* 2017;15(6):629–35. 14787210.2017.1309974. epub 2017 Apr 7. PMID: 28343419.
13. Gu J, Xiao H, Wu F, Ge Y, Ma J, Sun W. Prognostic factors of tuberculous meningitis: a single-center study. *Int J Clin Exp Med.* 2015;8(3):4487–93. PMID: 26064373; PMCID: PMC4443207.
14. Goyal V, Elavarasi A, Abhishek, Shukla G, Behari M. Practice trends in Treating Central Nervous System Tuberculosis and outcomes at a Tertiary Care Hospital: a Cohort Study of 244 cases. *Ann Indian Acad Neurol.* 2019 Jan-Mar;22(1):37–46. https://doi.org/10.4103/ain.AIAN_70_18. PMID: 30692758; PMCID: PMC6327709.
15. Wen L, Li M, Xu T, et al. Clinical features, outcomes and prognostic factors of tuberculous meningitis in adults worldwide: systematic review and meta-analysis[J]. *J Neurol.* 2019;266:3009–21.
16. Verma R, Mahapatro S, Kumar A, Rizvi I, Garg RK, Malhotra HS, Sharma PK, Uniyal R. Platelet dysfunction and coagulation assessment in patients of tuberculous meningitis. *Neurol Sci.* 2020;41(8):2103–10. <https://doi.org/10.1007/s10072-020-04299-4>. Epub 2020 Feb 29. PMID: 32114668.
17. Sy MCC, Espiritu AI, Pascual JLR 5. Th. Global frequency and clinical features of stroke in patients with tuberculous meningitis: a systematic review. *JAMA Netw Open.* 2022;5(9):e2229282. <https://doi.org/10.1001/jamanet-workopen.2022.29282>. PMID: 36048445; PMCID: PMC9437750.
18. Marais S, Thwaites G, Schoeman JF, et al. Tuberculous meningitis: a uniform case definition for use in clinical research. *Lancet Infect Dis.* 2010;10(11):803–12.
19. Philip N, William T, John DV. Diagnosis of tuberculous meningitis: challenges and promises[J]. *Malays J Pathol.* 2015;37(1):1–9.
20. Woldeamanuel YW, Girma B. A 43-year systematic review and meta-analysis: case-fatality and risk of death among adults with tuberculous meningitis in Africa. *J Neurol.* 2014;261(5):851–65. <https://doi.org/10.1007/s00415-013-7060-6>.
21. Kanesen D, Kandasamy R, Wong ASH, Tharakan J, Lim CJ, Abdullah JM. Clinical outcome of tuberculous meningitis with Hydrocephalus - A Retrospective Study. *Malays J Med Sci.* 2021;28(5):82–93. <https://doi.org/10.21315/mjms2021.28.5.8>. Epub 2021 Oct 26. PMID: 35115890; PMCID: PMC8793966.
22. Marais BJ, Heemskerck AD, Marais SS, et al. Standardized methods for enhanced quality and comparability of tuberculous meningitis studies. *Clin Infect Dis.* 2017;64(4):501–9. <https://doi.org/10.1093/cid/ciw757>.
23. Yang ZR, Zhang LF, Zhou BT, Shi XC, Cao W, Fan HW, Liu ZY, Li TS, Liu XQ. [Clinical features and influencing factors of long-term prognosis in patients with tuberculous meningitis]. *Zhonghua Nei Ke Za Zhi.* 2022;61(7):764–770. Chinese. <https://doi.org/10.3760/cma.j.cn112138-20220121-00069>. PMID: 35764559.
24. Rahman N, Pannu AK, Yadav R, Sethi S, Saroch A, Garg M, Kumar D, Bhalla A. Tuberculous meningitis in the elderly. *QJM.* 2022;115(6):381–387. doi: <https://doi.org/10.1093/qjmed/hcab162>. pmid: 34100953.
25. Feng B, Fei X, Sun Y, Zhang X, Shang D, Zhou Y, Sheng M, Xu J, Zhang W, Ren W. Prognostic factors of adult tuberculous meningitis in intensive care unit: a single-center retrospective study in East China. *BMC Neurol.* 2021;21(1):308. <https://doi.org/10.1186/s12883-021-02340-3>. Erratum in: *BMC Neurol.* 2021;21(1):308. Oct 25;21(1):406. PMID: 34376174; PMCID: PMC8353730.
26. Kalita J, Misra UK, Ranjan P. Predictors of long-term neurological sequelae of tuberculous meningitis: a multivariate analysis. *Eur J Neurol.* 2007; 14(1):33–7. <https://doi.org/10.1111/j.1468-1331.2006.01534.x>. Erratum in: *Eur J Neurol.* 2007;14(3):357. PMID: 17222110.
27. Goldberg DW, Tenforde MW, Mitchell HK, Jarvis JN. Neurological sequelae of adult meningitis in Africa: a systematic literature review. *open Forum Infect Dis.* 2017;5(1):ofx246. <https://doi.org/10.1093/ofid/ofx246>. PMID: 29322063; PMCID: PMC5753229.
28. Liu C, Huai R, Xiang Y, Han X, Chen Z, Liu Y, Liu X, Liu H, Zhang H, Wang S, Hao L, Bo Y, Luo Y, Wang Y, Wang Y. High cerebrospinal fluid lactate concentration at 48 h of hospital admission predicts poor outcomes in patients with tuberculous meningitis: a multicenter retrospective cohort study. *Front Neurol.* 2022;13:989832. <https://doi.org/10.3389/fneur.2022.989832>. PMID: 36277931; PMCID: PMC9583930.
29. Feng D, Xu L. The relationship between perceived discrimination and psychological distress among Chinese pulmonary tuberculosis patients: the moderating role of self-esteem[J]. *Psychol Health Med.* 2015;20(2):177–85.
30. Lu Y, Wang H, Zhu J, et al. Effect of targeted nursing intervention plus psychological counseling on quality of life, negative emotions, and complications in patients with extensively drug-resistant tuberculosis[J]. *Am J Translational Res.* 2021;13(12):13950.
31. Anurag Kumar Singh1,Hardeep Singh Malhotra,Ravindra Kumar Garg,et al.Paradoxical reaction in tuberculous meningitis: presentation, predictors and impact on prognosis.BMC Infectious Diseases,2016,16:306.
32. Huang HJ, Ren ZZ, Dai YN et al. Old age and hydrocephalus are associated with poor prognosis in patients with tuberculous meningitis: a retrospective study in a Chinese adult population[J]. *Medicine*, 2017, 96(26).

33. Cao X, Yang Q, Zhou X, Lv K, Zhou Z, Sun F, Ruan Q, Zhang J, Shao L, Geng D. Cerebral Infarction and Evan's ratio on MRI affect the severity and prognosis of tuberculosis meningitis patients. *Diagnostics (Basel)*. 2022;12(5):1264. <https://doi.org/10.3390/diagnostics12051264>. PMID: 35626418; PMCID: PMC9141437.
34. Donovan J, Figaji A, Imran D, Phu NH, Rohlwick U, Thwaites GE. The neurocritical care of tuberculous meningitis. *Lancet Neurol*. 2019;18(8):771–83. [https://doi.org/10.1016/S1474-4422\(19\)30154-1](https://doi.org/10.1016/S1474-4422(19)30154-1). Epub 2019 May 17. PMID: 31109897.
35. Davis AG, Nightingale S, Springer PE, Solomons R, Arenivas A, Wilkinson RJ, Anderson ST, Chow FC, Tuberculous Meningitis International Research Consortium. neurocognitive and functional impairment in adult and paediatric tuberculous meningitis. *wellcome Open Res*. 2019;4:178. doi.10.12688/wellcomeopenres.15516.1. PMID: 31984243; PMCID: PMC6971841.
36. Schaller MA, Wicke F, Foerch C, Weidauer S. Central Nervous System Tuberculosis: etiology, clinical manifestations and neuroradiological features. *Clin Neuroradiol*. 2019;29(1):3–18. <https://doi.org/10.1007/s00062-018-0726-9>. Epub 2018 Sep 17. PMID: 30225516.
37. Gu Z, Liu B, Yu X, Cheng T, Han T, Tong L, Cao Y. Association of blood neutrophil-lymphocyte ratio with short-term prognosis and severity of tuberculosis meningitis patients without HIV infection. *BMC Infect Dis*. 2023;23(1):449.

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