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Diagnostic and prognostic significance of chest radiographs in adult tuberculous meningitis: A retrospective study

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Abstract

Background: Tuberculous meningitis (TBM) is the most severe form of extra-pulmonary TB, carrying significant morbidity and mortality. Our study examined the diagnostic utility and prognostic value of abnormal chest X-rays (CXRs), alongside other clinical, laboratory and neuroimaging features in adult TBM. *Methodology:* This retrospective study used the Lancet consensus criteria to include all patients diagnosed with TBM at a tertiary referral centre from 2010-2020. Clinical, laboratory and radiological findings on admission were identified. The presence of tuberculomas, enhancement pattern, hydrocephalus, and infarction was assessed using brain imaging. Findings were compared to the functional outcome on the modified Rankin scale (mRS) at 90 days (good: mRS 0-2, poor: mRS 3-6). Correlation with functional outcomes was determined using logistic regression. Cases without imaging were excluded. *Results:* This study included 31 adults diagnosed with TBM (median age: 37 years, range: 18-67 years). Abnormal CXRs were seen in 51.61% of patients. Poor functional outcomes were observed in 51.61% of patients and were independently associated with abnormal CXRs (aOR 20.07, 95% CI 1.63-247.60), the absence of Bacillus Calmette-Guérin (BCG) inoculation (adjusted odds ratio (aOR) 7.89, 95% CI 1.01-61.55) and lethargy (aOR 15.89, 95% CI 1.28-196.86). We found significant differences between good and poor outcomes in patients with cerebrospinal fluid (CSF) polymorphs (median: 6% vs median: 43%), CSF lymphocytes (median: 88% vs median: 12%) and cerebral infarction (0% vs 100%).
Conclusion: Abnormal chest radiographs help guide the diagnosis of TBM while awaiting definitive CSF results. They also are independently associated with poor functional outcomes.

Keywords: Tuberculous meningitis, chest radiograph, diagnosis, prognosis

INTRODUCTION

Tuberculosis (TB) is the world's deadliest infectious disease.[1] While pulmonary TB is the most common form, extrapulmonary TB (EPTB) is not rare, representing 16% of all reported cases.[1] Of EPTB, central nervous system tuberculosis (CNS-TB) is the most severe. It constitutes 5–10% of all EPTB cases and approximately 1-2% of all active TB, with the primary manifestation being tuberculous meningitis (TBM).[2] TBM, though rare, has the highest TB-related morbidity and mortality, with case fatality rates of 20-50%[2-4], and neurological sequelae in 22-43% of cases.[5,6]

TBM remains a diagnostic challenge due to its non-specific presentation and the limited sensitivity of cerebrospinal fluid (CSF) tests in confirming *Mycobacterium tuberculosis*.[7] AFB smear has only a 10-15% sensitivity, while CSF culture, though more sensitive (50-60%)[8], may take up to three months. The World Health Organization (WHO) recommends Xpert MTB/RIF Ultra as the first-line test.[9] However, its

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negative predictive value (61.1% to 92.7%) remains insufficient for excluding TBM.[10]

Without reliable microbiologic or molecular techniques, diagnosis relies on a combination of clinical, laboratory, and radiological findings. As early treatment improves outcomes, identifying prognostic factors is crucial.[11] While previous studies have examined clinical, laboratory, and brain computed tomography/magnetic resonance imaging (CT/MRI) findings in relation to TBM prognosis[11-17], the role of chest radiographs remains underexplored.[18] The Lancet consensus criteria include pulmonary TB as a key diagnostic component[19], and chest X-rays (CXRs) demonstrate active or prior pulmonary TB in approximately 50% of TBM cases, supporting their diagnostic value.[20]

While miliary TB has been associated with poorer TBM outcomes[15], the broader diagnostic and prognostic significance of other chest radiograph abnormalities remains unclear. Most studies focus on paediatric populations, with limited data on abnormal CXRs in adult TBM.[21,22] This study aims to address this gap by evaluating the diagnostic utility and prognostic value of chest radiographs, alongside other clinical, laboratory and neuroimaging features in adult TBM.

METHODS

Study participants

This retrospective study included 31 of 51 patients diagnosed with TBM at a tertiary referral centre from 2011-2020. Patients were identified from University of Malaya Medical Centre's (UMMC) TB registry. Patient information and clinical notes were obtained from the electronic medical record (EMR) system with approval of the Ethical Review Committee (MREC ID: 202087-8959). Patients were included if they were aged ≥ 18 years, had complete clinical, laboratory and imaging data, and fulfilled the 2010 Lancet consensus criteria for TBM diagnosis.[19]

In line with this criterion, patients were diagnosed as either definite, probable or possible TBM based on clinical findings, CSF analysis, cerebral imaging and evidence of tuberculosis. The criteria for each category were:

(1) *Definite* TBM (microbiological identification or evidence from commercial nucleic acid amplification tests of CSF or positive histological findings);
(2) *Probable* TBM (diagnostic score of ≥ 10 points when cerebral imaging was unavailable, or ≥ 12 when cerebral imaging was available); and
(3) *Possible* TBM (diagnostic score of 6–9 points when cerebral imaging was unavailable or 6–11 points when imaging was available).

Patients with missing functional outcomes or had an alternative diagnosis on discharge were excluded.

Data collection

Patient data were collected following the guidelines of the Standardised Methods for Enhanced Quality and Comparability of TBM Studies.[23] Neurological status on admission was staged according to the modified British Medical Research Council (MRC) criteria.

(1) Stage I: the GCS score of 15 with no neurological deficit
(2) Stage II: GCS of 11–14 or GCS of 15 with focal neurological signs.
(3) Stage III: GCS ≤ 10.[24]

Documented clinical symptoms such as altered consciousness, headache, lethargy, nausea and vomiting were not attributable to sedative medications or other identifiable causes. Patient comorbidities, including retroviral disease, hypertension, and diabetes, were collected. CSF etiological tests included an acid-fast bacilli smear, TB culture, Xpert MTB/RIF Ultra and bacterial culture. Routine biochemical examination of CSF included assessments of appearance, erythrocytes, leukocytes, polymorphs, lymphocytes, large cells, glucose, and protein content.

Chest radiographs were evaluated for lymphadenopathy, consolidation, cavitation, nodules, fibrosis, pleural effusion, and miliary disease. Brain CT/MRI imaging was assessed for the presence of tuberculomas, enhancement patterns, cerebellitis, cerebritis, abscess, hydrocephalus, and infarction.

Therapeutic protocol

In line with local guidelines, patients received two months of intensive treatment, consisting of isoniazid (4-6 mg/kg/day; up to 300 mg/day), rifampicin (8-12 mg/kg/day; up to 600 mg/day), ethambutol (15-20 mg/kg/day; up to 1600 mg/day) and pyrazinamide (20-30 mg/kg/day; up to 2000 mg/day). This was followed by 10 months of treatment with isoniazid (4-6 mg/kg/day; up to 300 mg/day), rifampicin (8-12 mg/kg/day; up to 600 mg/day). Adjunctive steroids were given to reduce inflammation in all patients on admission.

Functional outcomes

The modified Rankin scale (mRS) score was used to evaluate patients' functional outcomes at 3-month follow-up. Scores of 0-2 indicated good outcomes, while scores of 3-6 indicated poor outcomes. The 3-month follow-up was chosen, as studies on time-specific mortality in TBM indicate that most deaths occur within this period.[11] The mRS scores were obtained by reviewing the hospital's medical records.

Patients were divided into good and poor outcome groups, and statistical differences between the groups were analysed to identify prognostic markers. All three TBM classifications (definite, probable, and possible) were analysed as a single group, as all patients receive anti-TB treatment regardless of classification. This also allowed for a larger sample size in each outcome group, thereby enhancing the statistical power of our analysis.

Chest radiograph

Baseline plain radiographs of the chest were performed in the posteroanterior (PA) view in either the erect or supine position.

Brain CT/MRI

Baseline brain imaging was performed using either computed tomography (CT) or magnetic resonance imaging (MRI). Both contrast and non-contrast-enhanced CT scans were included. For MRI, standard brain protocols included were T1-magnetisation-prepared rapid gradient echo (T1-MPRAGE), T2-weighted images (T2WI), T2-fluid-attenuated inversion recovery (T2-FLAIR), diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) mapping and gradient echo (GRE) sequences.

MRI brain was done using a 3.0 Tesla Signa® HDx MR System (GE Healthcare) or the Siemens Magnetom Prisma TIMDOT Engine 3T (Siemens Healthcare) with a dedicated 8-channel head coil at MRI 3T and 64-channel head coil. The patient was scanned in a supine position. The total examination time was approximately 30 minutes.

Statistical analysis

The data were compiled and expressed as median (range) or number (%). Patient's findings were compared according to functional outcome on the modified Rankin scale (mRS) at 90 days (good: mRS 0-2, poor: mRS 3-6), using Pearson's Chi-Square or Fisher's exact test for categorical variables and the Mann-Whitney test for quantitative variables (p values < 0.05 considered significant). Variables significantly associated with functional outcomes were included in a multivariate logistic regression model for further analysis. All analyses were conducted using SPSS 29.0 (IBM Inc., Armonk, NY, USA) software.

RESULTS

Patient demographics and clinical manifestations

A total of 31 patients (19 male and 12 female) were included in this study (Figure 1). Among them, 16 had poor functional outcomes, and 15 had good outcomes. The frequencies and associations of patient demographics and clinical features with functional outcomes are summarised in Table 1. The cohort was predominantly male (61.3%), with a median age of 37 years (18-67). Definite TBM was the most common diagnosis, accounting for 41.9% of cases, followed by probable and possible TBM (29.0% each). Most patients presented in advanced stages of TBM, with stage II (48.4%) and stage III (35.5%) being the most common, while only 16.1% presented in stage I TBM.

Of the patients, 38.7% did not receive Bacillus Calmette-Guérin (BCG) inoculation, and the median hospital stay was 23 days (range: 2–106). The most common clinical symptom was fever, reported in 74.2% of patients, followed by altered consciousness (71%), headache (64.5%), and lethargy (64.5%).

When comparing the two outcome groups, patients with poor outcomes tended to be older, with a median age of 43.5 years compared to 33 years in the good outcome group. Male sex was more common in the poor outcome group (75.0% vs 46.7%). Interestingly, retroviral disease (RVD) was found almost exclusively in the good outcome group (4 cases vs 1 in the poor outcome group), while diabetes mellitus (DM) and hypertension (HPT) were slightly more common in the poor outcome group, though these differences were not significant. The majority of patients with poor outcomes were in MRC stage II or III (43.8% each), while the majority of patients with good outcomes were in MRC stage II (53.3%). Notably, among all baseline characteristics, only lethargy and the absence of BCG inoculation were significantly associated with poor outcomes ($p < 0.05$).

Biochemical analysis of cerebrospinal fluid (CSF)

CSF analyses for the poor and good outcome

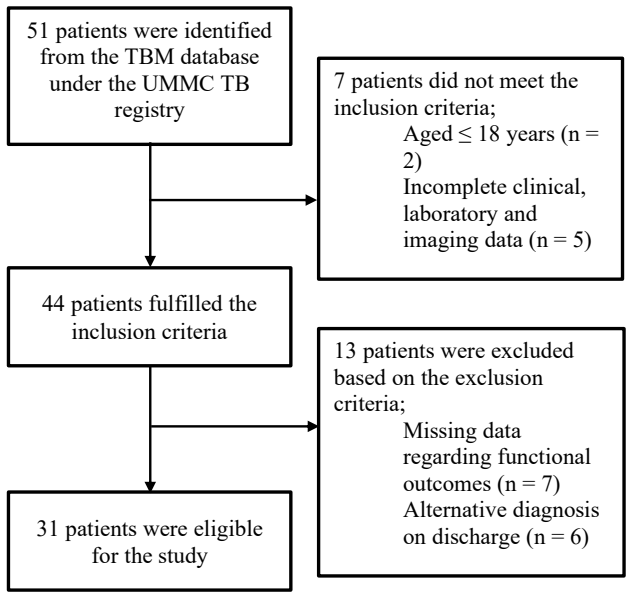

Figure 1. Flow diagram of patient selection

groups are detailed in Table 2. CSF analysis was performed in 28 (90.3%) patients. Three patients did not undergo CSF analysis, likely because sputum AFB smears were positive, and therefore CSF analysis was deemed unnecessary. Overall, CSF analysis revealed a typical pleocytosis of 22.5 (0-5640) cells/μL, elevated protein levels of 1.515 (0.18–17.70) g/L, elevated erythrocytes 15 (0-173600) cells/μL and low glucose levels of 2.05 (0.1–5.6) mmol/L. Patients with poor outcomes had significantly higher CSF polymorphs (median: 43% vs median: 6%) and significantly lower CSF lymphocytes (median: 12% vs median: 88%). Patients with poor outcomes also demonstrated a higher CSF erythrocyte count; however, this was not significantly associated with poor outcomes.

Chest X-ray abnormalities

All patients had CXRs, the findings of which are summarised in Table 3. Abnormal CXRs were observed in 16 (51.6%) patients and were significantly associated with poor outcomes, with 11 (68.8%) of these patients experiencing poor outcomes.

The most common abnormality was upper lobe consolidation, affecting 7 (22.6%) patients in both the right and left upper lobes (Figure 2A). Other findings included right lower lobe consolidation (12.9%), nodules (12.9%), fibrosis (12.9%) and miliary TB (12.9%). Less frequent abnormalities include pleural effusion (9.7%), cavitation (9.7%), right middle lobe consolidation (6.5%), left lower lobe consolidation (6.5%) and lymphadenopathy (3.2%).

Although specific CXR abnormalities lacked statistical significance, certain trends were observed with the poor outcome group. Miliary TB was exclusively seen in patients with poor outcomes. An example of miliary TB seen in one of our patients is depicted in Figure 2B. In contrast, abnormalities such as nodules, fibrosis, and pleural effusion were more evenly distributed between the poor and good outcome groups, with no significant differences observed.

Brain CT/MRI abnormalities

Brain imaging (CT/MRI) was performed on all patients, with the findings summarised in Table 4. Only acute findings related to the current infection, as determined by neuroradiologists (NR), were included. The most common abnormalities seen were leptomeningeal enhancement reported in 61.3% of patients, followed by basal enhancement (48.4%), tuberculoma (48.4%) and hydrocephalus (45.2%). Among all brain CT/MRI features, cerebral infarction was the only finding significantly associated with poor outcomes. It was exclusively observed in patients with poor outcomes, with all 5 (100%) affected individuals experiencing poor outcomes. An example of cerebral infarction from our study is shown in Figure 3.

While not statistically significant, leptomeningeal enhancement showed a trend

Table 1: Patient demographics and clinical manifestations between poor and good outcome groups

Characteristics/Variables	All patients (n=31)	Poor outcome (n=16)	Good outcome (n=15)	P value
Demographic features				
Male sex, n (%)	19 (61.3%)	12 (75.0%)	7 (46.7%)	0.106*
Age (years) - median [IQR]	37 (18-67)	43.5 (18-67)	33 (22-52)	0.122**
Comorbidities, n (%)				0.660***
Retroviral disease	5 (16.1%)	1 (6.3%)	4 (26.7%)	0.172***
DM	6 (19.4%)	4 (25.0%)	2 (13.3%)	0.654***
HPT	6 (19.4%)	4 (25.0%)	2 (13.3%)	0.454***
TBM diagnosis, n (%)				0.660***
Definite	13 (41.9%)	6 (37.5%)	7 (46.7%)	
Probable	9 (29.0%)	6 (37.5%)	3 (20.0%)	
Possible	9 (29.0%)	4 (25.0%)	5 (33.3%)	
MRC stage, n (%)				0.626***
Stage I	5 (16.1%)	2 (12.5%)	3 (20.0%)	
Stage II	15 (48.4%)	7 (43.8%)	8 (53.3%)	
Stage III	11 (35.5%)	7 (43.8%)	4 (26.7%)	
Other medical history, n (%)				
Absence of BCG inoculation	**12 (38.7%)**	**9 (56.3%)**	**3 (20.0%)**	**0.038***
Length of hospital stay (days)	23 (2-106)	40.5 (2-106)	23 (8-77)	0.332**
Signs and symptoms on admission, n (%)				
GCS on admission	12 (5-15)	11 (5-15)	13 (6-15)	0.157**
Symptom duration (> 5 days)	26 (83.9%)	14 (87.5%)	12 (80.0%)	0.654***
Fever	23 (74.2%)	14 (87.5%)	9 (60.0%)	0.113***
Altered consciousness	22 (71.0%)	12 (75.0%)	8 (53.3%)	0.704***
Headache	20 (64.5%)	10 (62.5%)	10 (66.7%)	0.809*
Lethargy	**20 (64.5%)**	**13 (81.3%)**	**7 (46.7%)**	**0.044*** **
Nausea & vomiting	15 (48.4%)	9 (56.3%)	6 (40%)	0.366*
Focal neurological deficits	14 (45.2%)	6 (37.5%)	6 (40%)	0.576*
Cough (> 2 weeks)	9 (29.0%)	5 (31.3%)	4 (26.7%)	1.000***
Weight loss	8 (25.8%)	5 (31.3%)	3 (20.0%)	0.685***
Convulsions	6 (19.4%)	4 (25.0%)	2 (13.3%)	0.654***
CN Palsy	6 (19.4%)	2 (12.5%)	4 (26.7%)	0.394***
Neck stiffness	5 (16.1%)	3 (18.8%)	2 (13.3%)	1.000***
Dyspnoea	4 (12.9%)	4 (25.0%)	0	0.101***
Irritability	4 (12.9%)	2 (12.5%)	2 (13.3%)	1.000***
Night sweats	1 (3.2%)	0	1 (6.7%)	0.484***
Photophobia	0	0	0	

Variables in bold are statistically significant ($p < 0.05$).

Abbreviations: IQR interquartile range, DM diabetes mellitus, HPT hypertension, TBM tuberculous meningitis, MRC British Medical Research Council, BCG Bacillus Calmette-Guérin, GCS Glasgow Coma Scale, CN cranial nerve

*Chi-square test

**Mann-Whitney test

***Fisher's Exact test

Table 2: Biochemical analysis of CSF between poor and good outcome groups

Variables	Reference range	All patients (n=31)	Poor outcome (n=16)	Good outcome (n=15)	P value
CSF biochemical analysis – median [IQR]					
Clear CSF appearance, n (%)		19 (67.9%)	9 (56.3%)[a]	10 (66.7%)[b]	0.435***
CSF erythrocytes, /μL		15 (0-173600)	62 (0-173600)[a]	6 (0-1920)[b]	0.084**
CSF leukocytes, /μL	0-10	22.5 (0-5640)	27 (0-5640)[a]	18 (0-480)b	0.780**
CSF polymorphs, %		**12 (0-100)**	**43 (0-100)[a]**	**6 (0-25)[b]**	**0.046****
CSF lymphocytes, %		**38 (0-100)**	**12 (0-100)[a]**	**88 (0-100)[b]**	**0.018****
CSF large cells, %		0	0[a]	0[b]	1.000**
CSF glucose, mmol/L	2.5-5.0	2.05 (0.1-5.6)	2.0 (0.1-5.6)[a]	2.3 (0.6-4.50)[b]	0.812**
CSF protein, g/L	0.08-0.32	1.515 (0.18-17.70)	1.53 (0.18-17.70)[a]	1.27 (0.38-11.81)[b]	0.532**
Positive CSF culture, n (%)		13 (41.9%)	6 (56.3%)	7 (46.7%)	0.605*

Variables in bold are statistically significant ($p < 0.05$).
Abbreviations: IQR interquartile range, DM diabetes mellitus, HPT hypertension, TBM tuberculous meningitis, MRC British Medical Research Council, BCG Bacillus Calmette-Guérin, GCS Glasgow Coma Scale, CN cranial nerve
*Chi-square test
**Mann-Whitney test
***Fisher's Exact test
[a]Data missing in 1 case
[b]Data missing in 2 cases

Table 3: Chest radiograph abnormalities between poor and good outcome groups

Variables	All patients (n=31)	Poor outcome (n=16)	Good outcome (n=15)	P value
CXR findings				
Normal CXR	**15 (48.4%)**	**5 (31.3%)**	**10 (66.7%)**	**0.049***
Abnormal CXR findings	**16 (51.6%)**	**11 (68.8%)**	**5 (33.3%)**	**0.049***
Individual CXR findings				
Lymphadenopathy	1 (3.2%)	0	1 (6.7%)	0.484***
Consolidation				
Right upper lobe	7 (22.6%)	5 (31.3%)	2 (13.3%)	0.394***
Right middle lobe	2 (6.5%)	2 (12.5%)	0	0.484***
Right lower lobe	4 (12.9%)	3 (18.8%)	1 (6.7%)	0.600***
Left upper lobe	7 (22.6%)	5 (31.3%)	2 (13.3%)	0.394***
Left lower lobe	2 (6.5%)	2 (12.5%)	0	0.484***
Cavitation	3 (9.7%)	1 (6.3%)	2 (13.3%)	0.600***
Nodules	4 (12.9%)	2 (12.5%)	2 (13.3%)	1.000***
Fibrosis	4 (12.9%)	2 (12.5%)	2 (13.3%)	1.000***
Pleural effusion	3 (9.7%)	1 (6.3%)	2 (13.3%)	0.600***
Miliary	4 (12.9%)	4 (25.0%)	0	0.101***

Variables in bold are statistically significant ($p < 0.05$).
Abbreviations: CXR chest X-ray
*Chi-square test
**Mann-Whitney test
***Fisher's Exact test

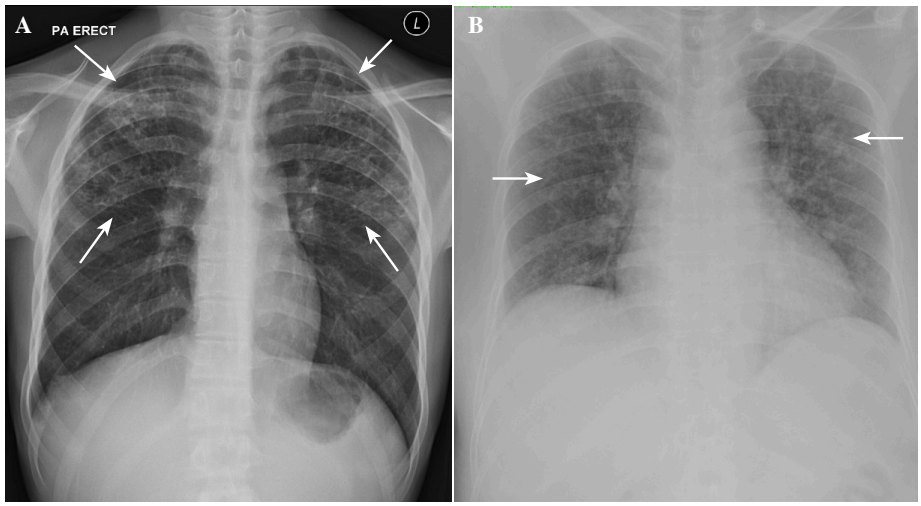

Figure 2. (A) CXR depicts bilateral upper lobe bronchiectasis with peribronchial thickening, fibrosis and patchy consolidation. (B) CXR in a different patient shows multiple ill-defined reticulonodular lesions in both lungs, suggestive of miliary TB.

toward poorer outcomes, with 75.0% of affected patients in the poor outcome group. Conversely, tuberculomas were associated with a trend toward good outcomes, as 9/15 (60.0%) of patients with this finding experienced good outcomes. Hydrocephalus was predominantly non-communicating in 8/14 (57.1%), with no significant differences

Table 4: Brain CT/MRI abnormalities between poor and good outcome groups

Variables	All patients (n=31)	Poor outcome (n=16)	Good outcome (n=15)	P value
Brain CT/MRI findings				
Leptomeningeal enhancement	19 (61.3%)	12 (75.0%)	7 (46.7%)	0.106*
Basal enhancement	15 (48.4%)	9 (56.3%)	6 (40.0%)	0.366*
Pachymeningeal enhancement	3 (9.7%)	3 (18.8%)	0	0.226***
Tuberculoma	15 (48.4%)	6 (37.5%)	9 (60.0%)	0.210*
Cerebellitis	3 (9.7%)	2 (12.5%)	1 (6.7%)	1.000***
Cerebritis	7 (22.6%)	5 (31.3%)	2 (13.3%)	0.394***
Abscess	5 (16.1%)	3 (18.8%)	2 (13.3%)	1.000***
Hydrocephalus	14 (45.2%)	8 (50.0%)	6 (40.0%)	0.772***
Hydrocephalus type				0.768*
Communicating	6 (19.4%)	3 (18.8%)	3 (20.0%)	
Non-communicating	8 (25.8%)	5 (31.3%)	3 (20.0%)	
Infarction	**5 (16.1%)**	**5 (31.3%)**	**0**	**0.043*** **
Surgical intervention	11 (35.5%)	7 (43.8%)	4 (26.7%)	0.320*
The interval between presence of symptoms and anti-TB therapy, days	5 (1-120)	3.5 (1-30)	5 (1-120)	0.297**

Variables in bold are statistically significant ($p < 0.05$).
Abbreviations: CT computed tomography, MRI magnetic resonance imaging
*Chi-square test
***Fisher's Exact test
**Mann-Whitney test

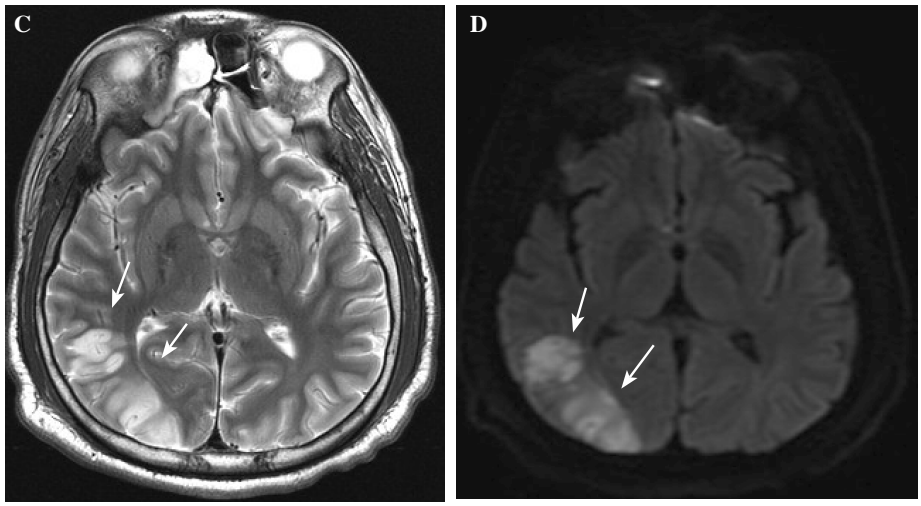

Figure 3. (C) Axial T2-weighted MRI shows hyperintensity over the right occipital lobe. (D) Axial diffusion weighted image of the same patient shows restricted diffusion in the right occipital lobe, consistent with an acute infarction.

between outcome groups. Other findings, such as pachymeningeal enhancement, cerebritis, abscesses, and cerebellitis, were infrequently observed and showed no significant association with outcomes.

Results of multifactorial analysis

Multivariate regression was performed using the significant variables: abnormal CXR, absence of BCG inoculation and lethargy. CSF lymphocytes and polymorphs were excluded due to missing data, and cerebral infarction was excluded due to an insufficient number of cases. From the analysis, three independent predictors of poor outcomes were identified (Table 5): Abnormal CXRs (adjusted odds ratio (aOR) 20.07, 95% CI 1.63-247.60), absence of BCG inoculation (adjusted odds ratio (aOR) 7.89, 95% CI 1.01-61.55) and lethargy (adjusted odds ratio (aOR) 15.89, 95% CI 1.28-196.86). This means that patients with abnormal CXRs were 20 times more likely to have poor outcomes. Absence of BCG inoculation was also strongly associated with poor outcomes, increasing the odds by approximately 7.89 times, and lethargy by nearly 16 times.

DISCUSSION

Our study investigated the role of abnormal CXRs, alongside other relevant clinical findings, in the diagnosis and prognostication of adult TBM. While most literature has focused on the diagnostic utility of CXRs in paediatric TBM, their relevance in adults remains underexplored, particularly their prognostic significance.[21,22] In our analysis, abnormal CXRs, absence of BCG inoculation and lethargy were independent predictors of poor outcomes in adult TBM. Among these, abnormal CXRs were particularly notable due to their dual diagnostic and prognostic relevance.

Radiological changes suggestive of pulmonary TB were seen in 51.6% of our patients, consistent with previous reports of 40–60%.[23,25,26] This supports the role of CXR in aiding diagnosis, though its modest yield limits its reliability for excluding TBM. Rather, it complements other clinical, laboratory and neuroimaging

Table 5: Multivariate logistic regression analysis of significant factors from univariate analysis

Variables	OR	95% CI	*P* value
Abnormal CXR	20.07	1.63-247.60	0.019
Absence of BCG inoculation	7.89	1.01-61.55	0.049
Lethargy	15.89	1.28-196.86	0.031

Variables in bold are statistically significant ($p < 0.05$).
Abbreviations: OR odds ratio, CI confidence interval, BCG Bacillus Calmette-Guérin, CXR chest X-ray

findings. In particular, miliary patterns on CXR, reflecting hematogenous dissemination, have been associated with CNS involvement.[27] Even in the absence of respiratory symptoms, such findings should prompt early neuroimaging and may indicate disseminated disease. This highlights the potential value of chest CT which can detect TB-related abnormalities missed on CXR, with studies showing superior sensitivity.[28] For example, a Turkish study found abnormalities in 43% of cases on CXR versus 88% on CT.[22] However, its use must be balanced against radiation exposure, cost, and availability. These findings reinforce the diagnostic value of CXR in adult TBM.

Beyond diagnosis, abnormal CXRs were also independently associated with poor outcomes. However, our study could not pinpoint specific CXR abnormalities linked to poor prognosis, likely due to the small sample size. An abnormal CXR may reflect a higher mycobacterial load, more advanced disease, or a later stage of infection, all of which may increase the risk of neurological morbidity and mortality. While not statistically significant, all patients with miliary tuberculosis had poor functional outcomes, aligning with past studies linking it to worse prognosis.[15,29]

These findings suggest that abnormal CXRs, in addition to aiding diagnosis, may serve as a useful prognostic marker. Although our study did not utilise chest CT, which may detect subtler abnormalities, routine CXR still proved valuable in identifying disease and stratifying risk. Future research should explore the prognostic value of specific radiographic patterns and validate these findings in larger cohorts.

Absence of BCG inoculation was also an independent poor prognostic factor. This has been well-documented in paediatric populations.[30,31] For example, a 20-year retrospective study of 38 children with CNS-TB found no permanent neurological sequelae among those BCG-vaccinated.[32] Additionally, a meta-analysis showed a 64% protective effect from BCG vaccination (OR 0.36, 95% CI: 0.18, 0.70). Our results suggest this prognostic role may extend to adults as well.

Lethargy emerged as a novel predictor, present in 81.3% of poor outcome patients. Though often described as fatigue or reduced energy, it lacks a standardised definition.[33] In our cohort, it may have reflected subtle reductions in Glasgow Coma Scale (GCS) scores. However, low GCS, which is an established predictor of poor prognosis,[15,30] was not significant in our analyses. This discrepancy may reflect inconsistencies in the documentation of lethargy in our study. Future research should aim to standardise the definition and documentation of lethargy in TBM.

Though excluded from the multivariate model due to missing data, poor outcomes were also significantly associated with higher CSF polymorphs, lower CSF lymphocytes, and cerebral infarction in univariate analysis. These findings are consistent with previous studies.[34-36] The association between high CSF neutrophil-to-lymphocyte ratio and poor outcomes remains unclear. Elevated CSF polymorphs (predominantly neutrophils), have been linked to poor prognosis, as these cells, while bactericidal, may also become infected.[34] Some studies suggest that high neutrophils and reduced lymphocytes reflect a heightened inflammatory state and may indicate persistent inflammation or impaired bacterial clearance.[37] These findings emphasise the importance of further research into neuroinflammation and its impact on outcomes in TBM.

Cerebral infarction is an established predictor of poor outcomes.[36] 16.1% of our patients had infarcts, all of whom had poor outcomes, falling within the known 6% - 47% range in previous studies.[38] Its mechanism is unclear but has been associated with leptomeningeal enhancement in TBM, where exudates surround arteries, leading to arterial narrowing and, subsequently, stroke.[39] Further research into the mechanism of infarction in TBM is required for improved preventive therapy. Other established poor prognostic factors such as advanced age, hydrocephalus and higher MRC[11,15], were not significant in our study, likely due to the small sample size.

In our cohort, 16 (51.6%) of our patients had poor outcomes at 90 days, including 6 (19.4%) deaths. These results were comparable to a local study reporting 58.3% morbidity and 19% mortality.[40] However, our morbidity rate (51.6%) was higher than the 28.7% reported in a systematic review of 32 studies.[11] This discrepancy may be due to our smaller sample size and our higher proportion of Stage II and III TBM cases (83.9% vs 63.7% in the systematic review), as advanced TBM stages are established predictors of worse outcomes.[11,17]

Our study has several strengths. To our knowledge, no previous studies have specifically examined the prognostic significance of chest radiographs in adult TBM. Additionally, the study adhered to validated guidelines and consensus definitions for patient inclusion and data reporting. However, limitations include its

retrospective design, single-centre sampling, reliance on hospital records, and small sample size. The wide confidence intervals (CI) for all three independent predictors indicate variability, likely due to sample size constraints. Future studies would benefit from a larger cohort and a multi-centre, prospective design to enhance the generalizability and robustness of the findings.

In conclusion, abnormal CXRs play an important dual role in adult TBM. While not diagnostic on their own, they support early suspicion and can guide diagnosis while awaiting definitive CSF results, which take several weeks to months to be ready. Abnormal CXRs were also independently associated with poor functional outcomes.

DISCLOSURE

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