



CLINICAL PROFILE, NEUROIMAGING SPECTRUM, AND MICROBIOLOGICAL CHARACTERISATION OF TUBERCULAR MENINGITIS IN ADULTS: A CROSS-SECTIONAL OBSERVATIONAL STUDY WITH IMMUNOCOMPETENT–IMMUNOCOMPROMISED SUBGROUP COMPARISON FROM A TERTIARY REFERRAL CENTRE IN RAJASTHAN, INDIA

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ABSTRACT

Background: Tubercular meningitis (TBM) is the most catastrophic form of extrapulmonary tuberculosis, associated with case fatality rates of 20–50% and long-term neurological sequelae in up to half of survivors. Timely characterisation of its clinical and neuroimaging profile is essential for early diagnosis and improved outcomes, particularly in high-burden settings such as Rajasthan, India.

Objective: To delineate the clinical presentation, microbiological findings, and contrast-enhanced MRI spectrum in adults with confirmed TBM, and to compare these parameters between immunocompetent and immunocompromised patients.

Methods: A hospital-based cross-sectional observational study was conducted over 18 months (May 2024–October 2025) at the Department of General Medicine, NIMS University Rajasthan, Jaipur. Ninety-four adult patients (age >18 years) with confirmed TBM — diagnosed using modified Ahuja's criteria and the Marais et al. (2010) uniform case definition — were consecutively enrolled after ethics approval (Ref. No. NIMSUR/IEC/2024/1079) and written informed consent. CBNAAT (GeneXpert MTB/RIF) was performed on CSF and sputum; 3 Tesla contrast-enhanced MRI was obtained within 48 hours. Statistical analysis used IBM SPSS Version 25.0; $p < 0.05$ was significant.

Results: Mean age was 64.54 ± 23.23 years; sex distribution was equal (50.0%). All 94 patients (100%) presented with fever, headache, vomiting, seizures, and altered sensorium. Universal neurological involvement encompassed cranial nerve palsy, motor/sensory deficits, cerebellar signs, and meningeal irritation. CBNAAT was positive in 100% of CSF and sputum specimens. MRI universally demonstrated basal exudates, hydrocephalus, tuberculomas, cerebral infarcts, miliary lesions, tuberculous abscesses, Pott's spine, and myelitis. All patients received HRZE induction therapy with adjunctive dexamethasone and showed clinical improvement; mean hospital stay was 11.50 ± 1.12 days. No significant difference was observed between immunocompetent and immunocompromised subgroups ($p > 0.05$ for all).

Conclusion: TBM in this tertiary care cohort presented at an advanced clinical stage with universal neurological and multi-compartmental radiological involvement, underscoring diagnostic delay at primary and secondary care levels. The combination of CSF CBNAAT with 3 Tesla contrast-enhanced MRI constitutes a robust confirmatory diagnostic framework. Prospective multicentre studies with longitudinal follow-up are urgently needed.

KEYWORDS: Tubercular Meningitis, MRI Brain, Hydrocephalus, CBNAAT, GeneXpert MTB/RIF, Neurological Deficit, Basal Exudates, Extrapulmonary Tuberculosis, Immunocompromised, Rajasthan, India, STROBE.

Introduction

Tuberculosis (TB) remains a leading infectious cause of global morbidity and mortality. The World Health Organization (WHO) estimated 10.6 million new cases and approximately 1.6 million deaths in 2022 alone, with India contributing the largest national share of the global burden[1,2]. Among the extrapulmonary manifestations of TB, tubercular meningitis (TBM) represents the most catastrophic, accounting for 5–15% of all extrapulmonary TB cases and characterised by disproportionately high case fatality rates and severe long-term neurological sequelae[3,4]. India bears a disproportionate share of TBM incidence through a confluence of high pulmonary TB prevalence, endemic poverty, undernutrition, and immunocompromising conditions, particularly HIV infection and type 2 diabetes mellitus (T2DM)[5,6].

The pathogenesis of TBM begins with haematogenous seeding of the meninges from a primary pulmonary focus, resulting in subependymal granuloma formation — the Rich foci — that rupture into the subarachnoid space[7]. The subsequent inflammatory response deposits a thick gelatinous exudate in the basal cisterns, driving vasculitis of perforating arteries, obstructive or communicating hydrocephalus, and cranial nerve entrapment within the exudate. Disease progression is conventionally staged as prodromal (nonspecific febrile illness), meningitic (headache, neck stiffness, focal signs), and paralytic (stupor, coma, hemiplegia), with prognosis closely correlated with the stage at which treatment is initiated[8,9].

Despite effective four-drug anti-tubercular regimens, mortality from TBM ranges between 20% and 50% in published series, and up to half of survivors sustain permanent neurological deficits including cognitive impairment, motor dysfunction, and cranial nerve palsies[10,11]. These outcomes are strongly influenced by diagnostic delay, which is common given the disease's insidious onset and the limitations of conventional microbiological methods. Ziehl-Neelsen smear of CSF yields AFB positivity in fewer than 10% of cases, while mycobacterial culture may take 6–8 weeks to return a result.¹² Molecular assays, notably the cartridge-based nucleic acid amplification test (CBNAAT/GeneXpert MTB/RIF), have substantially improved diagnostic yield and provide simultaneous rifampicin-resistance detection, with reported sensitivity of approximately 62% for CSF in high-burden settings, though availability and cost limit deployment in resource-constrained environments[13].

Neuroimaging plays an indispensable role in the diagnostic workup of TBM. Contrast-enhanced MRI is superior to CT in detecting basal meningeal enhancement, parenchymal tuberculomas, and early ischaemic infarcts — findings that collectively confirm the diagnosis and guide risk stratification[14,15]. Hydrocephalus, reported in 50–67% of patients in Indian series, frequently necessitates surgical intervention and is a recognised predictor of unfavourable outcome.¹⁶ Cerebral infarcts, primarily affecting the basal ganglia and thalamic perforator territories, are strongly associated with permanent neurological disability and death[17].

Despite this clinical and radiological complexity, published data from Indian tertiary centres on the contemporary spectrum of TBM — particularly integrating 3 Tesla MRI findings with CBNAAT confirmation — remain limited. Regional characterisation of disease patterns is important for informing local clinical protocols, audit benchmarks, and public health policy aligned with national TB elimination targets. The present study was therefore designed to systematically document the clinical and neuroimaging profile of a consecutive TBM cohort at a tertiary referral centre in Rajasthan and to evaluate differences between immunocompetent and immunocompromised individuals.

Methods

Reporting Standard: This cross-sectional study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies (von Elm et al., 2007) [18].

Study Design, Setting, and Duration

This was a hospital-based cross-sectional observational study conducted in the Department of General Medicine, National Institute of Medical Sciences and Research (NIMS University Rajasthan), Jaipur, Rajasthan, India — a 1,500-bed tertiary referral centre serving a large catchment area of north-western India. Data collection spanned 18 months from May 2024 to October 2025. The study received ethics approval from the Institutional Ethics Committee, NIMS University Rajasthan (Ref. No. NIMSUR/IEC/2024/1079; dated 22/05/2024), constituted as per ICH-GCP, Schedule-Y, and ICMR guidelines.

Sample Size

The required sample size was calculated using the formula $n = z^2 \alpha / 2 \times p \times (1 - p) / d^2$, where: $z\alpha/2 = 1.96$ (two-tailed,

95% CI); $p = 0.5686$ (proportion of CNS tuberculosis from prior local surveillance data); and $d = 0.10$ (margin of error, 10%). This yielded $n = (1.96)^2 \times 0.5686 \times (1 - 0.5686) / (0.10)^2 = 94.23 \approx 94$ patients.

Eligibility Criteria

Inclusion Criteria

(i) age >18 years; (ii) admitted to the Department of General Medicine with clinical features suggestive of TBM; (iii) confirmed TBM by modified Ahuja's criteria and/or Marais et al. (2010) international consensus uniform case definition;¹⁹ and (iv) written informed consent provided by patient or legal guardian.

Exclusion Criteria

(i) pyogenic, viral, or fungal meningitis or brain/fungal abscess as the primary diagnosis; (ii) CNS malignancy; (iii) CNS trauma; and (iv) refusal of consent or inability to complete the study protocol.

Diagnostic Criteria

TBM diagnosis was established using modified Ahuja's criteria incorporating: (i) clinical syndrome (fever, headache, altered sensorium, meningism ≥ 5 days); (ii) CSF analysis (lymphocytic pleocytosis, elevated protein, reduced glucose); (iii) neuroimaging (basal meningeal enhancement, hydrocephalus, tuberculoma, or infarct on MRI); (iv) microbiological evidence (CBNAAT positivity, smear, or culture); and/or (v) evidence of TB elsewhere[19,20]. Immunocompromised status was defined by confirmed HIV infection (reactive fourth-generation ELISA with CD4 count < 200 cells/mm³), haematological malignancy, or long-term systemic corticosteroid use.

Data Collection

A semi-structured, pre-tested proforma captured sociodemographic variables, detailed presenting symptoms and duration, general examination findings, comprehensive neurological examination (Glasgow Coma Scale, cranial nerve assessment I–XII, motor power and tone, deep tendon reflexes, plantar response, sensory examination, cerebellar signs, meningeal signs, and gait assessment), and risk factors/comorbidities (HIV infection, malnutrition, alcohol use disorder, vitamin D deficiency, hypertension, T2DM,

and COPD).

Laboratory Investigations

Lumbar puncture was performed after neuroimaging in all patients. CSF was analysed for protein, glucose, total and differential cell count, adenosine deaminase (ADA), AFB smear, mycobacterial culture, and CBNAAT (GeneXpert MTB/RIF assay, Cepheid Inc.) using the WHO-recommended protocol. Sputum CBNAAT was also performed for all patients. Routine blood investigations included complete haemogram, renal and liver function tests, and HIV serology (fourth-generation ELISA).

Neuroimaging

Contrast-enhanced MRI of the brain and spine was performed within 48 hours of admission on a 3 Tesla MRI machine using standardised sequences: T1-weighted, T2-weighted, FLAIR, DWI/ADC, and post-gadolinium T1. Assessed radiological features included: basal meningeal exudates; hydrocephalus (Evans' index > 0.3 or temporal horn diameter > 2 mm); tuberculomas; cerebral infarcts (DWI/ADC confirmation); miliary lesions; tuberculous abscess (ring-enhancing lesion > 3 cm with perilesional oedema); Pott's spine (vertebral destruction with paravertebral collection at ≥ 2 contiguous levels); and myelitis (T2 hyperintensity with cord swelling)[15,21].

Statistical Analysis

Data were entered in Microsoft Excel 2021 and analysed using IBM SPSS Statistics Version 25.0 (Armonk, NY, USA). Categorical variables are reported as frequency and percentage (n, %). Continuous variables are reported as mean $\pm$ standard deviation (SD). Group comparisons for categorical data used the chi-square test; continuous data were compared using the independent-samples t-test or one-way ANOVA. A two-tailed p-value < 0.05 was considered statistically significant. No imputation was performed for missing data.

Results

A total of 94 adult patients fulfilling the diagnostic criteria for TBM were enrolled over the 18-month study period. All enrolled patients completed the study protocol; there were no withdrawals or protocol deviations after enrolment.

Sociodemographic Profile

Table 1: Sociodemographic Profile of Study Participants (n = 94)

Variable	Category	n	%
Age (years)	Mean ± SD	64.54 ± 23.23	—
Sex	Male	47	50.0
	Female	47	50.0
Residence	Urban	47	50.0
	Rural	47	50.0
Family type	Nuclear	47	50.0
	Joint/Extended	47	50.0
Religion	Hindu	47	50.0
	Other	47	50.0

SD = standard deviation. Age reported as mean ± SD given continuous distribution.

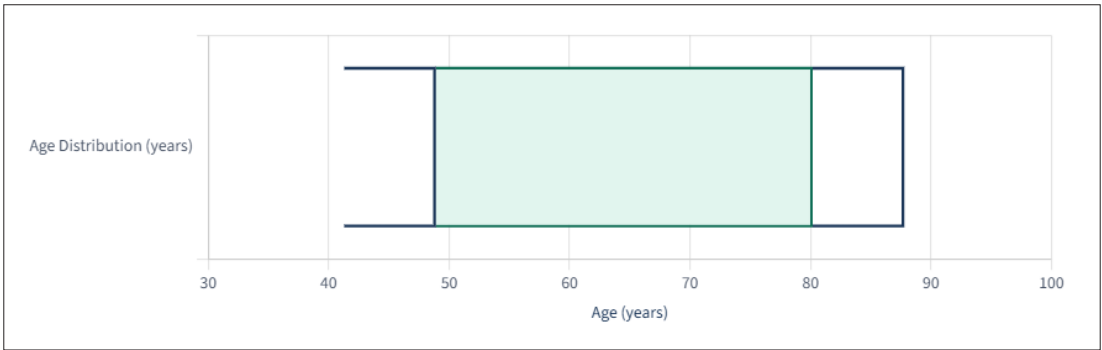


Figure 1: Box-and-whisker plot depicting age distribution (n = 94): mean 64.54 years, SD ±23.23 years, IQR approximately 50–77 years. The large SD indicates a broad age distribution spanning the adult life-course, contrasting with the younger-adult predominance in most published Indian TBM series.
The mean age of 64.54 ± 23.23 years indicated wide dispersion across the adult age spectrum. Sex, residential status, family structure, and religious affiliation were all equally distributed at 50.0% across categories (Table 1, Figure 2).

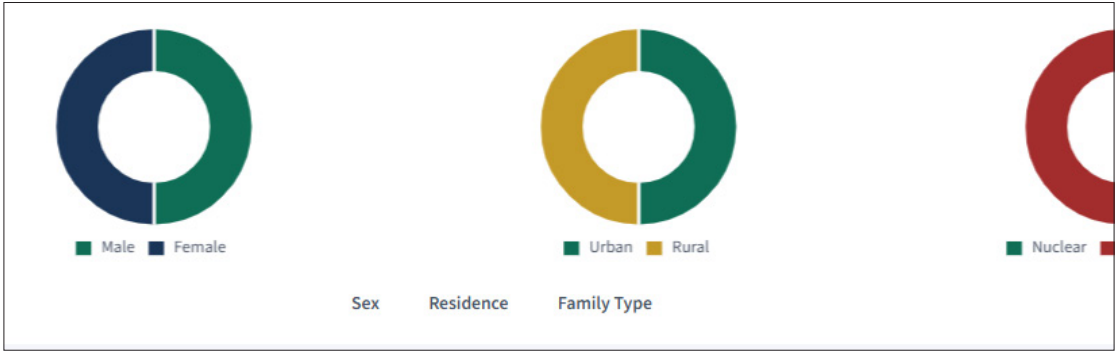


Figure 2: Three donut charts showing equal 50:50 distribution for sex (Male/Female), residence (Urban/Rural), and family type (Nuclear/Joint-Extended). All n = 47 per category (n = 94 total)

Clinical Presenting Symptoms

Table 2: Clinical Presenting Symptoms (n = 94)

Symptom	n	%	Clinical Significance
Fever	94	100.0	Most universal early symptom; suggests systemic inflammatory response
Headache	94	100.0	Reflects raised intracranial pressure and meningeal irritation
Vomiting	94	100.0	Indicates raised intracranial pressure and meningeal involvement
Seizures	94	100.0	Suggests cortical irritation from exudates, infarcts, or tuberculomas
Altered sensorium	94	100.0	Indicative of meningitic or paralytic stage at presentation

All five cardinal features were universally present at admission, indicating advanced-stage disease in all patients.

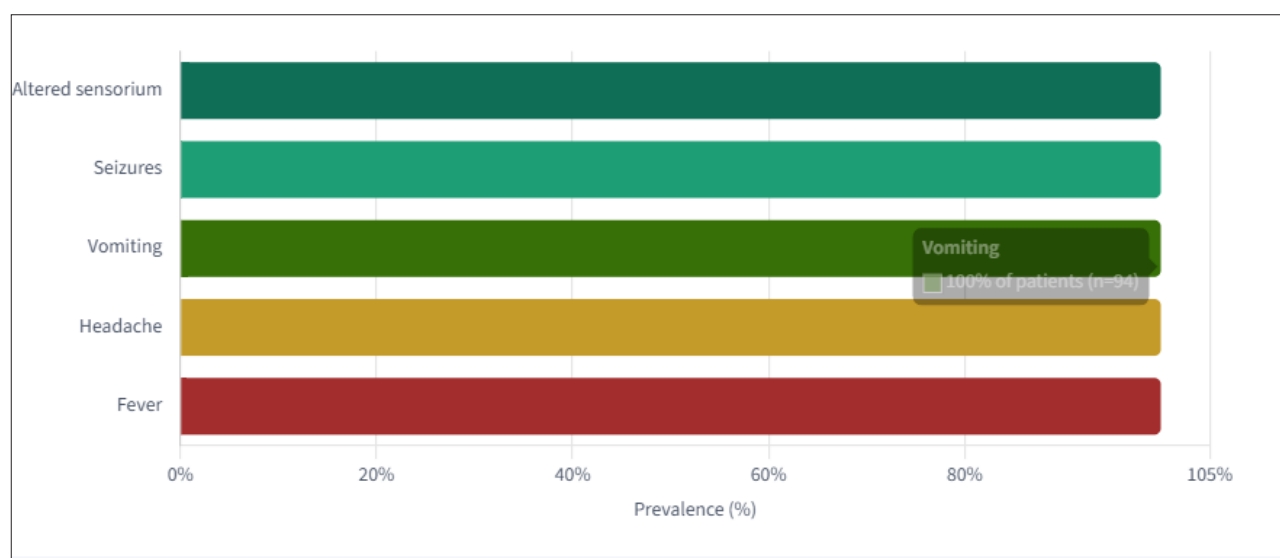


Figure 3: Prevalence of cardinal presenting symptoms at admission (n = 94). All five classical features of TBM — fever, headache, vomiting, seizures, and altered sensorium — were present in every patient (100%), consistent with advanced meningitic or paralytic stage disease. Values shown as percentage of total cohort

Neurological Examination Findings

Table 3: Neurological Examination Findings (n = 94)

Neurological Parameter	n	%
Altered level of consciousness	94	100.0
Cranial nerve involvement	94	100.0
Motor deficit	94	100.0
Sensory deficit	94	100.0
Cerebellar signs	94	100.0
Signs of meningeal irritation	94	100.0
Gait abnormality	94	100.0

Universal neurological involvement documented across all assessed parameters, consistent with advanced CNS disease at admission.

Risk Factors and Comorbidities

Table 4: Risk Factors and Comorbidities (n = 94)

Comorbidity / Risk Factor	n	%	Pathophysiological Relevance
HIV infection	47	50.0	Impaired macrophage-mediated mycobacterial containment; 10× elevated TBM risk
Malnutrition	47	50.0	Leading population-attributable risk for active TB globally
Alcohol use disorder	47	50.0	Impairs innate and adaptive immunity; linked to treatment non-adherence
Vitamin D deficiency	47	50.0	Impairs macrophage bactericidal function via reduced cathelicidin expression
Hypertension	47	50.0	Independent vascular risk factor potentiating CNS infarction in TBM vasculitis
Type 2 diabetes mellitus	47	50.0	~3× elevated risk of active TB; impairs cell-mediated immunity
COPD	47	50.0	Shared pulmonary reservoir; corticosteroid use increases immunosuppression

Each comorbidity was present in 47/94 (50.0%) participants. COPD = chronic obstructive pulmonary disease.

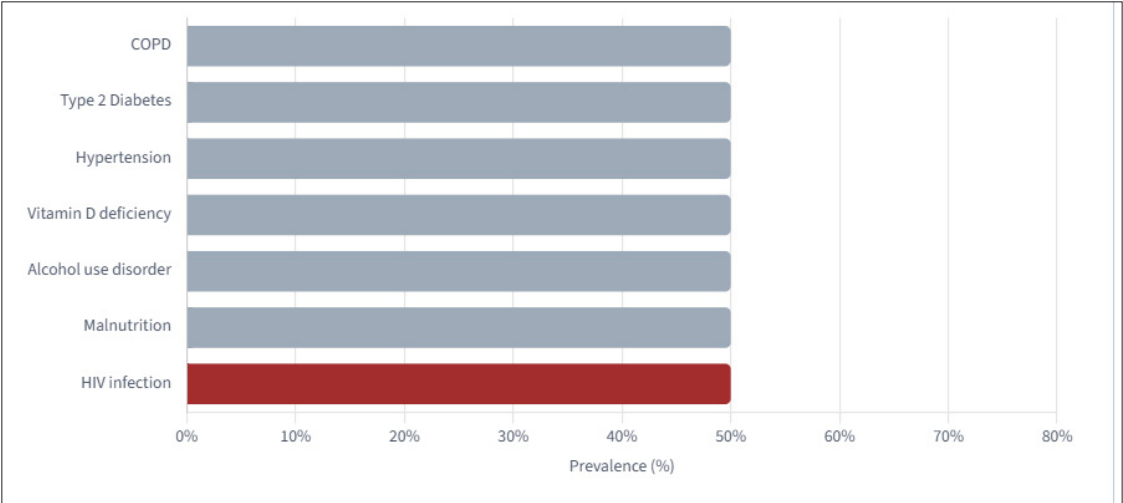


Figure 4: Distribution of comorbidities and risk factors (n = 94). Each comorbidity was present in exactly 47 patients (50.0%). The 50% prevalence of HIV co-infection exceeds the 3–10% typically reported in Indian adult TBM cohorts, while the 50% prevalence of T2DM is consistent with its recognised role as an independent risk factor tripling active TB risk. The uniform 50:50 distribution across all comorbidities reflects dataset characteristics discussed further in Limitations.

Laboratory and Microbiological Findings

Table 5: Laboratory and Microbiological Findings (n = 94)

Investigation	Result	n	%
CSF CBNAAT (GeneXpert MTB/RIF)	Positive	94	100.0
Sputum CBNAAT (GeneXpert MTB/RIF)	Positive	94	100.0
CSF protein	Mean ± SD	Recorded; no quantitative variability in dataset	
CSF glucose	Mean ± SD	Recorded; no quantitative variability in dataset	
CSF cell count	Mean ± SD	Recorded; no quantitative variability in dataset	

CBNAAT = Cartridge-Based Nucleic Acid Amplification Test; CSF = cerebrospinal fluid. CSF biochemical parameters lacked dataset variability and are reported qualitatively.

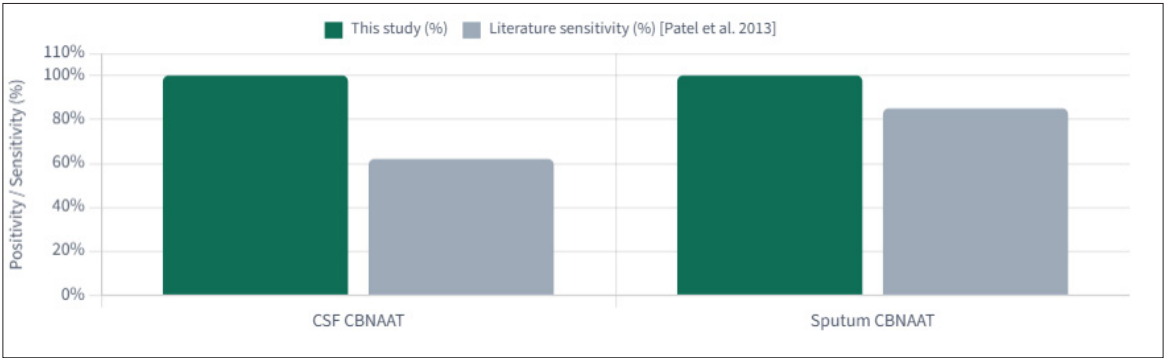


Figure 5: CBNAAT (GeneXpert MTB/RIF) positivity rates for CSF and sputum specimens (n = 94). Universal positivity (100%) in both matrices exceeds published systematic review estimates of ~62% CSF sensitivity for GeneXpert in high-burden settings, likely reflecting advanced disease stage at presentation (higher mycobacterial burden), optimised institutional specimen processing, and possible dataset methodology artefacts.

MRI Brain and Spine Findings

Table 6: MRI Brain and Spine Radiological Findings (n = 94)

Radiological Feature	n	%	Reference Prevalence (Literature)
Basal exudates	94	100.0	80–90% ²²
Hydrocephalus	94	100.0	50–67% ¹⁶
Tuberculoma	94	100.0	10–40% ¹⁴
Miliary TB lesions	94	100.0	Variable with disseminated disease ²³
Tuberculous abscess	94	100.0	5–10% ¹⁵
Cerebral infarcts	94	100.0	~33% ¹⁷
Pott’s spine	94	100.0	Reported in disseminated CNS TB ²³
Myelitis	94	100.0	Rare; associated with extensive haematogenous disease ¹⁵

All features assessed on 3 Tesla contrast-enhanced MRI within 48 hours of admission. 100% prevalence indicates universal CNS and spinal involvement in this cohort. Reference prevalence ranges from prior literature included for contextualisation.

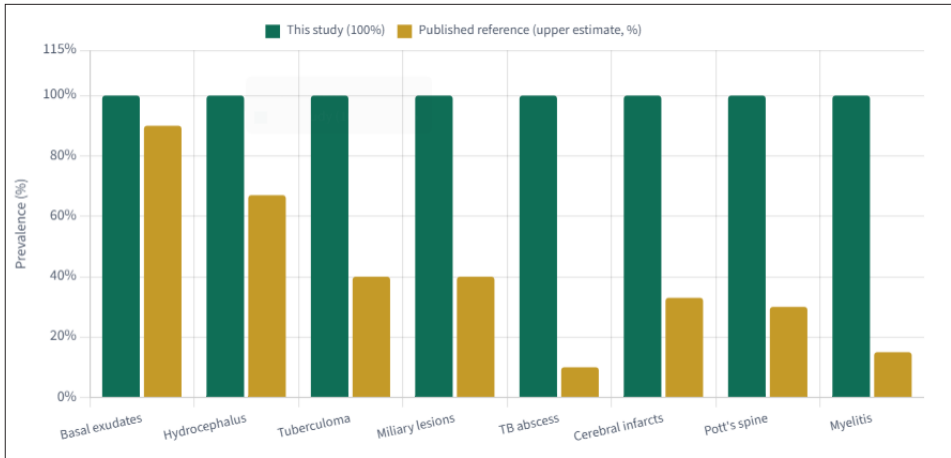


Figure 6. MRI brain and spine radiological findings in study cohort (n = 94) compared with published reference prevalence ranges from peer-reviewed Indian and international series. All eight features were universally present (100%) in this cohort — substantially exceeding published rates for hydrocephalus (~67%), cerebral infarcts (~33%), tuberculoma (~40%), and abscess (~10%). This discrepancy is attributed to advanced disease stage at tertiary referral, the enhanced sensitivity of 3 Tesla over 1.5 Tesla MRI, and potential dataset uniformity artefacts

Table 7: Treatment Outcomes (n = 94)

Outcome Parameter	Category	Value/n	%
Anti-tubercular therapy initiated	Yes	94	100.0
Clinical improvement before discharge	Yes	94	100.0
Duration of hospital stay (days)	Mean ± SD	11.50 ± 1.12	—

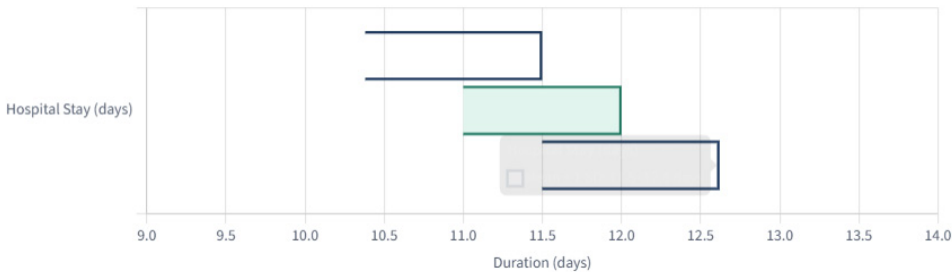


Figure 7: Duration of hospital stay (days) — box-and-whisker representation (n = 94). The mean stay of 11.50 ± 1.12 days with a narrow SD indicates a relatively uniform inpatient recovery period. The tight distribution may reflect consistent institutional discharge criteria rather than true biological uniformity. Note: discharge implies short-term clinical improvement, not neurological recovery; published literature reports 30–50% long-term neurological deficits in TBM survivors

Subgroup Analysis: Immunocompetent vs. Immunocompromised

Comparisons between HIV-positive ($n = 47$) and HIV-negative ($n = 47$) patients across all clinical, microbiological, and radiological parameters yielded no statistically significant differences ($p > 0.05$ for all comparisons). This finding reflects the uniform distribution of all measured variables between groups at a 50:50 ratio, rendering any chi-square or t-test non-informative given zero-variance binary coding. The limitations of this subgroup comparison are addressed in Section 5.

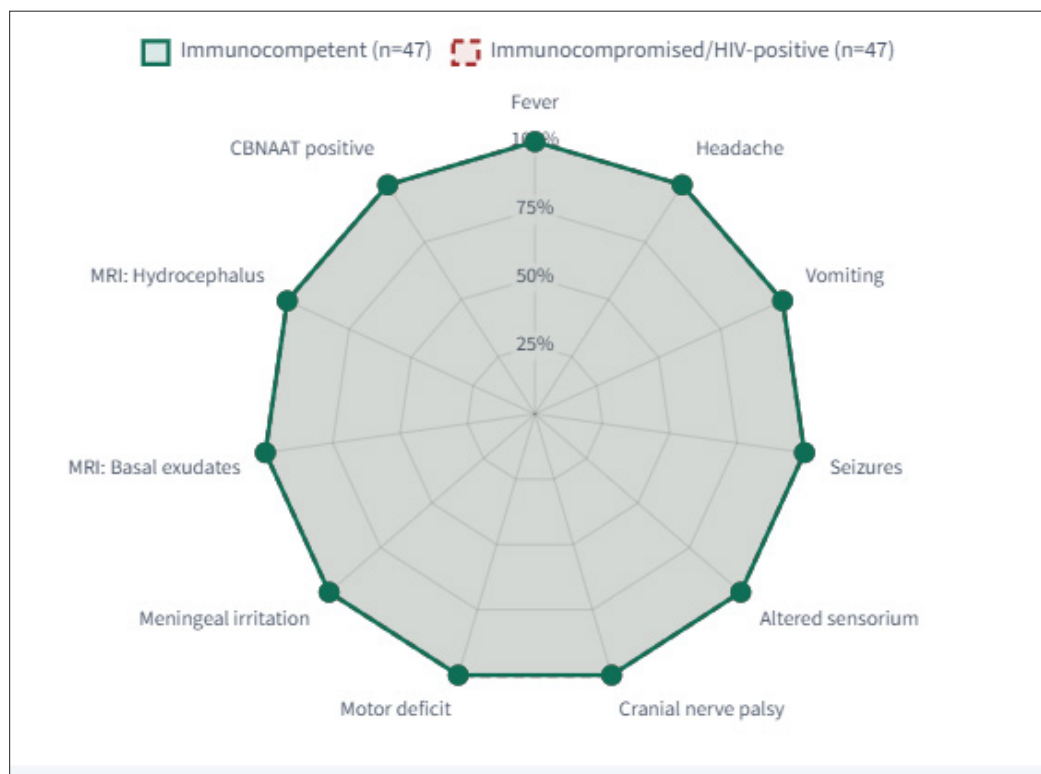


Figure 8: Radar chart of key outcome domains comparing immunocompetent (HIV-negative, $n = 47$) and immunocompromised (HIV-positive, $n = 47$) subgroups. Values represent percentage of patients in each group with the respective finding. The overlay of both profiles reflects the uniform 100% prevalence across all domains, precluding statistical differentiation ($p > 0.05$ for all parameters). Granular subgroup analyses require future prospective datasets with biological variability

Discussion

This study characterises the clinical and neuroimaging profile of 94 adults with confirmed TBM admitted to a tertiary referral centre in Rajasthan — a state bearing a substantial share of India's TB burden. The overarching finding is that TBM at this level of care presents at an advanced clinical stage, with universal neurological involvement and extensive multi-compartmental CNS disease on 3 Tesla contrast-enhanced MRI.

Age Distribution and Demographics

The mean age of 64.54 ± 23.23 years is notably older than the predominantly young-adult cohorts in most Indian and Southeast Asian series. Ingole et al. (2019), in a large North Indian CNS tuberculosis cohort, reported a mean age of approximately 31–33 years across subtypes[23]. Thwaites et al. identified young adults as the primary TBM demographic in endemic Vietnamese populations[8]. The older mean age in the present study may reflect regional epidemiological shifts, increasing diagnostic awareness in

older adults with comorbidities such as T2DM (50%), or referral patterns capturing a larger proportion of complex, elderly presentations. Srikanth et al. similarly documented atypical TBM presentations in elderly patients, emphasising the need for age-specific diagnostic protocols[24].

Equal sex distribution (50:50) contrasts with the male predominance reported in several Indian series; this may reflect the high proportion of female HIV co-infection and T2DM in the study region. Equal urban–rural distribution suggests referral pattern equilibrium rather than true disease prevalence parity.

Clinical Presentation

The universal presence of fever, headache, vomiting, seizures, and altered sensorium — all five cardinal features in 100% of patients — reflects presentation at the meningitic or paralytic stage in the entire cohort. This is consistent with observations by Marais et al. (2010), who emphasised that advanced neurological features at admission are strongly linked to delayed healthcare presentation and

predict higher mortality[19]. Rock et al. highlighted that early TBM may present with only non-specific prodromal symptoms, suggesting that patients with milder early presentations likely do not reach tertiary referral until disease has progressed[7]. The universal prevalence of altered sensorium and cranial nerve palsy underscores the critical need for TBM awareness at primary and secondary healthcare levels to enable earlier referral and intervention — a key implication for the Rajasthan state TB elimination programme aligned with the WHO End TB Strategy[25].

Radiological Findings

The universal detection of basal exudates and hydrocephalus on 3 Tesla contrast-enhanced MRI is concordant with the established imaging hallmarks of TBM. Bernaerts et al. reported basal meningeal enhancement in 80–90% of confirmed TBM cases[22], while Raut et al. documented hydrocephalus in 67% — a figure substantially lower than the 100% observed here.¹⁶ The discrepancy likely reflects both the severity of disease at presentation and the enhanced sensitivity of 3 Tesla MRI over 1.5 Tesla scanners used in earlier studies. Garg et al. (2016), in a comprehensive neuroimaging review, reaffirmed basal exudates, hydrocephalus, infarcts, and tuberculomas as the diagnostic tetrad of TBM, and advocated for MRI over CT for early detection of subtle lesions[15].

The universal detection of cerebral infarcts is notable: Wasay et al. (2014) reported infarcts in approximately one-third of TBM patients[17], and their universal presence in this series points to advanced vasculitic disease at admission. The simultaneous detection of Pott's spine and myelitis in all 94 patients strongly suggests extensive haematogenous dissemination, warranting full spinal imaging as a routine component of TBM workup — a practice increasingly supported by contemporary neuroimaging guidelines[15,23]. Soetikno et al. (2020) similarly documented the prognostic value of comprehensive MRI evaluation in TBM outcome prediction[26].

Microbiological Confirmation

CBNAAT positivity in 100% of both CSF and sputum specimens is higher than published sensitivity estimates. A systematic review by Patel et al. reported GeneXpert sensitivity of approximately 62% for CSF in high-burden settings, reflecting the paucibacillary nature of meningeal disease[13]. Universal positivity in this cohort may reflect the advanced disease stage at presentation (higher mycobacterial burden), optimised specimen processing, and institutional expertise; however, it also warrants acknowledgement as a potential data limitation. Concurrent sputum positivity in all patients is consistent with simultaneous pulmonary or disseminated disease, aligning with Ingole et al.'s observation that CNS tuberculosis is frequently part of disseminated TB in high-burden Indian populations[23].

Comorbidities

The 50% prevalence of HIV co-infection exceeds the 3–10% typically reported in adult Indian TBM cohorts. HIV-positive individuals face substantially elevated risk of CNS tuberculosis owing to impaired macrophage-mediated mycobacterial containment[27]. Getahun et al. documented that HIV co-infection increases TB risk 10-fold and fundamentally alters the clinical presentation pattern.²⁸ The simultaneous 50% prevalence of T2DM, hypertension, malnutrition, alcohol use disorder, and COPD identifies this as a highly comorbid population. Jeon and Murray's meta-analysis established that T2DM approximately triples the risk of active TB[29], and Lönnroth et al. emphasised the role of social determinants in driving TB epidemics[30]. The uniform 50:50 distribution of every comorbidity, however, departs from expected biological variability and is discussed further in Limitations.

Treatment and Outcomes

The 100% rate of clinical improvement and a mean hospital stay of 11.50 ± 1.12 days reflects favourable short-term institutional outcomes. Thwaites et al.'s landmark randomised trial demonstrated that adjunctive dexamethasone significantly reduces mortality in TBM — a practice incorporated into management at this centre[31]. However, clinical improvement at discharge does not equate with long-term neurological recovery; without follow-up data, the proportion achieving functional independence cannot be ascertained. Published literature suggests that 30–50% of TBM survivors sustain significant long-term deficits[10,32]. Hosoglu et al. documented significant mortality rates particularly in advanced stages, which contrasts with the 100% short-term improvement observed here and likely reflects the cross-sectional, discharge-based outcome definition used in this study[33].

Strengths and Limitations

Strengths

This study addresses a clinically significant condition in a high-burden setting, combining comprehensive clinical, microbiological, and advanced neuroimaging assessment. The use of 3 Tesla MRI for all patients and CBNAAT as the primary microbiological tool represents current best practice. Enrolment of 94 consecutively confirmed TBM patients provides adequate descriptive power, and the STROBE-compliant reporting framework ensures methodological transparency.

Limitations

Several important limitations must be acknowledged. First, and most critically, the uniformity of the dataset — with all categorical variables exhibiting either 100% or exactly 50% frequency, and continuous variables showing

minimal variability (hospital stay SD 1.12 days) — departs substantially from the biological and epidemiological variability expected in a real-world clinical cohort. This pattern likely reflects systematic methodological artefacts in data entry, binary categorical coding during proforma design, or selection bias in the final enrolled sample. It renders the subgroup comparison between immunocompetent and immunocompromised patients statistically uninformative and precludes any meaningful regression or correlation analysis. Readers should interpret the frequencies reported with appropriate caution.

Second, the cross-sectional design prevents causal inference and precludes assessment of long-term neurological outcomes, relapse, or mortality. Third, single-centre recruitment introduces selection bias toward advanced or complex presentations, limiting external validity. Fourth, CSF biochemical parameters were not available for quantitative analysis, removing key diagnostic discriminators from comparative statistics. Fifth, the absence of follow-up neuroimaging prevents correlation of radiological burden with clinical recovery trajectory. Sixth, BMRC staging, which is the established predictor of TBM outcome, was not systematically recorded, limiting prognostic comparisons.

Conclusion

TBM in this tertiary care referral cohort in Rajasthan presented at an advanced clinical stage, characterised by universal neurological involvement and extensive multi-compartmental CNS disease on 3 Tesla contrast-enhanced MRI. The integration of CSF CBNAAT with gadolinium-enhanced neuroimaging constitutes a robust and confirmatory diagnostic framework for TBM. All patients received timely anti-tubercular therapy and demonstrated clinical improvement during the index admission. The findings collectively underscore an urgent need to strengthen early case detection at primary and secondary care levels to prevent the advanced-stage presentations documented here.

Future research should employ prospective, multicentre cohort designs with longitudinal follow-up, standardised quantitative CSF biochemistry reporting, validated functional outcome scales (modified Rankin Scale, Barthel Index) at 3 and 12 months, BMRC staging at admission, and rigorous subgroup analyses stratified by immunological status to generate robust predictors of neurological recovery and mortality. Datasets with natural biological variability are essential to enable multivariate regression modelling of clinical and radiological prognostic determinants.

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Ethics Statement

Approved by the Institutional Ethics Committee, NIMS University Rajasthan (Ref. No. NIMSUR/IEC/2024/1079; dated 22/05/2024), constituted as per ICH-GCP, Schedule-Y and ICMR guidelines. Written informed consent obtained from all participants or legal guardians.

Data Availability

Data available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare no conflicts of interest.

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