

Original Article

Asian Pacific Journal of Tropical Medicine

apjtm.org

doi: 10.4103/apjtm.apjtm_60_24

Predictors of cerebrospinal fluid GeneXpert MTB/RIF positivity in patients with tuberculous meningitis: A prospective cohort study

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ABSTRACT

Objective: To identify the clinical, laboratory, and radiological markers that could predict a positive GeneXpert result in patients suspected of tuberculous meningitis.

Methods: In this prospective, observational study, patients with tuberculous meningitis were systematically evaluated. Various clinical, laboratory [including cerebrospinal fluid (CSF) microscopy, culture, and GeneXpert], and neuroimaging factors were examined. All participants were administered anti-tuberculous treatment and corticosteroids. A six-month follow-up was done to evaluate the outcome.

Results: Of the 116 patients studied, 54 (46.6%) tested positive for GeneXpert, while 62 (53.4%) were negative. Third cranial nerve involvement (*OR* 3.71, 95% *CI* 1.052-13.09, *P*=0.04) and the presence of basal exudates on neuroimaging (*OR* 5.22, 95% *CI* 2.03-13.42, *P*=0.001) emerged as independent predictive factors for a positive GeneXpert result. A positive CSF GeneXpert result (*P*=0.002) and drug resistance (*P*=0.004) were significantly linked to adverse outcomes. Additionally, a high score on the Medical Research Council stage III (*OR* 5.64, 95% *CI* 1.18-26.87, *P*=0.03) and elevated CSF cell counts (*OR* 1.002, 95% *CI* 1.00-1.001, *P*=0.03) were identified as independent predictors of poor prognosis.

Conclusions: Third cranial nerve involvement and the presence of basal exudates were significant indicators of a positive GeneXpert result. MRC stage III disability and elevated CSF cell counts predicted poor outcomes.

KEYWORDS: Tuberculous meningitis; *Mycobacterium tuberculosis*; Cerebrospinal fluid; Ziehl-Neelsen staining; GeneXpert

1. Introduction

Tuberculous meningitis (TBM) is one of the most severe manifestations of central nervous system tuberculosis, comprising 5%-10% of extra-pulmonary and 1%-5% of all tuberculosis cases. Despite treatment, TBM has a poor prognosis, with 50% of patients either dying or suffering from disabilities[1]. Tuberculous meningitis is challenging to diagnose and treat. Recent research highlights advances in molecular diagnostics, such as GeneXpert MTB/RIF, and new anti-tuberculosis drug regimens. Effective management of complications like brain infarcts and hydrocephalus is crucial. Rapid diagnosis and early treatment initiation are vital for improving

Significance

Tuberculous meningitis is one of the most severe manifestations of central nervous system tuberculosis. This study highlights the predictors of GeneXpert positivity based on clinical (third nerve palsy) and radiological (basal exudates) parameters. Elevated CSF cell counts were associated with poor outcome. These findings in patients alerts the clinician for a vigilant follow-up.

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How to cite this article: Gupta P, Kumar N, Garg RK, Malhotra HS, Rizvi I, Verma R, et al. Predictors of cerebrospinal fluid GeneXpert MTB/RIF positivity in patients with tuberculous meningitis: A prospective cohort study. Asian Pac J Trop Med 2024; 17(10): 465-472.

Article history: Received 23 January 2024 Revision 19 September 2024
Accepted 21 September 2024 Available online 26 October 2024

outcomes. Emerging drug resistance poses a threat, but new drugs and technologies provide hope[2].

Traditional diagnostic methods for TBM, such as microscopy for acid-fast bacilli (AFB) and *Mycobacterium* (*M.*) *tuberculosis* culture, have low sensitivity rates. For example, the sensitivity of standard Ziehl-Neelsen staining is around 10%, with only a slight improvement using fluorescence microscopy. *M. tuberculosis* culture, often regarded as the gold standard, takes weeks to produce results and has a sensitivity rate of only 40%-50%[3,4].

The introduction of genotypic tests such as the Xpert MTB/RIF assay has enabled faster and more accurate diagnosis of TBM. Xpert MTB/RIF assay provides results within 2 hours and is now part of the Indian Revised National Tuberculosis Control Program. However, its sensitivity varies widely across studies, and it still faces challenges, including the need for CSF sampling, which can be logistically difficult or medically contraindicated in certain cases[5,6].

In response to these challenges, our study aimed to identify clinical, investigational, and radiological factors that could predict the likelihood of a positive GeneXpert test result in suspected TBM cases. We also monitored patient outcomes over a six-month follow-up period.

2. Subjects and methods

This prospective cohort study was conducted between July 2021 and June 2023, in the Department of Neurology at King George's Medical University Lucknow India. Prior ethical approval was obtained from the Institutional Ethics Committee (No.732/Ethics/2021 dated 1/7/21). Before enrolment, written informed consent was taken from the patients or their legal guardians.

2.1. Inclusion criteria

We enrolled all the consecutive patients suspected of tuberculous meningitis according to the standardized case definition proposed by Marais *et al*[7]. Marais *et al*. criteria for diagnosing TBM include clinical symptoms, CSF findings, and neuroimaging results. Major criteria are longer duration of illness, focal deficits, specific CSF abnormalities, and neuroimaging signs like basal enhancement. Diagnosis is classified as definite, probable, or possible TBM based on a scoring system, incorporating clinical and laboratory evidence[7]. The eligible patients were admitted from the Neurology Emergency and Outpatient Department.

2.2. Exclusion criteria

Patients who were established with alternative diagnosis (*i.e.* non-tuberculous), patients with HIV co-infection, patients with tuberculous meningitis who were already taking anti-tuberculosis treatment, and patients who denied consent were excluded from the study (Figure 1).

2.3. Clinical evaluation

A detailed history was taken from all subjects. A comprehensive general and systemic examination was done. The neurological examination included higher mental functions, cranial nerve, motor system, sensory system, and assessment of signs of meningeal irritation.

2.4. Disease severity

The British Medical Research Council staging system was used to categorize patients at presentation. Patients with stage Ⅰ disease had a Glasgow Coma Scale score of 15 and no focal neurologic signs; patients with stage Ⅱ had meningeal irritation with slight or no alteration of sensorium and minor neurological deficit (like cranial nerve palsies) or no deficit (Glasgow coma scale score 11-14); and patients with stage Ⅲ had severe sensorium alteration, convulsions, focal neurological deficit, and involuntary movements (Glasgow coma scale score ≤10)[8].

2.5. Laboratory evaluation

At baseline, the workup included routine hematological and biochemical tests, a chest X-ray, and an enzyme-linked immunosorbent assay for human immunodeficiency virus.

CSF was collected in large volumes (10-15 mL) under full aseptic conditions and transported to the microbiology laboratory. A part of the sample was used for biochemical and microscopic examinations, including India-ink preparation. Rest (8-10 mL) CSF was centrifuged at 3 000×*g* for 15 min. After centrifugation the supernatant was discarded and pellets were used for further testing (AFB staining, GeneXpert, Liquid Culture). CSF sediments were inoculated into Mycobacteria Growth Indicator Tubes and monitored for growth and drug susceptibility testing. The GeneXpert test was conducted on CSF specimens according to the manufacturer's protocol.

2.6. Neuroimaging

All patients underwent MR imaging of the brain with contrast using a Signa Excite 1.5 Tesla device (General Electric Medical Systems, Milwaukee, WI, USA).

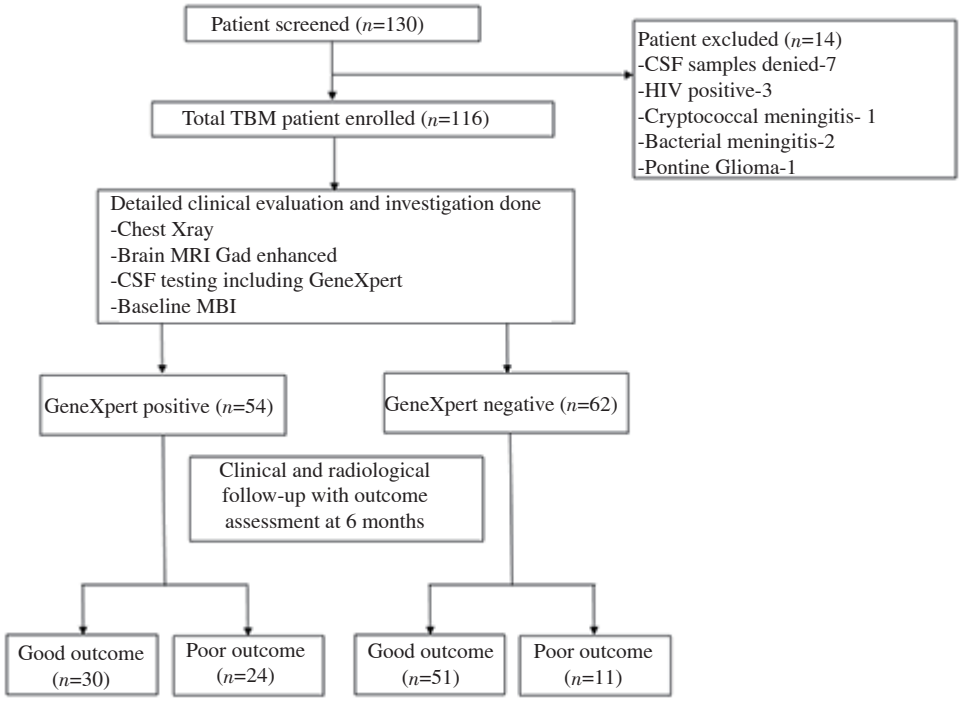


Figure 1. Flow diagram of the study. CSF, cerebrospinal fluid; HIV, human immunodeficiency virus; MBI, Modified Barthel Index; MRI, magnetic resonance imaging; TBM, tuberculous meningitis.

2.7. Treatment

All the patients were administered antitubercular medications following World Health Organisation standards for tuberculous meningitis therapy. During the intensive phase (first two months), all patients were given four drugs: isoniazid (5 mg/kg/day; maximum dosage 300 mg/day), rifampicin (10 mg/kg/day; maximum dose 600 mg/day), pyrazinamide (25 mg/kg; maximum dose 2 g/day), and intramuscular streptomycin (20 mg/kg/day; maximum dose 1 g/day). In the continuation phase (7 months), isoniazid (5 mg/kg/day; maximum dose 300 mg/day) and rifampicin were continued. All patients were also given corticosteroids in the form of dexamethasone. Intravenous dexamethasone was begun at 0.4 mg/kg/day and gradually decreased over the following 4 weeks, followed by oral dexamethasone for 4 weeks, commencing at 4 mg per day and gradually tapering by 1 mg per week[8,9]. Pyridoxine (20-40 mg/day) was administered to all patients.

Patients diagnosed with drug-resistant tuberculous meningitis were treated according to the World Health Organization's recommended guidelines for drug-resistant pulmonary tuberculosis, under the supervision of a tuberculosis expert at our institute[10].

2.8. Follow–up and outcome assessment

Patients were monitored for six months, with monthly evaluations in the neurology outpatient department. Outcomes were assessed based on the Modified Barthel Index (MBI) score. Poor outcome was defined as MBI$\leqslant$12 (Disability including death). Good outcome was defined as MBI 13-20[11].

2.9. Statistical analysis

IBM SPSS version 24.0 was used for data analysis. Continuous variables were summarized as mean±standard deviation (SD), and median (IQR), while categorical variables were expressed in percentages. Tests like the *Chi*-square/Fisher's exact test, and Mann-Whitney *U*-test were used for comparisons. Variables with $P<0.05$ in the univariate analysis were included in the multivariate analysis. Factors independently associated with GeneXpert positivity and poor outcome were identified using binary logistic regression in the multivariate analysis. A *P*-value below 0.05 was considered statistically significant.

Table 1. Comparison of baseline clinical, neuroimaging and laboratory parameters of cerebrospinal fluid GeneXpert positive and cerebrospinal fluid GeneXpert negative groups.

Variable	CSF GeneXpert positive group (*n*=54)	CSF GeneXpert negative group (*n*=62)	*P*-value	Odds ratio (95% confidence interval)
Age, years, median (IQR)^	23 (19, 30)	25 (19, 30)	0.64	NA
Sex				
Male	21 (38.9)	21 (33.9)	0.57	1.24 (0.58-2.65)
Female	33 (61.1)	41 (66.1)		
Duration of illness, days, median (IQR)^	30.0 (25.0, 60.0)	52.5 (28.7, 90.0)	0.14	NA
Fever	54 (100)	62 (100)	NA	NA
Headache	50 (92.6)	57 (91.9)	0.89	1.09 (0.27-4.30)
Vomiting	31 (57.4)	40 (64.5)	0.43	0.74 (0.35-1.57)
Seizure	29 (53.7)	24 (38.7)	0.10	1.83 (0.88-3.84)
Altered sensorium	39 (72.2)	36 (58.1)	0.11	1.88 (0.86-4.09)
Neck rigidity	52 (96.3)	59 (95.2)	0.76	1.32 (0.21-8.22)
Hemiparesis#	8 (14.8)	9 (14.5)	0.96	1.02 (0.36-2.87)
Paraparesis#	2 (3.7)	7 (11.3)	0.13	0.30 (0.60-1.52)
Papilledema#	8 (14.8)	15 (24.2)	0.21	0.54 (0.21-5.41)
Visual impairment	16 (29.6)	15 (24.2)	0.51	1.32 (0.58-3.00)
3rd CN involvement	15 (27.8)	5 (8.1)	**<0.01**	4.37 (1.47-13.05)
6th CN involvement	27 (50.0)	24 (38.7)	0.22	1.58 (0.76-3.31)
7th CN involvement#	6 (11.1)	1 (1.6)	**0.03**	7.62 (0.66-18.64)
Multiple CN involvement	16 (29.6)	10 (16.1)	0.08	2.19 (0.89-5.35)
Baseline MBI				
Stage Ⅰ#	8 (14.8)	20 (32.3)		
Stage Ⅱ	28 (51.9)	30 (48.4)	**0.03**	2.74 (1.09-6.88)
Stage Ⅲ	18 (33.3)	12 (19.4)		
Baseline MBI				
≤12	48 (88.9)	42 (67.7)	**<0.01**	0.26 (0.09-0.71)
13-20#	6 (11.1)	20 (32.3)		
Hydrocephalus	24 (44.4)	22 (35.5)	0.33	1.45 (0.69-3.07)
Basal exudates	45 (83.3)	25 (40.3)	**<0.01**	7.40 (3.07-17.80)
Meningeal enhancement	54 (100)	60 (96.8)	0.18	1.90 (1.59-2.26)
Infarcts	15 (27.8)	14 (22.6)	0.52	1.32 (0.57-3.06)
Tuberculomas	49 (90.7)	53 (85.5)	0.39	1.66 (0.52-5.30)
Chest X-ray abnormalities#	9 (16.7)	8 (12.9)	0.67	NA
CSF cells, median (IQR)^	135.0 (47.5, 212.5)	75.0 (9.5, 172.5)	**0.05**	NA
CSF protein, mg/dL, median (IQR)^	164.0 (107.7, 208.0)	141.5 (101.2, 221.2)	0.63	NA
CSF sugar, mg/dL, median (IQR)^	28.5 (18.0, 46.2)	36.0 (22.7, 62.0)	0.06	NA
Serum sodium, mmol/L, median (IQR)^	130.0 (125.0, 133.0)	132.0 (128.0, 135.0)	**0.02**	NA

^Data are expressed as median and interquartile range (IQR) and compared using Mann-Whitney *U* test; otherwise, data are expressed as *n* (%) and compared using *Chi* square (χ^2) test or #Fisher's exact test. *P*-value below 0.05 (in bold) was considered statistically significant. CN, cranial nerve; MBI, Modified Barthel Index.

3. Results

We screened 130 presumptive TBM patients, out of which 116 patients satisfied the defined inclusion criteria. The mean age was (25.8±10.4) years. The male-to-female ratio was 0.57.

In our cohort of 116 patients, 54 (46.6%) tested positive for GeneXpert and 62 (53.4%) tested negative (Figure 1 and Table 1). Among those who were GeneXpert positive, 15 (27.7%) also tested positive in culture and 9 (16.6%) had positive Acid-Fast Bacilli (AFB) staining. On the other hand, among the GeneXpert negative patients, 4 (6.5%) still tested positive in culture, but none showed positive AFB staining (Table 1).

3.1. Predictors of GeneXpert positivity

Univariate analysis revealed that a baseline MBI of ≤12 ($P<0.01$), Medical Research Council (MRC) stage Ⅲ ($P=0.03$), cranial nerve Ⅲ (3rd CN) involvement ($P<0.01$), cranial nerve Ⅶ (7th CN) involvement ($P=0.03$), serum sodium levels ($P=0.02$), cerebrospinal fluid (CSF) cell count ($P=0.05$), and the presence of basal exudates ($P<0.01$) were all significantly associated with GeneXpert positivity. However, upon a multivariate logistic regression analysis, cranial nerve Ⅲ involvement (*OR* 3.71, *CI* 1.052-13.09, $P=0.04$) and basal exudates (*OR* 5.22, *CI* 2.03-13.42, $P<0.01$) emerged as independent predictors for GeneXpert positivity.

Table 2. Outcome assessment at 6 months in patients with tuberculous meningitis.

Variable	Poor outcome (Death or MBI ⩽12) (*n*=35)	Good outcome (MBI: 13-20) (*n*=81)	*P*-value	Odds ratio (95% confidence interval)
Age, years, median (IQR)^	21 (18, 32)	25 (19, 30)	0.53	NA
Sex				
Male	11 (31.4)	31 (38.3)	0.48	0.74 (0.32-1.72)
Female	24 (68.6)	50 (61.7)		
Fever	35 (100)	81 (100)	NA	NA
Headache	31 (88.6)	76 (93.8)	0.33	0.51 (0.13-2.03)
Vomiting	21 (60.0)	50 (61.7)	0.86	0.93 (0.41-2.09)
Seizures	19 (54.3)	34 (42.0)	0.22	1.64 (0.74-3.64)
Altered sensorium	22 (62.9)	53 (65.4)	0.79	0.89 (0.39-2.04)
Neck rigidity	34 (97.1)	77 (95.1)	0.68	1.76 (0.19-16.39)
Hemiparesis	10 (28.6)	7 (8.6)	**<0.01**	4.23 (1.45-12.29)
Paraparesis#	4 (11.4)	5 (6.2)	0.45	1.96 (0.49-7.79)
Visual impairment#	7 (20.0)	24 (29.6)	0.28	0.59 (0.23-1.54)
Papilledema#	5 (14.3)	18 (22.2)	0.45	0.58 (0.19-1.72)
3rd CN involvement#	9 (25.7)	11 (13.6)	0.11	2.20 (0.82-5.92)
6th CN involvement	13 (37.1)	38 (46.9)	0.33	0.67 (0.29-1.50)
7th CN involvement#	4 (11.4)	3 (3.7)	0.12	3.35 (0.71-15.86)
Multiple CN involvement	10 (28.6)	16 (19.8)	0.29	1.62 (0.65-4.05)
Baseline MBI				
Stage Ⅰ#	3 (8.6)	25 (30.9)		
Stage Ⅱ	18 (51.4)	40 (49.4)	**<0.05**	NA
Stage Ⅲ	14 (40.0)	16 (19.8)		
Baseline MBI				
⩽12	31 (88.6)	59 (72.8)	0.08	0.34 (0.11-1.09)
13-20#	4 (11.4)	22 (27.2)		
Hydrocephalus	20 (57.1)	26 (32.1)	**<0.05**	2.82 (1.25-6.37)
Basal exudates	28 (80.0)	42 (51.9)	**<0.01**	3.71 (1.45-9.47)
Meningeal enhancement	35 (100)	79 (97.5)	1	1.44 (1.27-1.63)
Infarcts	12 (34.3)	17 (21.0)	0.13	1.96 (0.81-4.73)
Tuberculomas	33 (94.3)	69 (85.2)	0.22	2.87 (0.61-13.56)
Chest X-ray abnormalities#	7 (20.0)	10 (12.3)	0.36	NA
CSF cells, median (IQR)^	140 (68, 260)	85 (13, 180)	**0.02**	NA
CSF protein, mg/dL, median (IQR)^	175 (140, 252)	141 (102, 208)	0.07	NA
CSF sugar, mg/dL, median (IQR)^	27 (17, 47)	34 (22, 51)	0.13	NA
CSF GeneXpert positive	24 (68.6)	30 (37.0)	**<0.01**	3.70 (1.59-8.62)
Drug resistance#	6 (17.1)	0	**<0.01**	NA

^Data are expressed as median and interquartile range (IQR) and compared using Mann-Whitney *U* test; otherwise, data are expressed as *n* (%) and compared using *Chi* square (χ^2) test or #Fisher's exact test. *P*-value below 0.05 (in bold) was considered statistically significant. CN, cranial nerve; MBI, Modified Barthel Index.

3.2. Follow-up

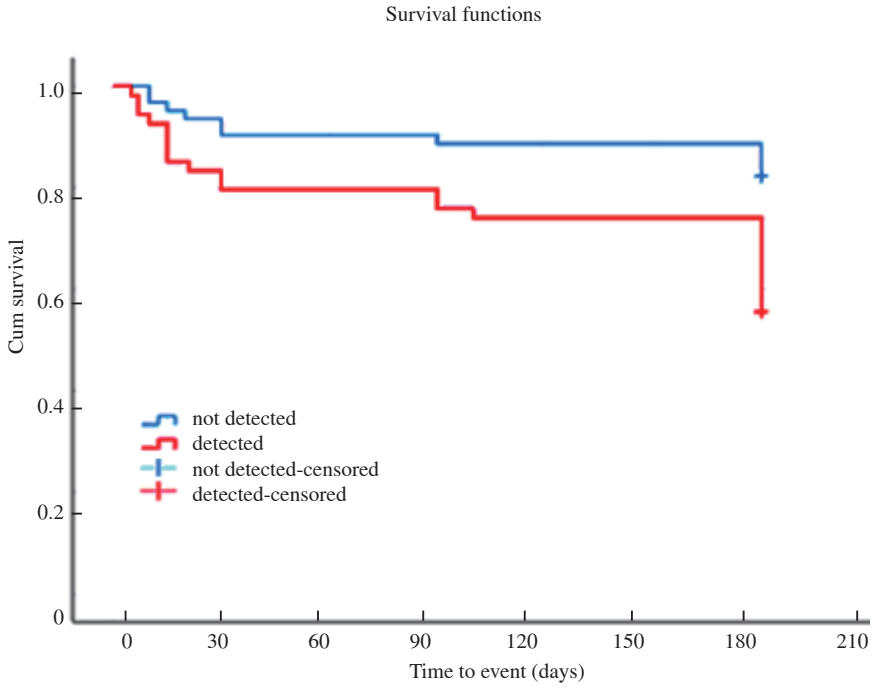
During follow-up, 21 patients died, out of which 14 (66.7%) patients were GeneXpert positive and 7 (33.3%) patients were GeneXpert negative. At 6 months, 35 (30.2%) patients showed poor outcomes (death or MBI ⩽12), while 81 (69.8%) patients showed good outcomes (MBI 13-20). Among the patients with poor outcomes, 24 (68.6%) patients were GeneXpert positive, while among the patients with good outcomes, 30 (37.0%) were GeneXpert positive (*P*<0.01) (Table 2).

3.3. Predictors of poor outcome

On univariate analysis of baseline clinical, laboratory, and imaging parameters, hemiparesis (*P*<0.01), MRC stage Ⅲ (*P*<0.05), hydrocephalus (*P*<0.05), basal exudates (*P*<0.01), CSF GeneXpert positivity (*P*<0.01), drug resistance (*P*<0.01) were significantly associated with poor outcome. On multivariate analysis using binary logistic regression analysis, MRC stage Ⅲ (*OR* 5.64, 95% *CI* 1.18-26.87, *P*=0.03) and CSF cell count (*OR* 1.002, 95% *CI* 1.00-1.001, *P*=0.03) were found to be an independent predictor of outcome. The Kaplan-Meier graph indicated significantly poorer survival among GeneXpert positive cases (Figure 2).

4. Discussion

In our study, 46.6% of the 116 patients were tested positive for GeneXpert. Third cranial nerve involvement and basal exudates on neuroimaging were strong predictors for a positive GeneXpert test.



CSF GeneXpert	Number at risk by time (days)						
	0	30	60	90	120	150	180
Negative	62	56	56	55	55	55	51
Positive	54	43	43	41	40	40	30

Figure 2. Kaplan-Meier survival curve in GeneXpert positive and GeneXpert negative groups.

Severe stage of TBM (stage Ⅲ) and elevated CSF cell counts were predictive factors for poor prognosis.

Tuberculous meningitis is an acute infection triggered by *M. tuberculosis*, which initially infects the lungs and then spreads through the bloodstream to the brain and spinal cord. There, they cause the formation of small tuberculous granulomas on brain and spinal cord surfaces. When these granulomas burst, they release bacteria into CSF, initiating a cascade of pathological processes. The most distinct feature is meningeal inflammation, accompanied by the formation of thick, gelatinous exudates at the basal part of the brain. The thick exudates can strangulate cerebral arteries of the Circle of Willis, leading to inflammation, constriction, and obstruction that results in brain infarcts. The optic chiasm and trunks of other cranial nerves also get encased within thick exudates, impacting their function. Furthermore, these exudates can block CSF flow, leading to increased intracranial pressure or hydrocephalus. Additionally, these exudates can affect the lower spinal cord and nerve roots, causing tuberculous radiculomyelopathy. The third cranial nerve involvement in TBM could indicate a more localized, possibly severe, manifestation of the disease[4,12].

Similarly, the presence of basal exudates, on MRI, is indicative of an inflammatory response in the subarachnoid space and adjacent brain structures. Its role as an independent predictor for GeneXpert positivity can be extrapolated to suggest a more aggressive or advanced disease state. In a retrospective study, Wen *et al*. analyzed the incidence of cranial nerve palsy in 114 patients diagnosed with TBM. The study found that approximately 33% of TBM patients experienced cranial nerve palsies. In this study, the optic nerve and oculomotor nerve were the most frequently affected nerves. Using logistic regression analysis, the study identified that focal neurological deficits, the presence of extracranial tuberculosis, and elevated CSF total white cell count were significant risk factors for developing cranial nerve palsy[13].

We noted that a higher number of deaths were recorded in GeneXpert positive TBM patients. Possibly, GeneXpert positivity represents a heavy *M. tuberculosis* load in the central nervous system leading to a higher risk of death. In a prospective study involving 102 HIV-positive Ugandans diagnosed with probable or definite TBM, Martyn *et al*. evaluated the relationship between CSF *M. tuberculosis* load, as determined by GeneXpert MTB/RIF Ultra (Xpert Ultra) PCR cycle threshold (Ct) values, and 2-week mortality. The findings indicate that subjects with low Ct values, representing a high TB bacillary load, had a 57% 2-week mortality rate, which was notably higher compared to those with intermediate (17%) and high (25%) Ct values and Xpert Ultra-negative cases (30%)[14].

In a study of 379 suspected TBM patients, the GeneXpert MTB/RIF

test showed 59.3% sensitivity and 99.5% specificity, outperforming traditional smear and culture methods in speed and accuracy. Adding a vortexing step increased sensitivity by 20%. Xpert MTB/RIF significantly advances early TBM diagnosis, improving outcomes[15]. Our study showed a significantly higher GeneXpert positivity rate (n=54) compared to culture positivity (n=15), which is notably higher than results reported in other studies. GeneXpert's high sensitivity and specificity allow it to detect *M. tuberculosis* in culture-negative samples, providing rapid results compared to the slower culture methods. The test's ability to identify DNA from both viable and non-viable bacteria, coupled with less susceptibility to sample contamination and degradation, explains the higher positivity rates.

Tuberculous meningitis is a severe *M. tuberculosis* infection. In a study from South India consisting of 293 CSF samples, GeneXpert showed 72.7% sensitivity and 98.5% specificity compared to *Mycobacteria* Growth Indicator Tubes 960 culture. Predominant *M. tuberculosis* strains were East African Indian lineage. GeneXpert is effective for TBM diagnosis, but negative results require further testing. Discrepancies in rifampicin resistance detection need resolution to prevent treatment failure[16].

In terms of prognosis, our study identifies severe disability (MBI $\leqslant$12) and increased CSF cell count as independent predictors of poor outcomes. Elevated CSF cell counts likely suggest a vigorous inflammatory response, potentially indicating an ongoing, uncontrolled infection that could result in poor outcomes, including neurological deficits. This diagnostic study examined the relationship between neutrophil count in CSF and cerebral infarction in MRI scans of adult patients with TBM. The study recruited 37 subjects. Higher neutrophil counts in CSF were significantly associated with cerebral infarction (P<0.05)[17].

The GeneXpert MTB/RIF Ultra assay shows 70% diagnostic sensitivity in tuberculous meningitis but can't rule out the disease. Diagnosing extrapulmonary tuberculosis is challenging due to diverse anatomical locations and low bacillary load. The GeneXpert® Ultra, endorsed by WHO, offers improved sensitivity over GeneXpert® by targeting IS6110, IS1081, and rpoB. Combining clinical features, imaging, histopathology, and GeneXpert® Ultra enhances extrapulmonary tuberculosis diagnosis for timely treatment initiation. Trials suggest enhanced rifampicin doses, additional antibiotics, and adjunctive aspirin with corticosteroids may improve outcomes[18].

The study has several key limitations. The study was conducted at a single centre, which may limit the generalizability of the results to other populations. The exclusion of patients with HIV co-infection could also limit the generalizability to all populations. The study also lacked long-term follow-up beyond six months, limiting the understanding of the chronic outcomes or long-term efficacy of treatment regimens in these two groups (based on the GeneXpert test). Another limitation of our study was that we did not use Xpert MTB/RIF Ultra, which is a rapid, highly sensitive test for tuberculosis and rifampicin resistance detection, especially effective for specimens with low bacillary burdens. BCG vaccination is universally administered in India. However, as our study included adult patients, BCG vaccination information was not collected. New technologies have identified molecules and pathways linked to its severity.

To conclude, the third cranial nerve involvement and the presence of basal exudates were independent predictors of GeneXpert positivity. Severe disability and increased CSF cell count were the independent predictors of poor outcomes.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Funding

The authors received no extramural funding for the study.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by PG, NK, RKG, HSM, IR, RV, PKS, RU, SP, AJ, and PJ. The first draft of the manuscript was written by PG, NK, and RKG and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Edited by Pan Y, Lei Y, Zhang Q