



# GeneXpert MTB/RIF Ultra For Diagnosis Of Central Nervous System Tuberculosis In The High Tuberculosis Prevalence Country - A Prospective Study From India

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## Introduction

- Tuberculous meningitis (TBM) kills nearly half the patients (mortality 40–60%) and disables the remaining half (54%) by severe residual neurological sequelae (1)
- TBM presents a diagnostic challenge due to overlapping clinical presentation, paucibacillary nature and limited volume of cerebrospinal fluid (CSF) sample
- Early diagnosis and initiation of antitubercular treatment are vital steps to reducing the impact of TB in high-burden countries.
- Conventional microbiological techniques of smear microscopy lacks sensitivity, and the culture is too lengthy. GeneXpert MTB/RIF assay (Xpert) ultra, a semi-automated platform has significantly improved the diagnosis of TB.(2,3)
- GeneXpert Ultra is more sensitive to the diagnosis and helps in paucibacillary samples like cerebrospinal fluid (CSF). Xpert Ultra has been reported to yield increased sensitivity with LOD of ~15.6 CFU/mL(2,3)
- This study aims to provide its utility in diagnosis of central nervous system tuberculosis (CNS TB) in high TB burden geography.

## Aims & Objectives:

- This prospective observational study included the suspected cases of CNS TB with age ≥12 years.
- Patients who presented with ≥ 5 days history of CNS symptoms suggestive of tuberculosis with a lancet score of ≥ 6 on combination of clinical, CSF and imaging criteria were included in the study.

## Materials & Method:

- The Institute Ethics Committee approved the study
- Adult TBM suspects (with symptoms and radiological examination outcomes) or TBM patients diagnosed according to clinical reference standard who underwent lumbar puncture as a part of routine care were prospectively and consecutively enrolled from April 2021 to May 2022 in tertiary care centre, AIIMS Jodhpur. Patients were categorized as definite-, probable-, possible-, and non-TBM cases using Lancet score. Non-TBM cases were excluded.
- We assessed clinical, radiological, microbiological, biochemical parameters along with treatment provided and outcomes of the patient.

- CSF was analysed for Acid fast bacilli (AFB) stain, GeneXpert Ultra and mycobacterial culture.
- The sensitivity, specificity, positive predictive value, and negative predictive value of different assays were calculated.

## Results

Clinical features	Percentage (n=107)
Altered sensorium	91
Loss of appetite	85.1
Weight loss	65
Focal neurological deficit	57
Headache	48.6
Fever	45.8
Night sweat	17.8
Neuro-Radiological findings	Percentage (n=107)
Leptomeningeal enhancement	83.2
Hydrocephalus	72.9
Vascular infarct	72
Basal exudate	70.1
Tuberculoma	47.7
Spinal Cord	17.7
CSF	Median (IQR)
Protein (mg/dl)	120 (74-129)
Glucose (mg/dl)	53 (34-77)
Chloride (mmol/L)	117 (102-140)
WBC (/μL)	54 (11.5-191)
	85% of cases Lymphomononuclear
ADA (IU/L)	11 (6-12)
Microbiological Results (in CSF)	Percentage (n=107)
GeneXpert MTB Detected	57.9%
MTB Culture positive	45.8%

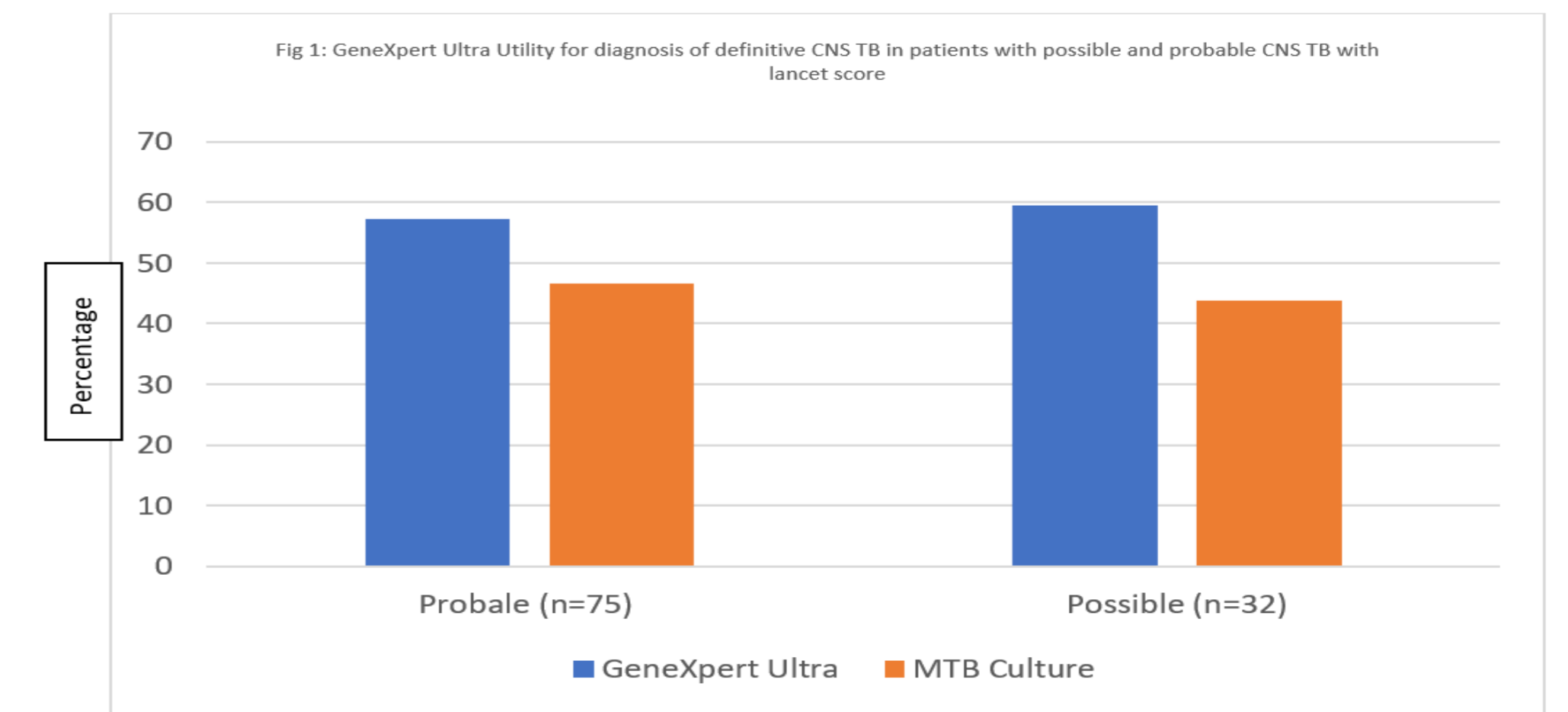
Table 1: Clinical and Laboratory Profiles of patients with CNS TB

Diagnostic performance	Percentage
Sensitivity	83.7
Specificity	63.8
Positive Predictive value	20.4
Negative predictive value	97.2

Table 2: Diagnostic utility of GeneXpert Ultra in CSF for diagnosis of CNS TB (MTB Culture positive is consider gold standard)

Lancet score classification (n=107)	CSF GeneXpert Ultra MTB Detected	CSF MTB culture positive
Probable CNS TB (n=75)	57.3% (n=43)	46.7% (n=35)
Possible CNS TB (n=32)	59.4% (n=19)	43.8% (n=14)

Table 3: GeneXpert Ultra Utility for diagnosis of definitive CNS TB in patients with possible and probable CNS TB with lancet score



- A total of 107 patients which included 27 definite TBM, 75 probable TBM, and 32 possible TBM patients. The mean age was 33.2±18.5 years analyzed.
- Clinical and laboratory profiles are shown in table 1.
- CSF mycobacterial culture was positive in 45.8% (n=49) of patients.
- However, CSF GeneXpert Ultra MTBC was detected in 57.9% (n=62) of patients.
- Sensitivity, specificity, PPV and NPV for GeneXpert Ultra were found 83.7%, 63.8%, 20.4% and 97.2% respectively. (Table 2)
- MTBC was detected in GeneXpert Ultra in 57.3% of cases with probable and 59.4% of cases with possible CNS TB with lancet score (Table 3, Figure 1)

## Conclusions

- GeneXpert Ultra has excellent sensitivity and negative predictive value for the diagnosis of CNS TB in CSF samples.
- The integration of the Xpert Ultra assay greatly changed the composition of TBM classifications in our study.
- Even with possible CNS TB according to the lancet score, it is better to consider antitubercular treatment in a high TB burden country.

## References:

- Sharma K, Sharma M, Shree R, Modi M, Goyal M, Narang D, Sharma A, Lal V, Sharma N, Ray P. Xpert MTB/RIF ultra for the diagnosis of tuberculous meningitis: a diagnostic accuracy study from India. Tuberculosis. 2020 Dec 1;125:101990.
- Shen Y, Yu G, Zhao W, Lang Y. Efficacy of Xpert MTB/RIF Ultra in diagnosing tuberculosis meningitis: A systematic review and meta-analysis. Medicine. 2021 Jul 7;100(29).
- Chin JH. Xpert MTB/RIF Ultra: the long-awaited game changer for tuberculous meningitis?. European Respiratory Journal. 2017 Oct 1;50(4).

