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**ORIGINAL RESEARCH**

# Prevalence and role of CBNAAT in diagnosing tubercular meningitis- A observational study

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**ABSTRACT**
Tuberculous meningitis (TBM) is the most severe form of tuberculosis. Microbiological confirmation is rare, and treatment is often delayed, increasing mortalityand morbidity.Dueto paucibacillarynatureofCSF,it isdifficult to demonstrate tubercle bacilli by the standard staining procedures which is the gold standard for diagnosis, thus leading to a large number of cases being undiagnosed or misdiagnosed. Meticulous examination of a smear from a large volume of cerebrospinal fluid (CSF) remains the most sensitive technique but is not practical in most laboratories. The Xpert MTB/RIF represents a significant advance in the early diagnosis of this devastating condition. So, this study was done with the aim to know the Prevalance and role of CBNAAT in the diagnosing of tubercular meningitis. Out of 70 patients included in the study, 7 were Definite TBM, 42 were probable TB, 16 were possible TBM and 5 were not TBM. Total 21 patients had M. TB detected intheir CSFon CBNAAT,out of a total of 65 TBM patients.The sensitivity of CBNAAT in our study was 32.3%
**Keywords:** CBNAAT, Gene Xpert, Tubercular meningitis, CSF.


## INTRODUCTION

The first description of TBM dates back to 1836 when six cases of acute hydrocephalus in children characterized by ''an inflammation of the meninges, with the deposit of tubercular matter in the form of granulations, or cheesy matter" were described in the Lancet.[1] Among various forms of extrapulmonary TB, tuberculous meningitis (TBM) is the most severe form and remains a major global health problem with the case fatality rate for untreated TBM reaching almost 100 %,[2] even after more than 100 years. Early recognition of TB meningitis is of paramount importance because the clinical outcome depends greatly upon the stage at which the therapy is initiated,[3] and delay in treatment often leads to permanent neurological damage. The diagnosis of TBM has been a continuous challenge. Definitive diagnosis requires demonstration of tubercle bacilli in CSF, which can be done either by smear microscopy or culture. Smear microscopy is inexpensive and rapid but insensitive (0–20 %)due to low microorganism densities in CSF, while culture techniques are unacceptably slow which makes it unsuitable as a routine technique forrapid confirmatory diagnosis.[2,4] Thus, diagnosis of tubercular meningitis basically remains presumptive and is based on clinical symptoms, neurologic signs, CSF findings, CT scans, and response to anti-TB drugs.Cartridge Based Nucleic acid-based amplification test(CBNAAT) or GeneXpert has now emerged as potentially important tool for diagnosing TBM. The Gene Xpert System (Cepheid) is a single use cartridge- based real-time PCR fully automated system that performs sample decontamination, sonication ,automated nucleic acid amplification, and fluorescence-based quantitative PCR.[5-7] The published Xpert MTB/RIF detection threshold is approximately 100 - 130 colony forming units (cfu)/ml of sample.[5,6] .According to recent WHO guidelines, Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test in testing cerebrospinal fluid specimens from patients presumed to have TB meningitis in order to reach quick diagnosis. If sufficient volume of material is available, concentration methods should be used to increase yield. So, the present study was undertaken to evaluate the role of CBNAAT in early detection of tubercular meningitis and to also detect rifampin

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resistance in this era of alarming rise of multi- drug resistant strains of mycobacterium.

## MATERIALS AND METHODS

This Observational study was carried out in the Dept of Pulmonary medicine, Govt. Medical College, Amritsar after approval from the Institution ethical committee. All the patients being admitted in the wards from January 2024 to September 2024, with signs and symptoms suggestive of tubercular meningitis were included in the study after taking their or guardian's (in case of unconscious patients or children) informed consent.

### Inclusion criteria

1. Patients having clinical features of meningitis with or without signs of meningeal irritation.
2. Patients with a sub acute onset of symptoms(>5 days) or a positive contact history.
3. MRI brain findings suggestive of tubercular meningitis.
4. CSF showing features of pleocytosis, predominantly lymphocytosis, decreased glucose levels, high protein levels and an ADA >10 IU/L.
5. Presence of tuberculosis elsewhere(egmiliary tuberculosis or abdominal TB)

### Exclusion criteria

1. Patients with features suggestive of pyogenicmeningitis.
2. Patients refusing to give consent

Complete history including past or family history of tuberculosis was taken. Complete physical examination was done including level of consciousness, signs of meningeal irritation (neck stiffness, Kerning's sign, Brudzinski's sign), cranial nerve involvement, etc. Lumbar Puncture was done after ruling out papilloedema after taking consent and CSF was subjected to cytology, biochemistry, ADA, fungal stain, smear for AFB, culture and CBNAAT. Other investigations like TLC, DLC, ESR, blood culture, mantoux, HIV etc were done. Chest Xray and MRI were done in relevant cases. Then, the cases were divided into probable TBM, possible TBM and definitive TBM according to Diagnostic Criteria in the Uniform Tuberculous Meningitis Research Case Definition as given by Suzaan Marais et al as published in The Lancet.[12]Xpert MTB/RIF results were not included in the case definition, because it was the test under evaluation. Definite TBM was defined as a clinical syndrome consistent with TBM, with acid-fast bacilli seen on CSF smear or M. tuberculosis isolated in CSF MGIT culture. Patients in the "probable TBM" group had a diagnostic score of 10 or more without cerebral imaging (MRI or CT scan) or 12 or more with cerebral imaging, with at least 2 points from CSF or cerebral imaging criteria. Patients in the "possible TBM" group had a diagnostic score of between 6 and 9 if cerebral imaging was not performed or between 6 and 11 if cerebral imaging was performed. All patients who had a score below 5 were classified as not having TBM**.**

## RESULTS

In our study, 70 patients were included who had features suggestive of tubercular meningitis. Out of these, 50 were male and 20 were female. 28 patients were of age group 0-15 years, 17 patients were in age group 16-30 years and 25 patients were aged > 30 years.

According to the universal case definition, the patients were divided into probable, possible and definitive TBM. Out of 70 patients included in this study, 7 were Definite TBM, 42 were probable TB, 16 were possible TBM and 5 were not TBM. To calculate statistical values, Definitive, probable and possible TBM were grouped together. So, total study patients were divided into two groups: TBM and Not TBM. Total 21 patients had M. TB detected in their CSF on CBNAAT, out of a total of 65 TBM patients

**Table1- Age distribution of patients**

| Age group | No. of patients | Percentage |
|---|---|---|
| 0-15years | 28 | 40% |
| 16-30years | 17 | 24% |
| >30 years | 25 | 36% |

**Table 2: Categorisation of patients according to the diagnostic criteria in the uniform tuberculous meningitis research case definition**

| Category | No. of patients | Percentage |
|---|---|---|
| Definitive TBM | 7 | 10% |
| Probable TBM | 42 | 60% |
| Possible TBM | 16 | 23% |
| Not TBM | 5 | 7% |

**Table 3: No. of patients with MTB detected on CBNAAT.**

| Category | Total no | MTB detected | MTB not detected |
|---|---|---|---|
| TBM | 65 | 21 | 44 |
| Not TBM | 5 | 0 | 5 |

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**Table 3(a): No. of patients with MTB detected on CBNAAT.**

| Category | Total no. | MTB detected | MTB not detected |
|---|---|---|---|
| Definitive TBM | 7 | 4(57%) | 3(43%) |
| Probable TBM | 42 | 13(31%) | 29(69%) |
| Possible TBM | 16 | 4(25%) | 12(75%) |
| Not TBM | 5 | 0 | 5 |

**Table 4: No. of patients with R-resistance on CBNAAT**

| Category | Total no | MTB detected | MTB not detected | Rifampicin resistance detected |
|---|---|---|---|---|
| TBM | 65 | 21 | 44 | 0 |
| Not TBM | 5 | 0 | 5 | 0 |

## DISCUSSION

Tuberculosis (TB) is a global health concern. India is highest TB burden country in the world and accounts for one fourth of the global TB burden cases. In 2015, an estimated 28 lakh cases occurred and 4.8 lakh people died due to TB.[13] Extra pulmonary Tuberculosis (EPTB) accounts for about 15 to 20% of all cases of Tuberculosis in India. The percentage may be higher in children and in HIV infected individuals. In HIV positive patients, EPTB accounts for more than 50 per cent of all cases of TB. Exact prevalence of CNS TB in India is not known, but it accounts for an estimated 1% of all cases of TB, which equates to around 17 000 cases in India in2014 (WHO, 2015). Case fatality rates for the most common form of CNS TB, i.e. TB meningitis, are high[15].A definitive diagnosis of mycobacterium infection depends on detection of the Mycobacterium Tuberculosis in CSF. It can be either done by smear microscopy which has very low sensitivity in CSF sample or by culture which has good sensitivity but takes too long to give the results.So, CBNAAT was proposed as a promising tool to detect M.TB early with increased sensitivity as compared to smear microscopy.

Sensitivity of CBNAAT in CSF has been variable among various studies. The pooled sensitivity of CBNAAT in CSF in a meta-analysis was 80.9%.[16]Other studies showed sensitity ranging from 40%[17] to 59.3%[18]. Its use for diagnosis of TBM has also been endorsed by INDEX TB guidelines. Thus, this study was planned to determine the sensitivity and utility of CBNAAT in diagnosis of TBM at a tertiary care centre in Punjab**.**

The sensitivity of CBNAAT in our study was 32.3%which is comparable with results of other studies. Thus, Gene Xpert MTB/RIF assay is an efficient and reliable technique for detection of M. TB in CSF samples. Its simplicity, speed and automation, and detection of resistance at the same time makes this technique a very attractive tool for the rapid diagnosis ofTB meningitis, especially in suspected cases.

This findings suggest that CBNAAT important role in the diagnosis of tubercular meningitis, particularly in places with high burden and limited availability of resources. CBNAAT could be the best aid for physicians in diagnosing TBM if more awareness is brought among them regarding its utility. Our study highlighted that CBNAAT can be a faster alternative to time taking methods like culture DST and at the same time a more efficient alternative to other rapid methods like AFB smear examination in the diagnosis of TBM.

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