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Original Article

Assessment of CBNAAT for the Diagnosis of Smear Neagative pulmonary Tuberculosis: A Prospective Study

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ABSTRACT

Background: Tuberculosis (TB) continues to be a major global public health concern and remains a significant challenge in India. Prompt and accurate diagnosis is essential for effective management and control of the disease. Conventional diagnostic methods, such as sputum smear microscopy, have limited sensitivity, particularly in smear-negative pulmonary TB cases. Hence, there is a critical need for rapid and highly sensitive diagnostic tools like the Cartridge-Based Nucleic Acid Amplification Test (CBNAAT).This study aims to evaluate the role of CBNAAT in the detection of *Mycobacterium tuberculosis* (MTB) in patients with sputum smear-negative pulmonary tuberculosis. **Methodology:** This study was conducted at Narayana Medical College, Nellore, and included 45 patients diagnosed with sputum smear- negative pulmonary tuberculosis based on predefined inclusion and exclusion criteria. The study was carried out over a period from January 2019 to November 2020.**Results:** The majority of patients belonged to the 41–60 years age group, with a higher prevalence observed among males. Chronic obstructive pulmonary disease (COPD) was the most common comorbidity, followed by diabetes mellitus. CBNAAT demonstrated a sensitivity of 96.43% and a specificity of 88.24% in diagnosing sputum smear-negative pulmonary tuberculosis.

Keywords*: CBNAAT, Diagnosis,Smear negative TB.*

INTRODUCTION

Tuberculosis (TB) remains the leading cause of death from a single infectious microorganism worldwide[1]. The rising global incidence of TB, along with the emergence of drug-resistant forms, highlights the urgent need for rapid and accurate diagnostic techniques[2]. Each year, approximately 8.7 million new TB cases and 1.4 million deaths are reported globally[3]. India bears the highest burden of TB cases in the world, according to the World Health Organization (WHO)[4].

Conventional diagnostic methods for TB are often time-consuming and show variable sensitivity and specificity. This contributes to increased morbidity, mortality, and the development of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB([5,6]). Although culture remains the gold standard for TB diagnosis, it is a slow and technically demanding process, taking 2–8 weeks for results and requiring biosafety level II/III laboratories, which are not widely accessible([7.8]). Sputum smear microscopy for Acid-Fast Bacilli (AFB) is a rapid method, but its sensitivity is relatively low[9].

In response to these limitations, nucleic acid amplification techniques have gained importance due to their rapidity, improved sensitivity, and higher specificity[10]. One such advancement is the GeneXpert MTB/RIF assay, an automated, easy-to-use, real- time PCR-based diagnostic tool[11]. It simultaneously detects Mycobacterium tuberculosis and rifampicin resistance within a few hours, making it highly valuable for early diagnosis and treatment initiation. The WHO now recommends its implementation in national TB control programs, particularly in developing countries([11,12]).

Under India's Revised National Tuberculosis Control Program (RNTCP), sputum smear microscopy remains the initial diagnostic test for suspected TB cases. The introduction of Light Emitting Diode Fluorescent Microscopy (LED-FM), recommended by WHO in 2011, has improved diagnostic sensitivity by at least 10% compared to conventional microscopy, while also offering operational and cost advantages. Most Designated Microscopy Centers (DMCs) are now equipped with LED-FM[13].

With the implementation of the End TB Strategy, Cartridge-Based Nucleic Acid Amplification Test (CBNAAT), also known as GeneXpert, has been increasingly used for rapid detection of TB and rifampicin resistance. This fully automated system provides results in less than two hours, enabling same-day treatment initiation and reducing loss to follow-up. It requires minimal biosafety infrastructure and training and can be installed in non-conventional laboratory settings[14].

This study was undertaken to evaluate the role of CBNAAT in diagnosing sputum smear-negative TB cases, along with its added advantage of upfront drug sensitivity testing (DST). The findings may help inform policy decisions on whether CBNAAT alone can be used in routine programmatic settings, potentially replacing the combined use of LED-FM and CBNAAT.

AIMS AND OBJECTIVES

To assess the role of CBNAAT (Cartridge-Based Nucleic Acid Amplification Test) in the diagnosis of sputum smear-negative pulmonary tuberculosis.

METHODOLOGY

Study Design:

An institution-based prospective observational study.

Study Period:

Two years (January 2019 to November 2020).

Study Area:

Department of Respiratory Medicine, Narayana Medical College & Hospital, Nellore.

Inclusion Criteria:

1. Patients aged 18 years and above.
2. Patients with smear-negative pulmonary tuberculosis.
3. Patients who provided informed consent to participate in the study.

Exclusion Criteria:

1. Patients who did not provide consent.
2. Patients with sputum smear positive for Acid-Fast Bacilli (AFB) on microscopy.
3. Patients who are known or suspected cases of HIV infection.
4. Patients receiving anti-tubercular therapy (ATT) for more than one month.

Sample Size:

A total of 45 patients with smear-negative presumptive pulmonary tuberculosis attending the Pulmonology outpatient department during the study period were included, based on the inclusion and exclusion criteria.

Ethical Approval:

The study protocol was approved by the Institutional Ethical Committee.

Study Procedure:

After obtaining informed consent, a detailed clinical history was recorded for each patient. A provisional diagnosis of pulmonary tuberculosis was made based on WHO criteria[15], including symptoms such as cough for two weeks or more, unexplained fever for two weeks or more, loss of appetite, weight loss, and suggestive findings on chest X-ray.

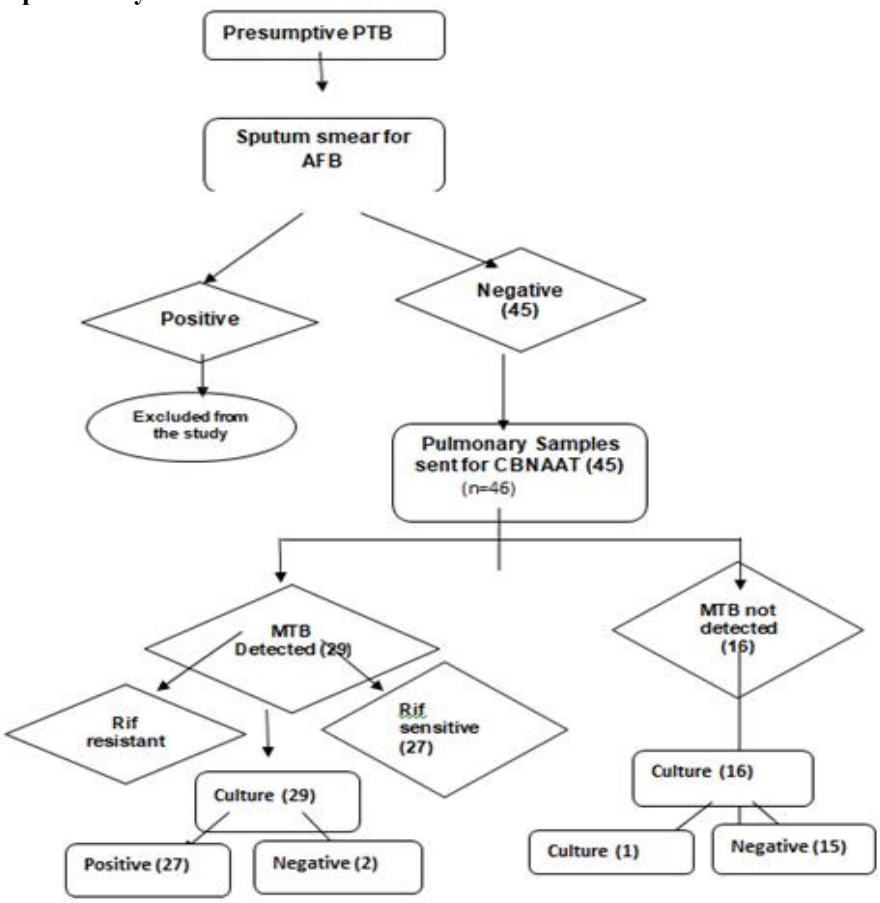
All patients underwent relevant investigations, including chest radiography and HIV testing (ICTC). Two sputum samples were collected from each patient and examined using fluorescent microscopy under the RNTCP laboratory attached to Narayana Medical College & Hospital. Patients found to be smear-positive were excluded from the study.

For smear-negative patients, further samples were collected for CBNAAT testing. These included sputum samples where available. In patients unable to produce sputum, alternative specimens such as bronchoalveolar lavage (BAL) fluid, CT-

guided transthoracic lung biopsy tissue, or endobronchial biopsy samples were obtained.

BAL fluid was collected via bronchoscopy[16], lung tissue samples were obtained through CT-guided transthoracic needle biopsy[17], and endobronchial samples were collected using bronchoscopy guided biopsy techniques[18].

Study procedure for pulmonary TB:



RESULTS

The most commonly affected age group in this study was 41–60 years (26.67%), followed by 61–80 years (24.44%) and 40–49 years (17.78%).Out of the total 45 participants, 33 were males and 12 were females, indicating a higher prevalence among males.Regarding educational status, 66.66% of the participants were literate, while 33.33% were illiterate.In terms of employment status, 64.44% of the participants were employed, whereas 35.55% were unemployed(Table 1).

Table 1: Sociodemographic profile of study participants (n=45)

Variable	Number	Percentage
Age		
<20	1	2.22
21-40	9	20
41-60	20	44.44
61-80	14	31.11
>80	1	2.22
Sex		
Males	33	73.34
Females	12	26.66
Education		
Illiterate	15	33.33
Literate	30	66.66
Occupation		
Employed	39	86.66
Unemployed	16	35.55

Among personal habits, a history of smoking was the most common (48.89%), followed by alcohol consumption (42.22%), while tobacco chewing was reported in a smaller proportion of patients (8.89%).Regarding comorbidities, chronic obstructive pulmonary disease (COPD) was the most prevalent condition (31.11%), followed by diabetes mellitus (26.66%), hypertension (15.56%), and asthma (13.33%). A past history of tuberculosis was noted in 11.11% of patients, while chronic kidney disease (CKD) was observed in only 2.22% of cases.(Table 2)

Table 2:Distribution of Personal Habits and Comorbidities among Study Participants

Personal history	**Yes(number)**	**Percentage**
H/O Smoking	22	48.89
H/O Alcohol	19	42.22
H/O Tobacco chewing	4	8.89
Comorbidities	**Number**	**Percentage**
Diabetes Mellitus	**12**	**26.66**
Hypertension	**7**	**15.56**
Asthma	**6**	**13.33**
COPD	**14**	**31.11**
CKD	**1**	**2.22**
Past H/O TB	**5**	**11.11**

The distribution of chest X-ray findings among the 45 cases shows that **pneumonia** was the most common finding, observed in 12 cases (26.67%). This was followed by **pleural effusion**, seen in 10 cases (22.22%). A normal chest X-ray (NAD) was reported in 9 cases (20%).Less frequent findings included **cavity, fibrosis, military pattern, lung abscess, and mediastinal mass**, each accounting for 2 cases (4.44%). Rare findings such as **haemothorax, fibro cavity, right hilar prominence, and hydropneumothorax** were each observed in only 1 case (2.22%) (Fig.1)

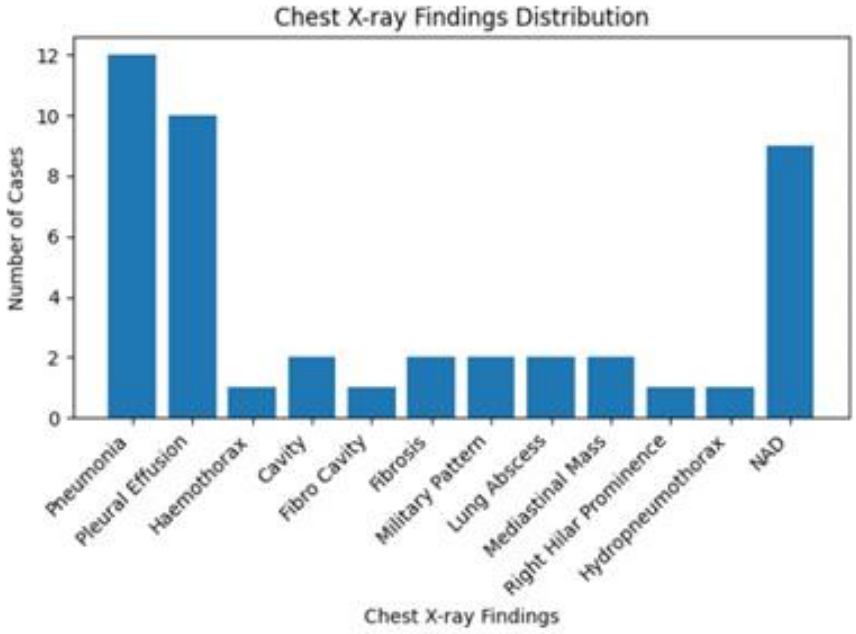


Figure 1: X-Ray findings of the study participants

The distribution of specimens among the 45 cases shows that **bronchoalveolar lavage (BAL) fluid** was the most commonly used specimen, obtained in 30 cases (56.52%). This was followed by **sputum samples**, which were collected in 11 cases (39.13%).More invasive procedures were less frequently used, with **biopsy of endobronchial mass** performed in 2 cases (2.17%) and **CT-guided lung tissue sampling** also done in 2 cases (2.17%).(Figure 2)

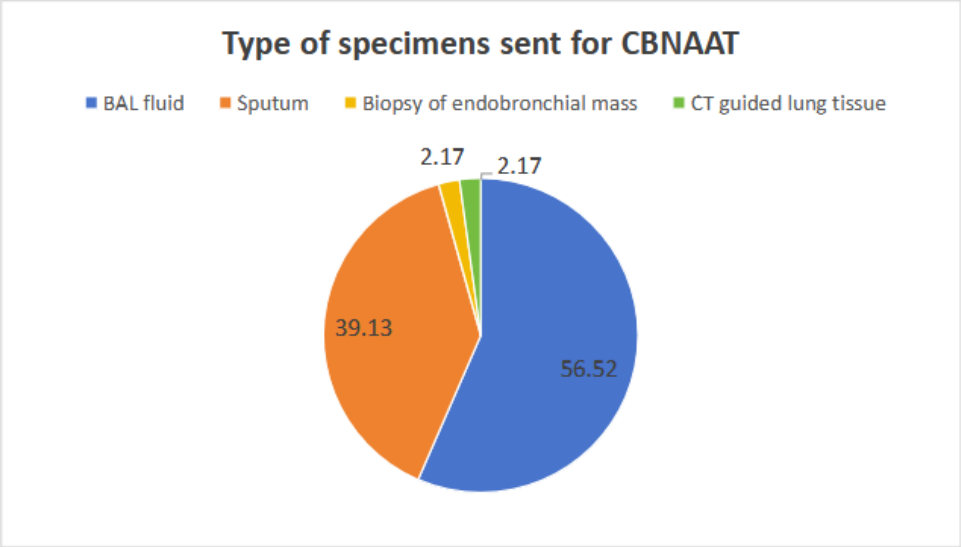


Figure 2: Type of specimens sent for CBNAAT

Out of 45 sputum smear–negative samples, 29 (64.44%) tested positive by CBNAAT, while 16 (35.55%) were CBNAAT negative.(Figure 3)

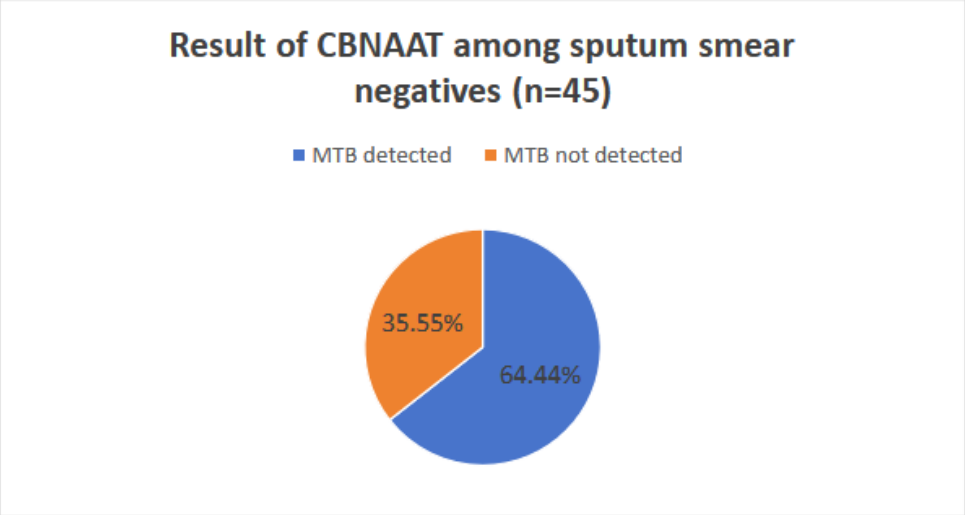


Figure 3: Result of CBNAAT

Table 3: Comparison of CBNAAT Results with Culture Findings (n = 45)

CBNAAT Result	Culture Positive	Culture Negative	Total
Positive	27	2	29
Negative	1	15	16
Total	28	17	45

CBNAAT showed a sensitivity of **96.43%**, specificity of **88.24%**, positive predictive value of **93.10%**, negative predictive value of **93.75%**, and an overall diagnostic accuracy of **93.33%** compared to culture. Its rapid turnaround time and high diagnostic accuracy make it a valuable tool for early diagnosis and management, especially in resource-limited settings.

DISCUSSION

The present study showed that the most commonly affected age group was 41–60 years (26.67%), followed by 61–80 years (24.44%) and 40–49 years (17.78%). This finding is comparable with the study by Sharma Shubhkaran et al[19]., where the majority of patients (87.7%) belonged to the 21–60 years age group. Similarly, R. Dewan et al[20]. reported a mean age of 35 ± 9 years, with the 41–60 years group being the most commonly affected, which is in agreement with the present study. Variations in age distribution observed in different studies may be attributed to differences in sample size and study population.

In terms of gender distribution, males (33 out of 45) were more commonly affected than females (12 out of 45). This observation is consistent with findings from Nageswar Rao Gopathi et al[21]., where 65% of patients were males and 35% were females. Similarly, Meghna Patel et al[15]. also reported a higher prevalence of tuberculosis among males.

Regarding educational status, 66.66% of participants were literate, while 33.33% were illiterate. Comparable findings were reported by Vandana Bhoi et al[22]., where 23.1% of participants were illiterate. The higher proportion of literate individuals in the present study may be due to better health-seeking behavior among this group.

In the present study, 64.44% of participants were employed, while 35.55% were unemployed. In contrast, Vandana Bhoi et al[22]. reported a lower proportion of unemployed individuals (29.6%), indicating some variation that may be related to socioeconomic differences.

Among personal habits, 48.89% of patients had a history of smoking, 42.22% reported alcohol consumption, and 8.89% had a history of tobacco chewing. These findings are somewhat comparable to Sharma Shubhkaran et al[23]., where 33% of patients were smokers and 31.5% were alcohol consumers.

The most common comorbid condition observed in this study was chronic obstructive pulmonary disease (COPD) (31.11%), followed by diabetes mellitus (26.66%), hypertension (15.56%), asthma (13.33%), past history of tuberculosis (11.11%), and chronic kidney disease (2.22%). In contrast, Bhavanarushi Sreekanth et al[24]. reported diabetes mellitus as the most common comorbidity, indicating some variation in comorbidity patterns.

Radiologically, the most common chest X-ray finding in the present study was pneumonia (26.67%), followed by pleural effusion (22.22%), while 20% of patients showed no abnormalities. In contrast, other studies have reported different patterns. Nageswar Rao Gopathi et al[21]. found cavitation (53%) to be the most common finding, whereas Ganesh Chandra Mohapatra et al[25]. reported infiltration (79%) as the predominant abnormality.

Among the 45 sputum smear-negative cases, the samples sent for CBNAAT included bronchoalveolar lavage (BAL) fluid (56.52%), sputum (39.13%), and tissue samples such as endobronchial biopsy and CT-guided lung biopsy (2.17%). Of these, 29 samples (64.44%) were CBNAAT positive, while 16 (35.55%) were negative.

When compared with culture (the gold standard), CBNAAT demonstrated a sensitivity of 96.43% and specificity of 88.24%, with a positive predictive value of 93.10% and a negative predictive value of 93.75%, indicating high diagnostic accuracy.

These findings are comparable with other studies. Meghna Patel et a[26]l. reported CBNAAT positivity in 53.26% of smear-negative cases, while Archana B. et al[27]. reported a higher positivity rate of 75.89%. K. Raj Kumar et al[28]. found CBNAAT positivity in 41.6% of BAL samples. Additionally, R. Dewan et al[20]. reported rifampicin resistance in 25% of cases detected by CBNAAT.

Further evidence supports the effectiveness of CBNAAT. A study conducted in 2011 in Hyderabad[29] demonstrated an incremental case detection of 10.8% over fluorescent microscopy. A multicentric study by Boehme et al[7]. showed nearly 100% sensitivity of CBNAAT. Under the RNTCP program, CBNAAT identified an additional 2,493 pulmonary TB cases among more than 30,000 suspects in 2012[30]. Moreover, CBNAAT increased TB detection by 23% among culture-confirmed cases compared to smear microscopy[31]. Rifampicin resistance detection rates in other studies, such as Bhavanarushi Sreekanth et al[32]., were reported to be low (1.86%), but still clinically significant.

CONCLUSIONS

CBNAAT is a highly effective and rapid diagnostic tool for detecting tuberculosis, especially in sputum smear-negative patients. It shows high sensitivity and specificity and helps in early and accurate diagnosis. The test also detects rifampicin resistance, allowing timely initiation of appropriate treatment. Most patients in the study were middle-aged males with risk factors like smoking, alcohol use, and comorbidities such as COPD and diabetes. Overall, CBNAAT improves early detection, reduces complications, and supports better management of tuberculosis especially in resource-limited settings

LIMITATIONS

The study had a small sample size and was conducted at a single center, which may limit the generalizability of the findings. HIV-positive patients were excluded, reducing applicability to this high-risk group. Variability in sample types and lack of long-term follow-up may have influenced the results and outcome assessment.

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