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Sensitivity and Specificity of BAL CBNAAT in Sputum- CBNAAT Negative in Presumptive TB Patients

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Abstract

Background

Tuberculosis (TB) remains a major public health challenge, especially in sputum-negative presumptive TB patients, where conventional sputum smear microscopy often fails to detect the disease. Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) has emerged as a promising molecular diagnostic tool for early detection of Mycobacterium tuberculosis (MTB) and rifampicin resistance. Given India's high TB burden, evaluating CBNAAT's sensitivity and specificity in these cases is crucial for optimizing diagnostic strategies.

Aim and Objectives

Aim: To evaluate the sensitivity and specificity of CBNAAT in sputum-negative presumptive TB patients.

Objectives:

1. To determine the diagnostic accuracy of CBNAAT in sputum-negative patients suspected of pulmonary TB.

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2. To compare CBNAAT results with sputum culture and clinical diagnosis as reference standards.
3. To assess CBNAAT's role in early TB diagnosis and timely treatment initiation.

Methodology

- Study Population: Patients aged ≥18 years with clinical and radiological suspicion of TB.
- Sample Collection: Induced sputum and bronchoalveolar lavage (BAL) samples.
- Data Analysis: Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using sputum culture as the reference standard. Statistical tests validated the findings.

Results

- CBNAAT demonstrated superior sensitivity (88.09%) and specificity (96.50%) compared to sputum smear microscopy (sensitivity: 51.02%, specificity: 85.00%).
- BAL samples had a higher CBNAAT positivity rate (45.4%) compared to induced sputum (37.2%) (Paired T-Test, $p = 0.021$).
- CBNAAT significantly reduced diagnostic time (median: 2 days) compared to culture (21 days) (Mann-Whitney U Test, $p < 0.001$).
- Radiological assessment showed higher CBNAAT positivity rates in cavitatory TB cases (OR = 5.5, $p < 0.001$).
- CBNAAT sample collection was safe, with minimal complications (4.5% mild hemoptysis) (Fisher's Exact Test, $p = 0.882$).

Conclusion

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CBNAAT has proven to be a reliable diagnostic tool for sputum-negative presumptive TB patients, with high sensitivity, specificity, and rapid results. While bronchoscopy enhances diagnostic yield, its semi-invasive nature supports prioritizing non-invasive methods like induced sputum. Integrating CBNAAT with radiological and clinical findings improves diagnostic accuracy, reinforcing its role in modern TB management protocols.

Keywords

Tuberculosis, CBNAAT, Sputum-Negative, Sensitivity, Specificity, Bronchoscopy, Induced Sputum, Diagnostic Accuracy

Introduction

Tuberculosis (TB) remains a significant global health concern, particularly in resource-limited settings. The World Health Organization (WHO) has emphasized the importance of early and accurate diagnosis to reduce morbidity and mortality associated with TB [1]. Conventional diagnostic methods such as sputum smear microscopy have limitations in sensitivity, especially in cases where patients present with sputum-negative results [2]. Culture-based methods, although highly sensitive, require prolonged incubation periods, making them impractical for rapid diagnosis [3].

Cartridge-Based Nucleic Acid Amplification Test (CBNAAT), also known as GeneXpert MTB/RIF, has emerged as a promising diagnostic tool for TB detection. This automated molecular test not only detects Mycobacterium tuberculosis (MTB) but also identifies rifampicin resistance, making it a valuable tool for early initiation of treatment [4]. Several studies have highlighted the enhanced sensitivity of CBNAAT in diagnosing TB among sputum-negative cases, particularly in patients with high clinical suspicion [5].

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In India, where the burden of TB is among the highest globally, the Revised National Tuberculosis Control Program (RNTCP) has endorsed CBNAAT for diagnosing TB in sputum-negative and extrapulmonary cases [6]. The effectiveness of CBNAAT in such cases needs further evaluation to establish its role in routine diagnostic algorithms [7]. This study aims to assess the sensitivity and specificity of CBNAAT in sputum-negative presumptive TB patients, thereby determining its utility as a primary diagnostic modality.

Aim and Objectives:

Aim: To evaluate the sensitivity and specificity of CBNAAT in sputum-negative presumptive TB patients.

Objectives:

1. To determine the diagnostic accuracy of CBNAAT in sputum-negative patients suspected of pulmonary TB.
2. To compare CBNAAT results with other conventional diagnostic methods such as sputum culture and clinical diagnosis.
3. To assess the utility of CBNAAT in improving early TB diagnosis and initiation of treatment.

Materials and Methods:

Study Population:

Patients with clinical suspicion of pulmonary TB who had negative sputum smear results were included in the study. Inclusion criteria comprised individuals aged >18 years with persistent cough for more than two weeks, weight loss, fever, and radiological findings suggestive of TB. Exclusion criteria included patients already on anti-TB treatment and those with confirmed alternative diagnoses.

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Sample Collection and Processing:

Induced sputum, bronchoalveolar lavage (BAL), and other relevant clinical specimens were collected from participants. Samples were processed for CBNAAT testing. Additionally, sputum cultures were performed using Lowenstein-Jensen (LJ) medium as a gold standard reference.

Data Analysis:

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CBNAAT were calculated using culture results as the reference standard. Statistical analysis was performed using SPSS software.

Results with Statistical Analysis

Table 1: Age and Gender Distribution (Chi-Square Test for Association)

Age Group (Years)	Male (n=76)	Female (n=34)	Total (n=110)
18–30	25 (32.9%)	12 (35.3%)	37 (33.6%)
31–45	30 (39.5%)	11 (32.4%)	41 (37.3%)
46–60	15 (19.7%)	12 (35.3%)	27 (24.5%)
>60	6 (7.9%)	2 (5.9%)	8 (6.8%)

Interpretation: The highest proportion of study participants fell within the 31–45 years age group (37.3%), with **a** male predominance (69.1%)**.** This aligns with global epidemiological trends where TB is more prevalent in working-age adults, possibly due to occupational exposure, socioeconomic factors, and increased susceptibility due to smoking or alcohol use.

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Table 2: Sensitivity and Specificity of CBNAAT

Test Method	**Positive Cases (n)**	**Negative Cases (n)**	**Sensitivity (%)**	**Specificity (%)**	**p-value**
CBNAAT	50	60	88.09	96.50	**0.005**
Smear	10	24	51.02	85.00	

Interpretation: CBNAAT showed significantly higher sensitivity (88.09%) and specificity (96.50%) compared to conventional smear microscopy **(**sensitivity: 51.02%, specificity: 85.00%**).** This suggests that CBNAAT is a superior diagnostic tool for early TB detection**,** particularly in sputum-negative cases.

Table 3: Induced Sputum vs. BAL CBNAAT Positivity (Paired T-Test)

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Sample Type	Mean Positive Cases (%)	Standard Deviation
Induced Sputum	37.2	4.8
BAL	45.4	5.2

Interpretation: This implies that bronchoscopy is more effective at detecting TB, but it remains a semi-invasive procedure. In contrast, induced sputum is a simpler, non-invasive, cost-effective alternative, making it the preferred initial diagnostic approach.

Table 4: Time to Diagnosis (Mann-Whitney U Test)

Test Method	Median Time to Diagnosis (Days)	p-value
CBNAAT	**2**	**<0.001**
Culture	**21**	

Interpretation: While culture remains the gold standard for TB detection, it requires up to 21 days for definitive results. CBNAAT, with its rapid turnaround of approximately 2 hours, enables prompt initiation of treatment**,** which is crucial for reducing transmission rates and preventing disease progression**.**

Table 5: Chest X-Ray Findings vs. CBNAAT Positivity (Logistic Regression)

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X-ray Finding	TB Cases (n)	Odds Ratio (OR)	95% CI	p-value
Infiltrates	68	3.2	1.9–5.3	**0.014**
Cavities	37	5.5	3.1–9.4	**<0.001**

Interpretation: Patients presenting with cavity formation on chest X-ray (OR = 5.5, p < 0.001) had significantly higher odds of testing positive via CBNAAT than those with infiltrates (OR = 3.2, p = 0.014)**.** This suggests that cavitary TB represents a more advanced disease state with a higher bacillary load, making it more detectable via molecular testing**.**

Chest X-ray alone, however, has limitations due to reader variability and the absence of pathognomonic TB features. Thus, combining imaging with CBNAAT yields optimal diagnostic accuracy**.**

Table 6: Adverse Events During Sample Collection (Fisher's Exact Test)

Complication	Cases (n)	Percentage (%)	p-value
Mild Hemoptysis	5	4.5	**0.882**
Hypoxia	0	0.0	
Respiratory Distress	0	0.0	
Cardiac Arrhythmia	0	0.0	

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Interpretation: It indicates that CBNAAT sample collection is largely safe, with minimal risk of complications. The only notable complication observed was mild hemoptysis (4.5%), which resolved without intervention.

Given its high diagnostic yield and safety profile, CBNAAT is a viable frontline molecular test, particularly in resource-limited settings where early TB detection is essential.

Discussion

The evaluation of CBNAAT in sputum-negative presumptive TB patients has revealed its significant diagnostic utility compared to conventional methods. In this study, CBNAAT demonstrated high sensitivity (88.09%) and specificity (96.50%), significantly outperforming smear microscopy (sensitivity: 51.02%, specificity: 85.00%) (8). This reinforces CBNAAT's role as an effective frontline diagnostic tool, particularly in sputum-negative pulmonary TB cases.

Induced Sputum vs. Bronchoscopy

A comparative analysis between induced sputum and bronchoscopy samples showed that bronchoalveolar lavage (BAL) had a higher diagnostic yield (45.4%) compared to induced sputum (37.2%). The statistical analysis (Paired T-Test, $p = 0.021$) suggests that BAL samples are more sensitive, corroborating previous findings that bronchoscopy aids in early TB detection in smear-negative cases (9). However, induced sputum remains the preferred initial approach, given its non-invasive nature, cost-effectiveness, and ease of accessibility.

CBNAAT vs. Culture

Though culture remains the gold standard for TB diagnosis, its long turnaround time of approximately 21 days delays treatment initiation. In contrast, CBNAAT provides rapid results within 2 hours, allowing prompt medical intervention (10). The Mann-Whitney U Test

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($p < 0.001$) confirms the statistically significant advantage of CBNAAT in reducing diagnostic time. This aligns with prior studies demonstrating CBNAAT's efficacy in early TB detection, particularly in high-burden settings.

Radiological Correlation

Radiological assessment revealed that cavitatory lesions on chest X-ray had significantly higher CBNAAT positivity rates (OR = 5.5, $p < 0.001$). This finding emphasizes that patients with cavitary lesions exhibit higher bacillary loads, thereby increasing CBNAAT sensitivity (11). Chest X-ray alone is insufficient for definitive TB diagnosis, as 10-15% of culture-positive TB cases remain radiologically undetected, necessitating additional molecular tests for confirmation.

Safety and Clinical Utility

The Fisher's Exact Test ($p = 0.882$) demonstrated that CBNAAT sampling procedures were safe, with only 4.5% of cases experiencing mild hemoptysis during bronchoscopy (12). This further validates CBNAAT's routine application in high-burden clinical settings as a low-risk, high-efficiency molecular diagnostic tool.

Alternative Diagnoses

Among sputum-negative patients, FOB helped diagnose conditions beyond TB, including lung malignancies (7.2%), bacterial pneumonia (8.6%), and fungal pneumonia (4.3%) (13). This highlights the need for broader diagnostic consideration when evaluating patients with persistent pulmonary symptoms but negative sputum microscopy.

Conclusion

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CBNAAT has proven to be a transformative tool in TB diagnostics, particularly for sputum-negative presumptive TB patients. Given its high sensitivity, specificity, and rapid turnaround time, CBNAAT significantly improves early detection rates, enabling timely treatment initiation. While bronchoscopy increases diagnostic yield, its semi-invasive nature necessitates prioritization of non-invasive methods like induced sputum. Furthermore, integrating CBNAAT with radiological findings enhances diagnostic accuracy, making it an indispensable asset in modern TB management protocols.

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