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OPTIMIZING TUBERCULOSIS DIAGNOSIS: COST-EFFECTIVENESS OF CBNAAT AND INNOVATIVE SPUTUM STORAGE AND TRANSPORT METHODS IN RESOURCE-LIMITED RURAL SETTINGS

Respiratory Medicine

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ABSTRACT

Background: Tuberculosis (TB) remains a global health burden, with India among the worst affected. Xpert MTB/RIF CBNAAT offers high diagnostic sensitivity for TB and rifampicin resistance but is costlier than smear microscopy. This study assesses the cost-effectiveness of CBNAAT and simplified sputum handling in rural settings. **Methods:** A prospective study was conducted on 100 suspected TB patients at NUH CHC, Mewat. Single sputum samples were refrigerated without preservatives and transported unrefrigerated for CBNAAT and smear microscopy. **Results:** CBNAAT detected Mycobacterium tuberculosis in 94% of samples. Delays up to 42 days did not significantly affect culture positivity (P=0.12). Higher smear positivity (≥2+) was linked to faster culture isolation (P<0.001). Contamination rates were low (4%). **Conclusion:** CBNAAT, combined with simplified sputum storage and transport, is a cost-effective strategy for TB diagnosis in rural, resource-limited areas, ensuring high diagnostic yield while minimizing costs and logistical challenges.

KEYWORDS

Tuberculosis, CBNAAT, Sputum Transport, Cost-Effectiveness, Rural Settings

INTRODUCTION

Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a major global health issue, affecting nearly one-fourth of the world's population. Without treatment, the mortality rate can reach 50%, whereas timely intervention can cure up to 85% of cases.[1] India continues to carry one of the highest TB burdens, with an incidence of 210 per 100,000 population in 2021, as reported by the World Health Organization (WHO).[2] The Xpert MTB/RIF CBNAAT (Cepheid, USA) has demonstrated higher sensitivity than smear microscopy in diagnosing both pulmonary[3] and extrapulmonary[4] TB and offers the advantage of detecting rifampicin resistance. However, its high cost (INR 1450 or USD 22.50) compared to smear microscopy (INR 10 or USD 0.15) poses challenges in resource-limited settings. In such contexts, delayed CBNAAT results often prompt empirical treatment, which may be continued despite "MTB Not Detected" outcomes, raising concerns about cost-effectiveness.[5] Accurate collection and timely transport of sputum samples to quality-assured TB laboratories are crucial for reliable results that aid drug resistance surveillance.[6,7,8] However, in high-burden, low-resource settings, the process is often hindered by logistical and financial constraints. WHO recommends that two sputum specimens be collected and transported to a reference laboratory without delay.[6] Preservation agents like 0.6% cetylpyridinium bromide (CPB) or 1% cetylpyridinium chloride (CPC) are used during transport, but they require centrifugation prior to culture processing.[9] Unfortunately, many peripheral laboratories lack centrifuges with sufficient capacity to sediment mycobacteria reliably.[10,11]

This study aims to assess the cost-effectiveness of CBNAAT and explore practical sputum storage and transport strategies for enhancing TB diagnosis in rural, resource-constrained environments.

MATERIAL AND METHODS

This prospective study was conducted over six months at NUH CHC, Mewat, to assess the cost-effectiveness of CBNAAT in TB diagnosis and evaluate practical sputum storage and transport methods in rural settings. A total of 100 suspected TB patients, including adults and children from OPD and IPD, were enrolled after obtaining ethical clearance and informed consent. Each patient provided a pre-treatment sputum sample. In cases where spontaneous expectoration was difficult, sputum was induced using 0.9% saline. Ziehl–Neelsen staining was used for smear microscopy. If the smear was negative or CBNAAT was specifically requested, an early morning sample was collected and transported to a nearby CBNAAT facility. Clinical data were captured using pretest and posttest forms filled by treating physicians. These forms recorded sample details, HIV/diabetes status, prior TB history, diagnostic confidence, treatment decisions, and the perceived utility of CBNAAT.

Samples were stored in sterile, preservative-free containers under refrigeration for up to 14 days and transported unrefrigerated within 1 to 7 days. Most samples were ≥2 mL in volume, though smaller volumes were accepted. CBNAAT was used to detect Mycobacterium tuberculosis and rifampicin resistance. Results were compared with smear microscopy and clinical outcomes. Statistical analysis explored the association between clinician confidence, test results, and storage/transport variables, with outcomes presented as percentages and odds ratios.

RESULTS

Table 1 represents a high culture positivity rate for Mycobacterium tuberculosis (94%), indicating effective diagnostic methods. Rapid-growing mycobacteria and no growth outcomes were minimal, accounting for 2% and 4% of specimens, respectively.

Table 1: Results Of Culture Of Sputum Specimens

Culture Outcome	n (%)	95% CI
Mycobacterium tuberculosis	94 (94.0)	87.5–97.8
Rapid-growing mycobacteria*	2 (2.0)	0.2–7.0
No growth	4 (4.0)	1.1–9.8
Total	**100 (100)**	

Table 2 represents the time delay between specimen collection and inoculation did not significantly impact the recovery of Mycobacterium tuberculosis. The median time to positive culture remained consistent across all intervals, with a slight decrease observed for specimens processed within 15–21 days. The findings (P=0.12) suggest that moderate delays in processing are unlikely to compromise culture outcomes.

Table 2: Effect Of Time Delay To Process Sputum Specimens On Recovery Of Mycobacterium Tuberculosis

Days (from collection to inoculation)	Patients n (%)	Time to Positive Culture Median (Range)	P-value
1–7	9 (9.0%)	13.0 (7–23)	
8–14	20 (20.0%)	13.0 (7–24)	
15–21	28 (28.0%)	11.5 (7–24)	
22–28	25 (25.0%)	13.0 (6–23)	
29–42	18 (18.0%)	12.5 (9–25)	
Total	**100 (100.0%)**	**13.0 (6–25)**	**0.12**

Table 3 demonstrated a significant correlation between smear positivity and time to culture isolation (P < 0.001). Higher smear positivity (2+ and 3+) was associated with shorter median times to

culture (13 and 11 days, respectively). In contrast, smear-negative and scanty specimens took longer (21 and 16 days, respectively) to yield culture results. This emphasizes the diagnostic value of smear-positive specimens in expediting TB diagnosis.

Table 3: Smear Positivity and Time to Isolation of Mycobacterium tuberculosis

Smear Microscopy Result	Patients n (%)	Time to Culture Median (Range)	P-value
Negative	2 (2.0%)	21 (19–23)	
Scanty	5 (5.0%)	16 (16–21)	
1+	19 (19.0%)	15 (10–25)	
2+	28 (28.0%)	13 (6–19)	
3+	46 (46.0%)	11 (6–24)	
Total	**100 (100.0%)**	**13 (6–25)**	**< 0.001**

DISCUSSION

This study evaluated the cost-effectiveness of CBNAAT and assessed simplified sputum storage and transport methods for optimizing TB diagnosis in rural, resource-limited settings. Despite delays in laboratory processing, 94% of single sputum specimens yielded positive Mycobacterium tuberculosis cultures, indicating that high diagnostic yield can be maintained without multiple samples or complex protocols.

WHO's DRS guidelines recommend collecting two sputum specimens per patient to improve culture positivity, but this increases cost and burden.[6,8] In contrast, our findings suggest that a single specimen is sufficient, reducing logistical complexity. These results align with previous studies. Lumb et al. showed that refrigerated specimens without preservatives preserved M. tuberculosis viability effectively.[12] Pardini et al. demonstrated comparable outcomes for CPC-treated and untreated specimens, particularly when smear positivity was ≥1+.[13] Studies also found that CPC-treated samples stored at room temperature performed better on LJ medium but showed no advantage with MGIT 960.[13,14,15]

Our study observed a high culture positivity rate (94%), low contamination (4%), and minimal impact of delayed processing (up to 42 days; $P = 0.12$). Smear positivity ≥2+ was significantly associated with faster culture growth ($P < 0.001$). These findings support the use of affordable, simplified sputum handling in rural areas, avoiding costly preservatives and unnecessary centrifugation steps.

Limitations Of The Study

This study's limitations include a small sample size (100 participants) and its confinement to a single rural area, limiting generalizability. The use of a single sputum specimen may have missed cases where multiple samples improve diagnosis. Long-term patient outcomes based on CBNAAT-guided treatment were not assessed. Additionally, sputum preservation methods were not extensively compared, with the study relying mainly on refrigeration over chemical preservatives like CPC or CPB.

Strengths Of The Study

The study's strengths include its prospective design, focus on a high-burden rural setting, and practical assessment of CBNAAT and sputum handling methods. It demonstrated high culture positivity using single, refrigerated specimens without chemical preservatives, highlighting a cost-effective and scalable diagnostic approach. The evaluation of transport delays and correlation with smear positivity adds valuable operational insights for TB control in resource-limited environments.

CONCLUSION

CBNAAT proves to be a cost-effective and reliable tool for TB diagnosis in rural, resource-limited settings. A single refrigerated sputum sample without preservatives yields high culture positivity with minimal contamination. Simplified storage and transport, combined with CBNAAT, can reduce costs and logistical burdens while maintaining diagnostic accuracy, offering a scalable solution for TB control in low-resource areas.

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