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Bronchoalveolar Lavage CBNAAT in Sputum-Negative Presumptive Tuberculosis: Diagnostic Yield and Clinicoradiological Predictors in a High-Burden Tertiary Setting

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ABSTRACT

Background: Patients with persistent clinicoradiological suspicion of pulmonary tuberculosis may remain negative on sputum smear microscopy and sputum CBNAAT, delaying confirmation and treatment.
Objective: To determine the diagnostic yield of bronchoalveolar lavage (BAL) fluid CBNAAT and identify clinical and radiological predictors of positivity.
Materials and Methods: This observational study enrolled 70 adults at a tertiary respiratory centre in Jodhpur, India. All had two sputum samples negative for acid-fast bacilli and one sputum sample negative on CBNAAT. Fibreoptic bronchoscopy with BAL was performed, and samples were tested by AFB smear, CBNAAT and mycobacterial culture. Diagnostic performance was estimated against the final composite diagnosis. Associations with BAL CBNAAT positivity were explored using univariate and multivariable logistic regression.
Results: The mean age was 45.04 ± 13.91 years and 45 (64.3%) participants were men. BAL CBNAAT was positive in 21/70 patients (30.0%; 95% CI 20.5-41.5), BAL culture in 24 (34.3%) and BAL AFB smear in 11 (15.7%). Pulmonary tuberculosis was the final diagnosis in 26 patients (37.1%). BAL CBNAAT showed 80.8% sensitivity, 100% specificity, 100% positive predictive value, 89.8% negative predictive value and 92.9% accuracy. Fever, loss of appetite and night sweats were associated with positivity on univariate analysis. Upper-lobe involvement (crude OR 5.00) and cavitation (crude OR 13.94) were strong radiological predictors; upper-lobe involvement remained independently associated after adjustment (adjusted OR 6.56, 95% CI 1.54-27.97; p=0.011). Bronchoscopy also established alternative diagnoses in 44 patients and caused only minor, self-limited complications.
Conclusion: BAL CBNAAT provides rapid, highly specific confirmation in a clinically challenging sputum-negative population. Culture remains complementary, while upper-lobe disease can help prioritize patients for bronchoscopy.

Keywords: *Bronchoalveolar lavage; CBNAAT; sputum-negative tuberculosis; Xpert MTB/RIF; bronchoscopy; diagnostic yield; predictors.*

INTRODUCTION

Tuberculosis remains a major public-health problem, and current global estimates continue to place India among the countries contributing the largest share of incident disease. Rapid bacteriological confirmation is central to interrupting transmission, identifying drug resistance and avoiding unnecessary empirical therapy.[1]

The diagnostic pathway is particularly difficult when patients have persistent symptoms and radiological abnormalities suggestive of pulmonary tuberculosis but remain negative on routine sputum examination. Smear microscopy is insensitive in paucibacillary disease, and even sputum CBNAAT may be unrevealing when bacillary load is low or the

sample is inadequate. Bronchoscopy permits targeted lower-respiratory sampling from the radiologically involved segment, while BAL can be processed simultaneously for smear, molecular testing, culture and evaluation of competing diagnoses.[2-6]

Studies across different settings have shown that Xpert MTB/RIF on bronchoscopic specimens substantially outperforms smear microscopy and can provide clinically actionable results before culture becomes available. Nevertheless, reported yields vary with disease prevalence, patient selection and radiological phenotype. Evidence from high-burden Indian tertiary centres remains important because the threshold for invasive testing must balance diagnostic delay, bronchoscopy resources and the possibility of alternative disease.[2-10]

We therefore evaluated BAL fluid CBNAAT among patients with presumptive pulmonary tuberculosis who were negative on both sputum AFB smear and sputum CBNAAT. The study also examined clinicoradiological features associated with BAL CBNAAT positivity, with the aim of identifying patients most likely to benefit from bronchoscopy.

MATERIALS AND METHODS

Study design and participants

This observational study was conducted in the Department of Respiratory Medicine, Kamla Nehru Chest Hospital, Dr. S.N. Medical College, Jodhpur, Rajasthan. Consecutive eligible adults with clinical and radiological suspicion of pulmonary tuberculosis were enrolled after written informed consent. Eligibility required two sputum samples negative for AFB smear and one sputum sample negative on CBNAAT. Patients with sputum-confirmed tuberculosis, extrapulmonary tuberculosis, resting SpO_2 below 90%, bleeding diathesis, recent myocardial infarction or another contraindication to bronchoscopy were excluded. The calculated minimum sample was 67; 70 participants were included.

Bronchoscopy and laboratory evaluation

After pre-procedure clinical and laboratory assessment, flexible fibreoptic bronchoscopy was performed under local anaesthesia and protocol-based conscious sedation with continuous cardiorespiratory monitoring. The bronchoscope was wedged in the segment corresponding to the principal radiological abnormality. Pre-warmed sterile normal saline was instilled in aliquots, with a total volume of approximately 100-150 mL according to tolerance and return. BAL fluid was divided for AFB smear microscopy, CBNAAT, mycobacterial culture and cytological or other microbiological assessment when clinically indicated. Participants were monitored for immediate adverse events after the procedure.

Outcomes and statistical analysis

The primary outcome was BAL CBNAAT positivity (diagnostic yield). Secondary outcomes included the yield of BAL smear and culture, diagnostic performance against the final composite diagnosis, alternative diagnoses, complications and predictors of BAL CBNAAT positivity. Final diagnoses were assigned from the available clinical, radiological, microbiological, cytological or histopathological evidence and follow-up assessment. Continuous data are presented as mean ± standard deviation and categorical data as number (percentage). Categorical associations were tested using the chi-square test or Fisher exact test as appropriate. Crude odds ratios were calculated, followed by an exploratory multivariable logistic-regression model including variables significant on univariate analysis. A two-sided p value <0.05 was considered significant. Analyses were performed using SPSS (IBM Corp., Armonk, NY, USA).

Ethics

The Institutional Ethics Committee of Dr. S.N. Medical College approved the study (SNMC/IEC/2026/Plan/1237; 9 January 2026). Written informed consent was obtained from every participant, and confidentiality was maintained.

RESULTS

Seventy patients completed bronchoscopy and BAL evaluation. The mean age was 45.04 ± 13.91 years (range 19-72), and 45 (64.3%) were men. Cough, weight loss and fever were the dominant presenting features. Consolidation was the most frequent imaging abnormality in the full cohort, whereas upper-lobe disease and cavitation were enriched among BAL CBNAAT-positive patients (Table 1).

Table 1: Baseline clinical and radiological profile (n=70)

Characteristic	Value
Age, years	45.04 ± 13.91
Male sex	45 (64.3)
Current smoker	28 (40.0)
Former smoker	11 (15.7)
Alcohol use	27 (38.6)
Diabetes mellitus	15 (21.4)

Characteristic	Value
Previous tuberculosis	16 (22.9)
Tuberculosis contact	24 (34.3)
Cough	62 (88.6)
Weight loss	44 (62.9)
Fever	42 (60.0)
Loss of appetite	36 (51.4)
Night sweats	20 (28.6)
Upper-lobe involvement	28 (40.0)
Cavitary lesion	13 (18.6)
Bilateral involvement	21 (30.0)
Consolidation	33 (47.1)

Values are mean ± SD or n (%).

BAL CBNAAT was positive in 21 patients, corresponding to a diagnostic yield of 30.0% (95% CI 20.5-41.5). BAL mycobacterial culture had the highest positivity rate (34.3%), while BAL AFB smear was positive in 15.7%. Among the 26 patients assigned a final diagnosis of pulmonary tuberculosis, CBNAAT identified 21, culture 24 and smear 11. CBNAAT therefore achieved a sensitivity of 80.8%, specificity of 100%, positive predictive value of 100%, negative predictive value of 89.8% and accuracy of 92.9% (Table 2).

Table 2: Yield and diagnostic performance of BAL investigations

Test	Positive n (%)	Sensitivity %	Accuracy %
BAL CBNAAT	21 (30.0)	80.8	92.9
BAL AFB smear	11 (15.7)	42.3	78.6
BAL culture	24 (34.3)	92.3	97.1

All three tests had 100% specificity and positive predictive value against the final composite diagnosis. Negative predictive values were 89.8% for CBNAAT, 74.6% for smear and 95.7% for culture. BAL, bronchoalveolar lavage; CBNAAT, cartridge-based nucleic acid amplification test; AFB, acid-fast bacilli.

On univariate analysis, fever, loss of appetite and night sweats were significantly associated with BAL CBNAAT positivity, while weight loss showed a non-significant trend. The strongest unadjusted association was observed for night sweats (OR 6.83). Radiologically, upper-lobe involvement (OR 5.00) and cavitation (OR 13.94) were strongly associated with positivity; bilateral involvement and consolidation were not (Table 3).

Table 3: Univariate predictors of BAL CBNAAT positivity

Predictor	Positive n=21	Negative n=49	Crude OR (95% CI)	p
Fever	17 (81.0)	25 (51.0)	4.08 (1.20-13.89)	0.032
Weight loss	16 (76.2)	28 (57.1)	2.40 (0.76-7.60)	0.179
Loss of appetite	15 (71.4)	21 (42.9)	3.33 (1.11-10.04)	0.038
Night sweats	12 (57.1)	8 (16.3)	6.83 (2.17-21.57)	0.001
Upper-lobe disease	14 (66.7)	14 (28.6)	5.00 (1.67-15.00)	0.004
Cavitary lesion	10 (47.6)	3 (6.1)	13.94 (3.28-59.32)	<0.001
Bilateral disease	9 (42.9)	12 (24.5)	2.31 (0.78-6.82)	0.158
Consolidation	10 (47.6)	23 (46.9)	1.03 (0.37-2.86)	1.000

In the exploratory multivariable model, upper-lobe involvement remained independently associated with BAL CBNAAT positivity (adjusted OR 6.56, 95% CI 1.54-27.97; p=0.011). Cavitation retained a large effect estimate but did not reach conventional statistical significance after adjustment (adjusted OR 6.51; p=0.062). Fever was borderline significant, while appetite loss and night sweats were attenuated (Table 4).

Table 4: Exploratory multivariable logistic-regression model

Variable	Adjusted OR	95% CI	p
Fever	4.97	0.98-25.23	0.053
Loss of appetite	2.65	0.62-11.31	0.187
Night sweats	2.95	0.58-14.98	0.191
Upper-lobe involvement	6.56	1.54-27.97	0.011
Cavitary lesion	6.51	0.91-46.42	0.062

The model is exploratory because only 21 BAL CBNAAT-positive events were available.

Pulmonary tuberculosis was the most frequent final diagnosis but accounted for only 37.1% of the cohort. Bronchoscopy and the subsequent diagnostic work-up also identified inflammatory, infectious, granulomatous and malignant alternatives (Table 5). Bronchoscopy was uncomplicated in 60 patients (85.7%). Transient desaturation occurred in five (7.1%), minor bleeding in three (4.3%) and short-lived post-procedure fever in two (2.9%); no major life-threatening complication was recorded.

Table 5: Final diagnoses among the study participants

Final diagnosis	n (%)
Pulmonary tuberculosis	26 (37.1)
Nonspecific inflammation	13 (18.6)
Bacterial pneumonia	9 (12.9)
Post-tuberculosis sequelae	6 (8.6)
Sarcoidosis	5 (7.1)
Organizing pneumonia	4 (5.7)
Malignancy	4 (5.7)
Fungal infection	3 (4.3)

DISCUSSION

In this sputum AFB- and CBNAAT-negative cohort, BAL CBNAAT established rapid microbiological confirmation in 30% of all patients and in 21 of 26 patients with final pulmonary tuberculosis. Its sensitivity of 80.8% was substantially higher than BAL smear microscopy and approached the performance reported for bronchoscopic Xpert testing in several prior studies. Lee et al. observed 81.6% sensitivity and 100% specificity in bronchoscopy specimens, closely mirroring our findings. Theron et al. similarly demonstrated that BAL Xpert improved accuracy and reduced empirical treatment in smear-negative or sputum-scarce disease.[2,3]

The overall 30% positivity rate is best interpreted as incremental yield after a deliberately restrictive sputum-negative selection process. Published yields vary because some studies enrol sputum-scarce patients, others include only culture-confirmed disease, and the prevalence of tuberculosis differs widely. Khalil and Butt, Gowda et al., Pan et al. and Kilaru et al. each found that BAL Xpert provided clinically useful additional confirmation and outperformed smear microscopy. A 2021 meta-analysis also concluded that Xpert on BAL has high pooled diagnostic performance against culture and composite reference standards.[5,7-10]

Culture remained the most sensitive investigation in our cohort, but CBNAAT offers the practical advantage of rapid availability. The two tests should therefore be regarded as complementary rather than competing. A positive BAL CBNAAT provided strong rule-in evidence, whereas a negative result did not fully exclude disease and required continued culture, histopathological evaluation when appropriate and clinical follow-up. This approach is consistent with more recent bronchoscopic series and systematic reviews.[10-13]

A notable contribution of this study is the assessment of predictors. Constitutional symptoms were useful enrichment features on univariate analysis, especially night sweats, but their effects were attenuated when radiological variables entered the model. Upper-lobe involvement emerged as the most stable independent predictor, while cavitation showed a strong but imprecise adjusted association. These findings are biologically plausible because upper-zone and cavitary disease generally reflect a higher local bacillary burden, making targeted lavage more likely to recover detectable mycobacterial DNA. They also support using imaging to select the bronchial segment and to prioritize bronchoscopy when resources are constrained. Imtiaz and Batubara likewise reported clinically meaningful relationships between bronchoscopic yield and clinicoradiological features.[12]

Bronchoscopy also prevented diagnostic anchoring on tuberculosis. Nearly two-thirds of the cohort ultimately had an alternative diagnosis, including bacterial pneumonia, sarcoidosis, organizing pneumonia, fungal infection and

malignancy. This broader diagnostic value is important in tertiary practice, where empirical antitubercular treatment can delay disease-specific management. The procedure was generally well tolerated, with only minor complications, supporting its selective use in appropriately screened patients.[6,13,14]

Strengths and limitations

The study addressed a well-defined, clinically difficult population and applied a uniform BAL work-up incorporating smear, molecular testing and culture. It also assessed both rapid diagnosis and patient-selection variables. Limitations include the single-centre design, modest sample size and selection of patients fit for bronchoscopy. The multivariable model had only 21 positive events and may be overfitted; its estimates should be considered hypothesis-generating. In addition, the final composite diagnosis was informed by BAL microbiology, creating potential incorporation bias in the reported diagnostic-performance measures. Long-term outcomes, cost-effectiveness and time to treatment were not assessed, and the results may not generalize to children, severely hypoxaemic patients or immunocompromised populations.

CONCLUSION

BAL fluid CBNAAT provided rapid confirmation in 30% of patients whose sputum AFB smears and sputum CBNAAT were negative, with high specificity and clinically useful sensitivity. Mycobacterial culture remained more sensitive and should be performed concurrently. Upper-lobe involvement independently predicted CBNAAT positivity, while cavitation showed a strong association and may further enrich patient selection. In high-burden tertiary settings, targeted bronchoscopy with BAL is a valuable next diagnostic step when clinicoradiological suspicion persists after negative sputum testing, both for confirming tuberculosis and for identifying important alternative diagnoses.

ETHICS AND DISCLOSURES

Ethics approval and consent: Approved by the Institutional Ethics Committee, Dr. S.N. Medical College, Jodhpur (SNMC/IEC/2026/Plan/1237). Written informed consent was obtained from all participants.
Financial support and sponsorship: Nil.
Conflicts of interest: None declared.

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