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Diagnostic utility of flexible bronchoscopy in smear-negative and atypical lung infections: identifying tuberculosis, fungal, and non-tuberculous mycobacteria infections and malignancy

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Abstract

Fiber-optic bronchoscopy (FOB) plays a crucial role in the diagnosis and management of various pulmonary diseases by offering direct visualization of the airways and enabling targeted sampling for microbiological and histopathological evaluation. This study aimed to assess the clinical, radiological, microbiological, and histopathological profiles of patients undergoing FOB.

A retrospective analysis of 103 participants who underwent the procedure over one year was conducted. After obtaining informed consent, demographic and clinical information was recorded, and relevant radiological findings were noted. The procedure was performed under local anesthesia. In all cases with inconclusive sputum evaluation, bronchoalveolar lavage (BAL) was conducted, with additional brushing and biopsy performed in selected participants. The collected samples were analyzed to determine the underlying etiology. Among the 103 individuals studied, 52.4% were female, with a mean age of 54.82 years, and the majority (82.5%) were over 40 years old. Cough was the most common symptom (73.78%), followed by breathlessness. The frequent comorbidities included diabetes (27.18%) and hypertension (18.4%). Radiological patterns commonly included consolidation (59%) and cavitary lesions (30.1%). On bronchoscopy, secretions (67%) and inflamed mucosa (26%) were the most frequent findings. BAL cultures were positive in 48% of cases, with Klebsiella being the predominant organism. Tuberculosis was confirmed in 32% of the cases. Histopathology confirmed malignancy in 5.8%, mainly adenocarcinoma. In 24.2% of participants, the procedure was inconclusive.

Overall, FOB was found to be a safe and valuable tool in diagnosing a spectrum of pulmonary conditions, especially in smear-negative tuberculosis, fungal and atypical infections, and malignancies, aiding targeted therapy and better clinical outcomes.

Key words: FOB, *Mycobacteria tuberculosis*, lung malignancy, bronchoalveolar lavage.

Introduction

Fiberoptic Bronchoscopy (FOB) is an essential tool for clinicians involved in the care of patients with lung diseases. Since Shigeto Ikeda introduced FOB to clinical practice in 1966, it has become a vital method for diagnosing and managing various pulmonary conditions. FOB has significantly improved the early diagnosis of diseases such as tuberculosis, lung malignancies, and both infectious and non-infectious disorders by providing valuable samples from the lower respiratory tract. This early intervention can help prevent complications associated with delayed or missed diagnoses. Often, clinical and radiological findings alone are insufficient to differentiate between various conditions. In such instances, bronchoscopy enables precise sampling and offers critical insights that aid in accurate diagnosis and treatment.

Materials and Methods

This retrospective cross-sectional study analyzed data from 103 participants who underwent fiberoptic bronchoscopy at a tertiary care center in Mangalore, with approval from the Institutional Ethics Committee. The study focused on subjects who underwent fiberoptic bronchoscopy (FOB) between April 2023 and May 2024, following inconclusive results from their initial sputum evaluation. Following the acquisition of informed consent, demographic and clinical information, as well as relevant radiological findings, were collected. Bronchoscopy was performed under local anesthesia, and bronchoalveolar lavage (BAL) was conducted for all participants. Brushing and biopsy were performed in selected cases based on radiological assessments. Findings from bronchoscopy, BAL reports indicating organism growth, and histopathological and cytological results were meticulously documented and analyzed.

Results

In this study involving 103 participants who underwent FOB, females constituted 52.4% of the cohort, with a mean age of 54.83 ± 16.18 years; notably, 49.5% were aged over 60. Common comorbidities included diabetes (27.18%) and hypertension (18.4%). Additionally, previous pulmonary tuberculosis and obstructive airway diseases were observed in 7.8% of participants. Other comorbid conditions included rheumatoid arthritis (9.7%), malignancy (6.8%), cerebrovascular accident (CVA) (3.9%), chronic kidney disease (CKD) (4.9%), and renal vascular disease (RVD) (2.9%) (Table 1).

Cough was the predominant symptom reported by 70.9% of participants, followed by breathlessness (41.7%) and fever (31.1%). Additional symptoms included chest pain (14.6%), weight loss (10.7%), and hemoptysis (8.7%). Radiologically, consolidation was observed in 59.2% of cases, while cavitary lesions were present in 30.1%. Other frequent findings included

bronchiectasis (19.4%) and centrilobular nodules (11.7%). Additional radiological abnormalities included lung collapse (8.7%), pleural effusion (7.8%), fibrosis (10.7%), "tree-in-bud" patterns (6.8%), abscesses (1.9%), miliary nodules (2.9%), and masses (2.9%) (Table 2).

Bronchoscopy findings included secretions (68%) and inflamed airways (26.2%), bleeding (5.8%) and growths (4.9%) noted. Mucus plug was found in 8.7 % and extrinsic compression in 1.9% of participants (Table 3).

BAL culture growth was observed in 48% of participants, with Klebsiella identified in 17.5% and Pseudomonas in 6.8%. Additionally, Mycobacterial tuberculosis (TB) was detected in 5.8% of cases, while non-tuberculous mycobacteria (NTM) were found in 3.9%. The GeneXpert assay identified Mycobacterium tuberculosis (MTB) in 31.06% of participants. Fungal organism growth was noted in 10.7% of the cohort (Table 4).

Cytological analysis of the BAL samples revealed malignant cells in 2 participants, representing 1.9% of the cohort. Brushing was performed on 49 participants, with 41.7% showing no atypia and 5.8% exhibiting atypia.

Among the 103 participants, 35.9% were diagnosed with bacterial infections, while pulmonary tuberculosis was identified in 32%. Fungal infections were noted in 10.7%, and NTM were found in 4.9%. Mucus plugs were present in 2.9% of cases, and anaerobic infections were detected in 1.9%. Malignancy was diagnosed in 5.8% of participants, with adenocarcinoma being the most common type. However, even after bronchoscopic evaluation, no specific organism was identified by microscopy, and no definitive histopathological diagnosis was achieved in 24% of the participants (Table 5).

Discussion

Fibreoptic bronchoscopy is an essential technique for diagnosing a range of respiratory diseases. This safe and effective procedure has transformed the diagnosis of lung infections by allowing clinicians to obtain samples for culture and sensitivity testing. As a result, it plays a critical role in guiding appropriate treatment strategies and improving patient outcomes.

In our study, most participants were over 40 years old, aligning with findings by Mullerova *et al.* and Merino-Sanchez *et al.* [1,2]. Comorbidities were common, particularly diabetes (27.2%) and hypertension (18.2%), with fewer cases of rheumatoid arthritis, post-TB sequelae, CKD, and RVD. These results highlight the increased risk of lung diseases among immunocompromised individuals, often requiring bronchoscopy. Cough was the most frequent symptom (70.9%), followed by dyspnoea and fever, consistent with studies by Prakash UB *et al.* and Prabhakar K *et al.,* underscoring its importance in respiratory evaluation [3,4].

Radiologically, consolidation was the most common finding (59.2%), followed by cavitary lesions. Less frequent features included bronchiectasis, centrilobular nodules, masses, and lung collapse. In most patients with consolidation, bronchoscopy identified an underlying cause—predominantly infections. Similar to studies by Alamoudi *et al.* and Alzeer *et al.,* chest infections were the leading indication for bronchoscopy [5,6]. Pulmonary tuberculosis emerged as the most common infection in our cohort, followed by bacterial pathogens like *Klebsiella* and *Pseudomonas*. These findings align with Sawy *et al*., though Taha *et al*. reported malignancy as the most common cause in their study [7,8]. In our study, adenocarcinoma was the leading non-infective cause of consolidation. Bronchoscopy failed to yield a diagnosis in small proportion of consolidation cases, highlighting its limitations and the need for multimodal diagnostic strategies.

For cavitary lesions, MTB was the most common cause, followed by bacterial infections; fungal infections were rare. TB was also the most frequent cause in cases presenting with both cavities and consolidation. Given India's TB burden, early diagnosis—especially in smear-negative cases—is essential to avoid complications. MTB was confirmed in 32% of cases using BAL PCR and culture, consistent with Sultan Q *et al.* and prior reports on variable diagnostic yields in smear-negative TB patients [9-11].

BAL cultures were positive in 56% of cases, with *Klebsiella* (17.5%) as the most commonly isolated organism, followed by *Pseudomonas* (6.8%). In our cohort, bronchoscopy led to a change in the treatment plan in approximately 20% of patients by enabling the collection of BAL samples for aerobic culture, which allowed for targeted antibiotic adjustments. This finding aligns with broader literature, where BAL-directed antimicrobial modification was possible in 29% to 75% of ICU patients, depending on the study population and clinical indications [12,13]. The ability to tailor antibiotics based on culture and sensitivity data is crucial, especially given the rising challenge of antimicrobial resistance [12]. Bronchoscopy facilitated the addition of anaerobic coverage in 2% of patients, a step that is often overlooked in routine management of respiratory infections. Recent evidence suggests that anaerobes and oral bacteria are more frequently implicated in community-acquired pneumonia (CAP) than previously recognized.

Other organisms included fungi, MTB, and NTM. Bronchoscopy confirmed pulmonary tuberculosis in 32% of patients, facilitating timely initiation of anti-TB therapy and preventing unnecessary treatment. This aligns with studies showing bronchoscopy—particularly when combined with transbronchial biopsy—as a reliable diagnostic tool in sputum-negative or non-productive TB cases [14,15]. The sensitivity of BAL alone can reach 60%, and increases with histopathology and post-bronchoscopy sputum analysis [14]. Early, accurate diagnosis is essential to avoid both overtreatment and undertreatment, and to reduce nosocomial

transmission. Notably, antimicrobial therapy adjustments based on BAL findings improved clinical outcomes; a recent study reported therapy modifications in 63.9% of cases, yielding a higher response rate (63% vs. 45%) [12]. This highlights the clinical value of bronchoscopy in guiding targeted treatment. Our BAL culture yield aligns with findings by Velez *et al*. and Kottmann *et al*., who reported yields of 51.6% and 55.8%, respectively [16,17]. While Vivek K. U *et al*. reported a lower yield of 38%, their study—along with those by Lin *et al*. and Singh AK *et al*. also identified *Klebsiella* as the most common isolate, consistent with our observations [18-20].

Bronchoscopy identified fungal infections in 10.7% and NTM infections in 5% of patients, facilitating timely initiation of appropriate therapies that might have otherwise been delayed or missed. Radiologically, most patients with fungal culture positivity exhibited consolidation (55%) , followed by cavitary lesions, whereas those with NTM infections commonly presented with consolidation and nodular lesions. The utility of BAL in accessing lower respiratory tract specimens is vital for accurate microbiological diagnosis, especially when sputum samples are unreliable or non-invasive tests are limited [21,22]. BAL is particularly valuable in diagnosing NTM infections, where a single positive culture can confirm disease in cases with inconclusive sputum and radiologic findings that mimic malignancy [21,23]. Accurate species identification through BAL also guides treatment choices and duration for fungal and NTM infections, both of which require tailored management due to variable drug susceptibilities [22].

Bronchoscopy also facilitated the diagnosis of malignancy in 5.8% of patients, confirmed through histopathological examination (HPE) of biopsy samples and, in some cases, by brushing cytology, including 3% initially misdiagnosed with infections. This underscores a common diagnostic challenge, as lung cancers especially adenocarcinoma can clinically and radiologically mimic infections, leading to delays in appropriate treatment [21,24]. Flexible bronchoscopy remains a key diagnostic tool, allowing direct visualization and biopsy of suspicious lesions, and is crucial when imaging is inconclusive [24]. Early, accurate diagnosis through bronchoscopy helps prevent inappropriate therapy and accelerates initiation of definitive oncologic care.

Conclusions

Bronchoscopy remains an indispensable diagnostic tool in the evaluation of patients with pneumonia, particularly those presenting with radiological consolidation or cavitary lesions and smear-negative MTB. As a safe and highly effective procedure, bronchoscopy offers substantial diagnostic yield for a range of pulmonary infections and malignancies. Through BAL and tissue biopsy, it facilitates accurate microbiological and histopathological diagnoses, guiding targeted treatment and improving clinical outcomes. Our findings highlight the critical

role of bronchoscopy in confirming tuberculosis, identifying fungal and NTM infections, and diagnosing malignancy in cases with non-specific clinical and imaging features. Bronchoscopy significantly influences patient management by reducing diagnostic delays, enabling tailored therapy, and supporting antibiotic stewardship. Its use should be judiciously considered based on clinical context, balancing diagnostic benefit with safety and resource availability.

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Table 1. Baseline characteristics of the subjects who underwent flexible bronchoscopy.

		N	Percentage
Age group (years)	<20 years	4	3.9
	20-39 years	14	13.6
	40-59 years	34	33
	60 years	51	49.5
	Mean ± SD	54.83 ± 16.18 years	
Gender	Female	54	52.4
	Male	49	47.6
Co morbidity	Type 2 DM	28	27.2
	Hypertension	19	18.4
	Old pulmonary tuberculosis	8	7.8
	Obstructive airway diseases	8	7.8
	Rheumatoid arthritis	10	9.7
	Malignancy	7	6.8
	Cerebrovascular accidents (CVA)	4	3.9
	Chronic kidney disease (CKD)	5	4.9
	Retro viral diseases (RVD)	3	2.9

Table 2. Clinical characteristics of the subjects who underwent bronchoscopy.

		N	Percentage
Symptoms	Chest pain	15	14.6
	Weight loss	11	10.7
	Cough	73	70.9
	Breathlessness	43	41.7
	Fever	32	31.1
	Haemoptysis	9	8.7
	Vomiting	1	1
Radiological features	Cavity	31	30.1
	Consolidation	61	59.2
	Collapse	9	8.7
	Effusion	8	7.8
	Abscess	2	1.9
	Bronchiectasis	20	19.4
	Central nodule	12	11.7
	Miliary nodule	3	2.9
	Mass	3	2.9
	Fibrosis	11	10.7
	Tree on bud	7	6.8

Table 3. Distribution of study subjects according to Bronchoscopy features.

Bronchoscopy features	N	Percentage
Secretion	70	68
Growth	5	4.9
Mucous plug	9	8.7
Inflamed airway	27	26.2
Bleeding	6	5.8
Extrinsic compression	2	1.9

Table 4. Distribution of study subjects according to microbial growth.

Growth		N	Percentage
Bacterial	Pseudomonas	7	6.8
	Klebsiella	18	17.5
	Enterococcus	3	2.9
	Acinetobacter	3	2.9
	MTB	6	5.8
	NTM	4	3.9
	Others	6	5.8
Fungal		11	10.7

Table 5. Distribution of study subjects according to final diagnosis.

Diagnosis	N	Percentage
Inclusive	25	24.3
Bacterial infection	37	35.9
Fungal infection	11	10.7
PTB	33	32
Mucous plug	3	2.9
Anaerobic infection	2	1.9
NTM	5	4.9
Malignancy	6	5.8
	SCC	1 (0.97%)
	Adeno carcinoma	3 (2.9%)
	Neuro endocrine tumour	2 (1.94%)