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Original Article

Internal Medicine Section

Clinicoradiological Profile of Endobronchial Tuberculosis: A Cross-sectional Study

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ABSTRACT

Introduction: Tuberculosis (TB) is a disease that causes severe mortality and morbidity worldwide, including India. Endobronchial Tuberculosis (EBTB) is an uncommon form of TB, which is often underdiagnosed due to the difficulty in diagnosis. This form of TB often has a poor prognosis and long-lasting sequelae.

Aim: To study the proportion of EBTB in clinically diagnosed pulmonary TB and to study the clinicoradiological and bronchoscopic profile of EBTB.

Materials and Methods: This study was a hospital-based record-based cross-sectional study that included patients with sputum smear negative for Acid-Fast Bacilli (AFB) and *Mycobacterium tuberculosis* (*M. tuberculosis*) not detected on Nucleic Acid Amplification Test (NAAT), who were clinically diagnosed with TB. Bronchoscopy was performed on such patients, and samples were sent for investigations, including histopathology and NAAT. Demographic characteristics, bronchoscopy and radiology findings, and microbiology results were documented. Quantitative variables were summarised as means, and categorical variables were presented as percentages.

Results: A total of 198 underwent bronchoscopy, of which 20 (10%) were diagnosed with EBTB. The mean age was 22 years, and 65% were females. The most common clinical feature in these patients was fever, the most common radiological presentation was lobar collapse, and the most common bronchoscopy feature was a tumorous lesion. NAAT detected *M. tuberculosis* in the bronchial wash in 50% of patients diagnosed with EBTB. A total of 45% of patients had TB which was diagnosed on histopathology.

Conclusion: EBTB was diagnosed in 10% of smear-negative, NAAT-negative cases. The use of NAAT on bronchoscopy wash samples resulted in a high yield in diagnosis.

Keywords: Bronchial diseases, Bronchoscopy, Pulmonary, Radiology

INTRODUCTION

TB is a major health problem that results in significant mortality and morbidity. In 2020, the World Health Organisation (WHO) estimated an incidence of 10.6 million cases worldwide, with 1.4 million cases in India [1]. India reported 1.8 million TB cases in 2020, with 1.29 million cases being pulmonary TB [2]. In the state of Kerala, 20,832 cases were reported in 2020, with 12,426 (59.6%) being pulmonary TB [2].

EBTB is defined as tuberculosis infection of the tracheobronchial tree with microbial and histopathological evidence [3]. The diagnosis of EBTB is difficult due to non specific symptoms, signs, and radiological presentation. EBTB may present with or without parenchymal involvement. In 10-20% of patients with EBTB, a normal Chest X-Ray (CXR) may be observed. The yield of sputum microscopy is as low as 16% (16-53%) [3-8]. When sputum smear and CXR findings are not definitively indicative of TB, bronchoscopy and Computed Tomography (CT) thorax play a role in the diagnosis. Morbidity is high as it heals with scarring and functional impairment of airways; hence, early diagnosis and treatment are necessary [8]. Bronchoscopic biopsy is the best method for diagnosing EBTB, with a yield of 30-84% [9]. The availability of newer molecular tests like Cartridge-Based Nucleic Amplification Test (CB-NAAT) can increase the yield in Broncho-Alveolar Lavage (BAL) compared to sputum AFB smears [10].

The diagnostic algorithm for the National TB Elimination Program in India (NTEP) recommends AFB smears and CXR for all presumptive pulmonary TB patients [11]. For those with CXR suggestive of TB but AFB smear negative, a NAAT is recommended. For those negative for *M. tuberculosis* on NAAT too, a clinical diagnosis of TB can be made by the treating physician [11]. In patients with a microbiologically confirmed TB (either AFB smear positive or NAAT result of *M. tuberculosis* detected), further evaluation for EBTB is not done.

In clinical practice, a diagnosis of TB is mostly made based on radiological grounds. Further evaluation by bronchoscopy, which would reveal the diagnosis of EBTB, is not usually conducted. This study examines the proportion of EBTB in clinically diagnosed TB and the clinicoradiological and bronchoscopy profile in patients with EBTB in the setting, which has not been previously reported. Hence, this study was conducted to evaluate these aspects and describe this profile with the aim of determining the proportion of patients with sputum AFB smear-negative, NAAT-negative TB who have features of EBTB on bronchoscopy and to describe clinicoradiological features in such patients.

MATERIALS AND METHODS

A record-based retrospective cross-sectional study was conducted in the Department of Pulmonary Medicine, Government Medical College, Thrissur, Kerala, India, during the period 2017 to 2020. Institutional Ethical Committee (IEC) clearance was obtained in March 2022, and data collection and analysis were carried out from 1st April 2022 for a period of six months. Ethics clearance was obtained from the IEC of Government Medical College, Thrissur, with clearance number IEC/GMCTSR/2022/025 dated 24-03-2022.

Inclusion criteria: Patients with a clinical diagnosis of Pulmonary TB, with sputum smear results negative for AFB and sputum NAAT results showing *M. tuberculosis* not detected, were included in the study.

Exclusion criteria: Patients who were not fit or unwilling for bronchoscopy were excluded from the study.

Patients were recruited at the NTEP unit of the Medical College. Presumptive TB patients, whose sputum samples were negative on both AFB smear microscopy and sputum NAAT, underwent bronchoscopy. Among these, those with endobronchial lesions on bronchoscopy and meeting the diagnostic criteria of EBTB were further evaluated. During the study period, 3,052 patients

were diagnosed with TB in the institution. Of these, 1,543 patients diagnosed with EPTB were excluded. Among the remaining 1509 cases with pulmonary TB, 1165 with microbiologically confirmed (Smear and NAAT) were also excluded. Of the remaining 344, 198 underwent bronchoscopy.

EBTB was diagnosed based on the following diagnostic criteria [6-8]:

- Endobronchial or tracheal lesions with the following:
  - AFB smear positive from Bronchial washing sample
  - CBNAAT positive for *M. tuberculosis* from Bronchial washing sample
  - Histopathologically caseating granuloma consistent with TB from bronchial brushing or bronchial biopsy.

The patient records were extracted from the department's documents, including the NTEP reports, bronchoscopy register, and case sheets. Patient identifiers were removed before the data was analysed. The parameters included in the study were clinical features, blood investigations, radiological investigations, sputum AFB and sputum CBNAAT, Fiberoptic Bronchoscopy (FOB) appearance, bronchoscopic washing cytology, AFB staining and CB-NAAT, Bronchial brushing cytology and AFB, and bronchoscopic biopsy histopathology.

STATISTICAL ANALYSIS

The data were collected using a structured questionnaire and then entered into MS Excel for analysis using EpiInfo7. Quantitative variables were summarised as the mean and categorical variables were presented as percentages.

RESULTS

Out of the total 3052 patients diagnosed with TB from 2017-2020, 1509 had Pulmonary TB. Among the 344 patients with smear-negative Pulmonary TB, 198 underwent bronchoscopy, and 20 were diagnosed with EBTB. All EBTB cases were sputum AFB and CBNAAT negative. Sixty-five percent of the EBTB cases were female, and the mean age was 22 years and age range of (14-71 years).

Clinical Features

Fever was the most common presenting symptom (85%), followed by loss of appetite and weight loss (75%), and cough (70%) [Table/Fig-1]. Mean duration between onset of symptoms and presentation was one month in 80% of patients.

Symptom	n (%)
Fever	17 (85)
Loss of appetite	15 (75)
Loss of weight	15 (75)
Cough	14 (70)
Haemoptysis	6 (30)
Hoarseness of voice	2 (5)
Chest pain	2 (5)

[Table/Fig-1]: Clinical features of the study patients.

Radiological Features

Lobar collapse:

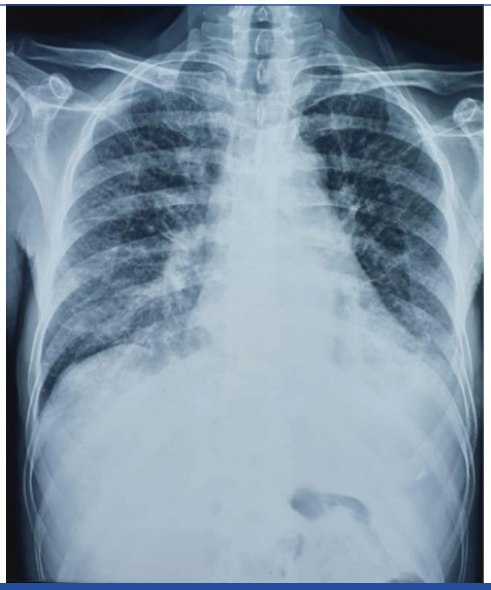
The most common radiological feature was lobar collapse, observed in six patients, followed by consolidation and hilar prominence, each seen in four patients [Table/Fig-2,3]. Centrilobular nodules in CT were observed [Table/Fig-4].

Bronchoscopic Features

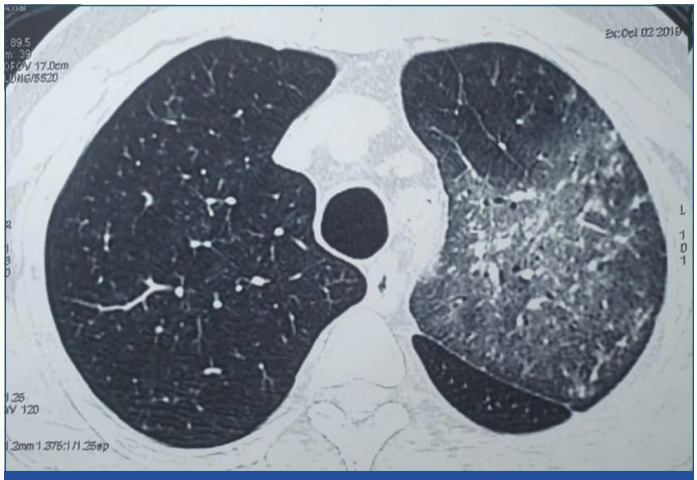
The most common bronchoscopic pattern in patients with EBTB was a tumorous pattern, seen in 7 (35%) patients with EBTB [Table/Fig-5,6].

Radiological feature seen	n (%)
Lobar collapse	6 (30)
Hilar prominence	4 (20)
Consolidation	4 (20)
Diffuse nodular shadow	3 (15)
Thick walled cavity	2 (10)
Patchy alveolar shadow	1 (5)

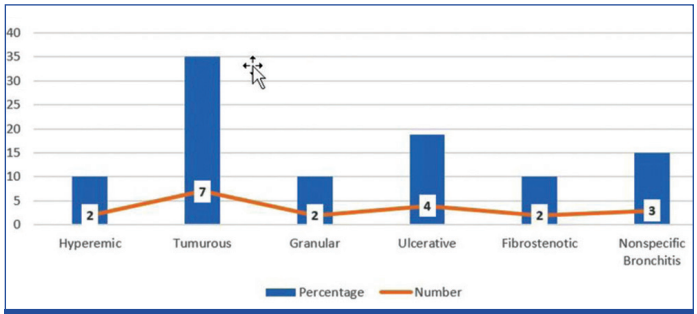
[Table/Fig-2]: The radiological features of the study patients.



[Table/Fig-3]: Chest X-ray (CXR) of the patient shows straightening of left heart border suggestive of left lower lobe collapse.



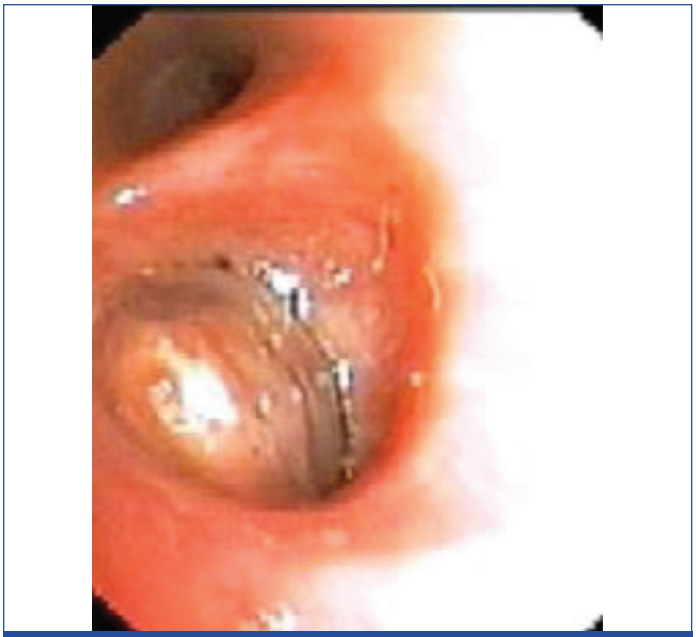
[Table/Fig-4]: CT chest picture of the patient showing centrilobular nodules.



[Table/Fig-5]: Endobronchial appearance on bronchoscopy.
(X-axis denotes the appearance and Y-axis the percentage of Endobronchial TB (EBTB) patients with the mentioned Bronchoscopic appearance)

Diagnosis of Endobronchial TB (EBTB)

The diagnosis of EBTB is made by histopathology (HPR), AFB staining, and CBNAAT. Bronchial washing showed positive AFB staining in four patients (20%) and positive AFB culture in LJ media in two patients (10%), other findings are shown in [Table/Fig-7].

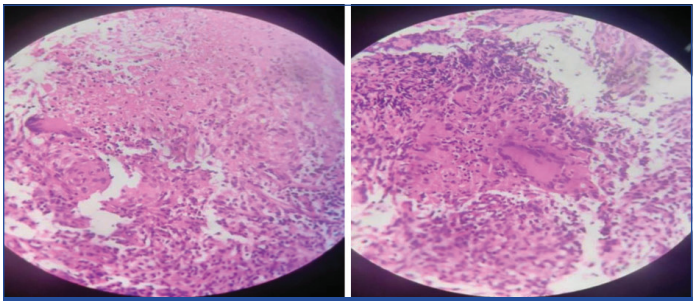


[Table/Fig-6]: The bronchoscopic pattern seen in one of the patients- Tumorous type.

Diagnostic test	n (%)
Positive CBNAAT	10 (50)
TB on histopathology	9 (45)
Positive AFB staining	4 (20)
Positive *Mycobacterium tuberculosis* culture	2 (10)
Both HPR and CBNAAT positive	3 (15)
All three HPR, CBNAAT and AFB smear positive	1 (2)

[Table/Fig-7]: Diagnostic test on bronchoscopy in patients diagnosed as Endobronchial TB (EBTB).
CBNAAT: Cartridge based nucleic acid amplification test; AFB: Acid fast bacilli; HPR: Histopathology report

The most common histopathology pattern was caseating granuloma [Table/Fig-8]. Others were epithelioid granuloma without necrosis both consistent with TB. Chronic inflammatory cell infiltration was seen in six patients (30%), and non specific results were found in five patients (25%). Biopsy CBNAAT and culture were not available during that period in our setting [Table/Fig-9].



[Table/Fig-8]: Histopathological appearance of Endobronchial TB (EBTB) showing granuloma with caseation necrosis (H&E, 10x).

Appearance	n (%)	Inference
Caseating granuloma	6 (30)	Suggestive of tuberculosis
Epithelioid granuloma without necrosis	3 (15)	Suggestive of tuberculosis
Chronic inflammatory cell infiltration	6 (30)	Suggests inflammation
Non specific results	5 (25)	Cannot infer a conclusion

[Table/Fig-9]: Histopathology results seen in the patients.

DISCUSSION

In this study, approximately 10% of clinically diagnosed TB cases were diagnosed as EBTB when bronchoscopy was performed. A significant proportion of these cases were diagnosed by NAAT, and a nearly equal number were diagnosed by histopathology. The most common symptom in this study was fever. However, in other studies (Sharma D et al., Valdès CLH et al., and Simsek A et al.,) cough was reported as the most common symptom [12-14]. Similarly, the most common CXR finding in this study was collapse, whereas study by Simsek A et al., found upper lobe mass-like lesion and nodular shadow as the most common features, respectively [14].

The primary bronchoscopy feature in this study was a tumorous lesion. In a study by Chung HS and Lee JH, 10 out of 34 cases were tumorous lesions [15]. In a study by Simsek A et al., four out of 18 cases were of the tumorous type [14]. These findings differ from those reported by Ozkaya S et al., where 34.7% were edematous hyperemic type, and Kim HJ et al., who found actively caseating, oedematous-hyperemic, and ulcerative EBTB to be the most common EBTB subtypes, occurring in 49%, 21%, and 20% of their patients, respectively [10,16]. The diagnostic test yielding more positive results in this study was NAAT on bronchial lavage specimens, which is a microbiology test. A study by Simsek A et al., revealed BAL AFB positivity of 62.5% and 97.5% for culture. 44% had a definite histopathological picture suggestive of TB [14].

EBTB is a tuberculous infection of the tracheobronchial tree. EBTB in the earlier era was a postmortem finding until bronchoscopy became available [17]. While this is not a different disease entity, it evokes interest because of the difficulty in diagnosis and the worse prognosis. These changes may be visible through the bronchoscope starting with an area of reddishness in the airways, progressing to multiple tubercles, which may develop into ulcers, finally resulting in granulation tissue formation, giving the appearance of an intrabronchial tumor [3,13]. This was the most common presentation in this study.

The diagnostic yield in expectorated sputum specimens may be low in EBTB (15 to 60%) [3,10,16]. The yield can be increased when BAL is performed. Bronchoscopy is the best investigation in a patient with sputum AFB and NAAT negative, with a high yield resulting in establishing a diagnosis [3,7,10,16]. Biopsy and histopathology generally show caseating granulomas. The yield of bronchoscopic biopsy is 30-84% [3,18]. NAAT of bronchial washing, if positive, is diagnostic. Strictures can occur after treatment [18-20]. Interventional pulmonology may improve treatment in patients with EBTB with such sequelae [21].

This study shows that EBTB is diagnosed in about 10% of clinically diagnosed TB cases, i.e., those negative on sputum smear examination for AFB and NAAT. Bronchoscopy is essential for the diagnosis of these patients. Hence, it is essential that bronchoscopy is available and used in all patients with clinically diagnosed TB. The strength of this study is that such data is not available from this part of the country.

Limitation(s)

The limitation of this study was that not all patients with smear-negative/NAAT-negative results could undergo bronchoscopy. This should be seriously looked into in the future, as there is a high possibility of underlying malignancy mimicking TB. Biopsy CBNAAT and Biopsy AFB culture were not available at the time of the study, which might have missed many cases of TB. Further, Rifampicin sensitivity of these cases couldn't be done. Hence, in the time of genetic testing, testing by CBNAAT and culture may be done for all suspected cases.

CONCLUSION(S)

EBTB was present in 10% of smear-negative/NAAT-negative cases. The most common radiological feature in these patients was lobar collapse, and the most common bronchoscopy finding was a tumorous lesion. Availability of NAATs has resulted in better diagnosis of patients, and the yield of NAAT positivity was 50%. The other patients could be diagnosed based on histopathology. This study suggests that all patients with presumptive TB who were smear

AFB-negative and NAAT-negative may undergo bronchoscopy, which can lead to the diagnosis of EBTB, confirming the diagnosis and also prognosticating the disease.

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