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## Bronchoscopy in immediate diagnosis of smear negative tuberculosis

Bronchoskopia w szybkim rozpoznaniu gruźlicy u chorych bez obecności prątków w bezpośrednim badaniu płwociny

The authors declare no financial disclosure

### Abstract

**Background:** Tuberculosis is a major public health problem. Almost 30% of cases of tuberculosis are known to be sputum smear negative. There is a diagnostic dilemma in such cases leading to inadvertent delays in management of these cases. The present study was planned to assess the role of bronchoscopy in immediate diagnosis of smear negative pulmonary tuberculosis.

**Material and methods:** The present study is a retrospective analysis of 132 sputum smear negative tuberculosis suspects who underwent bronchoscopic evaluation during the period 2002–2013. The diagnosis of tuberculosis was based on the finding of bacilli in aspirate or in tissue biopsy or the demonstration of caseous necrosis on tissue biopsy.

**Results:** The present study showed that bronchoscopy could lead to immediate, accurate diagnosis in 68.2% of suspected smear negative cases. Bronchial aspirate and bronchoalveolar lavage alone were diagnostic in 51.5% of such cases while tissue biopsy added to the yield in another 16.5% cases.

**Conclusions:** The results of the present study suggests an important place of bronchoscopy in immediate diagnosis of suspected smear negative tuberculosis, thus avoiding inadvertent delays in diagnosing and instituting appropriate treatment.

**Key words:** tuberculosis, bronchoscopy, bronchial aspirate, bronchioalveolar lavage, endobronchial biopsy, transbronchial lung biopsy  
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### Streszczenie

**Wstęp:** Gruźlica jest poważnym problemem zdrowia publicznego. Prawie u 30% chorych na gruźlicę bezpośrednie badanie płwociny na prątki jest ujemne. Prowadzi to do niezamierzonych opóźnień w leczeniu tych przypadków. W niniejszym badaniu zaplanowano ocenę roli bronchoskopii w szybkim rozpoznaniu gruźlicy u tych chorych.

**Materiał i metody:** Niniejsze badanie jest retrospektywną analizą 132 chorych z podejrzeniem gruźlicy, u których nie stwierdzono prątków w bezpośrednim badaniu płwociny i którzy zostali poddani bronchoskopii w okresie 2002–2013. Gruźlicę rozpoznawano na podstawie stwierdzenia prątków w wydzielinie oskrzelowej lub w płukaniu oskrzelowo-pęcherzykowym względnie w materiale uzyskanym z biopsji. Rozpoznawano również gruźlicę na podstawie stwierdzenia martwicy serowatej w materiale z biopsji.

**Wyniki:** Wynik niniejszego badania wykazał, że w wyniku bronchoskopii było możliwe ustalenie rozpoznania w 68,2% przypadków, w których badanie płwociny było negatywne. Potwierdzenie uzyskano po stwierdzeniu prątków w wydzielinie oskrzelowej lub płukaniu oskrzelowo-pęcherzykowym w 51,5% przypadków a na podstawie badania materiału z biopsji w 16,5%.

**Wnioski:** Wyniki niniejszego badania wskazują na ważne miejsce bronchoskopii w szybkiej diagnostyce gruźlicy u chorych z ujemnym bezpośrednim badaniem płwociny. Pozwala to na uniknięcie opóźnień w rozpoznawaniu gruźlicy i na szybkie podjęcie odpowiedniego leczenia.

**Słowa kluczowe:** gruźlica, aspiracja oskrzelowa, płukanie oskrzelowo-pęcherzykowe, biopsja oskrzeli, przezoskrzelowa biopsja płuc  
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## Introduction

Tuberculosis is a major public health problem especially in developing countries like India. Worldwide, 8.6 million new cases of tuberculosis emerged in 2012 [1]. Despite availability of highly effective antitubercular therapy, tuberculosis accounted for about 1.3 million deaths worldwide in 2012 [1]. Tuberculosis is the second leading cause of death from an infectious disease worldwide, after human immunodeficiency virus. On epidemiological analysis of tuberculosis in India, prevalence per million reduced from 4,650 in year 1990 to 2,300 in 2012 [2]. In absolute numbers, prevalence has reduced from 4 million to 2.8 million annually. Incidence per million population has reduced from 2,160 in year 1990 to 1,760 in 2012. Tuberculosis mortality per million population has reduced from 380 in year 1990 to 220 in 2012 [2].

According to the Global tuberculosis report 2013, there were 1.29 million notified tuberculosis cases in India in 2012 out of which about 30% were smear negative cases [1]. The diagnosis of tuberculosis is often delayed in these smear negative cases. A follow up study of suspected smear negative tuberculosis patients, 70% progressed to active disease in next 12 months if left untreated [3]. A major challenge in tuberculosis control is early and accurate diagnosis in such cases. The various methods currently available to diagnose such cases are induced sputum, radiological guided transthoracic needle aspiration, gastric lavage especially in children and bronchoscopy. The present study was planned to assess the role of bronchoscopy in early diagnosis of smear negative suspected cases of pulmonary tuberculosis.

## Material and methods

The present study is a retrospective analysis of sputum smear negative tuberculosis suspect patients presenting to one of the respiratory unit at Vallabhbhai Patel Chest Institute Delhi during the period of 2002–2013. All the patients who were diagnosed as tuberculosis after bronchoscopy during this period were included in the study.

The suspicion of tuberculosis was considered in patients with cough or fever of more than 2 weeks duration with or without weight loss, hemoptysis and with radiological opacity (consolidation/ cavity/ infiltrates/lymph nodes). These patients were either sputum smear negative twice or were not producing sputum and hence microbiological confirmation of tuberculosis could not be obtained.

**Table 1. Bronchoscopy in tuberculosis patients**

Gross bronchoscopy finding	n (%)*
Edema and/or narrowing of segment	10 (7.5%)
Mucous pooling in affected bronchus	6 (4.5%)
Endobronchial nodules	5 (3.8%)
Hyperemia	4 (3%)
Bronchoscopy procedure	n°/N (%)**
Bronchial aspirate/bronchoalveolar lavage for AFB	68/132 (51.5%)
Endobronchial biopsy	25/67 (37.3%)
Transbronchial lung biopsy	20/44 (45.5%)
Transbronchial needle aspiration	2/6 (33%)
Combined yield of various procedures	90/132 (68.2%)

\*n — number of patients, n° — number of patients diagnosed by a particular procedure, \*\*N — number of patients who underwent the particular procedure, percentage of patients shown in bracket

Fibreoptic bronchoscopy (FOB) was performed in patients willing for the procedure and if they were clinically fit. The various bronchoscopy procedures performed were bronchial aspirate (BA), bronchoalveolar lavage (BAL), endobronchial biopsy (EBB), transbronchial lung biopsy (TBLB) and trans-bronchial needle aspiration (TBNA), either individually or in varying combinations depending on the need of individual case. Samples so obtained were sent for Ziehl Nielsen (ZN) staining and cytological/histopathological examination.

## Results

There were 132 suspected cases of tuberculosis which were included in the present study comprising of 74 (56%) males and 58 (44%) females. The study population had age varying from 10 to 80 years with a mean of 41.4 years. Out of these, there were three children with age less than 15 years.

The most common presenting symptoms were cough (83.3%), breathlessness (59%), fever (39.4%), weight loss (28%) and hemoptysis (19%). Fever was more common (42.2%) in patients later proved to be having tuberculosis by bronchoscopy as compared to patients (30.95%) that were not proved to be having tuberculosis.

Radiologically, consolidation was the commonest presentation and it was more common (40%) in patients ultimately proved to be having tuberculosis as compared to patients (23.8%) that were not proved to be having tuberculosis. Other presentations were cavity, lymph node, nodule/s, mass lesions.

**Table 2. Studies on immediate bronchoscopic diagnosis of tuberculosis**

Study	Year of publication	Country	Immediate diagnosis (n/N)
Sarkar et al. [6]	1980	India	73% (22/30)
Russel et al. [13]	1986	USA	12% (3/25)
Palenque et al. [11]	1987	Spain	34% (17/50)
Chawla et al. [7]	1988	India	72% (36/50)
Wongthim et al. [8]	1989	Thailand	75% (53/71)
Khoo et al. [14]	1989	UK	9% (3/35)
Chan et al. [12]	1990	China	14% (4/28)
Zainudin et al. [9]	1991	Malaysia	55% (18/33)
Fujii et al. [10]	1992	Japan	44% (14/32)
Bachh et al. [4]	2007	India	48.3% (29/60)
Present Study	2014	India	68.2% (90/132)

n — TB confirmed by bronchoscopy; N — total number of patients

The abnormalities found on gross bronchoscopic examination of the tracheo-bronchial tree of the tuberculosis patients were edema and/or narrowing of a bronchial segment in 10 patients, mucus pooling in 6, endobronchial nodules in 6 patients and hyperemia in 5 patients (Table 1).

Bronchoalveolar lavage and bronchial aspirate were smear positive for acid fast bacilli in 51.5% subjects (68 cases).

Endobronchial biopsy (EBB) was performed in 67 patients, out of which evidence of caseous necrosis and/or AFB positivity was seen in 25 cases (37.3%). Similarly, transbronchial lung biopsy (TBLB) was suggestive of tuberculosis in 20 out of 44 cases (45.5%). Transbronchial needle aspiration (TBNA) showed AFB positivity in 2 out of 6 cases (33%). EBB, TBLB and TBNA increased the diagnostic yield by 16.7% (22 cases) over and above that provided by lavage and aspirate alone (Table 1).

The combined diagnostic yield of all the bronchoscopic procedures in confirming the diagnosis of tuberculosis was 68.2% (n = 90). All these patients were started on anti-tubercular treatment (ATT) and on follow up both clinical and radiological response was observed. Of these 13 patients had history of prior ATT intake and hence, were treated with appropriate regimen. In remaining 42 cases who could not be proven tuberculosis by the above methods, empirical ATT trial was instituted, considering the high prevalence of TB in India as well as consistent clinical and radiological presentation. On follow up of these 42 patients, again both clinical and radiological response was observed which confirmed the diagnosis of TB.

No serious complications were encountered except pneumothorax in one patient which resolved by oxygen and observation alone.

## Discussion

Flexible fiberoptic bronchoscopy provides material, aspirate as well as biopsy, from localized affected areas of lung aiding in early diagnosis of smear negative tuberculosis. In the present retrospective analysis, we have shown the immediate diagnostic yield of bronchoscopy in smear negative suspected cases of tuberculosis to be 68.2%.

A number of studies [4–14] have looked into the role of bronchoscopy in immediate diagnosis of suspected smear negative tuberculosis. The results of the various studies done on smear negative tuberculosis have been summarized in Table 2. The immediate yield in various studies on sputum smear negative tuberculosis has ranged varied from 9% to 75% worldwide [4–14]. In Indian studies bronchoscopy has given immediate diagnostic yield in 48% to 73% [4, 6, 7]. A study by Bachh et al. [4] showed bronchoscopy was helpful in diagnosis of sputum smear negative pulmonary tuberculosis in 83.33% cases, with immediate diagnosis possible in 48.33% patients. In another study on 40 suspected tuberculosis smear negative patients, overall diagnosis was confirmed in 24 (60%) patients [5]. Sarkar et al. [6] performed bronchoscopy in 30 patients with suspected pulmonary tuberculosis and obtained immediate diagnosis of pulmonary tuberculosis in 22 cases (73%). In study by Chawla et al. [7], bronchoscopy was done in 50 sputum smear-ne-

gative patients suspected to have pulmonary tuberculosis and early diagnosis was made in 36 (72%) patients. In, another four year study by Wongthim et al. [8] on 112 bronchoscopies performed for suspected smear negative tuberculosis, tuberculosis was diagnosed in 71 cases with immediate diagnosis in 58%. Similarly, studies by Zainudinet et al. [9] and Fujiet et al. [10] have reported immediate diagnosis in 55% and 44% of cases.

In contrast, a number of other studies have shown a lower diagnostic yield for immediate diagnosis of tuberculosis by bronchoscopy. Palenque et al. [11] could obtain immediate diagnosis in 34% cases. Chan et al. [12] was able to provide immediate diagnosis in only 14% of cases. Similarly in studies by Russel et al. [13] and Khoo et al. [14], immediate diagnosis by bronchoscopy was possible in only 12 and 9 percent of cases studied respectively.

The present study found the yield of bronchoalveolar lavage/aspirate alone in tuberculosis cases to be 51%. This is similar to the results obtained by Baughman et al. [15] and Sharma KK et al. [16] who obtained a yield of BAL smear positivity for AFB of 68% and 64.7% respectively. However, studies by VijayanVK et al. [17], Tueller et al. [18] and Worodria et al. [19] have shown a comparatively poor BAL smear positivity of 9%, 47% and 25.4% respectively.

In countries in which tuberculosis presents a great problem and without enough facilities for making culture, tuberculosis may be diagnosed in the presence of symptoms and discovery of acid fast bacilli in the direct smear of the sputum. RNTCP (Revised National Tuberculosis Control Programme) in India recommends treatment with ATT in patients with even single sputum smear positive for AFB in presence of consistent clinical presentation. As a corollary to this, patients with AFB positive bronchoscopic specimens and consistent clinico-radiologic presentation can be diagnosed as TB.

The limitations of the current study are its retrospective nature and the unavailability of culture of the bronchoscopy specimen. Culture results were not evaluated in the study as the primary aim of the study was to assess the role of bronchoscopy in immediate diagnosis of tuberculosis. However in spite of the limitations, the study was able to achieve a diagnostic yield of 68% in the subjects studied.

### Conclusion

India is among the 22 high burden countries of pulmonary tuberculosis, and due to high contagious nature of the disease, its early

recognition is of utmost importance. The results of present study suggest an important place of bronchoscopy in immediate diagnosis of smear negative tuberculosis. This will likely avoid the inadvertent delays in diagnosing and instituting appropriate treatment, thus minimizing the risks of untreated tuberculosis to both the individual as well as the community. There is need for increased use of bronchoscopy in striving to make confirmed diagnosis of tuberculosis in smear negative cases. Furthermore, the high yield of acid fast bacilli obtained by bronchial washings could play an important role in providing drug susceptibility patterns in the settings of high drug resistant tuberculosis.

### Conflict of interest

The authors declare no conflict of interest.

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