

## Yield of Bronchoalveolar Lavage in Clinico Radiologically Suspected Cases of Sputum Smear Negative Pulmonary Tuberculosis

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**Abstract:** Tuberculosis (TB) is a major public health problem in India. Diagnosis of active Pulmonary TB (PTB) is often delayed due to Acid-fast bacilli (AFB) smears of respiratory specimens (at least two or more specimens) are necessary for the prompt diagnosis of PTB, but AFB smears has poor sensitivity (30-70%) despite high specificity (98-99%). Mycobacterial culture are more sensitive than AFB smears (80-85%), but culture results usually require 3-8 weeks. Every attempt to establish a definitive diagnosis of tuberculosis should be made in patients who are either unable to produce sputum voluntarily or are smear negative by conventionally obtained sputum sample. Fibreoptic bronchoscopy guided bronchoalveolar lavage is a relatively safe and useful procedure for diagnosis of suspected cases of pulmonary tuberculosis when smears of expectorated sputum do not reveal mycobacterium. The study was conducted in the department of chest medicine of Medical College, Kolkata from January 2017 to March 2017. Patients attending TB clinic under department of chest medicine were randomly selected and a total of 70 patients were recruited. On examination of BAL fluid, 17.1% found to be AFB smear positive on Ziehl-Neelsen staining and upon BACTEC culture, 25.7% showed positive growth of Mycobacterium Tuberculosis. This showed that Bronchoalveolar lavage can be a viable tool to confirm the diagnosis of sputum smear negative cases for diagnosis and treatment of Pulmonary Tuberculosis.

**Key Words:** Pulmonary Tuberculosis (PTB), Fibreoptic bronchoscopy, Bronchoalveolar lavage (BAL), Smear negative.

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### I. Introduction

Tuberculosis (TB) is a major public health concern in India. India accounts for one fourth of the global Tuberculosis burden. In 2015, an estimated 28 lakh cases occurred and 4.8 lakh people died due to TB [1]. The global strategy to control TB is prompt diagnosis, notification and successful treatment of patients with active, transmissible disease. Early diagnosis of active Pulmonary Tuberculosis (PTB) is critical for control of TB.

Unfortunately, diagnosis of active PTB is often delayed due to less than half of these patients have a positive sputum smear (23-29% in 2009 in Korea) and isolation of Mycobacterium Tuberculosis (MTB) takes a long time [2,3,4]. Acid-fast bacilli (AFB) smears of respiratory specimens (at least two or more specimens) are necessary for the prompt diagnosis of PTB, but AFB smears has poor sensitivity (30-70%) despite high specificity (98-99%). Mycobacterial culture are more sensitive than AFB smears (80-85%), but culture results usually require 3-8 weeks [5].

The diagnosis of TB and decision to start treatment of sputum smear negative TB is usually dependent upon clinical features, but 20% of PTB patients are completely asymptomatic whereas 42-86% of PTB patients may be symptomatic. Sputum smear negative PTB patients are especially likely to show no or mild respiratory symptoms and systemic manifestations [6]. Murray et al. found that in the pre-AIDS (Acquired Immunodeficiency Syndrome) era, there were 1.22 cases of smear negative PTB for every case of smear positive PTB [7]. After that, a study from western Canada by Long et al. found that for every smear positive PTB case there were 2.52 smear negative PTB and extra-pulmonary cases [8]. The association of AFB negative smear along with lesser number of bacilli and minimal non-cavitary radiographic patterns might imply that smear negative cases are less infectious. However a DNA finger printing study from San Francisco attributed 17% of TB transmission to smear negative, culture positive tuberculosis cases [9].

Therefore every attempt to establish a definitive diagnosis of tuberculosis should be made in patients who are either unable to produce sputum voluntarily or are smear negative by conventionally obtained sputum sample. World Health Organization (WHO) recommends detection of acid-fast bacilli in respiratory specimens

as the initial approach to the diagnosis of TB [10]. As a routine examination method for detection of AFB, sputum smear microscopy remains a fundamental tool but may be negative in 20-70% of all cases of active tuberculosis [11]. Data from longitudinal surveys from Bangalore district, India indicate that at 18 months of follow up, the mortality rate for smear negative culture positive cases was 14.1% compared to 34.7% observed in smear positive patients [12]. Thus, early diagnosis of active smear negative PTB is of utmost importance.

## **II. Aims & Objective**

To assess the role of fiberoptic bronchoscopy in the diagnosis of sputum smear negative pulmonary tuberculosis.

To evaluate the diagnostic yield of bronchoalveolar lavage fluid for AFB smear in the diagnosis of tuberculosis in clinically and radiologically suspected cases who are sputum smear negative.

To evaluate the diagnostic yield of bronchoalveolar lavage fluid in BACTEC culture (for Mycobacterium Tuberculosis) for the diagnosis of tuberculosis in clinically and radiologically suspected cases who are sputum smear negative.

## **III. Materials And Methods**

Medical College, Kolkata is a tertiary care hospital cum teaching institution. Chest medicine department of Medical College, Kolkata runs a Tuberculosis clinic under National Revised Tuberculosis Control Program (RNTCP) for treatment of TB patients. Randomly selected patients from TB clinic were chosen to be recruited in the study. The inclusion and exclusion criteria were as follows:-

### ***Inclusion criteria***

Patients of both gender aged 15 years and above

History, clinical features of the patients highly suggestive of pulmonary tuberculosis.

Sputum smear – two in number, negative by Ziehl-Neelsen staining method under RNTCP.

Chest radiograph (CXR) of the patient suggestive of pulmonary tuberculosis.

### ***Exclusion criteria***

Sputum positive pulmonary tuberculosis by Ziehl-Neelsen staining under RNTCP.

Extra-pulmonary tuberculosis

Severe dyspnoeic patients

Immunosuppressed patients particularly HIV (Human Immunodeficiency Virus) positive patients

Unstable cardiovascular status (Arrhythmia and Angina)

Uncooperative patients

The study was conducted in the department of chest medicine of Medical College, Kolkata. Time period of the study was from January 2017 to March 2017. Patients attending TB clinic under department of chest medicine were randomly selected to participate in the study. Over the period of recruitment a total of 70 patients were recruited as per study protocol. This was an interventional, cross-sectional real world study to determine the feasibility of using fiberoptic bronchoscopy to obtain bronchoalveolar lavage a diagnostic tool in sputum smear negative pulmonary tuberculosis. Suspected smear negative TB patients were identified with detailed history, clinical manifestations and radiological evidence suggestive of pulmonary tuberculosis. History childhood infection, possible contact and symptoms over last 2-3 weeks were given importance [12,13,14,15,16]. As for clinical features or symptoms of unexplained weight loss, cough, fever & malaise, haemoptysis over last two to three weeks were noted with any other complaints. CXR were taken to be suggestive of TB after confirmation by two persons, one pulmonologist and one radiologist, both of whom are blinded to the ongoing trial. To obtain bronchoalveolar lavage, consenting patient was admitted for a day on the day of bronchoscopy. Fiberoptic bronchoscope (Pentax FB – 15P<sup>TM</sup>) was used to do the procedure. Bronchoalveolar lavage (BAL) fluid sample thus obtained was examined for AFB smear and BACTEC culture for Mycobacterium Tuberculosis.

## **IV. Results**

70 patients were recruited in the study. 53 were male (75.7%) and 17 were female (24.3%) participants. Among the recruited patients, majority (70%) belong to 21-40 years age category. Table 1 is showing number of patients according age and gender.

**Table 1: Age and sex distribution of study population**

Age in Years	No of Cases	%	Male	%	Female	%
11-20	3	4.3	0	0	3	4.3
21-30	30	42.9	22	41.5	8	47.0
31-40	19	27.1	15	28.3	4	23.5
41-50	4	5.7	4	7.5	0	0
51-60	9	12.9	8	15.0	1	5.8
61-70	5	7.1	4	7.5	1	5.8
total	70	100	53	75.7	17	24.3

16 patients (22.9%) were from urban areas and 54 patients (77.1%) were from rural areas. We found that cough was the commonest symptoms with over 88% patient reporting it as a primary symptom. Fever was almost equally reported by 85% patients followed by haemoptysis reported by 38% patients. Table 2 enumerates different symptoms reported by patients in the study group.

**Table 2: Presenting symptoms in the study population**

Symptoms	Number of cases	%
Cough/Expectoration	62	88.6
Fever	60	85.7
Haemoptysis	27	38.6
Chest pain	12	17.1
Shortness of breath	8	11.4
Heaviness of chest	2	2.9

As for radiological evidence of pulmonary tuberculosis, most patients (55.71%) had pulmonary infiltrate followed by cavitory lesion in 30% of the cases. Fewer cases also showed nodular pattern and military mottling. Table 3 shows all the different radiological evidence of tuberculosis in Chest x-rays.

**Table 3: Frequency of chest radiological pattern in study population**

Radiographic pattern	Frequency	%
Pulmonary infiltrate	39	55.7
Cavity	21	30
Nodular shadow	6	8.6
Miliary mottling	4	5.7

Interestingly in our study group, majority of the patients i.e 82.9% had unilateral lung involvement with only 17.1% had bilateral involvement. Although looking at zonal involvement, we found that right upper zone is the most common lung area involved in pulmonary tuberculosis. Table 4 shows distribution of zonal involvement as follows.

**Table 4: Distribution of zonal involvement in study population**

Zonal involvement in CXR	Number of cases	%
Right upper zone	42	60.0
Left upper zone	8	11.4
Right mid zone	6	8.6
Left mid zone	1	1.4
Lower lung fields	3	4.3
Diffuse parenchymal involvement	10	14.3

All 70 patient included in the study were sputum smear negative. On examination of BAL fluid, 12 cases (17.1%) found to be AFB smear positive on Ziehl-Neelsen staining and upon BACTEC culture, 18 cases (25.7%) showed positive growth of Mycobacterium Tuberculosis. This showed that Bronchoalveolar lavage can be a viable tool to confirm the diagnosis of sputum smear negative cases for continuation and adjustment of antituberculous chemotherapy.

## V. Discussion

In our study female patients were outnumbered by male patients. Gender biasness in tuberculosis is much doubted as no concrete evidence has been found in studies done across the world. But one study from Brazil and majority authors describe greater incidence of sputum positive pulmonary tuberculosis among males [17,18]. These data corroborate with our study findings in sputum smear negative cases. Compared to developed countries where TB is more common among elderly population, in developing countries young and middle aged people are more affected. The trend towards increasing age being significant in comparison to twenty years ago is being observed in recent times [19]. In Scotland during 1993, 64% of Caucasian patients with TB were aged over 55 years; in comparison 85% of Asian patients were under 55 years [20]. One study from Pakistan ,

involving 5023 PTB cases showed that pulmonary tuberculosis affect the most economically productive segment of the society, i.e. the people between 15 to 59 years age group [21]. The present study showed significantly higher prevalence in rural population which is consistent with the findings of higher prevalence of rural areas (469 vs 307 per 100000 population) as documented by National Family Health Survey 3 (NFHS-3) [22]. Raine et al. found poverty, illiteracy etc. to be the major contributing factors for TB in rural population [23]. Presenting clinical symptoms of pulmonary tuberculosis has remained remarkably consistent over multiple decades, continents, and clinical settings; cough occurs among 70-90%, weight loss among 43-75%, haemoptysis in 21-29%, and fever among 75-80% [12-16]. Of the systemic effects fever is most common symptom [24,25]. Cough is the most frequent symptom referable to the site of lung infection [26, 27]. In our study, pulmonary infiltrate was the most common radiographic finding appeared in 55.7% of patients. If we consider cavities with concomitant infiltrates, 85.7% patients were showing such features. Aktogu et al. also reported that the pulmonary infiltrate was the most common radiographic finding in 99% patients in their study [16]. Cavities when present are considered to be the most important X-ray finding corroborating active disease in adults. The frequency of appearance of cavity in chest X-ray in adults vary from 40 to 87% [16, 27, 28]. Our study showed miliary pattern represented 5.7% of the total cases. Though miliary tuberculosis is more common in primary form of the disease, it may occur in 7% of post primary cases also [16, 29, 30]. The nodular form constitutes one of the less common manifestation. Nyman et al. found 7% in their study, Khan et al found 9% whereas in our study, in 8.6% of the cases nodular pattern were observed [30,31]. In two large series consisting of 204 & 500 patients, the sites of cavitory disease were found to involve apical and/or posterior segments of the upper lobes in 83-85% of cases and the superior segments of the lower lobes in 11-14% of cases [ 32, 33]. Parenchymal involvement occurs in more than one segment in majority of the cases [34, 35]. From our study, it is revealed that comparing data between smear positive and smear negative cases, there would be insignificant difference in clinical presentation and radiographic findings. So confirmation of tuberculosis can only be from AFB positive sputum smear or culture positive for Mycobacterium Tuberculosis. Sputum smear negative patients are a dilemma for physician whether to start ATD or not and also more important is the fact that 74% of these patients develop active tuberculosis in next 5 years if not treated properly [36]. Bronchoscopy and related procedures like BAL, bronchial aspirate, bronchial brushing, transbronchial biopsy and post bronchoscopy sputum examination may be an alternative way to reach an early diagnosis. BAL is considered to be the best bronchoscopic specimen available for diagnosis of pulmonary tuberculosis [37]. Caminero et al. opined that bronchoscopy should be performed in all patients with negative sputum smear and concluded that BAL should be a routine procedure as it is simple and relatively safe procedure [38]. The diagnostic yield of overall bronchoscopic procedure in our study was 25.7%. It consisted of positive BAL smear for AFB in 17.1% and positive for mycobacterial culture which is 25.7%. S. Charoenratanakul et al. reported diagnostic yield of positive BAL smear in 7.5% of cases and culture positivity in 155 of cases [ 39]. Other studies have found higher rates of detection. Vijayan et al. found BAL fluid culture was positive in 34% cases [40]. Similar findings have reported by Kennedy et al [41]. Baughman et al. studied 50 patients and found sensitivity of positive smear and positive culture in BAL as 68% and 92% respectively [42]. Purohit et al. carried out fiberoptic bronchoscopy in 50 patients and found that BAL was positive for AFB smear in 42% cases whereas BAL culture was positive for 70% patients [43]. While in some studies bronchoscopic specimen had a comparatively lower yield, other studies have produced significant results also; thereby implying the importance of BAL fluid in the diagnosis of sputum smear negative pulmonary tuberculosis. Sputum smear negative pulmonary tuberculosis is a paucibacillary condition and the dilution of epithelial lining fluid by the instilled saline might be responsible for the low yield from BAL specimens in some studies. In addition, the local anaesthetic used for bronchoscopy might also have suppressed the growth of M. Tuberculosis [44].

The pre and post bronchoscopy sputum culture and transbronchial biopsy were not done in our study. This is a major limitation of the study as investigation of these specimens could have augmented the diagnostic yield of bronchoscopy as suggested by different studies in literature.

## **VI. Conclusion**

Tuberculosis and more so pulmonary tuberculosis is still one of the biggest public health concern in the developing countries and with increasing number of HIV infected patients it is also on the rise in few developed countries across the world. Sputum smear negative pulmonary tuberculosis pose a real challenge in controlling and treating tuberculosis as such. Every available resources should be utilised to detect and treat these cases as early as possible.

To conclude, fiberoptic bronchoscopy guided bronchoalveolar lavage is a relatively safe and useful procedure for diagnosis of suspected cases of pulmonary tuberculosis when smears of expectorated sputum do not reveal mycobacterium. To enhance yield transbronchial lung biopsy should be combined with BAL fluid study and post bronchoscopy sputum should be sent routinely for culture of mycobacterium tuberculosis.

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