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Original Research Paper

Pulmonary Medicine

# ROLE OF FIBEROPTIC BRONCHOSCOPY IN DIAGNOSIS OF SPUTUM NEGATIVE PULMONARY TUBERCULOSIS

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**ABSTRACT** Tuberculosis is a disease caused by Mycobacterium tuberculosis. It is a systemic disease, predominantly affecting the lungs. Globally, tuberculosis affects around 10.4 million people per year, and kills around million of them, with the majority of patients presenting with pulmonary disease. One of the key challenges to global tuberculosis control is correct diagnosis. The diagnosis of Pulmonary Tuberculosis can be obtained from microscopy and culture of a number of different sources including expectorated sputum, induced sputum, gastric washings and bronchoscopy. Fiberoptic bronchoscopy (FOB) can provide an early confirmative diagnosis in such patients. Among the bronchoscopic materials, bronchoalveolar lavage (BAL) is the best diagnostic material for the diagnosis of PTB.

**KEYWORDS :** Bronchoscopy, GeneXpert, Sputum, MGIT, LIPA, WHO.

## INTRODUCTION

Tuberculosis is a disease caused by Mycobacterium tuberculosis. It is a systemic disease, predominantly affecting the lungs. One of the key challenges to global tuberculosis control is correct diagnosis, and WHO has prioritized improving diagnostic guidelines and tests. However, the sensitivity of a diagnostic test depends on the quality of the sputum samples obtained.

Microscopy is inexpensive and the most frequently used laboratory test globally, but it is only likely to be positive if the concentration of acid-fast *Mycobacterium tuberculosis* bacilli exceeds 10,000 per ml of sputum. Tuberculosis culture techniques generally have greater sensitivity than microscopy, and PCR has intermediate sensitivity between that of culture and microscopy. However, culture and PCR tests, which are more expensive than microscopy, can only diagnose tuberculosis in samples containing sufficient concentrations of *Mycobacterium tuberculosis*.

Thus, poor quality sputum samples can lead to missed tuberculosis diagnoses for all tests, since diagnostic sputum samples inevitably contain respiratory secretions from both the healthy airway tract and the diseased lung together with variable amounts of saliva. Recommended sputum collection methods vary globally and their relative merits for tuberculosis diagnosis are poorly characterized.

The diagnosis of Pulmonary Tuberculosis can be obtained from microscopy and culture of a number of different sources including expectorated sputum, induced sputum, gastric washings and bronchoscopy. Amongst the various methods, bronchoalveolar lavage (BAL) has been used with great success as a tool for recovering pathogenic micro-organisms from the lower respiratory tract of individuals with pulmonary infiltrates.

Case finding and effective treatment are the fundamental binomial for disease control. The strategy for finding cases consists of sputum smear microscopy (two or three samples) of individuals with cough and sputum for more than 2 weeks, being the main diagnostic method due to its low cost, easy collection and short turnaround time. Despite the high positive predictive value (PPV) in our country (95%), sputum smear microscopy has an average sensitivity of 40-60%. In addition, the test is positive in only 20% of patients with minimal lung injury, and approximately 30% of patients cannot expectorate sputum spontaneously, especially in the early forms of the disease. Other factors which interfere with the diagnostic performance of smear microscopy include: collection and analysis technique, secretion volume and storage conditions.

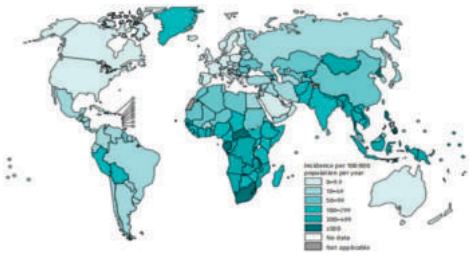

**Figure 1** - Estimated TB incidence rates, 2020.

## MATERIAL AND METHODS

This prospective, interventional study was conducted under Department of Respiratory Medicine and District DR TB Centre, MGM Medical College and Hospital, Navi Mumbai.

Prior approval of Institutional Ethics Committee was taken before start of the study.

A written signed informed consent was taken from the patients prior to enrolling the subjects in the study.

Ethical clearance was obtained from Ethical Clearance Committee of the institution for the study.

### Duration Of Study

November 2019 to November 2021

### Study Population

All the cases who are suspected to have pulmonary TB (PTB) and are sputum smear negative or are not able to produce sputum attending the OPD or in IPD and meeting the inclusion and exclusion criteria.

### Inclusion Criteria

1. Patients aged more than 18 years of either gender.
2. Patients with clinical suspicion of Pulmonary TB including symptoms of cough with or without expectoration for >2 weeks Significant weight loss, hemoptysis & loss of appetite.
3. Patients having any abnormality on chest radiography as per definition of presumptive pulmonary tuberculosis given by NTEP. A persistent cough of more than two weeks that brings up phlegm and blood at times, Breathlessness,

which is usually mild to begin with and gradually gets worse Lack of appetite and weight loss A high temperature of 38°C (100.4°F) or above Extreme tiredness or fatigue Night sweats, Chest pains.
4. Patients who are sputum smear negative.
5. Patient who cannot produce sputum.

**Exclusion Criteria**
1. Patients aged less than 18 years of age.
2. Patient who are not fit for bronchoscopy.
3. Patient who refused for bronchoscopy.
4. Patients who are sputum positive (smear or GeneXpert).
5. Patients who do not consent to participate in the study.

**Sample Size**
A sample of 72 cases of suspected PTB were included in the study.

**Stastical Analysis**
The data was analyzed using statistical software (IBM SPSS, IBM Corporation, Armonk, NY, USA). Descriptive statistics: The Numerical/Continuous data were expressed as Mean ± Standard Deviation and the Categorical data were expressed as Percentages. Analytical statistics: The Numerical/ Continuous data were analyzed by the Unpaired t test. Bar charts and Pie diagrams were used for the presentation of the data as applicable. P value of less than 0.05 was considered as —statistically significant and indicated by —* in the Tables.

**Procedure**
BRONCHOALVEOLAR LAVAGE (BAL)
In diffuse lung involvement, BAL should be performed either from the right middle lobe or the lingula. In patients with suspected Pneumocystis jirovecii or Cytomegalovirus (CMV) pneumonia with diffuse lung involvement, BAL should be performed bilaterally from more than one lobe, including the upper lobe. In focal/patchy lung involvement the site of BAL should be guided by high-resolution computerized tomography (HRCT) thorax findings. At least 100 ml of normal saline should be instilled while performing BAL and total quantity should not exceed 200 ml. The required amount of fluid should be instilled in 2–5 aliquots, and smaller aliquots should be used in patients with COPD. Either manual suction or wall suction can be used for aspiration of fluid during BAL.

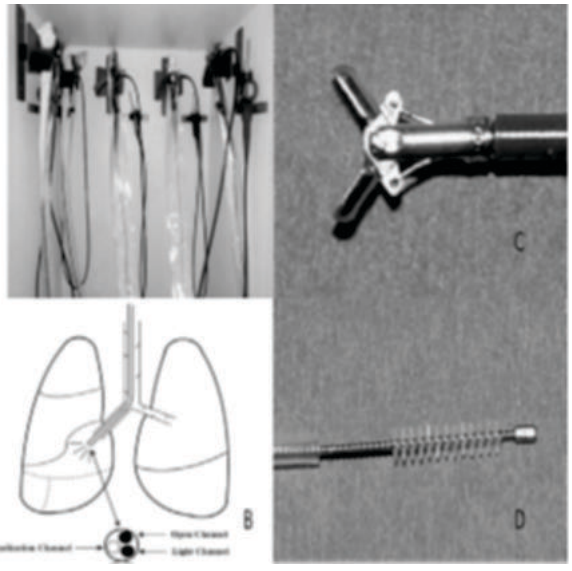


**Figure 2** - A. Fiberoptic bronchoscopes. B. Placement of different channels in a flexible broncho videoscope. C. Tip of endobronchial biopsy forceps. D. Cytology brush tip shown outside its sheath.


**Figure 3**- Bronchoscopy images from patients with different Endobronchial tuberculosis sub-types: (A) actively ca-seating, (B) edematous–hyperemic, (C) fibro-stenotic, (D) granular, (E) ulcerative, and (F) tumorous.

**Figure 4**- Extensive cavitary lung disease due to Mycobacterium tuberculosis visualized by plain chest radiography (left) and computed tomography (right). Note the typical upper lobe predominance and extensive fibronodular infiltrates.

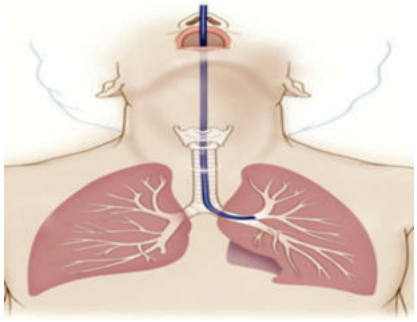

**Figure 5** – Bronchoscopy Procedure for Left Lung Lavage.

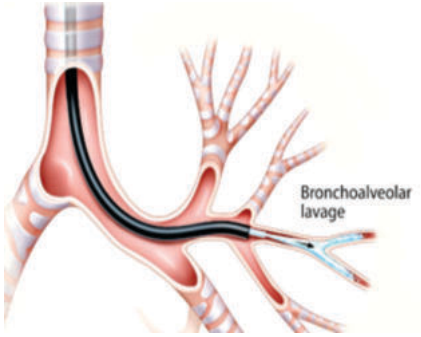


**Figure 6** – Bronchoalveolar Lavage

**RESULTS**
Table 1 show the age and gender-wise distribution of the study population. There was a slight male preponderance in the study group with no difference in the mean age amongst the two genders; P value: 0.603.

**Table 1**: Age (in years) and gender-wise distribution of the study population

| Age Groups | Females | | Males | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Up-to 30 | 9 | 12.50% | 18 | 25.00% | 27 | 37.50% |
| 31 to 40 | 6 | 8.33% | 7 | 9.72% | 13 | 18.05% |
| 41 to 50 | 2 | 2.78% | 7 | 9.72% | 9 | 12.50% |
| 51 to 60 | 6 | 8.33% | 7 | 9.72% | 13 | 18.05% |
| 61 to 70 | 2 | 2.78% | 8 | 11.12% | 10 | 13.90% |
| Total | 25 | 34.72% | 47 | 65.28% | 72 | 100% |
| Mean ± SD | 39.36 ± 14.55 | | 41.40 ± 16.41 | | 40.69 ± 15.72 | |
| Range | 20 to 70 years | | | | | |
| P value | 0.603 | | | | | |
| Statistical Significance | Not Significant | | | | | |

Distribution of the study population according to the chest X ray findings (Table 2)

**Table 2** - Infiltrations were the most common (87.50%), followed by cavitations (27.78%).

| Parameter | Number | Percentage |
|---|---|---|
| Infiltrations | 63 | 87.50% |
| Cavitations | 20 | 27.78% |
| Associated Pleural Effusion | 5 | 6.94% |
| Fibrotic Changes | 5 | 6.94% |

All the cases were sputum smear negative for AFB. On BAL smear, 45.83% of the cases were positive for AFB while on BAL GeneXpert 54.17% of the cases were positive for TB. On MGIT culture 66.67% of the cases were positive. (Table 3)

**Table 3** - Distribution of the positive cases according to the various procedures.

| Procedure | Number | Percentage |
|---|---|---|
| Sputum For AFB | 0 | 0% |
| BAL AFB Smear | 33 | 45.83% |
| BAL Genexpert | 39 | 54.17% |
| BAL MGIT Culture | 48 | 66.67% |

**Table 4** - Distribution of the positive cases according to the various procedures.

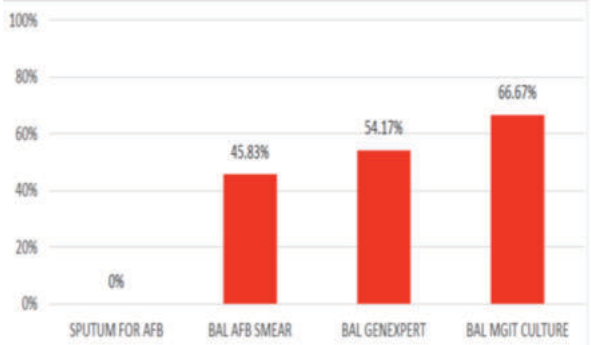


Table 5 shows the sensitivity and specificity of the various tests. Both sensitivity and specificity of BAL GeneXpert were more than BAL AFB smear.

**Table 5** Table 6 and 7 show that rifampicin resistance by BAL GeneXpert was present in 28.21% of the total cases detected positive by BAL sample (n=39)

| Procedure | Sensitivity | Specificity |
|---|---|---|
| BAL AFB Smear | 65.31% | 95.65% |
| BAL Genexpert | 81.25% | 100% |

**Table 6** - Distribution of the study population according to the Rifampicin resistance by the BAL GeneXpert.

| BAL Genexpert | Number | Percentage |
|---|---|---|
| Rifampicin Resistant | 11 | 28.21% |
| Primary Rifampicin Resistance | 2 | 18.18% |
| Secondary Rifampicin Resistance | 9 | 23.07% |
| Not Resistant | 28 | 71.79% |
| Total | 39 | 100% |

**Table 7** - Distribution of the study population according to the Rifampicin resistance by the BAL GeneXpert.

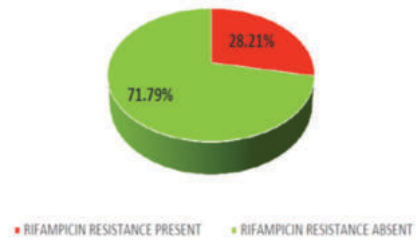


**Table 8** - Distribution of the study population according to the diagnostic categories.

| Parameter | Number | Percentage |
|---|---|---|
| NTM | 2 | 2.78% |
| Clinically Diagnosed Tb | 4 | 5.56% |
| PTB Drug Sensitive | 35 | 48.61% |
| MDR PTB | 11 | 15.27% |
| CAP | 12 | 16.67% |
| Adenocarcinoma | 3 | 4.17% |
| Aspergillus | 2 | 2.78% |
| Candidiasis | 1 | 1.38% |
| Squamous-cell Carcinoma | 2 | 2.78% |
| Total | 72 | 100% |

**Table 9**

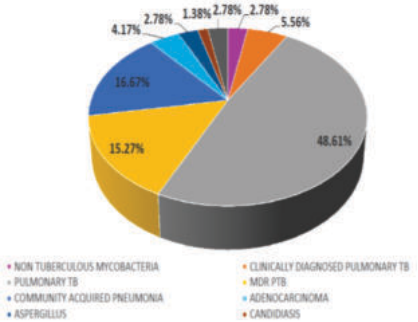


Table 8 and 9 shows the distribution of the diagnosis of the study population. PTB (48.61%), CAP (16.67%) and MDR-PTB (15.27%) were the most common diagnosis while cancer and other infective etiologies were present in less than 5% of the cases, each.

## DISCUSSION

Tuberculosis has existed for millennia and continues to remain a major global public health problem. It is an infectious disease caused by *Mycobacterium tuberculosis*, typically affects the lungs but can also affect other sites and spreads when a person with TB expels the bacteria into the air while coughing or sneezing. TB is one of the top 10 causes of death worldwide and the leading cause of death from an infectious disease. The BRICS countries (i.e., Brazil, Russia, India, China, and South Africa) account for 53% of all tuberculosis cases in the world. In 2016, there were an estimated 1.3 million tuberculosis deaths among HIV negative individuals and an additional 374,000 deaths among HIV-positive individuals. An estimated 10.4 million people (adults, 90%; males, 65%; and people living with HIV, 10%) fell ill with tuberculosis (i.e., were incident cases) in 2016. Drug-resistant tuberculosis is a persistent threat, a total of 490,000 cases of multi-drug-resistant tuberculosis having occurred in 2016, with an additional 110,000 cases of rifampicin-resistant, isoniazid-susceptible tuberculosis.

According to WHO guidelines for control of tuberculosis, the initial approach is the detection of AFB in respiratory specimens (sputum) with bacteriological methods. Although mycobacterial culture is the gold standard and most specific test for the diagnosis, it requires 3-8 weeks to grow. Therefore, the culture is not available to guide the initial therapy. Sputum examination for acid-fast bacilli (AFB) is simple and inexpensive, but it is positive in 44% of cases and even less in children.

Approximately more than 50% of the pulmonary tuberculosis is sputum smear-negative. Clinical and radio-logical based diagnosis can lead to either over- or under-diagnosis of tuberculosis. Mortality of sputum smear-negative, culture-positive tuberculosis cases are about 14.1%, insisting on the importance of diagnosis of sputum smear-negative PTB. On the other hand, unnecessary anti-tuberculosis treatment may cause drug resistance and economic burden.

Fiberoptic bronchoscopy (FOB) can provide an early confirmative diagnosis in such patients. Among the bronchoscopic materials, bronchoalveolar lavage (BAL) is the best diagnostic material for the diagnosis of PTB. However, due to its invasive nature and being expensive, not much data is available regarding its efficacy in the diagnosis of smear negative PTB and other conditions. Therefore, the present study was conducted to assess its utility in Indian scenario.

## CONCLUSION

In the present study, a total of 72 cases with negative sputum smear for AFB were included. Demographic details were recorded. Detailed past, personal and family histories were recorded. Findings of physical examination were noted. Laboratory and radiological investigations were done and findings were noted. BAL samples were obtained and subjected to smear, GeneXpert and MGIT culture. Other relevant procedures were carried out for the diagnosis. Details of diagnosis and treatment were recorded and data was analyzed.

A slight male preponderance with majority distribution in younger population (less than 40 years) was observed. Weight loss, fever and cough were the predominant symptoms (more than 70% of the cases, each) while chest and joint pains were the least common symptoms (Less than 10% of the cases, each). Positive past history (27.78%), family history (8.33%) and history of contact with TB cases (15.28%) was present in minority of the cases. DM (23.61%) and hypertension (12.50%) were the most common comorbidities while others accounted for up-to 13% of the total cases. 2.78% of the cases were HIV positive. Addictions were present in less than 20% of the cases, each, with tobacco chewing being the most common addiction (18.06%). Majority of the cases were malnourished, with low BMI (66.66%). Infiltrations and cavitations were the most common radiological finding on both, chest X ray and CT scan. These were most commonly distributed in the upper zones.

The detection rate by BAL AFB smear was 45.83%, BAL GeneXpert was 54.17% and by BAL MGIT culture was 66.67%. With BAL MGIT culture as the gold standard, it was observed that the sensitivity, specificity, positive and negative predictive values of BAL AFB smear were less than BAL GeneXpert. Rifampicin resistance was present in 28.21% of the total cases detected positive by BAL sample (n=39). Majority of the cases were diagnosed by the BAL. Trans-bronchial biopsy, trans-bronchial needle aspiration and bronchial brushing were required to be performed in less than 10% cases each, for aiding diagnosis.

**Conflict Of Interest:** None to declare

**Source of funding:** Nil

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