EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 3
313-318
Year: 2019

ROLE OF FIBEROPTIC BRONCHOSCOPY IN DIAGNOSIS OF SUSPECTS OF PULMONARY TUBERCULOSIS

Dr. Mamata Heda*[1], Dr. Pankaj Wagh*[2], Dr. Shivam Puniani[2], Dr. Jigneshkumar Patel[2], Dr. Rakesh Rajpurohit[2], Dr. Ravindra Chordia[3], Dr. Gaurav Dubey[4], Dr. Pankaj Gujar[4] and Dr. Anil Rohankar[5]

[1]Associate Professor, Department of TB and Respiratory Diseases, Dr Panjabrao Alias Bhausaheb Deshmukh Memorial Medical College, Amravati 444603, Maharashtra, India.
[2]Junior Resident, Department of TB and Respiratory Diseases, Dr Panjabrao Alias Bhausaheb Deshmukh Memorial Medical College, Amravati 444603, Maharashtra, India.
[3]Professor and Head of Department, Department of TB and Respiratory Diseases, Dr Panjabrao Alias Bhausaheb Deshmukh Memorial Medical College, Amravati 444603, Maharashtra, India.
[4]Assistant Professor, Department of TB and Respiratory Diseases, Dr Panjabrao Alias Bhausaheb Deshmukh Memorial Medical College, Amravati 444603, Maharashtra, India.
[5]Senior Resident, Department of TB and Respiratory Diseases, Dr Panjabrao Alias Bhausaheb Deshmukh Memorial Medical College, Amravati 444603, Maharashtra, India.

***Corresponding Author: Dr. Pankaj Wagh & Dr. Mamata Heda**
Junior Resident, Department of TB and Respiratory Diseases, Dr Panjabrao Alias Bhausaheb Deshmukh Memorial Medical College, Amravati 444603, Maharashtra, India.

Article Received on 24/12/2018 **Article Revised on 15/01/2019** **Article Accepted on 06/02/2019**

ABSTRACT

Introduction: TUBERCULOSIS is a disease caused by Mycobacterium tuberculosis (MTB) which is a gram positive, aerobic, acid and alcohol fast bacillus. India has the maximum number of tuberculosis cases worldwide accounting for one fourth of the global TB cases. The diagnosis of pulmonary TB can be obtained from microscopy and culture of a number of different sources including regular sputum, induced sputum, gastric washings and bronchoscopy. Fiberoptic bronchoscopy can provide excellent material for diagnosis of suspected cases of pulmonary TB when smear of expectorated sputum do not reveal mycobacteria. **Aims & Objectives:** To assess the diagnostic role of fiberoptic bronchoscopy in diagnosis of suspect cases of pulmonary tuberculosis. **Material And Methods:** After consent, 82 patients with sputum smear negative for AFB and chest x ray suggestive of pulmonary TB, underwent fiberoptic bronchoscopy. Bronchoalveolar lavage(BAL), Bronchial brushings, Transbronchial lung biopsy(TBLB) was done and sample analysed by smear microscopy, CBNAAT and Cytopathology. **Results:** The final diagnosis of PTB was established in 51/82 (62%) cases by combining all Bronchoscopic aided procedures. The sensitivity of BAL CBNAAT, BAL fluid direct smear, Bronchial Brushing smear and TBLB are 90.2%, 41.2%, 23.5% and 7.8% respectively. **CONCLUSION:** Flexible fiberoptic bronchoscopy is a useful tool in early diagnosis of pulmonary tuberculosis in sputum smear negative patients. Bronchoscopy with various Bronchoscopic aided procedures reveals a higher bacteriological confirmation of diagnosis in patients with strong clinical and radiological evidence suggestive of pulmonary tuberculosis.

KEYWORDS: Mycobacterium Tuberculosis, Fiberoptic Bronchoscopy, Bronchoalveolar Lavage(BAL), CB NAAT, Transbronchial lung biopsy (TBLB).

INTRODUCTION

Tuberculosis (TB) is one of the major health problems in India. India has the maximum number of tuberculosis cases worldwide accounting for one fourth of the global TB cases. In 2013, out of the estimated global annual incidence of 9 million TB cases, 2.1 million were estimated to have occurred in India.[1]

The diagnosis of pulmonary TB can be obtained from microscopy and culture of a number of different sources including regular sputum, induced sputum, gastric washings and bronchoscopy. The sensitivity, specificity and diagnostic yield of each of these tests vary widely between studies.[2] Sputum microscopy and culture are relatively easy to perform but can be negative in a substantial proportion of pulmonary TB patients with reported sensitivities ranging from 25 to 45%.[2-4] Microbiological diagnosis is the main stay for the effective treatment of pulmonary tuberculosis for obtaining the correct sputum sample, patient education is imperative. However, even if the correct sample is expectorated, the bacillary population has to be at least 10000 per millilitre, to get the smear positive for acid fast bacilli (AFB).[5] Moreover, it depends on the

previous treatment, default behaviour, and effective cough. Again 31%of the new cases may be smear-negative for AFB.[6] Sputum induction with hypertonic saline requires additional resource allocation and manpower training, but has been shown to increase the diagnostic yield of sputum examination in several studies.[7-9] Several studies have confirmed the higher diagnostic yield of bronchoscopy over sputum examination in the diagnosis of pulmonary TB both from higher microscopy and higher culture positivity results.[10-12] Clinicians often face a real dilemma when a patient suspected with active pulmonary TB has multiple negative induced-sputum results. They have a choice to either proceed with empiric treatment for pulmonary TB or to perform an invasive test like bronchoscopy in order to confirm the diagnosis. The question then is whether bronchoscopy offers any additional diagnostic yield in patients suspected with active pulmonary TB and with multiple negative induced-sputum results. The existing literature on this subject reports varying diagnostic yields for bronchoscopy depending on the study design and patient population studied. Higher diagnostic yields are obtained from patients undergoing bronchoscopy because of an inability to expectorate any sputum. This is in contrast to patients who underwent bronchoscopy after an adequate sputum sample was determined to be smear negative.[10] Other studies however have shown no additional yield of bronchoscopy over sputum induction.[13,14]

We performed this study to answer the clinical question as to whether bronchoscopy provides additional diagnostic yield after multiple negative induced-sputum smear testing.

AIMS AND OBJECTIVES

To assess the diagnostic role of fibreoptic bronchoscopy in diagnosis of suspect cases of pulmonary tuberculosis.

MATERIAL AND METHODS

An institutional based **observational study** was undertaken with 82 patients to evaluate the significance of fiberoptic bronchoscopy in the diagnosis of PTB among patients who have chest X-ray suggestive but remain undiagnosed because of a negative sputum smear for AFB.The present clinical study was conducted in the Department of Respiratory Medicine of a tertiary care centre.The study duration was one and half year.

Considering the prevalence as 38% from the study of Nikbakhsh N et al[15], sensitivity and specificity of BAL specimens as 60% and 91% respectively with absolute precision of 10%, confidence level of 95% and confidence interval of 14, the number of patients in our study to achieve statistical significance is 49. But we were considered 82 cases for our study. Those patients with HIV infection, Bleeding diathesis, recent history of myocardial infarction and arrhythmias were excluded from the study.

Methodology

All patients attending OPD & IPD at our tertiary care centre satisfying the inclusion and exclusion criteria were taken for the study. Clinical symptoms consisted of cough, fever, breathlessness, loss of apetite, chest pain, hemoptysis and weight loss. The enrolled patients were subjected to a protocol, which included detailed recording of history regarding mode of onset and duration of illness, Complete physical examination, routine investigations like CBC, ESR, RBS, HIV, HbsAg, ECG and chest x ray. Sputum examination for AFB -2- samples (1-spot sample & 1-early morning sample) carried out by Ziehl & Neelsen staining technique. Radiologically chest x ray showed one or more of the following lesions like infiltration, consolidation, military mottling, cavity and fibrosis. Fiberoptic bronchoscopy was used to examine bronchial tree and obtain BAL, Bronchial Brushing and Transbronchial lung biopsy. The bronchoscopy was performed transnasally using fujinon bronchoscope by 2 bronchoscopists under local anaesthesia. All patients received lignocaine 10% spray to the nose and throat and lignocaine 2% solution to the vocal cords, trachea and bronchi. A thorough examination of bronchial tree was carried out and bronchoalveolar lavage (BAL) bronchial brushing, transbronchial lung biopsy(TBLB) were collected. The specimen obtained was placed on slides for Ziehl-Neelsen stain. Bronchial biopsy was performed on abnormal looking mucosa and stained with Eiosin-hematoxylin and Ziehl- Neelsen stains.

OBSESRVATIONS AND RESULTS

Majority of the patients (44%) were from the age group of 31-40years.There was male preponderance (55%) while female patients constituted 45% of the study group. 72(88%) and 58(71%) patients presented with cough and fever respectively followed by breathlessness 42(51%), loss of appetite 36(44%), chest pain 34(41%), haemoptysis 28(34%) and weight loss 13(16%). Radiological findings showed that upper zone was most commonly involved.Infiltration was present in 40 patients followed by consolidation (30), cavity(05), military mottling(04) and fibrosis (03). Bronchoscopic findings showed no pathological lesion in 33 (40%) patients. Out of 49 patients where bronchoscopy revealed some pathology, 25(31%) patients had discharge from bronchus, 16 (20%) patients had unhealthy mucosa /granuloma, 6 (7%) patients had bleeding from bronchus while growth was visible only in 2(2%) patients**(Table-1).** Bronchoalveolar Lavage (BAL) was done in all 82 cases. Smear examination for AFB was positive in BAL fluid in 21 (26%) (male-10(22%) & female-11(30**%**)) **(Fig-1)**. CB NAAT of bronchoalveolar lavage fluid was done in all 82patients. CB NAAT was positive in 46 (56%) patient out of which 23 are males and 23 are females**(Fig-2)**. All 21 cases which were positive in BAL Fluid Direct smear were also positive in BAL CB NAAT. Bronchial brushings were taken from the affected segment in 82 cases. Smear examination for AFB was positive in bronchial brushings in 12 (15%)

cases**(Fig-3)**. Out of 12 positive cases 9 were also positive in BAL direct smear and BAL CB NAAT and 3 cases were positive only in Bronchial Brushing smear. Bronchial biopsies were done only in 29 out of 82 patients, where biopsy was feasible. Trans-Bronchial lung biopsy (TBLB) showed caseating epitheloid granuloma in 4 (14%) patients out of which 2 were positive in all i.e BAL fluid direct smear, BAL CB NAAT and bronchial brushing smear and 2 were positive only in TBLB. 4(14%) patients were positive for Malignancy and nonspecific inflammation in 21 (72%) patients**(Table-2)**.

We diagnosed 51 cases out of 82 (62%) by combining all Bronchoscopic aided procedure. BAL CB NAAT was the most effective method where diagnosis was accurate in 46 cases with sensitivity of 90.2% (46/51) followed by BAL fluid smear and Bronchial Brushing smear where diagnosis was accurate in 21 and 12 cases with a sensitivity of 41.2% (21/51) and 23.5% (12/51) respectively. Using TBLB the diagnosis was 4 out of 51 positive patients with a sensitivity of 7.8% (4/51)**(Fig-4)**. In our study BAL CB NAAT had the highest yield (46/82) of 56% followed by BAL fluid smear (21/82) of 26%. Bronchial brushing smear and TBLB comparatively had low diagnostic yield of (12/82)15% and (4/29)14% respectively**(Table-3)**.

Table 1: Bronchoscopic Findings.

Bronchoscopic Findings	N	%
Normal Appearance	33	40%
Abnormal Appearance*		
Discharge from bronchus	25	31%
Unhealthy mucosa/granuloma	16	20%
Bleeding from bronchus	6	7%
Growth	2	2%

* - Multiple findings in some cases

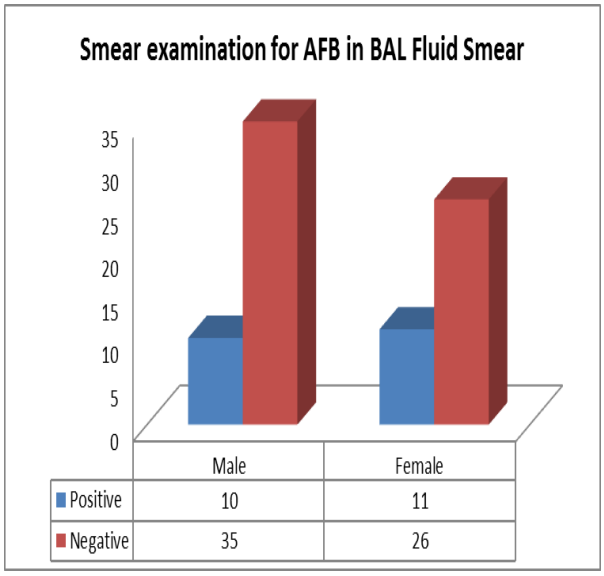

Fig 1: Smear examination for AFB in BAL Fluid Smear.

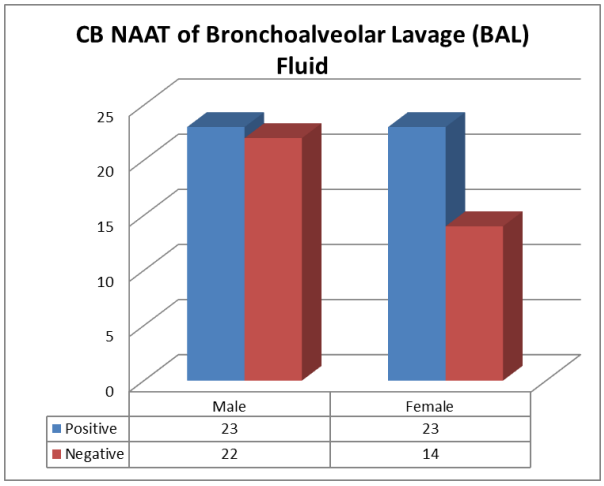

Fig 2: CB NAAT of Bronchoalveolar Lavage (BAL) Fluid.

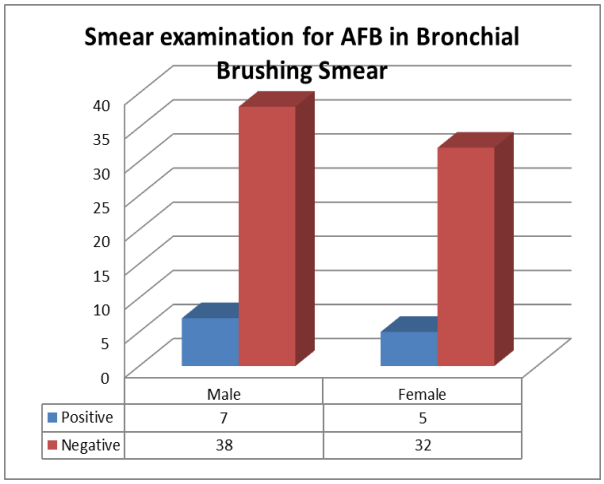

Fig 3: Smear examination for AFB in Bronchial Brushing Smear.

Table 2: Cytopathological Results of TBLB Samples.

Cytopathology	N	%
Caseating Epithelioid granuloma	4	14%
Malignancy	4	14%
Non-specific inflammation	21	72%
Total	29	100%

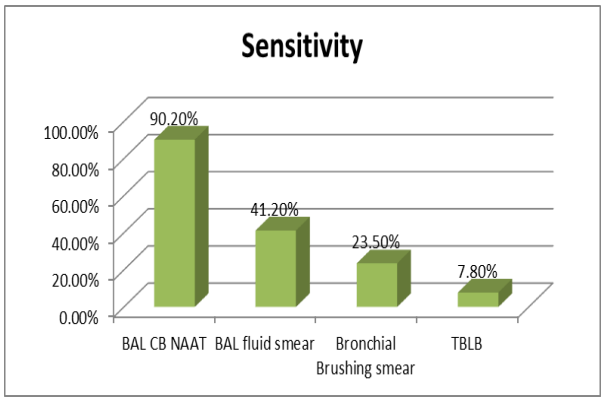

Fig. 4: Sensitivity of Various Bronchoscopic Aided Methods.

Table 3: Total Yield of Various Bronchoscopic Aided Methods.

Diagnostic Techniques	Positive Cases	Total Cases	Total Yield
BAL CB NAAT	46	82	56%
BAL fluid smear	21	82	26%
Bronchial Brushing smear	12	82	15%
TBLB	4	29	14%

DISCUSSION

The WHO Expert Committee on Tuberculosis recommends that patients of pulmonary tuberculosis in whom the disease has not been confirmed bacteriologically should be classified as "suspects" till the presence of AFB is demonstrated and a patient with persistent symptoms whose sputum does not contain AFB should be followed up and anti-tubercular treatment should be given only if the diagnosis can be confirmed bacteriologically.

In the present study, majority of the patients (44%) were from the age group of 31-40years followed by 26% from the age group of 41-50 years,13% from the age group of 51-60 years, 11% from the age group of 21-30 years, and 6% from the age group of >60 years. There was male preponderance (55%) while female patients constituted 45% of the study group. This was comparable to the study done by **Kumar A et al**[18] on total 33 patients, 22 (66.66%) were male and 11 (33.33%) were female. The youngest patient was 18 years of age and the oldest was 73 years old. The maximum number 11 (33.33%) of patients belonged to 20-29 years age group followed by 40-49 years age group.

In our study, 72(88%) and 58(71%) patients presented with cough and fever respectively. The other symptoms were breathlessness 42 (51%), loss of appetite 36(42%), chest pain 34(41%), haemoptysis 28 (34%) and weight loss 13(16%).These patients characterstics were similar to the study done by **Bhaglani DK et al**[17] **and Patel D et al.**[20]

Radiological findings in the present study showed that upper zone was most commonly involved- infiltration was present more in right upper zone (12), left upper zone (6), Bilateral (4). Consolidation in right upper zone (5), left upper zone (3), Bilateral (2), Cavity in left upper zone (1), Bilateral military mottling (4) and Fibrosis in right upper zone (3). **Bhaglani DK et al**[17] in an Institutional based Prospective Study reported among patients with active PTB, 23 had right sided lesion and 8 had left sided lesion. Bilateral lesion was seen in 21 patients 50 patients (75.76%) had infiltrates and 16 patients (24.24%) had cavitatory lesions.

Bronchoscopic findings in our study showed no pathological lesion in 33 (40%) patients. Out of 49 patients where bronchoscopy revealed some pathology, 25 (31%) patients had discharge from bronchus, 16 (20%) patients had unhealthy mucosa /granuloma, 6 (7%) patients had bleeding from bronchus while growth was visible only in 2(2%) patients. This was comparable to the study done by **Prakash P et al**[19] where Bronchoscopic examination revealed no pathological lesion in 21 (42%) of 50 patients. Out of 29 patients where bronchoscopy revealed some pathology, 14 cases (28%) had discharge from bronchus, 11 cases (22%) had unhealthy mucosa /granuloma, 5 cases (10%) had external compression and another 5 cases (10%) had bleeding from bronchus, while growth was visible only in 2 cases (4%).

Bronchoalveolar Lavage (BAL) was done in all 82 cases in the present study. Smear examination for AFB was positive in BAL fluid in 21 (26%) (male -10(22%) & female-11(30%)). This study was comparable to study done by **Kumar A et al**[18] where BAL was done in 27 patients and BAL fluid smear showed AFB in 5 (18.5%) patients.

CB NAAT of bronchoalveolar lavage fluid was done in all 82patients of our study. CB NAAT was positive in 46 (56%) patient out of which 23 are males and 23 are females. This is comparable to study done by **Mohanty T et al in 2017**[21] on 100 patients, 74 males and 26 females. SI sputum smear positive 29 out of 100. BAL CBNAAT yield 38/71 (54%).

Bronchial brushings were taken from the affected segment in 82 cases in our study. Smear examination for AFB was positive in bronchial brushings in 12 (15%) cases.This is comparable to study done by **Kumar A et al**[18] where out of 33 patients, bronchial brushing was done in 16 patients. Bronchial brushing smear was positive for AFB in 4 (25%) patients. Also study done by **Prakash P et al**[19] where bronchial brushing smear positive in 12(41.4%) cases.

It was observed in the present study that Bronchial biopsies were done only in 29 out of 82 patients, where biopsy was feasible. Trans-Bronchial lung biopsy (TBLB) showed caseating epitheloid granuloma in 4 (14%) patients and 4(14%) patients were positive for Malignancy and nonspecific inflammation in 21 (72%) patients. This is comparable to study done by **Kumar A et al**[18] where TBLB was done in 13 patients.Out of 13 patients, epithelioid granuloma was seen in 2 (15.38%) patients, malignancy in 3 (23.07%) patients and nonspecific inflammation in 8 (61.54%) patients. **Prakash P et al**[19] study reported TBLB were done only in 12 out of 50 patients, which showed caseating epitheloid granuloma in 3 cases (25%) out of which AFB could be demonstrated in two (16.66%). Cytopathological yield of Transbronchial lung biopsy ranges between 10-68%. **Willicox PA et al**[22] reported

result of 68%, while **Panda BN et al**[23] reported 10%. **Kulpatti DDS et al**[24] reported 12%, and **Charoenratanakaul S et al**[25] reported 17%.

In our study, BAL CB NAAT was the most effective method where diagnosis was accurate in 46 cases with sensitivity of 90.2% (46/51) followed by BAL fluid smear and Bronchial Brushing smear where diagnosis was accurate in 21 and 12 cases with a sensitivity of 41.2% (21/51) and 23.5% (12/51) respectively. Using TBLB the diagnosis was 4 out of 51 positive patients with a sensitivity of 7.8% (4/51). **Mohanty T et al in 2017**[21] study shows BAL CBNAAT yield 38/71 (54%), with a sensitivity of 88.09%. **Jacomelliet M et al**[26] study showed BAL sensitivity and specificity of 60% and 100% respectively.

In our study, BAL CB NAAT had the highest yield (46/82) of 56% followed by BAL fluid smear (21/82) of 26%. Bronchial brushing smear and TBLB comparatively had low diagnostic yield of (12/82)15% and (4/29)14% respectively. In **Bhaglani DK et al**[17] Study among the 66 cases studied the total number of PTB cases diagnosed was 52 (78.78%), where smear +ve on ZN staining was 15 (22.72%) and total number of PTB cases showed growth on MGIT 960 TB culture was 48 (72.72%). The total number of cases, of other diseases diagnosed was 6 (9.09%). **Kumar A et al**[18] study showed that maximum number, 8 (24.24%) patients were diagnosed with the help of BAL fluid smear and Bronchial brush smear, and Post Bronchoscopy sputum and TBLB helped further in diagnosis of pulmonary tuberculosis. So by using all the four techniques fiberoptic bronchoscopy helped in diagnosis of 10 (30.30%) patients. Thus in total 33 sputum smear negative suspected pulmonary tuberculosis cases, at microscopy centre under RNTCP, early diagnosis of pulmonary tuberculosis was established in 10 (30.30%) cases and in 3 (9.09%) cases diagnosis of malignancy was established.

Prakash P et al[19] study diagnosed of 24 cases out of 50 (48%) by combining all the bronchoscopic aided procedures. Of these 24 cases diagnosed as tuberculosis, BAL was the most effective method where diagnosis was clinched in 21 cases (21/24) with a sensitivity of 87.5 % followed by brushings where diagnosis was clinched in 13 cases (13/24) with a sensitivity of 54.17%. TBLB clinched the diagnosis in 3 out of 24 positive patients (3/24) with a sensitivity of 12.5%. Bronchial brushings had the highest yield (13/29) of 44.8% followed by BAL (21/50) of 42%. TBLB comparatively had low diagnostic yield of 25%. In our study, out of 82 cases 51(62.2%) cases were diagnosed as a Pulmonary Tuberculosis by combining all Bronchoscopic aided procedures. Of these 51 cases diagnosed as tuberculosis, BAL CB NAAT was the most effective method where diagnosis was clinched in 46 patient with a sensitivity of 90.2% followed by BAL fluid smear where diagnosis was clinched in 21 cases with a sensitivity of 41.2%. Bronchial brushing smear was effective in diagnosis of 12 cases with a sensitivity of 23.5% and TBLB was effective in diagnosis of 4 cases with a sensitivity of 7.8%.The total no of cases, of other diseases diagnosed was 31 (37.8%), out of which 27 cases were diagnosed as Bacterial Pneumonia which were resolved by a course of antibiotics and 4 cases were diagnosed as Malignancy.

CONCLUSION

India is among the 22 high burden countries of PTB, and due to high contagious nature of PTB, its early recognition is of utmost importance. The results of present study suggest that FOB is a useful tool in diagnosing SSN-PTB patients. FOB reveals a high bacteriological confirmation of diagnosis in SSN-PTB patients. FOB is also a safe procedure. FOB also helps in ruling out non-PTB conditions like bacterial pneumonia. FOB and various bronchoscopy guided procedures can provide a rapid and definitive diagnosis of PTB in sputum negative patients.

REFERENCES

1. Zumla A, George A, Sharma V, Herbert RH, Oxley A, Oliver M. The WHO 2014 global tuberculosis report—further to go. The Lancet Global Health, Jan 1, 2015; 3(1): e10-2.
2. Merrick ST, Sepkowitz KA, Joan W, Damson L, McKinley P, Jacobs JL. Comparison of induced versus expectorated sputum for diagnosis of pulmonary tuberculosis by acid-fast smear. American journal of infection control, Dec 1, 1997; 25(6): 463-6.
3. Nelson SM, Deike MA, Cartwright CP. Value of examining multiple sputum specimens in the diagnosis of pulmonary tuberculosis. Journal of clinical microbiology, Feb 1, 1998; 36(2): 467-9.
4. Kim TC, Blackman RS, Heatwole KM, Kim T, Rochester DF. Acid-fast bacilli in sputum smears of patients with pulmonary tuberculosis. Prevalence and significance of negative smears pretreatment and positive smears post-treatment. The American review of respiratory disease, Feb, 1984; 129(2): 264-8.
5. Katoch VM. newar diagnostic techniqe for tuberculosis. Indian J Med Res., 2004; 120: 418-28.
6. India TB. Revised national TB control programme annual status report. New Delhi: Government of India, 2012 Mar.
7. Al Zahrani K, Al Jahdali H, Poirier L, Rene P, Menzies D. Yield of smear, culture and amplification tests from repeated sputum induction for the diagnosis of pulmonary tuberculosis. The International Journal of Tuberculosis and Lung Disease, Sep 1, 2001; 5(9): 855-60.
8. Bell D, Leckie V, McKendrick M. Use of the induced sputum procedure in the investigation of smear-negative pulmonary tuberculosis. Clinical infectious diseases, May 15, 2004; 38(10): 1504-5.
9. Conde MB, Loivos AC, Rezende VM, Soares SL, Mello FC, Reingold AL, Daley CL, Kritski AL.

Yield of sput um induction in the diagnosis of pleural tuberculosis. American journal of respiratory and critical care medicine, Mar 1, 2003; 167(5): 723-5.
10. Chawla R, Pant K, Jaggi OP, Chandrashekhar S, Thukral SS. Fibreoptic bronchoscopy in smear-negative pulmonary tuberculosis. European Respiratory Journal, Oct 1, 1988; 1(9): 804-6.
11. Conde MB, Soares SL, Mello FC, Rezende VM, Almeida LL, Reingold AL, Daley CL, Kritski AL. Comparison of sputum induction with fiberoptic bronchoscopy in the diagnosis of tuberculosis: experience at an acquired immune deficiency syndrome reference center in Rio de Janeiro, Brazil. American journal of respiratory and critical care medicine, Dec 1, 2000; 162(6): 2238-40.
12. Ganguly KC, Hiron MM, Mridha ZU, Biswas M, Hassan MK, Saha SC, Rahman MM. Comparison of sputum induction with broncho-alveolar lavage in the diagnosis of smear-negative pulmonary tuberculosis. Mymensingh medical journal: MMJ, Jul, 2008; 17(2): 115-23.
13. McWilliams T, Wells AU, Harrison AC, Lindstrom S, Cameron RJ, Foskin E. Induced sputum and bronchoscopy in the diagnosis of pulmonary tuberculosis. Thorax, Dec 1, 2002; 57(12): 1010-4.
14. Anderson C, Inhaber N, Menzies D. Comparison of sputum induction with fiber-optic bronchoscopy in the diagnosis of tuberculosis. American journal of respiratory and critical care medicine, Nov, 1995; 152(5): 1570-4.
15. Novin Nikbakhsh, Masomeh Bayani, Sepideh Siadati. The value of Bronchoalveolar Lavage in the diagnosis of Sputum Smear negative Pulmonary Tuberculosis. Iran J Pathol, 2015; 10: 35-40.
16. World Health Organization- Global tuberculosis report 2013/ Global plan to stop TB. http://www.stoptb.org/news/stories/2013/ns13_067 .asp(accessed 1/10/2015)
17. Bhaglani DK, Sarkar M, Singh D, Negi RS, Sharma S. Role of Fiber-Optic Bronchoscopy in Sputum Smear Negative Pulmonary Tuberculosis. National Journal of Medical Research, 2016; 134.
18. Kumar A, Gupta AK, Khan MH. Role of flexible fiberoptic bronchoscopy in suspected sputum smear negative pulmonary tuberculosis cases at microscopy centre under RNTCP. Int J Med Sci Public Health, 2014; 3: 31-34.
19. Prakash P, Agarwal P, Agarwal P, Singh DP, Gupta A. Role of Bronchoscopy in Diagnosing Sputum Smear Negative Pulmonary Tuberculosis. Annals of Applied Bio-Sciences, Mar 10, 2016; 3(1): A113-117.
20. Patel D, Kamdar DJ. Sputum versus bronchial washings for diagnosis of pulmonary tuberculosis-a prospective study of 53 patients. International Journal of Research in Medical Sciences, Mar 28, 2017; 5(4): 1266-9.
21. Mohanty T, Panigrahi SK, Pattnaik M, Panda G, Routray D, Patra JK, Meher BK. Study on diagnostic modalities in smear negative pulmonary tuberculosis with special reference to sputum induction (SI CBNAAT), bronchoscopy (BAL CBNAAT and BAL culture). Journal of Evidence Based Medicine and Healthcare, Jan 1, 2017; 4(47): 2858-62.
22. Willcox PA, Benatar SR, Potgieter PD. Use of the flexible fibreoptic bronchoscope in diagnosis of sputum-negative pulmonary tuberculosis. Thorax, Aug 1, 1982; 37(8): 598-601.
23. Panda BN, Rajan KE, Jena J, Nema SK, Murali M, Patil AP. Diagnostic yield from flexible fiberoptic bronchoscopy in sputum negative pulmonary tuberculosis cases. INDIAN JOURNAL OF TUBERCULOSIS, 1995;42: 207-10.
24. Kulpati DDS, Hira HS. Diagnosis of smear negative pulmonary tuberculosis by flexible fiberoptic bronchoscopy Indian J Tub, 1986; 33: 179-82.
25. Charoenratanakul S, Dejsomritrutai W, Chaiprasert A. Diagnostic role of fiberoptic bronchoscopy in suspected smear negative pulmonary tuberculosis. Respiratory medicine, Oct 1, 1995; 89(9): 621-3.
26. Jacomelli M, Silva PR, Rodrigues AJ, Demarzo SE, Seicento M, Figueiredo VR. Bronchoscopy for the diagnosis of pulmonary tuberculosis in patients with negative sputum smear microscopy results. Jornal Brasileiro de Pneumologia, Apr, 2012; 38(2): 167-73.