Original Article

Fiberoptic bronchoscopy, as a valuable diagnostic option in sputum negative pulmonary tuberculosis: A prospective study

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Abstract

Context: World Health Organization recommends bacteriological confirmation of pulmonary tuberculosis (PTB) by the detection of acid-fast bacilli (AFB) in respiratory specimens. However about 40-60% of patients with PTB suspected clinically or radiologically may fail to produce sputum, or when it is available, AFB may be negative on repeated smear examination. These sputum smear negative patients and those who fail to produce any sputum can be diagnosed by flexible fiberoptic bronchoscopy. **Aims**: Our study was an attempt to analyze the role of fiberoptic bronchoscopy in sputum smear negative PTB patients with respect to their association with clinical and radiological profile. **Materials and Methods:** In this prospective, open label, observational study, 40 cases of sputum smear negative PTB were subjected to bronchoscopic examination after taking informed consent and samples like bronchial aspirate, bronchoalveolar lavage and post bronchoscopy sputum were collected. The data was analysed and the results were given in percentage. **Results**: Out of the total 40 patients, overall diagnosis was confirmed in 24 (60%) patients. Of these 24 patients, 17 patients were confirmed for PTB whereas 7 had other diagnoses. **Conclusion:** The study concludes that fiberoptic bronchoscopy is a useful tool in diagnosing sputum smear negative PTB patients with respect to their association with clinical and radiological profile, and also identifies individuals at a higher risk for progression of disease, at an early stage despite not meeting routine bacteriological criteria for confirmation of PTB.

Key words: AFB-negative, pulmonary tuberculosis, AFB-negative sputum, fiberoptic bronchoscopy, pulmonary tuberculosis

Introduction

Pulmonary Tuberculosis (PTB) is a major public health problem, and its diagnosis is based on isolation of the organism from respiratory specimens, especially sputum samples. World Health Organization (WHO) recommends bacteriological confirmation of pulmonary tuberculosis by the detection of acid-fast bacilli (AFB) in respiratory specimens.[1] However in children, gastric lavage is recommended for the collection of respiratory secretions.[2]

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Access this article online	
Quick Response Code:	Website: www.ijabmr.org
	DOI: 10.4103/2229-516X.106355

Difficulties arise when a patient who is suspected of active tuberculosis, both clinically and radiologically, does not produce sputum. About 40-60% of patients with active pulmonary tuberculosis suspected clinically or radiologically may fail to produce sputum, or when it is available AFB may be negative on repeated smear examination.[3] Henceforth, more aggressive procedures need to be undertaken in these patients in order to establish the diagnosis.

A number of studies confirm the usefulness of fiberoptic bronchoscopy in the diagnosis of pulmonary tuberculosis.[4-6] In the series reported by Chan *et al.*,[5] 34 patients with suspected PTB who were sputum smear negative, were subjected to fiberoptic bronchoscopy. PTB was confirmed in 29 of them. Flexible fiberoptic bronchoscopy with bronchial aspiration and bronchoalveolar lavage under local anaesthesia is a relatively safe procedure and well tolerated by most of the patients.[7-10] Its safety and diagnostic yield have been reported before.[11,12] Complications are known but rare in occurrence.[13,14]

This study was carried out to know the usefulness of bronchoscopy in sputum smear negative pulmonary

tuberculosis patients diagnosed on clinical and radiological grounds, by direct visualization of bronchial tree and collecting specimens such as bronchial aspirate, bronchoalveolar lavage, transbronchial needle aspiration cytology and post-bronchoscopy sputum and to assess the positivity of these specimens through smear examination for AFB by Ziehl-Neelsen staining method, culture of the specimens for *Mycobacterium tuberculosis* on Lowenstein-Jensen media and cytological examination of transbronchial needle aspiration (TNA).

Materials and Methods

Study population

The study was conducted in the Department of Medicine, Bokaro General Hospital, Bokaro Steel City. The subjects of the study group were chosen from among the patients attending the outpatient department and those admitted in the wards. For the purpose of our study, the patients selected were those who were diagnosed as a case of pulmonary tuberculosis on clinical and radiological grounds but who were sputum smear negative on three consecutive occasions as per RNTCP 2009 guidelines.[15]

Forty patients with clinical history and physical findings or chest X-ray lesions suggestive of pulmonary tuberculosis or with three consecutive sputum smear examinations negative for acid-fast bacilli were included in this prospective, non randomised and observational study. Patients with any contraindications for bronchoscopic procedure, those not giving consent and patients on anti-tubercular treatment were excluded from the study.

After a detailed clinical history, thorough physical examination and routine investigations, assessment for the fitness of patients for bronchoscopy procedure was done. Written informed consent was obtained from all the patients undergoing bronchoscopy procedure. Fiberoptic bronchoscopy was performed using KARL STORZ bronchoscope introduced through transnasal route after proper lubrication with xylocaine ointment. All procedures were carried out as per the International recommendations.[16,17] A thorough examination of the bronchial tree was carried out and bronchial aspirate (BA), bronchoalveolar lavage (BAL), TNA and post-bronchoscopy sputum (PBS) were collected. All these specimens were sent to the Department of Microbiology, with a code number where these samples were processed, stained and cultured.

The data was analysed and the results were given in percentage in accordance with previous related studies. Different statistical aggregates like mean and median were used to analyse numerical parameters. Graphical representation of the results was done and appropriate statistical methods were employed to ascertain the yield of the various specimens obtained after bronchoscopy.

Results

Out of 40 patients included in the study, 33 (82.5%) patients were males and 7 (17.5%) were females. The age of patients in this study group ranged from 16 to 73 years (mean age was 38.5 ± 9.5 years).

Bronchoscopic examination revealed no pathological lesion in 19 (47.5%) of 40 patients. Out of 21 patients where bronchoscopy revealed some pathology, 6 patients showed features suggestive of tuberculosis (endobronchial inflammation with distortion and stenosis of bronchi/tubercles/necrotic red patches), 8 patients had generalized chronic inflammation, and 7 patients had features of acute inflammation [Table 1].

Through bronchoscope, BA and BAL were collected and smeared for ZN staining for AFB. TNA was done in all the 40 patients from the affected segment of the lung and aspirate sent for cytological examination. After bronchoscopy, PBS was also taken for ZN staining for AFB. In study group of 40 patients, 6 (15%) patients were positive for AFB by ZN staining from BA, 7 (17.5%) patients were positive in BAL smear and 7 (17.5%) patients were positive on PBS smear. One smear each was exclusively positive for AFB on BAL smear and PBS smear. TNA cytology was suggestive of mycobacterial disease in 5 (12.5%) patients which included exclusive positivity in one patient [Table 2].

Table 1: Bronchoscopy results in study group suggestive of pathology (*n*=21)

Bronchoscopic features	*N* (%)
Suggestive of tuberculosis	6 (28.6)
Endobronchial inflammation with distortion and stenosis of bronchi	3
Granulomata and tubercles with caseous material	1
Necrotic red patches due to sloughed mucosa	2
Generalized chronic inflammation	8 (38.5)
Acute inflammation	7 (33.3)

Table 2: Result of microscopic examination of bronchial specimens

Bronchoscopic specimens	Positive specimens *N* (%)	Exclusively positive specimens *N* (%)
BA smear	6 (15)	0 (0)
BAL smear	7 (17.5)	1 (2.5)
PBS smear	7 (17.5)	1 (2.5)
TNA cytology	5 (12.5)	1 (2.5)

BA: Bronchial aspirate; BAL: Broncoalveolar lavage; PBS: post-bronchoscopy sputum; TNA: Transbronchial needle aspiration

All specimens collected through bronchoscope were cultured for mycobacteria. BA culture for *M. tuberculosis* was positive in 8 (20%) patients whereas BAL culture was positive in 12 (30%) patients, and PBS culture was positive in 11 (27.5%) patients. Two specimens of BA culture were exclusively positive whereas three BAL cultures were exclusively positive. No PBS culture was exclusively positive [Table 3].

After TNA cytology, in 7 (17.5%) patients no abnormality was observed and in 20 (50%) patients non-specific chronic inflammatory changes were present. Caseating granuloma with epithelioid cells suggestive of mycobacterial disease was seen in 5 (12.5%) patients. Features of acute inflammation were found in 5 (12.5%) patients and in 3 patients TNA cytology gave the diagnosis of malignancy [Table 4].

When all results were combined together it was found that in the study group of 40 patients, 24 (60%) patients could be diagnosed. Out of these 24 patients, 17 (42.5%) patients were diagnosed as a case of pulmonary TB, while 7 (17.5%) patients had a diagnosis other than pulmonary TB [Table 5].

All 40 patients participating in our study were divided into 6 categories depending upon the extent of lesion[18] and presence or absence of cavity on chest X-rays. Out of these 40 patients, 6 (15%) patients had mild disease with cavity, 19 (47.5%) patients had mild disease on X-ray chest without cavity. Five (12.5%) patients had moderate disease with cavity on X-ray chest and 6 (15%) patients had moderate radiological disease without cavity. Two (5%) patients had extensive disease with cavity and remaining 2 (5%) patients were having extensive disease without cavity on chest X-ray [Table 6].

Table 3: Culture results of bronchial specimens for Mycobacterial Spp

Bronchoscopica specimens	Positive specimens *N* (%)	Exclusively positive specimens *N* (%)
BA culture	8 (20)	2 (5)
BAL culture	12 (30)	3 (7.5)
PBS culture	11 (27.5)	0 (0)

BA: Bronchial aspirate; BAL: Broncoalveolar lavage; PBS: post-bronchoscopy sputum

Table 4: Transbronchial needle aspiration cytology findings in study group

Cytological findings	*N* (%)
No abnormality	7 (17.5)
Non specific chronic inflammation	20 (50)
Caseating granuloma	5 (12.5)
Acute inflammation	5 (12.5)
Malignancy	3 (7.5)

N = Number of patients

Table 5: Diagnostic yield of bronchoscopic specimens

Diseases diagnosed	*N* (%)
Total PTB cases diagnosed	17 (42.5)
With smear (BA+BAL+PBS)	11 (27.5)
With culture (BA+BAL+PBS)	5 (12.5)
With TNA cytology	1 (2.5)
Total other diseases cases diagnosed	7 (17.5)
Malignancy	3 (7.5)
Bacterial pneumonia	4 (10.0)

N=Number of patients; PTB: Pulmonary tuberculosis; BA: Bronchial aspirate, BAL: Broncoalveolar lavage; PBS: post-bronchoscopy sputum; TNA: Transbronchial needle aspiration

Table 6: Patients distribution according to radiological picture

Category	Radiological feature	*N* (%)
A1	Mild disease with cavity	6 (15)
A2	Mild disease without cavity	19 (47.5)
B1	Moderate disease with cavity	5 (12.5)
B2	Moderate disease without cavity	6 (15)
C1	Extensive disease with cavity	2 (5)
C2	Extensive disease without cavity	2 (5)

N = Number of patients

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.[19]

In areas with high transmission, the risk of infectivity of sputum smear negative PTB to young household contacts has been estimated to be quite high.[20-22] Published observations suggest that over 50% of smear negative patients would need chemotherapy by the end of 12 months if left untreated.[23,24] Data from longitudinal surveys[25] 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 with 34.7% observed in smear positive patients. Many patients with PTB who are co-infected with HIV with late stage HIV disease (CD4+ count less than or equal to 200 per mm^3) and those who are severely immunosuppressed are more likely to be sputum smear-negative.[26] Thus, early diagnosis of active sputum smear negative PTB disease is important.

With the advent of Fiberoptic bronchoscopy (FOB), diagnosis of PTB in sputum smear negative patients has become possible. The main advantage with this instrument is the ability to visualize the bronchial tree and collect samples directly from the bronchial pathology site. TNA has enabled

pulmonologists to sample tissue well beyond the visible range of bronchoscope.[25] Though FOB procedures have some risk of complications like hemoptysis, pneumothorax; it is considered to be a relatively safe procedure.[27]

After bronchoscopic examination of 40 patients, 6 (15%) patients had pathological features suggestive of tuberculosis, like endobronchial inflammation with distortion, granuloma and ulcerations in the mucosal wall, which was comparable to the study by So *et al*.[28] who found endoscopically visible lesions such as localized red swollen mucosa, stenosis or plaques of caseous material in 12 (18%) of the 65 patients.

As shown in a number of previous studies, the positivity of BA varies from 13%[29] to 61%.[30] So *et al*.[28] obtained a positive yield of 38% in bronchial aspirate while Danek *et al*.[31] observed BA smear positive in 24% cases. Anand reported the diagnostic yield of BA smear to be 28%, BA culture to be 32%, while BA was the exclusive means of diagnosis in 16% patients.[32] In our study BA smear was positive in 6 (15%) patients whereas when both BA smear and BA culture were combined, the positivity increased to 8 (20%) patients. Thus the data generated in our study is comparable to previous studies.

In our study the BA culture was positive in 8 (20%) patients. In previous studies, it varied from 4%[29] to 72%.[28] At the end of our study BAL smear was diagnostic in 7 (17.5%) patients which is comparable to previous studies where it was reported to be 12% by Pande *et al*.,[33] and 26% by Mohan *et al*.[34] BAL culture yielded *M. tuberculosis* in 12 (30%) patients in our study which was comparable to the 25% yield obtained in the study done by Mohamed S. Sawy *et al*.[35]

Combining all the results of bronchoscopic procedures in our study, a definitive diagnosis of tuberculosis was possible in 17 (42.5%) of the 40 patients. BAL smear was exclusively positive in one case; BAL culture in 3 patients and PBS smear also had one patient exclusively positive. PBS smear revealed AFB in 7 (17.5%) patients. In various other previous studies, PBS smear revealed AFB positivity ranging from 23% to 37%. Twenty one percent positivity was noted by Danek *et al*.,[31] 26% by Purohit *et al*.,[36] 28% by Anand *et al*.,[32] 35% by Wallace *et al*.,[29] 37% by So *et al*.[28] and 23% by Kulpati *et al*.[37]

Flexible FOB is a relatively safe procedure with risks such as spread of tuberculosis following bronchoscopy,[38,39] iatrogenic transmission of other infections by bronchoscope,[40] hemoptysis and pneumothorax. However transmission of infection through bronchoscope can be prevented by following proper disinfection guidelines like double-disinfection technique.[41]

Major advantage of bronchoscopy in suspected patients with negative sputum smear examination for AFB, is the isolation of mycobacteria at an early stage when the destruction of lung tissue is minimal and the risk of spreading the disease to contacts can be decreased by early diagnosis and treatment.

The study concludes that flexible fiberoptic bronchoscopy is a useful tool in diagnosis of pulmonary tuberculosis in sputum smear negative patients. Bronchoscopy reveals a higher bacteriological confirmation of diagnosis in patients with strong clinical and radiological evidence suggestive of pulmonary tuberculosis and those having more risk factors.

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How to cite this article: Quaiser S, Agarwal A, Khan R, Haque SF. Fiberoptic bronchoscopy, as a valuable diagnostic option in sputum negative pulmonary tuberculosis: A prospective study. Int J App Basic Med Res 2012;2:123-7.

Source of Support: Nil. **Conflict of Interest:** None declared.