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ORIGINAL ARTICLE

Role of FOB (Fiber Optic Bronchoscopy) in Diagnosis of Smear Negative Pulmonary Tuberculosis: A Prospective, Observational Study in a Tertiary Care Hospital in Bangladesh

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Abstract:

Background: *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 fibreoptic bronchoscopy in sputum smear negative PTB patients with respect to their association with clinical and radiological profile.*

Materials and Methods:*This prospective , open level, observational study was conducted on 80 suspected sputum/ smear negative PTB cases attending Respiratory Medicine Department of Dhaka Medical College& Hospital. Patients were subjected to bronchoscopic examination after taking informed consent and samples like bronchial aspirate, bronchoalveolar lavage and post bronchoscopy sputum were collected and smear were prepared and culture for MTB done from collected specimens. The data were analysed and results were given in percentage.*

Results: *Out of total 80 patients, overall diagnosis was confirmed in 46 (57.5%) patients. Of these 46 patients, 32 patients were confirmed for PTB whereas 14 had other diagnoses.*

Conclusion: *Our study suggests that fibreoptic bronchoscopy can provide excellent material for diagnosis of suspected cases of pulmonary tuberculosis in whom smears of expectorated sputum do not reveal mycobacteria.*

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Introduction

Pulmonary Tuberculosis is a major public health problem worldwide. According to WHO estimates, 12 million people were suffering from active TB disease in 2011 causing 1.4 million death globally.

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The initial diagnostic approach to suspected cases of pulmonary tuberculosis is to demonstrate *Mycobacterium Tuberculosis* in stained smear of expectorated sputum. In most of the tuberculosis centers, even after meticulous search, the bacteriological positive yield from sputum is around 16 to 50% and large portion remain negative in spite of clinical profile and radiological lesions being consistent with diagnosis of pulmonary tuberculosis[5]. Early diagnosis of pulmonary tuberculosis prevents progression of disease, morbidity, spread of disease and permanent damage by fibrosis.

A number of studies confirm the usefulness of fiber optic 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].

Thisstudy 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, broncho-alveolar lavage and post bronchoscopy sputum and assess the positivity of these specimens through smear examination for AFB by Ziehl-Neelsen staining method and culture of the specimens for Mycobacterium tuberculosis on Lowenstein-Jensen media.

Materials and method

This study was conducted in the Department of Respiratory Medicine, Dhaka Medical College from June 2014 to June 2016. The subjects of the study group was chosen from among the patients attending the outpatient department and those admitted in the wards (under respiratory medicine department and also cases referred from other discipline/departments).

Clinically suspected cases of pulmonary tuberculosis, aged 16 – 75 years, with three sputum smears negative for AFB and a chest radiograph suggestive of pulmonary tuberculosis were included in the study. Patients with bleeding diathesis, history of myocardial infarction or arrhythmia, extra-pulmonary tuberculosis, history of anti tubercular treatment (ATT) for more than one month and those with severe dyspnea were excluded from the study.

A detailed history, clinical examination and routine investigations were carried out on suspected cases of tuberculosis. Three sputum samples (spot, morning and spot) were tested in DOTS corner of DMCH for presence of AFB in smear. In patients with suspected smear negative pulmonary tuberculosis, a sputum sample was sent for sputum culture and the patients were taken for bronchoscopy.Prior to the procedure an informed written consent was obtained from the patient/ patients attendant. The procedure was carried out electively in early morning with the patient fasting overnight. Patients were pre-medicated 30- 45 minutes prior to bronchoscopy with 0.6 mg atropine and nebulization was done with 2%xylocaine via nedulizer. Bronchoscopy was carried out under local aneasthesia.

Bronchial washing was performed by instilling 0.9% isotonic saline at room temperaturethrough the internal channel of the fiberoptic bronchoscope and aspirated into a trap connected to suction tubing. Usually 15-30 ml of fluid instilled with each washing and about one fourth to half of this volume was retrieved in the suction trap. Upto one-fourth of the instilled amount retrieved was considered successful. The bronchial washing was sent for AFB staining, AFB culture, and for cytology and cell count. In cases where an endobronchial growth was seen washing, brushing and biopsy was performed.

After the procedure, the patient was observed for 2 hours in post procedure room for any bronchoscopy related complications. The first sample sputum (post bronchoscopic sputum) was collected and sent for analysis along with bronchial washings.

Results

Bronchoscopy was performed in 80 patients.

Characteristics of the patients were given in Table 1.

Table-I
Patients characteristics

Sex:	
Male	53 (66.3%)
Female	27 (33.7%)
Mean age:	
Total	43.2 ± 14.6
Male	45.2 ± 15.2
Female	39.2 ± 12.9
Mean duration of illness	2.2 months
Symptoms:	
Cough	67 (83.7%)
Expectoration	52 (65%)
Fever	55 (68%)
Constitutional symptoms	59 (73.7%)
Dyspnoea	23 (28.7%)
Haemoptysis	16 (20%)
Chest pain	14 (17.5%)
Asymptomatic	4 (5%)
Chest radiography: Site of lesion	
Right	39 (48.7%)
Left	27 (33.7%)
Bilateral	14 (17.5%)
Type of lesion:	
Cavitory	11 (13.7%)
Non cavitory	69 (86.3%)

The most common bronchoscopic finding was congestion with mild to moderate hyperaemia with whitish plaques of variable size in between, observed in 43 (53.7%). In 14 (17.5%) patient sulceration, erosion or granulation was seen. In all patients with cavitary lesion the mucosa was ulcerated and swollen. In 5 patients ulcerative lesion was observed with extensive areas of pulmonary involvement radiographically. In 16 patients (20%) the segmental opening were narrowed and slightly deformed.Endobronchial growth was seen in 3 (3.8%) patients.

Through bronchoscope Bronchial aspirate (BA) and Bronchoalveolar lavage (BAL) were collected and smeared for ZN staining for AFB. After bronchoscopy Post bronchoscopy sputum (PBS) was taken for ZN staining for AFB.

In study group of 80 patients, 12(15%) patients were positive for AFB by ZN staining from BA, 14(17.5%) patients were positive in BAL smear and 14 (17.5%) patients were positive on PBS smear. 2 smear each was exclusively positive for AFB on BAL smear and PBS smear.

Table-II
Results of microscopic examination of bronchial specimen

Bronchoscopic specimen	Positive specimen N (%)	Exclusively positive specimen (%)
BA smear	12 (15)	0 (0)
BAL smear	14 (17.5)	2 (2.5)
PBS smear	14 (17.5)	2 (2.5)

All specimens collected through bronchoscope were cultured for mycobacteria. BA culture for mycobacteria was positive in 16 (20%) patients whereas BAL culture was positive in 24 (30%) patients and PBS culture was positive in 11 (27.5%) patients. 4 specimens of BA culture was exclusively positive whereas 6 BAL cultures were exclusively positive. No PBS culture was exclusively positive.

Table-III
Culture results of bronchial specimens for Mycobacterial Spp

Bronchoscopic specimen	Positive specimen N (%)	Exclusively positive specimen (%)
BA culture	16 (20)	4 (5)
BAL culture	24 (30)	6 (7.5)
PBS culture	22 (27.5)	0 (0)

When all results were combined together it was found that in the study group of 80 patients, 46 (57.5%) patients could be diagnosed. Out of these 46 patients,32 (40%) patients were diagnosed as a case of pulmonary TB, while 14 (17.5%) patients had a diagnosis other than TB.

Table-IV
Diagnostic yield of bronchoscopic specimens

Diseases diagnosed	N (%)
Total PTB cases diagnosed	32 (40)
With smear (BA + BAL + PBS)	22 (27.5)
With culture (BA + BAL + PBS)	10 (12.5)
Total other diseases diagnosed	14 (17.5)
Malignancy	6 (7.5)
Bacterial pneumonia	8 (10)

No serious complications were encountered during the study, except pneumothorax (less then 10%) in one patients and minimal hemoptysis (less then 10 ml) in six patients. No specific treatment was required to manage these complications.

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 and anti-tubercular treatment should be given only if the diagnosis can be confirmed bacteriologically [19].

In areas of 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 treatment by the end of 12 months if left untreated [23,24]. Data from longitudinal surveys in Bangalore district,India[25]indicate that at 18 months follow up, the mortality rate from 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 disease and those who are severely immunosuppressed are more likely to be smear negative [26]. Thus, early diagnosis of active sputum smear negative PTB disease is important.

In the earlier days of rigid bronchoscopy, patients with tuberculosis were seldom subjected to bronchoscopy for diagnostic purpose. With the advent of fiberoptic bronchoscopy, smear and culture for mycobacteriafrom the bronchial aspirate, bronchial brushing, bronchial washing, broncho-alveolar lavage fluid, post-bronchoscopy sputum and biopsy materialhave been used in various studies for diagnosing pulmonary tuberculosis. The main advantage with this instrument is the ability to visualize the bronchial tree and collect samples directly from the bronchial pathology site. 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 80 patients, the most common bronchoscopic finding was congestion with mild to moderate hyperemia with whitish plaques of variable size in between, observed in 43 (53.7%). In 14 (17.5%) ulceration, erosion or granulation was seen. In all patients with cavitary lesion the mucosa was ulcerated and swollen. In 5 patients ulcerative lesion was observed with extensive areas of pulmonary involvement radiographically. In 16 patients (20%) the segmental opening were narrowed and slightly deformed. Which was comparable to the study of So et al [28] who found endoscopically visible lesions such as localized red swollen mucosa, stenosis or plaques of caseous material in 33 (50.8%) of the 65 patients.

As shown in a number of previous studies, the positivity of smear from BA varies from 13% [29] to 61% [30]. So Syet el [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 [30]. In our study BA smear was positive in 12 (15%) patients whereas when both BA smear and BA culture were combined, the positivity increased to 16 (20%) patients. Thus the data generated in our study is comparable to previous studies.

In our study the BA culture was positive in 16 (20%). In previous studies it varied from 4% [29] to 72% [28]. At the end of our study BAL smear was diagnostic in 14 (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 24 (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 32 (40%) of the 80 patients. BAL smear was exclusively positive in 2 cases, BAL culture in 6 patients and PBS smear also had 2 patients exclusively positive.PBS smear revealed AFB in 14 (17.5%) patients. In various other previous studies PBS smear revealed AFB positivity ranging from 23 to 37%. 21% 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 risk 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 disease to contacts can be decreased by early diagnosis and treatment.

The study concludes that flexible 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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