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Role of fiberoptic Bronchoscopy in diagnosis of smear negative pulmonary TB

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ORIGINAL ARTICLE

Role of Fiberoptic Bronchoscopy in Diagnosis of Smear Negative Pulmonary Tuberculosis

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Abstract

Background: **Several studies have demonstrated the value of bronchoscopy in individuals with a positive history of pulmonary tuberculosis (PTB) but a negative sputum smear. Unfortunately, there is a lack of information on when bronchoscopy is most beneficial.**

Aim and objectives: **To assess the use of bronchoscopy for the diagnosis of TB in patients with negative sputum smears.**

Patients and methods: **This study is a retrospective study, was conducted at Azhar Assiut University Hospital during the period from 2020 to 2022.**

Result: **BAL culture for *Mycobacterium tuberculosis* (MTB) was positive in 22 (44%) patients, Bronchial brushing culture was positive in 14 (46.7%) cases, and (postbronchoscopy sputum) was positive in 13 (26%) patients.**

Conclusion: **With a high sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV), fiber optic bronchoscopy (FOB) is an effective method for the fast identification of active PTB in sputum smear-negative PTB-suspected patients. However, the main issue is that contaminated bronchoscopes might cause nosocomial transmission of TB, and other infectious pathogens, so strong cleaning processes and protocols should be developed to prevent this.**

Keywords: Bronchoscopy, Fiber optic bronchoscopy, Pulmonary tuberculosis, Sputum smear

1. Introduction

The World Health Organization anticipated in 1990 that tuberculosis (TB) would remain the world's seventh leading cause of morbidity until the year 2020.[1]

Mycobacterium tuberculosis (MTB) must be seen in stained smears of expectorated sputum as the first step in diagnosing instances of pulmonary tuberculosis (PTB). The bacteriological positive yield from sputum in most TB hospitals is only 16–50%, and a sizable proportion of cases remain negative despite a clinical profile and radiographic abnormalities that are compatible with a diagnosis of PTB.[2]

When a thorough search for acid fast bacillus (AFB) in expectorated sputum has repeatedly failed, when sputum expectoration is absent, or when sputum induction is unsuccessful, a diagnosis of TB can be made with the help of fiber optic bronchoscopy (FOB) and bronchial washing analysis for AFB, including culture for MTB.

Around 10 million new cases of TB will be diagnosed each year by the end of 2019. Around 12 000 cases of TB were reported in Egypt. Due to the TB control program, the disease burden was reduced in Egypt. Compared with 2000 TB incidence rate reduced from 26/100 000 to 12/100 000 in 2018.[3]

Sputum smear-negative PTB is still a prevalent issue. Those patients are considered as continuous sources of infection to the community due to delays in diagnosis and treatment of these patients.

Early treatment renders patients noninfectious, stops the spread of TB, and lowers the incidence of multidrug-resistant TB, as we found in our study using FOB as the major method for diagnosis of smear-negative PTB.

The purpose of this study was to evaluate the utility of bronchoscopy for the diagnosis of TB in patients with negative sputum smears.

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2. Patients and methods

50 suspected TB patients and their smears of expectorated sputum did not reveal mycobacteria or those with difficulty and scanty expectorations.

2.1. Inclusion criteria

Age greater than or equal to 18 years, Patients with radiological or clinical evidence of active PTB, sputum cultures that are negative for acid fast bacilli or patients unable to produce sputum for acid fast bacilli culture, and patients who have received both a chest radiography and a chest computed tomography (CT) scan for PTB within the last month are candidates for anti-TB treatment.

2.2. Exclusion criteria

Patients with a positive AFB smear, patients with a clinical diagnosis of PTB based on clinical and radiological TB findings who did not improve clinically with empirical antibiotics but improved clinically and radiographically with anti-TB medication, and patients with contraindications for bronchoscopy such as an uncorrectable bleeding tendency disorder, Inability to lie in the supine position, Respiratory insufficiency requiring ventilatory support and Serious cardiac arrhythmia, hemodynamic instability.

2.3. Methods

From each patient, the following data had been collected upon admission.

2.3.1. Complete full history taking, including

Age, sex, history of Fever, chills, Diarrhea, Sore throat, Fatigue, body aches, loss of weight or loss of appetite, history of Hemoptysis, past history of TB or recent contact with TB patient, special Habits Of Medical Importance.

2.3.2. Clinical examination

General examination in the form of Vital signs, Signs of (Dyspnea, Pallor, Cyanosis, Jaundice, and Lymph node enlargement).

2.3.3. Chest examination

In the form of Inspection, palpation, percussion, and auscultation are all part of the pulmonary examination. The inspection procedure starts as soon as a patient is contacted and continues for the duration of the entire consultation. Tenderness and the degree to which the chest has expanded can be evaluated by palpation and verified with percussion. The more sensitive procedure of auscultation verifies prior results and may aid in the identification of previously unrecognized disease conditions.

2.3.4. Auscultation

It is best to do a chest auscultation with the patient seated or standing in a calm room. The scapulae should be moved laterally as much as feasible by crossing the patient's arms anteriorly when examining the posterior thorax.

2.4. Investigations

2.4.1. Laboratory study: complete blood picture (CBC)

Hb %, red blood cells (RBCs), white blood cells (WBCs), platelet count, erythrocyte sedimentation rate (ESR), Renal function test: serum creatinine, blood urea and urine analysis. Liver Test Profile: aspartate transaminase (AST) and alanine transaminase (ALT), serum albumin, serum bilirubin, gamma-glutamyl transferase (GGT), prothrombin time and international normalized ratio (INR). Coagulation profile (INR, APTT, platelets and fibrinogen). Arterial blood gases (ABG): acidity (pH) and the levels of oxygen and carbon dioxide in the blood from an artery and Electrocardiography (ECG).

2.4.2. Radiological investigations

Chest radiography, chest and Abdomen ultrasonography, and computerized tomography.

2.4.3. Direct sputum smear for acid fast bacilli in three consecutive days

Coughing is the most commonly used method of sputum collection.

2.4.4. Bronchoscopy

No patients had anything to eat or drink for at least 6 h before their bronchoscopies. Before a bronchoscopy, the patient was given information about the process. Firstly an I V line was done. Midazolam was infused into each patient's IV prior to and/or throughout the procedure at doses ranging from 5 to 15 mg, depending on the patient's state. Before beginning the procedure, local lidocaine (10%) was sprayed transnasally and orally. The larynx was numbed with a 2% lidocaine solution; a typical dose is 4–6 ml. A bronchial wash was performed by instilling about 10 ml of 0.9% saline and then collecting it in a pot/trap using suction through the bronchoscope to obtain superficial airway cells. To prevent infection and blood loss, BAL was done before any additional bronchoscopy

procedures. The chest CT was used to pinpoint the exact location of the BAL procedure.

Bronchial brushings were conducted by introducing a covered brush into a bronchial segment, exposing it, stroking the bronchial wall, covering it again, extracting it, and either placing it in a cell preservation medium or wiping it on a plate (which is then sprayed with a cell fixing solution).

Bronchial biopsies were collected using biopsy forceps, and 5–7 were taken to maximize yield.

2.4.5. Administrative and ethical design

The Faculty of Medicine granted official permission. An official permit was received, as well as approval from the faculty of medicine's ethical committee (Institutional Research Board IRB).

2.5. Statistical analysis

Information was gathered, tabulated, and analyzed using SPSS 22.0 for Windows. It was determined whether or not the data had a normal distribution by using the Shapiro-Wilk test. The qualitative data were represented as frequencies and relative percentages. χ^2 and Fisher exact tests were used to calculate the differences between qualitative variables as specified. If the data were parametric, it was displayed as a mean and standard deviation (SD), whereas if it was not, it was shown as a median and range.

Table 1. Demographic distribution of the studied patients.

	All patients ($n = 50$)
Age (years)	
Mean ± SD	38.51 ± 10.46
Range	25–63
BMI (kg/m^2) Mean ± SD	26.92 ± 3.65
Sex	
Males	35 (70%)
Female	15 (30%)

3. Results

Table 1.

Most of the patients were males (70%) with age ranged between 25 and 63 years with mean age of 38.51 ± 10.46 years, meanwhile mean BMI is 26.92 ± 3.65 kg/m^2 (Fig. 1).

60% of the patients were smokers, 26% were diabetic, 18% were hypertensive, and 30% had a history of TB infection (Fig. 2).

According to this data, the most prevalent symptom was cough (82%), followed by shortness of breath (64%) while the least symptom was hemoptysis (18%) (Table 2).

This table shows that the most common finding was parenchymal consolidation 36% followed by cavitation (30%). This table shows that there were 38% of the patients showed no pathological lesion. Among those who showed pathological lesion; the most findings were edematous hyperemic mucosa (50%) and caseation (34%) (Table 3).

BAL was done in all 50 cases, while brushings were taken from the affected segment in 30 cases. Bronchial biopsies were done only in 11 out of 50 patients, where biopsy was feasible. PostBronchoscopy Sputums (PBS) was also taken in all 50 cases. Smear examination for AFB was positive in BAL fluid in 20 (40%) cases, in bronchial brushings in 13 (43.3%) cases, and in post bronchoscopy sputum in 12 (24%) cases. Biopsy showed caseating epitheloid granuloma in 2 (18.2%) cases (Table 4).

This table shows that 91.7% of the positive on combined procedures were also positive on BAL with true negative 100% with P value (0.000) that is highly statistically significant difference (Table 5).

BAL was significant procedure with sensitivity of 91.67% and specificity of 100% besides Negative

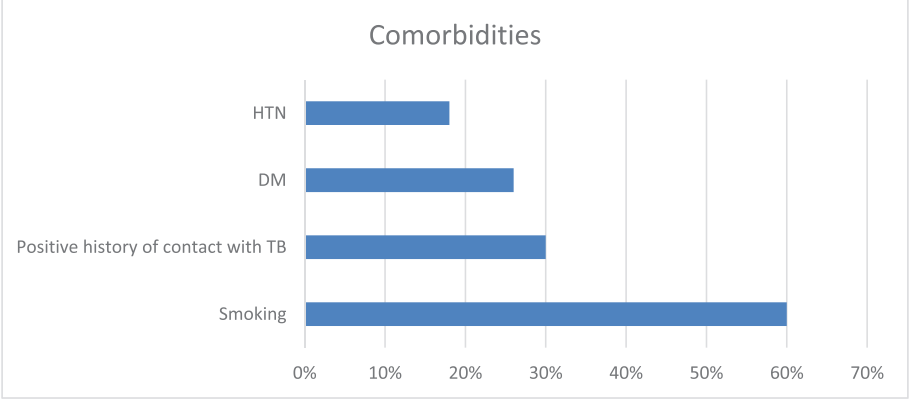

Fig. 1. Comorbidities and risk factors distribution.

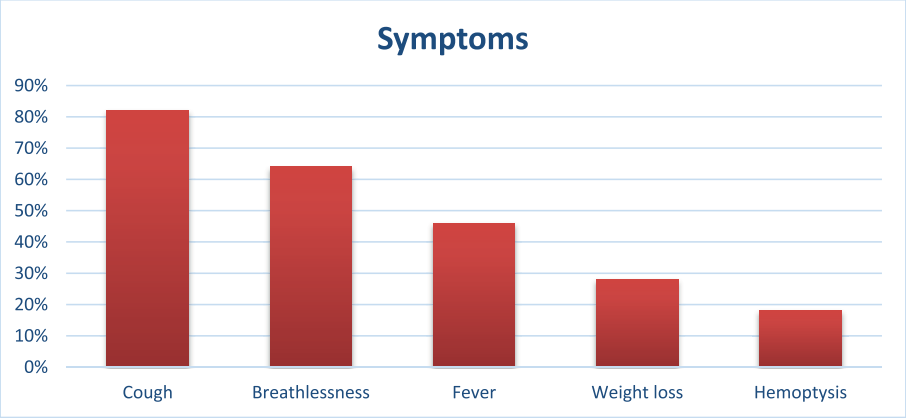

Fig. 2. Symptoms distribution, Cough was the most prevalent symptom.

Table 2. Radiological findings and Bronchoscopy findings among the studied patients.

Radiological findings	All patients ($n = 50$) N (%)
Parenchymal consolidation	18 (36%)
Cavitation	15 (30%)
Lymphadenopathy	11 (22%)
Miliary tuberculosis	8 (16%)
Tuberculoma	7 (14%)
Fibroproductive lesion	12 (24%)
Pleural effusion	6 (12%)
Bronchoscopic findings	
No pathological lesion	19 (38%)
Abnormalities	
Edematous hyperemic mucosa	25 (50%)
Caseating	17 (34%)
Discharge from bronchus	15 (33%)
Granuloma	6 (12%)
Bleeding from bronchus	5 (10%)

Predictive Value (NPV) was 92.9% and Positive Predictive Value (PPV) was 100% with accuracy of 96% in diagnosis of tuberculosis (TB) (Table 6).

This table shows that 54.2% of the positive on Combined procedures were also positive on Post-Bronchoscopy Sputums (PBS) with true negative 100% with P value (0.000) that is highly statistically significant difference (Table 7).

Table 3. Methods of examination and Positive smear examination for AFB of bronchial specimens among the studied patients.

Methods of examination	All patients ($n = 50$) N (%)
BAL	50 (100%)
Bronchial brushings	30 (60%)
Biopsies	11 (22%)
PBS	50 (100%)
Positive smear examination for AFB of bronchial specimens	
BAL fluid ($n = 50$)	20 (40%)
Bronchial brushings ($n = 30$)	13 (43.3%)
Biopsies ($n = 11$)	2 (18.2%)
PBS ($n = 50$)	12 (24%)

Table 4. BAL value in diagnosis of TB.

BAL	Combined procedures		Total	P
	Positive ($n = 24$) N (%)	Negative ($n = 26$) N (%)		
Positive	22 (91.7%)	0	22 (44%)	**0.000**
Negative	2 (8.3%)	26 (100%)	26 (56%)	
Total	24 (100%)	26 (100%)	100	

Table 5. Diagnostic value.

Statistic	Value	95% CI
Sensitivity	91.67%	73%–98.97%
Specificity	100%	86.77%–100%
Positive Predictive Value (PPV)	100%	–
Negative Predictive Value (NPV)	92.86%	77.52%–98%
Accuracy	96%	86.29%–99.51%

Table 6. PBS value in diagnosis of TB.

PBS	Combined procedures		Total	P
	Positive ($n = 24$) N (%)	Negative ($n = 26$) N (%)		
Positive	13 (54.2%)	0	13 (26%)	**0.000**
Negative	11 (45.8%)	26 (100%)	36 (74%)	
Total	24 (100%)	26 (100%)	100	

Table 7. Diagnostic value.

Statistic	Value	95% CI
Sensitivity	54.17%	32.82%–74.45%
Specificity	100%	86.77%–100%
Positive Predictive Value (PPV)	100%	–
Negative Predictive Value (NPV)	70.27%	60.47%–78.5%
Accuracy	78%	64.04%–88.47%

PBS was significant procedure with sensitivity of 54.2% and specificity of 100% besides Negative Predictive Value (NPV) was 70.3% and Positive Predictive Value (PPV) was 100% with accuracy of 78% in diagnosis of tuberculosis (TB).

4. Discussion

When comparing sputum examination to bronchoscopy for the diagnosis of PTB, bronchoscopy has been shown to have a better diagnostic yield due to a greater likelihood of microscopy and culture positive results Le Palud and colleagues.[4]

The primary objective of this research was to evaluate the use of bronchoscopy in making a diagnosis of tuberculosis in patients who tested negative for the disease using sputum smears. This cross-sectional study was conducted, including 50 suspected TB patients and their smears of expectorated sputum did not reveal mycobacteria or those with difficulty and scanty expectorations. The duration of the study ranged from 6 to 24 months.

Most of the patients were males (70%) with age ranged among 25 and 63 years with mean age of 38.51 ± 10.46 years, meanwhile mean BMI is 26.92 ± 3.65 kg/m^2.

The average patient age that was recorded in this study was 36.56 ± 12.05 years. 58% of the patients were men, while the remainder were women.

Furthermore, in the study of Bachh and colleagues,[5] the majority of their studied groups were males (66.7%) with mean age 39.20 ± 12.88 years.

The present study showed that 60% of the patients were smokers, 26% of the patients were diabetic and 18% of the patients were hypertensive. 30% of the patients has positive history of contact with TB. Regarding symptoms; the most common symptom was cough (82%) followed by breathlessness (64%), while the least symptom was hemoptysis (18%).

Similarly, Le Palud and colleagues[4] found that cough was the most common clinical symptom, occurring in 51.9% of patients, along with asthenia, lack of appetite, and weight loss in half of patients.

Cough was the most common symptom (n = 18, 60%), followed by loss of weight (n = 7, 23%), fever (n = 6, 20%), hemoptysis (n = 4, 13%), and chest pain (n = 4, 13%), according to research by Iyer and colleagues.[6] The current study showed that as regard radiological examination: the most common finding was parenchymal consolidation 36% followed by cavitation (30%).

The majority of patients in this research displayed cavitary lesions on their chest radiography (62%), which is consistent with previous reports of radiological characteristics compatible with the diagnosis of PTB.

While, in the study of Sarõbaş and Yõldõz,[7] radiologically, 15 (50%) patients had consolidation, 14 (46.6%) had cavitation lesion and consolidation, and 1 (3.3%) had cavitation, consolidation, and paratracheal opacity.

In the study in our hands, as regard bronchoscope findings; there were 38% of the patients showed no pathological lesion. Among those who showed pathological lesion; the most findings were edematous hyperaemic mucosa (50%) and caseation (34%).

In contrast with our results, study of Bansal and colleagues,[8] as they reported that the most common findings in bronchoscopy was pus or secretion (40%).

In the study of Bachh and colleagues,[5] Congestion with mild to moderate hyperemia (similar to our study) and white plaques of varying sizes were the most prevalent findings at bronchoscopic examination, being seen in 53 (70.6%) patients. The presence of ulceration, erosion, or granulation was noted in 21 individuals (28%). Every person who had a cavitary lesion had a large, ulcerated mucosa.

Moreover, Sarbaş and Yldz[7] demonstrated that normal endobronchial appearance was observed in 25 (83.3%) patients, but mucosal hyperemia, hemorrhagic secretion, and mucosal granuloma were observed in 2 (6.6%), 2 (6.6%), and 1 (3.3%), respectively. Our results showed that BAL was done in all 50 cases, while brushings were taken from the affected segment in 30 cases. Bronchial biopsies were done only in 11 out of 50 patients, where biopsy was feasible. PostBronchoscopy Sputums (PBS) was also taken in all 50 cases.

40% of the 50 patients in this research who had negative sputum smears also tested positive for AFB in their bronchoalveolar lavage, whereas the other 60% tested negative.

The present study showed that Smear examination for AFB was positive in BAL fluid in 20 (40%) cases, in bronchial brushings in 13 (43.3%) cases, and in post bronchoscopy sputum in 12 (24%) cases. Biopsy showed caseating epitheloid granuloma in 2 (18.2%) cases. As regard BAL culture for MTB was positive in 22 (44%) patients, Bronchial brushing culture was positive in 14 (46.7%) cases, and PBS culture was positive in 13 (26%) patients.

While, in the study of Le Palud and colleagues,[4] 23 cases of TB, respectively, were reported to have positive cultures on FOB (Fiberoptic bronchoscopy) and sputum samples. The remaining seven patients were diagnosed based on clinical and histological/radiological characteristics, with their positive responses to anti-TB treatment providing as confirmation.

In addition, Luhadia and colleagues[9] reported that their combined yield for AFB smear positivity was 45% (27/60) among their group A patients (31 new and 29 retreatment), and that it was 65% (26/40) among their group B patients (28 new cases and 12 retreatment). The overall yield for diagnosing pulmonary TB by FOB was therefore considerably greater in group B patients.

The current study showed that BAL was significant procedure with sensitivity of 91.67% and specificity of 100% besides NPV was 92.9% and PPV was 100% with accuracy of 96% in diagnosis of TB.

While, in the study of Jacomelli et al.,[10] for the diagnosis of TB, BAL showed sensitivity and a specificity of 60% and 100%, respectively.

In the study in our hands, Brushings was significant procedure with sensitivity of 58.3% and specificity of 100% besides NPV was 72.2% and PPV was 100% with accuracy of 80% in diagnosis of TB.

PBS was significant procedure with sensitivity of 54.2% and specificity of 100% besides NPV was 70.3% and PPV was 100% with accuracy of 78% in diagnosis of TB.

According to Khalil and Butt,[11] BAL gene Expert has a sensitivity of 91.86%, a specificity of 71.42%, a positive predictive value of 97.53%, and a negative predictive value of 41.66% when testing for MTB.

Altaf Bachh and colleagues[5] conducted a prospective study of 75 cases with sputum/smear-negative PTB and found that bronchial washings were the only method of diagnosis in 48.33% of cases.

4.1. Conclusion

With a high sensitivity, specificity, PPV, and NPV, FOB is an effective method for the fast identification of active PTB in sputum smear-negative PTB suspected patients. However, the main issue is that contaminated bronchoscopes might cause nosocomial transmission of TB and other infectious pathogens, so strong cleaning processes and protocols should be developed to prevent this. If a patient has smear-negative PTB, bronchoalveolar lavage will be a more accurate diagnostic tool. Because of this, it is strongly suggested for patients who have a negative sputum smear but are being treated for PTB.

Conflicts of interest

None declared.

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