Role of Bronchoscopy in Diagnosing Sputum Smear Negative Pulmonary Tuberculosis

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ABSTRACT

Background: In patients of pulmonary tuberculosis microscopic examination of sputum is the method of choice. Sputum examination for AFB microscopy is usually positive but even in advanced disease may be negative due to immunosuppression, poor quality of the sample collection, deficient preparation, staining or examination of the sputum smear. Clinical and radiological based diagnosis can lead either to over or under diagnosis of tuberculosis and unnecessary antitubercular treatment may cause drug resistance and economic burden. Fiberoptic bronchoscopy can provide excellent material for diagnosis of suspected cases of pulmonary tuberculosis when smears of expectorated sputum do not reveal mycobacteria.

Aim: To assess the role of bronchoscopy in diagnosis of pulmonary tuberculosis among patients who have clinico-radiological suspicion but remain negative for AFB on sputum examination.

Settings and design: After consent, 50 patients with sputum smear negative for AFB and chest X-ray suggestive of pulmonary tuberculosis, underwent fiberoptic bronchoscopy. Bronchoalveolar lavage (BAL), Bronchial brushings, Transbronchial lung biopsy (TBLB) and Post bronchoscopy sputum (PBS) were done and samples analyzed by smear microscopy, histopathology and or culture.

Result: Sensitivity of BAL, Brushing and PBS by smear and culture are 87.5%, 54.17% and 50% respectively. The final diagnosis of PTB was established in 24/50 (48%) cases.

Conclusion: Fiberoptic bronchoscopy with post bronchoscopy sputum is a useful tool for diagnosis and can thereby prompt treatment of sputum smear negative pulmonary tuberculosis patients.

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**Introduction**

India has the highest burden of tuberculosis in the world and account for nearly one fourth of the global burden of tuberculosis per year. Globally, the absolute number of incident TB cases per year has been falling since 2006 and the incidence rate (per 100 000 population) has been falling by 1.3% per year since 2002. Case fatality rate prior to RNTCP was generally greater than 25%. In RNTCP era, case fatality has remained less than 5% for new cases registered under this programme. “Smear negative – culture positive” state has been observed in 22 to 61% of the cases. With the advent of flexible fiberoptic bronchoscope, a more aggressive approach of investigation for sputum negative pulmonary TB has been adopted. Bronchoscopy and related procedures such as bronchial brushing, bronchoalveolar lavage, transbronchial biopsy and post bronchoscopy sputum examination may be alternative way of reaching the diagnosis as early as possible. Therefore, this study was undertaken to determine the role of bronchoscopy in the diagnosis of sputum smear negative pulmonary tuberculosis (SSNPTB).

**Methods**

This study was carried out in the Department of Medicine and Department of Pathology, and the duration of study was from August, 2011 to January, 2014. 60 patients were admitted with clinical and radiological suspicion of pulmonary tuberculosis. Clinical symptoms consisted of evening rise of temperature, night sweats, weight loss, anorexia associated with cough with or without expectoration, hemoptysis and dyspnea. Radiologically chest x-ray showed one or more of the following lesions like parenchymal consolidation, cavitation, miliary tuberculosis, lymphadenopathy, tuberculoma, fibroproductive lesion and pleural effusion. Out of these, six patients had associated cardiac diseases and were excluded from the study. Four patients did not give consent for the bronchoscopy, so they were also excluded from the study. So, finally 50 patients were included in this study. All these patients (18-60 years) had two negative pulmonary tuberculosis (SSNPTB).

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Fiberoptic bronchoscopy was carried out under local anesthesia and inspection of both bronchial tree was done. Special emphasis was given to the segments of radiographically suspicious areas. BAL fluid was collected in all patients, bronchial brushing and trans-bronchial lung biopsies were done in patients who had some kind of visible pathological lesion on bronchoscopy and in whom biopsy was feasible. Post bronchoscopy sputum sample were taken on next three occasions in all 50 cases (one immediately after bronchoscopy and other two on next two days). These specimens were further examined by Z-N staining and AFB culture by L-J media. Biopsies were examined histopathologically.

**Results**

Out of the 50 cases, 33 (66%) were males and 17 (34%) were females. Amongst the males, history of smoking was present in 30/33 (90.90 %) and in the females 6/17 (35.2%) were smokers. 44 cases (88%) were positive for history of contact with TB. Of these, 38 cases (76%) gave history of pulmonary tuberculosis in neighbourhood. Only six subjects reported negative history of contact with pulmonary tuberculosis. Of the six negative history cases, three were females and three were males. Nine patients (18%) had received whole course of anti-tubercular treatment before, 12 patients (24%) were defaulters, 29 patients (58%) were without any prior history of anti-tubercular treatment. 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%) (Table-I). BAL was done in all 50 cases where as brushings were taken from the affected segment in 29 cases. Bronchial biopsies were done only in 12 out of 50 patients, where biopsy was feasible. After bronchoscopy, Post Bronchoscopy Sputums (PBS) was also taken on three occasions in all 50 cases (one immediately after bronchoscopy and other two on next two days). Smear examination for AFB was positive in BAL fluid in 19 cases (38%), in bronchial brushings in 12 cases (41.4%), and in post bronchoscopy sputum in 11 cases (22%). Trans bronchial lung biopsy (TBLB) showed caseating epitheloid granuloma in three cases (25%) out of which AFB could be demonstrated in two (16.6%) (Figure 1). BAL culture for M. tuberculosis was positive in 21 patients (42%), Bronchial brushing culture was positive in 13 cases (44.8%). Post bronchoscopy sputum (PBS) culture was positive in 12 patients (24%) (Figure 2).

During our study, we were able to diagnose 24 cases out of 50 (48%) by combining all the bronchoscopic aided
procedures and using either smear examination for AFB or culture for AFB or caseating granulomas as the end result of our study. 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%. Using post bronchoscopy sputum (PBS) as the method of diagnosis, we were able to clinch the diagnosis in 12 out of 24 positive patients (12/24) with a sensitivity of 50% and TBLB clinched the diagnosis in 3 out of 24 positive patients (3/24) with a sensitivity of 12.5% (Figure 3). Bronchial brushings had the highest yield (13/29) of 44.8% followed by BAL (21/50) of 42%. TBLB and PBS comparatively had low diagnostic yield of 25% and 24% respectively, in our study (Table II).

Table II: Total Yield Of Various Bronchoscopic Aided Methods In Our Study (N= 50)

<table>
<thead>
<tr>
<th>Method</th>
<th>Cases Positive</th>
<th>Cases Done</th>
<th>Total Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAL FLUID</td>
<td>21</td>
<td>50</td>
<td>42%</td>
</tr>
<tr>
<td>BRONCHIAL BRUSHINGS</td>
<td>13</td>
<td>29</td>
<td>44.8%</td>
</tr>
<tr>
<td>PBS</td>
<td>12</td>
<td>50</td>
<td>24%</td>
</tr>
<tr>
<td>TBLB</td>
<td>3</td>
<td>12</td>
<td>25%</td>
</tr>
</tbody>
</table>
50 cases, they had 35 males and 15 females. Thus, the data generated in our study is comparable to this study.

Out of the 50 patients in our study, 43 patients presented with cough (86%), 40 patients (80%) had cough with expectoration, 30 (60%) patients had fever, 16 patients (32%) had hemoptysis and 12 patients (24%) presented with chest pain. These patients characteristics were similar to the study done by D.D.S. Kulpati et al.

In our study, 18 cases out of 50 (36%) were active smokers, while 18 of them (36%) quitted smoking for more than one year and 14 of them (28%) had never smoked before. This was higher than the study characteristics done by Chan H S et al. Amongst the 50 cases, when evaluated for history of contact with a case of pulmonary tuberculosis, 44 cases (88%) were positive. Of the six negative cases, three were females and three were males. This was higher than the study done by Kwan Hoi Yee et al. This high rate could be due to high prevalence of tuberculosis in India.

Among 50 patients, signs in the form of crepitations (with or without rhonchi) or bronchial breath sounds were found among 44 patients. Crepitations (with or without rhonchi) were found in 28 patients. Bronchial breath sounds were found in 16 patients.

Bronchoscopic examination revealed no pathology in 21 (42%) of these 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%). This was comparable to the study done by Panda et al where bronchoscopy was normal in 44% cases and 35% cases had discharge from bronchus, 21% cases had unhealthy mucosa / granuloma, 3% cases had external compression and another 3% cases had bleeding from bronchus, while growth was visible in 5% cases. In our study, the BAL fluid smears were taken in all 50 cases and were positive for AFB in 19 (38%) patients. In previous studies, it varied from 7.5% to 57.1% in studies done by SCharoenratanakul et al and Malekmohammad M et al respectively. BAL culture yielded M. tuberculosis in 42% patients in our study which was comparable to the 48% positivity (24 cases out of 50) by Wongthim et al. In our study, bronchial brush smears were done in 29 patients in whom bronchoscopy revealed some visible pathology. Bronchial brushings were positive for acid fast bacilli in 41.4% (12/29) patients; all of these were confirmed by positive culture. Bronchial brushings when subjected to culture yielded 44.8% positivity in our study. This was also comparable to the studies done by Willcox et al (42%) and Wongthim et al (51%).

In our study, Post bronchoscopy sputums were collected on 3 occasions and subjected to both smear for AFB and culture, yielding 22% (11/50) and 24% (12/50) respectively. This was comparable to the 23% positivity (7 out of 30 cases) in post bronchoscopy sputum studied by Wongthim et al. Kulpati et al also noted 25% positivity (5 out of 20 cases) by PBS culture and 26% AFB smear positivity was noted by Purohit et al.

In our study, transbronchial lung biopsies were taken from areas of suspicion in 12 cases, 3 cases (25%) showed caseating epithelioid granulomas with AFB positivity in 16.66% (2 cases out of 12). A.K.Jaiswal et al reported bronchoscopic guided biopsy for diagnosis of sputum negative tuberculosis to be 10% (2 out of 20 cases) in their study and D.D.S.Kulpati et al reported 20% (4 cases out of 20) in their study.

During our study, we were able to diagnose 24 cases out of 50 cases (48%) by combining all the bronchoscopic aided procedures and using either smear examination for AFB, culture for AFB or caseating epithelioid granulomas as the end result of our study. Out 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% which was comparable to the study by de Gracia et al where BAL had a sensitivity of 88% (15/17).

Using brushings, diagnosis was clinched in 13 cases (13/24) with a sensitivity of 54.17%. This was comparable to the previous studies by A.A Bachh et al and Chawla et al where brushings had sensitivity of 48.33% and 62% respectively. Using post bronchoscopy sputum as the method of diagnosis, we were able to clinch the diagnosis in 12 out of 24 positive patients (12/24) with a sensitivity of 50% which was comparable to the study by Panda et al where PBS had a sensitivity of 48.5% (17/35).

Trans bronchial lung biopsy clinched the diagnosis in 3 out of 24 positive patients (3/24) with a sensitivity of 12.5% which was comparable to the study by S.Y.So et al (7/57).

Conclusion
The study concludes that flexible fiberoptic bronchoscopy along with post bronchoscopy sputum examination is a useful tool in early 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. Thus bronchoscopic aided procedures should be undertaken in sputum smear negative pulmonary tuberculosis patients with a high index of clinico-radiological suspicion.

References
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