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**Original Research Article** 

### A Comparison of yield of bronchoalveolar lavage fluid examination versus post bronchoscopic sputum examination in the diagnosis of sputum smear negative pulmonary tuberculosis

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#### Abstract

**Aim**: To compare efficacy/yield of post bronchoscopic sputum (PBS) with Bronchoalveolar lavage (BAL) in the detection of sputum smear negative pulmonary tuberculosis (SSNPTB).

**Material and Methods**: Bronchoscopy was done in 72 patients of SSNPTB .BAL and Post Bronchoscopy Sputum (PBS) were collected and subjected to AFB staining and culture.

**Results**: Tuberculosis was confirmed by smear examination for AFB in BAL fluid in 30 cases (41.6%), by post bronchoscopy sputum in 18 cases (25%). BAL culture for M. tuberculosis was positive in 37(51.3%) patients whereas PBS culture was positive in 23 (32%) patients. We were able to diagnose 39 out of 72 cases (54.2%) by combining both BAL fluid and PBS smear examination and culture for AFB. Out of these 39 cases diagnosed, BAL was more effective method with sensitivity of 94.87 % and yield of 51.38% (37/72) whereas sensitivity and yield of PBS was 58.97% and (23/72) 31.94% respectively.

**Conclusions**: Patients of SSNPTB must be subjected to bronchoscopy and its guided procedures before starting empirical antitubercular treatment. In our study Bronchoalveolar lavage had more sensitivity and yield as compared to post bronchoscopy sputum in detection of SSNPTB.

**Keywords:** Bronchoalveolar lavage fluid, Bronchoscopy, Post bronchoscopic sputum, Sputum smear negative pulmonary tuberculosis.

#### Introduction

Pulmonary tuberculosis (PTB) is a leading health problem in the world especially in the developing countries. Despite the development of effective chemotherapy, it is estimated that about  $1/3^{rd}$  of the current global population is infected asymptomatically with tuberculosis, of whom only 5–10% develop clinical disease.<sup>[1,2]</sup> Though

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India is the second-most populous country in the world, India has more new TB cases annually than any other country. It accounted for one fourth of the estimated global incident T.B. cases in 2014.<sup>[3]</sup> In July 2013, the revised estimated prevalence & incidence rates of all form of T.B. in India were 211 and 171 cases per 100,000 population respectively. TB mortality in India was 2.4 lakh annually in 2013.<sup>[3]</sup> With RNTCP implementation, mortality has come down to half in the country which was over 5 million annually at the beginning of the Revised National TB Control Programme (RNTCP).

The World Health Organisation (WHO) recommends the detection of acid fast bacilli (AFB) in respiratory specimens as the initial approach to the diagnosis of PTB. Most clinicians do encounter patients having clinical history and radiological lesions suggestive of pulmonary tuberculosis but many of these patients either are not able to expectorate or sputum is repeatedly negative for acid fast bacilli. Flexible fiberopic bronchoscopy (FOB) is one of the tool which agitate bronchial secretions, gives access to the diseased area and also post bronchoscopy sputum collected after the procedure gives better bacteriological and histological yield.

The purpose of this study was to evaluate the value of sputum obtained post bronchoscopically (post-FOB) in the detection of tuberculosis, in comparison with results from the standard BAL smear and culture.

#### **Material and Methods**

This study was conducted between January 2014 and December 2015 in the Post Graduate Department of Medicine and Department of Pathology. 80 patients were admitted with clinical (cough with or without expectoration, weight loss, evening rise of temperature, hemoptysis) and radiological evidence<sup>[4]</sup> (parenchymal consolidation, cavitation, lymphadenopathy, pleural effusion) of pulmonary tuberculosis who were sputum smear negative on all 2 occasions. Of these, 8 patients were excluded as they did not give consent for this study. So, finally 72 patients were included in the study. The enrolled patients were subjected to a protocol, which include detailed history regarding mode of onset, duration of illness, history of drug intake and examination followed by battery of investigations which included radiological study with evidence of pulmonary tuberculosis. Bronchoscopy was done using fibroptic bronchoscope (model BE-TE2, manufactured by Olympus Corporation, Tokyo, Japan). In all the patients BAL was collected during the procedure and PBS (post bronchoscopy sputum) collected on next 3 occasions (one immediately after bronchoscopy and other two on next 2 days) was submitted to pathology department for AFB staining and culture.

#### **Inclusion criteria**

All adult patients (12 years onwards) with clinical and radiological evidence of pulmonary tuberculosis but with two sputum smear negative for AFB.

#### **Exclusion criteria**

Patients with bleeding diathesis, history of myocardial infarction or arrhythmia and those with severe dyspnea were excluded from the study. HIV-positive and who did not give consent for bronchoscopy were also excluded.

**Chest X-ray Classification of Disease:** The radiological classification of disease extent was as follows <sup>[5]</sup>:

0= No disease;

1= Mild/minimal PTB (when the lesions did not cross the area above the sternal cartilage of the second rib on one side);

2= Moderate/intermediate PTB (when moderately advanced lesions could be seen in one or both lungs, with disseminated lesions of low to moderate density extending throughout one lung or the equivalent in both lungs, or dense, confluent lesions limited to one-third of the volume of one lung); and

3=Severe/extensive well advanced PTB (when the lesions were even more extensive)

#### Procedure

Patients were kept nil per oral for at least 4 hours prior to procedure followed by premedication with intramuscular injection of 0.6 mg Atropine and 10 mg of Diazepam orally 30 to 45 min before the procedure. Local anaesthesia to upper respiratory tract was given using 2% XYLOCAINE through nebulizer, just before the procedure. After thorough examination of the bronchial tree, bronchoscope was then negotiated into the and sub-segmental segmental bronchi and bronchoalveolar lavage was taken from the involved area. For BAL fluid, sterilized buffered normal saline at body temperature was used. A 20 ml of this was instilled through the bronchoscope and promptly aspirated using low pressure suction. Total of 8-10 aliquotes (150-200 ml) were instilled. Lavage fluid was collected into a non siliconised sterilized container. After the procedure, the patient was observed for any complications like development of pneumothorax, hemorrhage, infection and cardiac arrythmias for 24-48 hours. The sputum samples for next 3 days after bronchoscopy (post-bronchoscopic sputum) were collected. All samples of BAL fluid and post bronchoscopic sputum were examined for AFB by Z-N staining and were cultured for mycobacterium tuberculosis on L-J media.

#### Results

The study population included 72 patients, 50 (69%) males and 22 (31%) females with the age group of 13-75 years, average age being 38.48 years. 32 patients (44%) belonged to the age group < 30 years. History of smoking was present in 33 (66%) males and in 3(14%) females. Most common symptom was cough in 52(72%) patients followed by expectoration in 42(58.33%), hemoptysis in 34(47.22%), fever in 17 (24%), and chest pain in 12(16%). 60 cases had history of contact. Of these, 50 cases had contact in neighborhood and 10 had household contacts.7 patients (10%) had taken ATT for full duration, 16(22%) were defaulters, 49(68%) were those without any prior history of ATT.

All 72 patients participating in our study were divided into 3 categories depending upon the extent of lesion on chest X-rays. 39 (54%) patients had minimal disease on X-ray chest; 29 (40%) patients had moderate disease on X-ray chest and 4 patients (6%) had advanced disease on X ray chest. (Table 1)

	Radiological feature	N (%)	TB Diagnosed
A	Minimal Disease	39 (54%)	15
В	Moderate Disease	29 (40%)	20
С	Advanced	4 (6%)	4

**Table 1:** Extent of chest x-ray lesion (n= 72)

Bronchoscopic examination revealed no pathological lesion in 26 (36%) of 72 patients. Among remaining 46 patients , 6 cases (8.2%) had discharge from bronchus, 40 cases (55%) had unhealthy mucosa /granuloma, 1 case (1.4%) had external compression and another 10 cases (14%) had bleeding from bronchus, while growth was visible only in 1 case (1.4%). (Figure 1)

**Figure 1**: Bronchoscopy findings in suspected cases of pulmonary TB (*n*=72)



In all cases, BAL and Post Bronchoscopy Sputum were collected and subjected to AFB examination by ZN staining and culture on LJ media.

In our study group of 72 patients, tuberculosis was confirmed by smear examination for AFB in BAL fluid in 30 cases (41.6%), by post bronchoscopy sputum in 18 cases (25%).BAL culture for *M. tuberculosis* was positive in 37(51.3%) patients whereas PBS culture was positive in 23 (32%) patients. 16 specimens of BAL culture were exclusively positive whereas two PBS culture were exclusively positive.(Table 2)

**Table 2:** Result of smear examination and AFB culture of BAL fluid and PBS (n=72)

Specime	Smear Examination		AFB Culture	
n	Positive	Exclusivel	Positive	Exclusivel
	Specimen	y Positive	specimen	y positive
	n(%)	Specimen	n(%)	specimen
		n		N(%)
BAL	30/72	12	37/72	16
	(41.6%)		(51.38%)	(22.2%)
PBS	18/72	0	23/72	2 (2.7%)
	(25%)		(32%)	

During our study, we were able to diagnose 39 cases out of 72 cases (54.2%) by combining both BAL fluid and PBS smear examination and culture for AFB. Out of these 39 cases diagnosed, BAL was more effective method with sensitivity of 94.87% whereas sensitivity of PBS was 58.97%.(Table 3)

**Table 3:** Sensitivity of bronchoalveolar lavageand post bronchoscopy sputum (n=72)

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Specime	Cases	Cases Positive	Sensitiv	Confidenc
n	Positiv	(By	ity (%)	e Interval
	e	smear/culture)		
BAL	37	39	94.87%	82.68 to
Fluid				99.37%
PBS	23	39	58.97%	42.10 to
				74.43%

Comparison of BAL& PBS using McNemar test revealed that there was a significant difference in the result of two test (p value= 0.0013). Bronchoalveolar lavage had more yield (37/72) of 51.38% compared vield of post as to bronchoscopy sputum examination (23/72)31.94%. Thus BAL gave a significantly higher yield than PBS. (Table 4)

**Table 4:** Yield of bronchoalveolar lavage and postbronchoscopy sputum (n=72)

Specimen	Cases	Cases	Cases	Total	
	Positive	Negative	Done	Yield	
BAL Fluid	37	35	72	51.38%	
PBS	23	49	72	31.94%	
MaNaman tast a 0.0012					

McNemar test, *p*=0.0013

#### 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 till the of "suspects" presence 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.<sup>[6]</sup>

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.<sup>[7]</sup>Published observations suggest that over 60% of smear negative patients would need chemotherapy by the end of 12 months if left untreated.<sup>[8,9]</sup>

In our study, we had selected 72 patients with sputum smear negative on 2 occasions; out of which 50 patients (70%) were males and 22 (30%) were females. This was comparable to the study done by Purohit et al <sup>[10]</sup> where in the sample size of 50 cases, they had 35 males (70%) and 15 females (30%).

Out of the 72 patients in our study, 52 patients complained of cough (72%), which was the most common symptom. This was similar to study done by Purohit et al, <sup>[10]</sup> D D S Kulpati et al <sup>[11]</sup> and A A Bachh et al<sup>[12]</sup> who have also reported cough as the most common symptom.

In our study, 36 cases had history of smoking, among these 30 cases (42%) were active smokers, while 6 (8%) quitted smoking for more than one year and 36 of them (50%) had never smoked before. This was slightly higher than the study done by X Qingliang et al<sup>[13]</sup> where history of smoking was present in 22.7%.

Based on history of ATT intake, 7 patients (10%) had received anti-tubercular treatment for full duration, 16 patients (22%) were defaulters, 49 patients (68%) were those without any prior history of anti-tubercular treatment. These characteristic were similar to the study done by Rajesh Kumar Jain et al <sup>[14]</sup> where past history of pulmonary tuberculosis was present in 26.66%.

Based on extent of lesion on chest X-rays,<sup>[5]</sup> patients were divided into 3 categories, 39 (54%) patients had minimal disease on X-ray chest; 29 (40%) patients had moderate disease on X-ray chest and 4 patients (6%) had advanced disease on X ray chest. This was almost similar to the study done by Choudhary S et al <sup>[15]</sup> where 63% patients had minimal disease on X-ray chest; 27% patients had moderate disease and 10% patients had advanced disease on X-ray chest.

Bronchoscopic examination revealed no pathological lesion in 26 (36%) patients. In remaining 46 patients, bronchoscopy revealed unhealthy mucosa (congestion with hyperaemia) in 40 patients (55%) which was the most common finding while second most common finding in our study was bleeding from bronchus accounting for 14% of all cases. This was slightly lower than the study done by A.A.Bachh et al <sup>[12]</sup> where 71% patients had congestion with mild to moderate hyperaemia with whitish plaque.

In our study, the BAL fluid smears were taken in all 72 cases and were positive for AFB in 30(41.66%) patients. In previous studies, it varied from 7.5% in S Charoenratanakul et al <sup>[16]</sup> to 57.1% in Malekmohammad M et al. <sup>[17]</sup>

BAL culture yielded M. tuberculosis in 51.38% patients in our study (37 cases out of 72) which was comparable to the 53% positivity (57 cases out of 108) by Choudhary S et al.<sup>[15]</sup>

In our study, Post bronchoscopy sputum were collected on 3 occasions and subjected to both smear for AFB and culture, yielding 25%(18/72) and 32% (23/72) positivity respectively. This was comparable to the 26% AFB smear positivity (13 cases out of 50) by Purohit et al<sup>[10]</sup> and 27.78% AFB smear positivity (30 cases out of 108) by

Choudhary S et al.<sup>[15]</sup> Also in previous studies, 27.5% positivity by PBS culture was noted by Saifquaiser et al<sup>[18]</sup> and 25% by D.D.S.Kulpati et al .<sup>[11]</sup>

During our study, we were able to diagnose 39 cases out of 72 cases (54.2%) by combining both BAL and PBS smear examination and culture for AFB. This rate of detection was 40% by J.Balakrishna et al, <sup>[19]</sup>60% by Saifquaiser et al <sup>[18]</sup> and 94% by S.Y.So et al<sup>[20]</sup>.Out of these 39 cases diagnosed, BAL was more effective method with sensitivity of 94.87%(CI of 82.68% to 99.37%) which was comparable to the study by de Gracia et al<sup>[21]</sup>where BAL had a sensitivity of 88% (15/17).

Using post bronchoscopy sputum as the method of diagnosis, we were able to diagnose 23 patients with a sensitivity of 58.97% (CI of 42.1% to 74.43%) which was lesser than the study by K.Pipatvech et al<sup>[22]</sup> and M.Malekmohammad et al<sup>[17]</sup> where PBS had a sensitivity of 72% (13/18) and 76.7% (43/56) respectively.

### Conclusion

We conclude that bronchoscopy proved to be a safe and effective method for the diagnosis of tuberculosis especially in sputum smears negative pulmonary TB. Combination of BAL and PBS increase the diagnostic sensitivity of this method. Our study found that sensitivity of BAL was more than PBS .We suggest that empirical treatment for tuberculosis should be avoided whenever possible, even in patients with clinical and radiological suspicion of the disease. All these patients should be subjected to bronchoscopic guided procedures for bacteriological confirmation.

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