

# The stand of induced sputum and bronchoscopy in the diagnosis of sputum smear-negative pulmonary tuberculosis

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**Abstract- Background & objectives:** Pulmonary tuberculosis diagnosis rely on demonstration of the acid- fast bacilli (AFB) in sputum samples. Difficult issue arises when a patient who is suspected of tuberculosis does not produce adequate amount of sputum. About 40-60% of patients with suspected pulmonary tuberculosis may fail to produce sputum. We conducted a prospective study to compare the stand of induced sputum and bronchoscopy in sputum Smear negative Pulmonary tuberculosis with clinical features and radiologically suggestive of active Pulmonary tuberculosis.

**Methods:** Demonstration of acid-fast bacilli in sputum induction, bronchial washing, bronchial brush, and post bronchoscopy sputum was done in all cases to compare the role of induced sputum and bronchoscopy.

**Results:** Induced sputum for AFB was positive in 14 (30.4%) cases and was negative in 32(69.6%) cases. Bronchial wash for AFB was positive in 21 (45.7%) cases and negative in 25 (54.3%) cases. Bronchial brush for AFB was positive in 23 (50%) cases and an equal number of negative case bronchial brush.

**Interpretation & conclusions:** Our study showed that bronchoscopy is essential in the diagnosis of Pulmonary tuberculosis followed by sputum induction in sputum smear negative Pulmonary tuberculosis patients. Bronchoscopy exhibit a higher bacteriological confirmation for diagnosis in patients with strong clinical and radiological evidence expressing pulmonary tuberculosis and those having more risk factors.

**Index Terms-** Bronchial brush, Bronchial wash, Induced sputum, Post bronchoscopy sputum, pulmonary tuberculosis

## I. INTRODUCTION

Pulmonary tuberculosis is a global health issue. India is one of the biggest contributors to the global burden of tuberculosis, accounting for 26% of all TB cases reported globally.(1,2) In 2011, out of the estimated global annual incidence of 10 million (range, 8.9–11.0 million) TB cases, nearly 2.64 million were estimated to have occurred in India.(1)

Pulmonary tuberculosis diagnosis relies on demonstration of the acid- fast bacilli (AFB) in respiratory specimens, especially sputum samples.(3–5) Identification of active pulmonary tuberculosis disease patients is an important component of TB control as early appropriate treatment renders these patients non-Infectious and interrupts the chain of transmission of TB. Under the programme conditions such as Revised National Tuberculosis Control Programme (RNTCP) of the Government of India, the diagnosis of Pulmonary Tuberculosis is based on sputum smear examination.(6,7)

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 suspected pulmonary tuberculosis may fail to produce sputum, or when it is available AFB may be negative on repeated smear examination. Hence, more invasive procedures need to be undertaken in these patients to establish the diagnosis.(8–12)

Anti-Tuberculosis Treatment is frequently started empirically, leading many a time to the avoidable risk of drug toxicity and expenditure. Diseases like bronchogenic carcinoma and diffuse lung diseases are sometimes missed because cases are put within the grey area of tuberculosis suspects. On the other hand, if not treated, 64% of sputum negative suspects could need chemotherapy within 12 months.(13)

Among various alternative methods, the use of fiberoptic bronchoscopy (FOB) is one of the most widely studied alternative diagnostic approaches among sputum negative patients.(14,15) Early FOB seems to be the best course of action in a patient with suspected sputum smear tuberculosis. With the changing economic scenario and availability of FOB facilities in developing countries, the picture is changing fast, hence its utility in smear-negative situations must be evaluated in our settings.(10)

This study was carried out to know the stand of induced sputum and bronchoscopy in smear-negative pulmonary tuberculosis patients diagnosed on clinical and radiological grounds, by direct visualization of the bronchial tree and collecting specimens, bronchial wash to get the positivity of these specimens

through smear examination for AFB by Ziehl –Nelson staining method.

## II. MATERIAL AND METHODS

This is one year Prospective and observational study undertaken after obtaining approval from the hospital ethical committee and was conducted in the Department of Pulmonary Medicine, SRMS-IMS Bareilly (UP). The present study was done on 46 patients who attended the outpatients Department of Pulmonary Medicine and those admitted in the wards of the Department of Pulmonary Medicine SRMS IMS Bareilly. We included those who were clinically diagnosed case of pulmonary tuberculosis as per RNTCP guidelines.

## III. STUDY DESIGN

Clinically diagnosed active pulmonary tuberculosis with inadequate sputum production or smear-negative patient were studied. We used 20 ml of 3% hypertonic saline solution delivered through an ultrasonic nebulizer for sputum induction. Induced sputum sample was subjected to Z-N staining and was examined for the presence of AFB. All these patients were subjected to the bronchoscopy procedure and various specimens like a bronchial wash, bronchial brush smear and post bronchoscopy sputum was subjected to ZN staining for AFB. Patients were also followed up after 6 months of starting Anti tubercular treatment.

### Inclusion criteria:

- All patients attended OPD and were admitted to wards with clinical history, physical findings and chest X-ray lesions suggestive of pulmonary tuberculosis.
- Sputum is either not produced or inadequate for examination (only saliva or sputum quantity < 2 mL) or sputum smear-negative for acid-fast bacillus (AFB) on two samples.

### Exclusion criteria:

- Those who did not give consent.
- Patients on anti-tubercular treatment.
- Sputum smear-positive patients.
- Patients who came out to be a case of lung cancer, pneumonia, inflammatory diseases etc. were excluded from our study.
- Contraindications for the bronchoscopic procedure.

## IV. METHODOLOGY

At the time of enrollment detailed medical history was taken and a complete physical examination of the patients was performed. The patients were subjected to the following investigations: Chest X-Ray PA view, CT Thorax (if required), Sputum examination for AFB: two samples (one spot sample and one early morning sample), Induced sputum (20 ml of 3 % hypertonic saline solution) for AFB, Fiberoptic bronchoscopy, Bronchial wash, Bronchial brushing, Bronchoscopy sputum for AFB.

## V. OBSERVATIONS AND RESULTS

For this study, a total of 46 patients in the sampling frame were enrolled and were subjected to demographic, clinical, radiological, microscopic, and fiberoptic evaluation.

It was observed that 21.7% of the patients were under the age groups 15-25 years, 36-45 years and 56-65 years each followed by 19.6% of the patients in 46-55 years and 8.7% in 26-35 years. It was also observed that the mean age of the group was  $44.61 \pm 16.77$  years. It was observed that 29 (63.0%) were male and 17 (37.0%) of the patients were female. Majority were farmers 16 (34.8%) followed by housewife 12 (26.1%), student 9 (19.6%). 8 (17.4%) cases were diabetic, 6 (13.0%) cases were hypertensive, 2 (4.3%) cases had a family history of Anti-tuberculosis treatment, 18 (39.1%) cases were cigarette/Bidi smokers, 8 (17.4%) cases were alcoholic and chullah smoke exposure each. (Table no 1)

Pulmonary tuberculosis (smear-positive) was diagnosed in 29 (63.0%) cases and Pulmonary tuberculosis (smear negative) was diagnosed in 17 (36.9%) cases based on results of induced sputum, bronchial wash, bronchial brush and post bronchoscopy sputum for AFB (Table no 2).

Out of 29 smear-positive Pulmonary tuberculosis case Induced sputum for AFB was positive on Z-N staining in 14 (48.3%) cases, bronchial wash for AFB was positive on Z-N staining in 21 (72.4%) cases, bronchial brush for AFB was positive on Z-N staining in 23 (79.3%) cases post bronchoscopy sputum for AFB was positive on Z-N staining in 11 (37.9%) cases and was diagnosed as smear-positive pulmonary tuberculosis. (Table no 3) Pulmonary tuberculosis (smear negative) was diagnosed in 17 cases based on clinic-radiological findings.

## VI. DISCUSSION

At the beginning, patient with pulmonary tuberculosis subjected to rigid bronchoscopy for therapeutic purpose. With the advancement and advent of flexible bronchoscopy, smear for mycobacteria from the bronchial aspirate, bronchial wash, bronchial brush, bronchoalveolar lavage fluid, post bronchoscopy sputum has been used in various studies for diagnosing pulmonary tuberculosis. The FOB facilitates rapid diagnosis and offers the additional advantage of the diagnosis of several conditions that may mimic pulmonary tuberculosis. The main advantage of bronchoscopy is the ability to look into the bronchial tree and can directly collect samples from the bronchial pathology site.(16)However, FOB is an invasive procedure and is associated with the increase risk of transmission of tuberculosis and other infections and also have little risk of complications like fever, hemoptysis, pneumothorax. Despite of invasive procedure, it is considered to be a relatively safe procedure.(17,18)

Sputum induction was first used during 19<sup>th</sup> century's six decade by Hensler et al. for the diagnosis of active Pulmonary tuberculosis. Hypertonic saline inhalation produces increased vascular permeability and induces mucus production by submucosal glands through the irritation of the airways mucosa and it also increases the osmolarity of the airway lining fluid which causing the patient to expectorate.(9,19)

In our study attempt was made to study the stand of induced sputum and bronchoscopy in the diagnosis of sputum smear-negative pulmonary tuberculosis.(9,19) Patients who came out to

be a case of lung cancer, pneumonia, inflammatory diseases were excluded from our study.

In our study to compare the role of bronchoscopy and induced sputum in sputum negative pulmonary tuberculosis, total forty-six patients were evaluated for induced sputum, bronchoscopy and post bronchoscopy sputum for AFB. Induced Sputum and bronchial wash for AFB was positive in 10 (34.5%) cases.

Those were active pulmonary tuberculosis diagnosed as by demonstration of acid-fast bacilli in bronchial washing, brush, sputum induction, post bronchoscopy sputum and smear negative Pulmonary tuberculosis was diagnosed in those who were negative for AFB in bronchial washing, brush, sputum induction, post bronchoscopy sputum and diagnosed as pulmonary tuberculosis on basis of clinico-radiological profile and also responded well to Anti-tubercular therapy given on empirical basis.(20) Patients were followed up after 6 months and all patients responded well to Anti-tubercular therapy, improvement was seen clinically as well as radiologically.

Out of the total of 46 patients in the present study microbiologically confirmed Pulmonary tuberculosis was diagnosed in 29 (63.0%) cases and clinically diagnosed Pulmonary tuberculosis was diagnosed in 17 (36.9%) cases based on induced sputum, bronchial wash, bronchial brush and post bronchoscopy sputum for AFB.

In smear-positive pulmonary tuberculosis 36-45 years of age was more common in 7 (24.1%) cases followed by 15-25 years and 46-55 years of age in 6 (20.7%) cases and in smear negative pulmonary tuberculosis 56-65 years of age was more common in 5 (29.4%) cases followed by 4 (24%) cases between 15-25 years of age. Among 46 patients in this study, 29 (63%) were male and 17 (37%) were female. In pulmonary tuberculosis (smear-positive) majority were male 18 (62.1%) followed by female 11 (37.9%) and in pulmonary tuberculosis (smear negative) majority were male 11 (64.7%) and females were 6 (35.2%). Gender distribution is equal in sputum positive, sputum negative and overall patients. In pulmonary tuberculosis (smear-positive) 5 (17.2%) cases were diabetic, 3 (10.3%) were hypertensive, 10 (34.5%) were smokers, alcoholic 2 (6.9%) and 4 (26.7%) had a history of chullah smoke exposure. While smear negative pulmonary tuberculosis, diabetic and hypertensive were 3 (20%) each, smoker 8 (47%), alcoholic 6 (35.2%) and chullah smoke exposure 4 (26.7%). Common co-morbidity in both group is diabetes and hypertension. We can draw conclusion from study that co-morbidity reduces the sensitivity of sputum smears test. So, in the suspected case tuberculosis with diabetes and hypertension bronchoscopy might be an effective tool for microbiological confirmation of bacilli and drug resistant.

In pulmonary tuberculosis both in smear positive and smear negative group cough was the most common symptoms followed by fever. Some patient also had breathlessness, loss of appetite, chest pain, hemoptysis and weight loss.

In a study by Jain et al. Immediate diagnosis of Pulmonary tuberculosis was possible in 33 (55%) cases. The diagnosis other than Pulmonary tuberculosis was established in 5 cases (8.33%), which included 2 cases (3.33%) of lung cancer, 2 cases (3.33%) of fungal (candida) pneumonia, and 1 case (1.66%) of bacterial (klebsiella sp.) pneumonia.(21)

In a study by Biswas S et al. radiological assessment of pulmonary tuberculosis has been done and they seen that exclusive upper zone involvement was in 67% of patients while 16% of other patients had multi-lobar involvement including upper zones. Patchy non-cavitary pacifications were seen in 91% of patients and only 4% of patients had cavitary lesions. (9)

In our study Infiltrative opacities were seen in the majority of the cases 33 (71.7%) followed by consolidation 13 (28.3%), cavity 5 (10.9%) and fibrosis 3 (6.5%). The majority of the cases had unilateral involvement. Among cases with unilateral involvement right side was more commonly involved 56.5% as compared to the left side 28.3%. Bilateral involvement was in 7 (15.2%). In our study Induced sputum for AFB shows similar result. Induced sputum was positive in 14/46 (30.4%) cases and among the smear, positive Induced sputum for AFB was positive in 14/29 (48.3%) cases. So induced sputum is not effective as bronchoscopy wash and brush sample for detection of tuberculosis. Our result was similar with Biswas et al study on induced sputum.

In the present study, Bronchoscopic visualization shows normal appearance in 16 (34.8%) cases, mucopurulent secretions in 16 (34.8%), mucosal hyperemia in 10 (21.7%), inflammation 8 (17.4%), the bleeding site was present in 3 (6.5%) cases and there was infiltrated growth, edematous, necrotic black patches in 1 (2.2%) case each.

Bronchial wash for AFB was positive in 21/46 (45.7%) cases and was negative in 25/46 (54.3%) cases, and among the smear, positive 29 cases bronchial wash for AFB was positive in 21 (72.4%) cases and was negative in 8 (27.6%) cases. Bronchial brush for AFB was positive in 23/46 (50%) cases and negative in 23/46 (50%) cases, and among the smear, positive cases Bronchial brush for AFB was positive in 23/29 (79.3%) cases and negative in 6/29 (20.7%) cases. Post bronchoscopy sputum for AFB was positive in 11/46 (23.9%) cases and negative in 35/46 (76.1%) cases, and among the smear-positive cases post bronchoscopy sputum for AFB was positive in 11/29 (37.9%) cases and negative in 18/29 (62.1%) cases.

Our study shows similarity with Wongthim et al. reported that over four years, 112 of the 1265 bronchoscopies were performed in patients with suspected PTB, who were smear-negative or were unable to produce sputum. Active PTB was diagnosed in 71 of them. Immediate diagnosis was possible in 38 of the 65 (58%) of these patients. Out of 71, 54 (76%) were diagnosed from bronchoscopy specimens. Bronchial brushings gave the highest diagnostic yield being positive in 33 of the 65 (51%; 4.6% exclusively positive) compared to bronchial washings which were positive in 24 of the 50. Post-bronchoscopy sputum smear was positive in seven out of 30 (23%). (9,22)

In the series reported by Chawla et al. studied 50 sputum smear-negative patients suspected to have PTB underwent FOB. Bronchial aspirate smears of twelve patients and post bronchoscopic sputum smears of fourteen patients were positive for AFB. Bronchial biopsy provided the diagnosis in 9 out of 30 patients. Brush smears were positive in 28 patients, being the only positive sample in ten cases. Early diagnosis could be made in 36 of the 50 (72%) patients and a definitive diagnosis was made in 45 (90%) of them. (23,24)The yield from brush smears was found to be significantly better when compared to bronchial aspirate smear and post-bronchoscopy smear.

Das Gupta et al. reported a study in which bronchoscopy with bronchial fluid aspiration, washings and biopsy was performed in 104 patients suspected clinically and radiologically of having pulmonary tuberculosis diagnostic yield in 92.30% (96/104) cases. Diagnostic yield for tuberculosis was in 69.22% (72/104) cases, it includes positive aspiration and washing smears in 38.46% (40/104) patients, positive mycobacterial culture alone in 26.92% (28/104) cases.(16)

In a study by McWilliams et al. studied and found that sputum induction (96.3%) is superior to that of Broncho-alveolar lavage (51.9%) and the overall cost of Broncho-alveolar lavage was three times of performing Sputum Induction. They suggested employing Sputum Induction, followed by BAL only in patients who were undiagnosed on Sputum Induction but had radiologically suggestive of active pulmonary TB.(17) This is shows opposite result than our study. It may because of a smaller number of patients taken in our study.

All patients with microbiologically confirmed tuberculosis case were treated with anti-tubercular treatment. In 17 clinically diagnosed pulmonary tuberculosis patients, Anti-tuberculosis treatment was started on a clinico-radiological basis. Patients were followed up after 6 months of starting Anti-tuberculosis treatment and they had a successful outcome.

## VII. CONCLUSION

Our study concluded that bronchoscopy is an essential tool in the diagnosis of pulmonary tuberculosis followed by sputum induction in clinically diagnosed sputum smear-negative patients. Bronchoscopy exhibit a higher microbiological confirmation of the diagnosis in those patients who have strong clinical and radiological suspicion of pulmonary tuberculosis and having more risk factors. The results from the current study reemphasize on the diagnostic use of the bronchoscopy. In clinically diagnosed pulmonary tuberculosis, the diagnosis of tuberculosis can successfully be established with bronchial brush and bronchial wash. Collectively all these procedures can identify around two-third of cases. Study highlighting the significant stand of bronchoscopy in the diagnosis of pulmonary tuberculosis.

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- Formal analysis, Data curation, Software, Validation, Investigation and Writing - **Dr Vikash Gupta**
- Writing - review and editing: **Dr Ankit Kumar**
- Approval of final manuscript: **Dr Vikash Gupta, Dr Rajeev Tandon, Dr Ankit Kumar**

**Tables:**

**Table 1 : Past history, Family history and Personal history of the patients enrolled in the study**

	Frequency	Percentage
<b>Past H/o</b>		
Diabetes Mellitus	8	17.4%
Hypertension	6	13.0%
<b>FAMILY/ H/o of ATT</b>		
No	44	95.7%
Yes	2	4.3%
<b>Personal H/o</b>		
Cigarette/Bidi Smoker	18	39.1%
Chullah Smoke exposure	8	17.4%
Alcoholic	8	17.4%

**Table 2 : Distribution of Patients(N=46) according to diagnosis based on results of induced sputum for AFB, bronchial wash for AFB, bronchial brush for AFB and post bronchoscopy sputum for AFB.**

Procedure	Positive	Negative
Induced Sputum	14(30.4%)	32(69.6%)
Bronchial Wash	21(45.7%)	25(54.3%)

Bronchial Brush	23(50%)	23(50%)
Post Bronchoscopy	11(23.9%)	35976.1%)
Overall Result(N=46)	29(63%)	17(36.9%)

**Table 3 : Distribution of Sputum Positive pulmonary tuberculosis(N=29) Patients according to diagnosis based on results of induced sputum for AFB, bronchial wash for AFB, bronchial brush for AFB and post bronchoscopy sputum for AFB.**

Procedure	Positive
Induced Sputum	14(48.2%)
Bronchial Wash	21(72.4%)
Bronchial Brush	23(79.3%)
Post Bronchoscopy	11(37.9%)
Overall (N=29)	29(100%)