

## Role of Sputum Induction in Sputum Smear Negative and Chest X-Ray Suggestive of Pulmonary Tuberculosis

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### ABSTRACT

**Background:** Sputum induction is a procedure used for patients who have difficulty in spontaneously producing sputum. So we have planned to conduct a study to find out the role of sputum induction in TB patients to increase the yield of sputum smear positivity in sputum smear negative pulmonary tuberculosis patients and the role of sputum induction in tuberculosis suspected patients having cough without expectoration.

**Materials & Methods:** The present study was carried out in 50 patients admitted with clinical & radiological features suggestive of pulmonary tuberculosis in the Department of TB & Respiratory diseases, R.N.T Medical College, Udaipur. Study protocol includes detailed history, clinical examination, routine blood investigations including ESR, chest x-ray, sputum induction and smear study by Ziehl-Neelson staining was done to all the patients included in the study.

**Results:** Our study showed that the total numbers of cases were 50, among which 40 (80%) cases were in the age group of below 60 years. Males in the study are 31 (62%) and females are 19 (38%). ESR was elevated to more than 30 mm/hr in 46 (92%) cases and less than 30mm/hr in 4 (8%) cases. Sputum production were absent in 40 (80%) cases. Maximum 30 (60%) cases had moderate disease, 14 (28%) cases had minimal disease and 6 (12%) cases had far advanced disease on chest x-ray. 30 (60%) cases had no

cavity on chest x-ray and 20 (40%) cases had cavity. 30(60%) cases had bilateral disease (B/L) and 20 (40%) cases had unilateral disease (U/L) on chest x-ray.

**Conclusion:** We concluded that the identification of smear positivity through sputum induction method with 3% hypertonic saline that allows sampling of the airways in a noninvasive fashion and is a less expensive approach than the technique like bronchial biopsy, bronchoalveolar lavage and gastric lavage.

**Keywords:** Sputum Induction, Pulmonary Tuberculosis, Chest X-Ray, Smear Positivity.

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### INTRODUCTION

Tuberculosis (TB) remains a major global health problem and causes ill-health among millions of people each year and ranks as the second leading cause of death from infectious disease worldwide. Though India is the second most populous country in the world, it has more new TB cases annually than any other country.<sup>1</sup>

Microbiological confirmation of pulmonary tuberculosis (TB) is becoming increasingly important because of emergence of multi-drug resistance and increased incidence of TB among patients with human immunodeficiency virus (HIV) infection. Moreover, rapid and precise diagnosis will reduce the risk of nosocomial transmission of TB. Direct sputum smear microscopy remains a fundamental tool of diagnosis, but may be negative up to 50% case of active pulmonary TB.<sup>2</sup>

A fairly good number of cases, strongly suspected of pulmonary TB are not confirmed bacteriologically. One reason for this may be related to the difficulties of obtaining adequate quantity of sputum specimen from TB suspected patients either due to dry cough or inadequate or scanty sputum (<2 ml).<sup>3</sup> Thus sputum remains negative in about 25-50% of all cases of active pulmonary TB. Alternative methods of obtaining sputum specimens are frequently needed in those patients with radiological suspicion of TB who are unable to expectorate or are smear negative. The methods used for increasing yield of sputum smear positivity are sputum induction (SI), bronchoalveolar lavage (BAL) and gastric washings (GW) specimens. These methods have their own advantages and disadvantages and diagnostic yield vary in respect of safety, tolerability, and feasibility in different set-ups.

Sputum induction is a procedure used for patients who have difficulty in spontaneously producing sputum. The patient inhales nebulised hypertonic saline solution, which liquefies airway secretions & promotes coughing and allows expectoration of respiratory secretions.<sup>4</sup> Sputum induction is simple, non-invasive, inexpensive and less time consuming and if successful, often precludes the need for bronchoscopy.<sup>5</sup> If sputum induction is not possible then we need bronchoscopy. It can be used in young children, post prandially and as an OPD (Out Patient Department) procedure. After a brief description, any person can perform it.

So we have planned to conduct a study to find out the role of sputum induction in TB patients to increase the yield of sputum smear positivity in sputum smear negative pulmonary tuberculosis patients and the role of sputum induction in tuberculosis suspected patients having cough without expectoration.

**MATERIALS & METHODS**

The present study was carried out in 50 patients admitted with clinical & radiological features suggestive of pulmonary tuberculosis in the Department of TB & Respiratory diseases, R.N.T Medical College, Udaipur.

Patients aged more than 18 years with features of pulmonary tuberculosis and having spontaneously produced 2 sputum smear negative samples or having dry cough/scanty sputum included,

**Inclusion Criteria**

1. Persistent cough for at least 2 weeks.
2. Patient with symptoms suggestive of pulmonary tuberculosis (weight loss, evening rise of temperature, night sweats, chest pain, loss of appetite).
3. Sputum either not produced or inadequate for examination (only saliva or sputum quantity <2ml) or sputum smear negative for acid fast bacillus (AFB) on two samples.
4. Chest radiograph showing changes consistent with active pulmonary tuberculosis.
5. Age more than 18 years.

**Exclusion Criteria**

1. Patients already on anti-tuberculosis therapy or who have taken anti-tuberculosis treatment previously.
2. Recent eye surgery.
3. Active hemoptysis
4. Patient with uncontrolled asthma or chronic obstructive pulmonary disease.
5. Unstable angina or arrhythmias.
6. Fractured ribs or other chest trauma.
7. Pneumothorax

**Study Method**

Study protocol includes detailed history, clinical examination, routine blood investigations including ESR, chest x-ray, sputum induction and smear study by Ziehl-Neelson staining was done to all the patients included in the study.

**Procedure of Sputum Induction**

Following signed informed consent and rinsing and gargling with water, in a well-ventilated room, reservoir device of nebulizer (INFI-NEB- compressor nebulizer, CN-01WB, Oertel Gbr, Germany) was filled with 10 ml of 3% hypertonic saline and subjects were asked to inhale mist until 2ml of sputum was obtained or for a maximum of 20 to 30 minutes.

Inhalation was interrupted every 5 minutes, so that patient could expectorate the sputum. The patients were closely monitored at all

times during the procedure and 1 h post-procedure. The nebulizer equipment was decontaminated after each session by thorough washing and soaking in glutaraldehyde.

**Table 1: Distribution of patients according to demographic profile**

Demographic profile	No. of cases (N=50)	%
<b>Age (yrs)</b>		
<60 yrs	40	80%
≥60 yrs	10	20%
<b>Sex</b>		
Male	31	62%
Female	19	38%
<b>BMI (Kg/M<sup>2</sup>)</b>		
<18.5 Kg/M <sup>2</sup>	48	96%
>18.5 Kg/M <sup>2</sup>	2	4%

**Table 2: Distribution of patients according to parameters**

Parameters	No. of cases (N=50)	%
<b>Sputum production</b>		
Absent	40	80%
Present	10	20%
<b>Successful induction</b>		
No	2	4%
Yes	48	96%
<b>Presence of cavity</b>		
Absent	30	60%
Present	20	40%
<b>Lesion side</b>		
B/L	30	60%
U/L	20	40%
<b>Severity of disease of chest X-ray</b>		
Minimal	14	28%
Moderate	30	60%
Far advanced	6	12%

**Table 3: Sputum positivity with demographic profile and various parameters of sputum examination**

Parameters		Induced sputum Zn Staining	
		Positive (n=17)	Negative (N=33)
<b>Age (yrs)</b>	<60 yrs	13	27
	≥60 yrs	4	6
<b>Sex</b>	Male	9	22
	Female	8	11
<b>BMI (Kg/M<sup>2</sup>)</b>	<18.5	17	31
	>18.5	0	2
<b>ESR (mm in Hg)</b>	<30	1	3
	≥30	16	30
<b>Lesion side</b>	B/L	12	18
	U/L	5	15
<b>Cavity</b>	Absent	6	24
	Present	11	9
<b>Sputum production</b>	Absent	13	27
	Present	4	6
<b>Severity of chest x-ray</b>	Minimal	2	12
	Moderate	12	18
	Far advanced	3	3

## RESULTS

Our study showed that the total number of cases were 50, among which 40 (80%) cases were in the age group of below 60 years. Males in the study are 31 (62%) and females are 19 (38%). ESR was elevated to more than 30 mm/hr in 46 (92%) cases and less than 30mm/hr in 4 (8%) cases. Sputum production were absent in 40 (80%) cases. In 48 (96%) cases sputum was induced successfully by induction method. Maximum 30 (60%) cases had moderate disease, 14 (28%) cases had minimal disease and 6 (12%) cases had far advanced disease on chest x-ray. 30 (60%) cases had no cavity on chest x-ray and 20 (40%) cases had cavity. 30 (60%) cases had bilateral disease (B/L) and 20 (40%) cases had unilateral disease (U/L) on chest x-ray (table 1 & 2). Our study showed that 8 out of 19 (42.11%) cases were positive in female and 9 out of 31 (29.03%) cases were positive in male after sputum induction. In far advanced disease 3 out of 6 cases (50%) were positive for AFB after sputum induction. In moderate advanced disease 12 out of 30 cases (40%) were positive after sputum induction. In patients with BMI less than 18.5 kg/m, 17 out of 48 (35.42%) cases were positive after sputum induction. 11 out of 20 (55%) cases were positive after sputum induction in patients having cavity on their chest x-ray. 12 out of 30 (40%) cases were positive after sputum induction in patients having bilateral lesion on their chest x-ray. 4 out of 10 (40%) cases were positive in patients having sputum production and 13 out of 40 (32.5%) were positive in patients having dry cough after sputum induction. 17 out of 50 (34%) cases were positive on ZN staining after sputum induction. (table 3)

## DISCUSSION

The present study was carried out in 50 patients admitted with sputum smear negative and clinical & radiological features suggestive of pulmonary tuberculosis in the Department of TB & Respiratory Diseases, Bari, Udaipur.

SI was first used by Hensler<sup>6</sup> et al., in the diagnosis of active TB. Hypertonic saline irritates the airways causing the patient to cough and increases the osmolarity of the airway lining fluid, which produces increased vascular permeability, and induces mucus production by submucosal glands.<sup>7</sup>

GW (Gastric Washings) is regarded as the standard procedure in diagnosis of TB in children who swallow their sputum and cannot expectorate.<sup>8-10</sup> However, this method has yielded variable results in different studies. The main drawbacks are: (1) Limited rate of positive cultures among the smear positive results making positive smear results unreliable, (2) requirement of 3 samples for evaluation, (3) requirement of overnight fasting, (4) invasive procedure, (5) cannot be easily performed on an out-patient basis, and (6) requires rapid processing to avoid killing by gastric acid. In different studies, the sensitivity of the GW smears was 61-80% while positive cultures were present in only 30%. The disproportionate GW smear and culture results were presumed to be due to non-neutralization of sample, in appropriate decontamination and presence of non-tuberculous mycobacteria.<sup>11-13</sup>

Bronchoscopy for BAL requires special facilities, is invasive, is not accessible in many areas of resource-limited setting. Cost of the procedure, concern regarding infection control, inhibition of mycobacterial growth with the use of local anesthetics during bronchoscopy, sampling from only one portion of the lung are its

major drawbacks.<sup>12,14,15</sup> In a study by Mc Williams et al. the yield of SI (96.3%) was superior to that of BAL (51.9%) and the overall cost of BAL was three times that of performing SI.<sup>16</sup> They suggested to employ SI, followed by BAL only in patients who were negative on SI, but had radiologically active pulmonary TB. In a similar study, the yield of SI and BAL was 19% and 12% respectively, but the direct cost of bronchoscopy was 8 times more as compared to SI.<sup>16</sup>

In comparison with the above two procedures, SI has several advantages, which include less invasiveness, high diagnostic yield, greater patient comfort and safety, low-cost, no age restriction, no need of fasting, out-patient procedure, no need for expert for performance and less time consuming. Adequate sputum sample was obtained in 93-97% of patients in different studies.<sup>3,17</sup> The yield of sputum smear positivity varied between 26% and 38%.<sup>16-18</sup>

Patients with clinical and radiological evidence of pulmonary tuberculosis but negative sputum for AFB is called smear negative disease, this is a common problem and seen more commonly among children, female, elderly and immuno-compromised. The low rate of smear positivity in these persons may be explained by the fact that they have either minimal disease or without extensive cavitation. Smear negative patients have minimal and non-cavitary disease with low bacillary count as compared to smear positive patients with far advanced disease with heavy bacillary burdens.

Sputum induction by 3% hypertonic saline nebulisation has been found to improve bacteriological diagnosis and is a simple, cheap and safe method. In the present study sputum induction procedure with 3% saline was carried out in 50 cases and it was successful in 48 cases, other 2 cases were not able to expectorate even after induction. In K.B.Gupta<sup>17</sup> et al, 100 patients were subjected for sputum induction out of which 97 produced sputum (97%). In A.M.A. Shatal et al<sup>19</sup>, 30 patients were subjected for sputum induction out of which 29 produced sputum (97%). The results of present study are comparable to above studies. In present study 48 out of 50 (96%) were able to produce sputum after sputum induction.

To confirm the bacteriological diagnosis of the induced sputum, ZN staining was done in the present study. Sputum smear staining was done by Z-N technique for all 50 cases. In K. B. Gupta et al<sup>17</sup>, 100 cases were studied and 38% cases were positive by ZN staining after sputum induction. In MC Williams et al<sup>16</sup>, 50 cases were studied and 26% cases were positive by Z-N staining after sputum induction. In Hartung et al<sup>18</sup>, 50 cases were studied and 29% cases were positive by Z-N staining after sputum induction. In the present study, 50 cases were studied and 34% cases were positive by ZN staining after sputum induction.

Biswas et al<sup>2</sup> studied the role of induced sputum in the diagnosis of pulmonary TB in 100 patients. They found that ninety five patients could produce adequate sputum after sputum induction (SI). Sputum from thirty two patients were found to be positive both in smear and culture, conclude that SI provides significant yield in the diagnosis of pulmonary TB; thus, increasing the case detection rate of smear positive pulmonary TB. The results of present study are comparable to above studies. In present study 48 out of 50 (96%) were able to produce sputum after sputum induction & 17 out of 50 (34%) cases were positive by ZN staining after sputum induction.

Radiologically, 6 out of 30 cases (20%) in our study, who were positive for AFB on smear after induction showed non-cavitary lesions on chest X-ray, explaining the fact that patients with non-cavitary lesions have high probability of smear negativity before sputum induction. In K.B.Gupta<sup>17</sup> et al, 100 cases were studied and 39% had non-cavitary lesions on chest X-ray, who were positive for smear after induction.

Requirement of electricity-driven nebulizer and a room with negative pressure ventilation are major limitations for its routine use. Moreover, necessity of about 30 minute's time to complete one SI may not be practical in a high burden country like ours. Our study has few limitations. Mycobacterial culture was not done. Larger studies are needed to assess its utility in different settings.

## CONCLUSION

We concluded that the identification of smear positivity through sputum induction method with 3%hypertonic saline that allows early diagnosis, monitoring and optimization of treatment of pulmonary tuberculosis is one of the most ambitious goals in respiratory medicine. The induced sputum technique allows sampling of the airways in a noninvasive fashion and is a less expensive approach than the technique like bronchial biopsy, bronchoalveolar lavage and gastric lavage.

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