

Original research article

A Cross Sectional Analysis of Sputum Induction in Radiological Suspected Smear Negative Pulmonary Tuberculosis Patients

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Abstract

Background: Tuberculosis (TB) is a communicable disease that is a major cause of ill health and one of the leading causes of death worldwide. The advantage of making early diagnosis prevents morbidity, progression & spread of the disease and lung damage by fibrosis.

Aims and Objective: To assess the value of sputum induction (SI) as a diagnostic tool in patients with suspected pulmonary TB who has no or inadequate sputum or have a sputum smear negative for acid fast bacillus (AFB).

Material and Methods: A cross sectional study of total 90 adult patients who were radiological suspected tuberculosis, detected smear negative initially included. Detailed history of each participant was taken which consists for chief complains, past history of tuberculosis or ATT, family history with thorough Clinical examination. After sputum induction, sputum samples were sent for fluorescent microscopy for AFB examinations under NTEP.

Results: Out of 90 chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis, sputum of 56 (62.2%) patients were converted to positive for AFB after sputum induction with 3% NaCl. Out of 90 chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis, 65 the patients (72.2%) had ESR ≥ 60 mm/hr and 41 (45.6%) had infiltrative lesion in their chest x-ray. Majority of cases 80 (88.9%) had cough. Out of which, 50 (55.6%) cases became sputum smear positive after sputum induction and 30 (33.3%) cases remained sputum smear negative after sputum induction.

Conclusion: Sputum induction with 3% NaCl for detection of Acid Fast Bacilli is much more simple, easy, reliable, rapid and accurate diagnostic method in suspected cases of pulmonary tuberculosis who are sputum smear negative and chest x-ray suggestive of pulmonary tuberculosis.

Key Words: Sputum Induction, Pulmonary Tuberculosis, Chest X-ray, Smear negative.

Introduction

Tuberculosis (TB) is a communicable disease that is a major cause of ill health and one of the leading causes of death worldwide. Until the coronavirus (COVID-19) pandemic, TB was the leading cause of death from a single infectious agent, ranking above HIV/AIDS. Worldwide, an estimated 9.9 million people (95% UI: 8.9–11 million) fell ill with TB in 2020, equivalent to 127 cases (UI: 114–140) per 100 000 population.^[1] The number of TB deaths is unacceptably high. With a timely diagnosis and correct treatment, almost all people with TB can be cured. The World Health Organization (WHO) recommends the detection of acid-fast bacilli (AFB) in respiratory specimens as the initial approach to the diagnosis of Pulmonary Tuberculosis.^[2] However, this method has a low sensitivity and has little value in patients who cannot produce sputum spontaneously.^[3,4] Early diagnosis is imperative for early patient management and successful patient outcomes. False-negative results and misdiagnosis of TB suspects are common in developing nations, as most TB control programmes use Ziehl-Neelsen (ZN) smear microscopy and fluorescent microscopy, which has poor sensitivity and more than one visits are required that leads to higher default. Mycobacterial culture, although considered as the gold standard but is slow and usually takes 2-6 weeks to yield a final result and requires proper infrastructure and technical expertise. The benefit of making early diagnosis prevents morbidity, progression & spread of the disease and lung damage by fibrosis. Hence this study has been undertaken to evaluate the significance of induction of sputum in the diagnosis of Pulmonary Tuberculosis among patients who have chest X-ray suggestive but remain undiagnosed because of a negative sputum smear for AFB, hence aiding in the early diagnosis and thereby prompt & accurate treatment of such patients. Sputum will be induced with inducing agent delivered through ultrasonic nebulizer. The specimens will be examined by fluorescent microscopy. The objective of study was to assess the value of sputum induction (SI) as a diagnostic tool in patients with suspected pulmonary TB who has no or inadequate sputum or have a negative sputum smear for acid fast bacillus (AFB).

Material and Methods:

This cross sectional study was carried out after obtaining approval from institutional ethics committee in department of respiratory medicine of tertiary care hospital of Surat. .About 6% prevalence was identified in the pilot study carried out in respiratory department. From this prevalence, 90 sample size was calculated using $4pq/L^2$ formula. Total 90 chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis were purposively enrolled. All patients were informed in detail about study and written consent was taken from the patients who were willing to participate. Patients who were more than 18 years of age, suspected case of pulmonary TB who were sputum negative and chest x-ray suggestive of Koch's lesion were included in the study. Patients who were on antitubercular drugs, having Asthma/COPD, active haemoptysis were excluded from study. Data collection was done by using a structured pre-prepared case Performa to enter the patient details, detailed clinical history including presenting complaints, history of Tuberculosis, history of anti-tuberculosis medications, past and family history of tuberculosis, and physical examination of patients who meet the inclusion criteria. After sputum induction, sputum samples were sent for fluorescent microscopy for AFB examinations under RNTCP (now NTEP). Data entry was done in Microsoft Excel. Data analysis was done by applying appropriate statistical tests (descriptive analysis, chi-square test).

Results:

The data obtained from 90 cases of Sputum negative and Chest x-ray suggestive of Pulmonary Tuberculosis that presented to Department of Respiratory Medicine, Tertiary care centre (medical college) were analysed. As per table 1, out of 90 chest x-ray positive (sputum

negative) suspected cases of pulmonary tuberculosis, sputum of 56 (62.2%) patients were converted to positive for AFB after sputum induction with 3% NaCl and sputum of 34 (37.8%) patients remained negative even after sputum induction.

Table 1: Results of sputum smear microscopy for AFB after sputum induction with 3% NaCl in chest x-ray positive (sputum negative) suspected cases of pulmonary Tuberculosis

Sputum smear microscopy after SI with 3% NaCl	No. of patients	Percentage (%)
Sputum AFB positive	56	62.2%
Sputum AFB negative	34	37.8%
Total	90	100%

After sputum induction, out of 56 patients who became sputum positive, 40 (71.4%) patients had duration of symptoms ≥ 2 weeks and 16 (28.6%) cases had duration of symptoms < 2 weeks. After sputum induction, out of 34 patients who remained sputum negative, 24 (70.6%) patients had duration of symptoms ≥ 2 weeks and 10 (29.4%) cases had duration of symptoms < 2 weeks. After sputum induction, out of 56 patients who became sputum positive, 45 (80.4%) cases had no any past history of ATT, 6 (10.7%) cases had completed ATT in past and 5 (8.9%) cases had defaulted ATT in past. After sputum induction, out of 34 patients who remained sputum negative, 23 (67.6%) cases had no any past history of ATT, 3 (8.8%) cases had completed ATT in past and 8 (23.5%) cases had defaulted ATT in past.

Table 2: Duration of symptoms-wise distribution of chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis after sputum induction with 3% NaCl

Duration of symptoms	Sputum positive after sputum induction (n-56)	Sputum negative after sputum induction (n-34)	Total (n-90)	p value
< 2 weeks	16 (28.6%)	10 (29.4%)	26 (28.9%)	0.80
2 – 4 weeks	20 (35.7%)	10 (29.4%)	30 (33.3%)	
> 4 weeks	20 (35.7%)	14 (41.2%)	34 (37.8%)	

Table 3: Past history of ATT-wise distribution of chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis after sputum induction with 3% NaCl

Past history of ATT	Sputum positive after sputum induction (n-56)	Sputum negative after sputum induction (n-34)	Total (n-90)	p value
No	45 (80.4%)	23 (67.6%)	68 (75.6%)	0.16
ATT completed	6 (10.7%)	3 (8.8%)	9 (10.0%)	
ATT defaulter	5 (8.9%)	8 (23.5%)	13 (14.4%)	

After sputum induction, Out of 56 patients who became sputum positive, 39 (69.6%) patients had ESR ≥ 60 mm/hr and 17 (30.4%) patients had ESR < 60 mm/hr. Out of 34 patients who remained sputum negative after sputum induction, 26 (76.5%) patients had ESR ≥ 60 mm/hr and 8 (23.5%) patients had ESR < 60 mm/hr.

Table 4: Laboratory parameter wise distribution of chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis after sputum induction with 3% NaCl

Lab parameter	Sputum positive after sputum induction (n-56)	Sputum negative after sputum induction (n-34)	Total (n-90)	p value
ESR (mm/hr)				
< 60	17 (30.4%)	8 (23.5%)	25 (27.8%)	0.48
> = 60	39 (69.6%)	26 (76.5%)	65 (72.2%)	
RBS (mg/dL)				
≤ 140	51 (91.1%)	31 (91.2%)	82 (91.1%)	0.98
> 140	5 (8.9%)	3 (8.8%)	8 (8.9%)	

Cough was the most common clinical feature in chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis. Out of 90 patients, 80 patients had problem of coughing. Out of those 80 patients, 50 (55.6%) cases became sputum positive after sputum induction and 30 (33.3%) cases remained sputum negative even after sputum induction. In present study most of the patients had duration of symptoms more than & equal to 2 weeks. Out of 90 patients, 64 patients had duration of symptoms ≥ 2 weeks. Out of those 64 patients, 40 (44.4%) cases became sputum positive after sputum induction and 24 (26.9%) cases remained sputum negative even after sputum induction. Out of total 90 cases, 10 cases were HIV reactive and 80 cases were HIV non-reactive. After sputum induction, Out of those 10 HIV reactive cases, 8 (8.9%) cases became sputum positive and 2 (2.2%) remained sputum negative. After sputum induction, out of 80 HIV non-reactive cases, 48 (53.3%) cases became sputum positive and 32 (35.6%) cases remained sputum negative. Out of 90 patients 8 cases had RBS > 140 mg/dl who diagnosed as diabetics according to FBS and 82 cases had RBS \leq 140 mg/dl. After sputum induction, out of those 8 cases with RBS > 140 mg/dl, 5 (5.6%) cases became sputum positive and 3 (3.3%) cases remained sputum negative. After sputum induction, out of those 82 cases with RBS \leq 140 mg/dl, 51 (56.7%) cases became sputum positive and 31 (34.4%) cases remained sputum negative. In present study, infiltrative lesion in chest x-ray was the most common lesion in chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis. Out of 90 patients, 41 patients had infiltrative lesion in their chest x-ray. Out of those 41 patients, 31 (34.4%) cases became sputum positive after sputum induction and 10 cases (11.1%) remained sputum negative even after sputum induction. Out of 90 patients, 10 cases had cavitary lesion in their chest x-ray. Out of those 10 cases, 6 (6.7%) became sputum positive and 4 (4.4%) cases remained sputum negative after sputum induction. Out of 90 patients, 8 cases had bilateral extensive lesion in their chest x-ray. Out of those 8 cases, 5 (5.6%) became sputum positive and 3 (3.3%) cases remained sputum negative after sputum induction. Out of 90 patients, 16 cases had bilateral fibrosis, bronchiectasis & calcified lesion in their chest x-ray. Out of those 16 cases, 5 (5.6%) became sputum positive and 11 (12.2%) cases remained sputum negative after sputum induction. Out of 90 patients, 15 cases had combination of above lesions in their chest x-ray. Out of those 15 cases, 9 (10%) became sputum positive and 6 (6.7%) cases remained sputum negative after sputum induction. In present study, lower zone involvement in chest x-ray was most commonly seen in chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis. Out of 90 patients, 39 patients had lower zone involvement in their chest x-ray. Out of those 39 patients, 29 (32.2%) cases became sputum positive after sputum induction and 10 (11.1%) cases remained sputum negative even after sputum induction. Out of 90 patients, 11 patients had upper zone involvement in their chest x-ray. Out of those 11 patients, 6 (6.7%) cases became sputum positive after sputum induction and 5 (5.6%) cases remained sputum negative even after

sputum induction. Out of 90 patients, 10 patients had middle zone involvement in their chest x-ray. Out of those 10 patients, 3 (3.3%) cases became sputum positive after sputum induction and 7 (7.8%) cases remained sputum negative even after sputum induction. Out of 90 patients, 30 patients had multiple zones including bilateral involvement in their chest x-ray. Out of those 30 patients, 18 (20%) cases became sputum positive after sputum induction and 12 (13.3%) cases remained sputum negative even after sputum induction. The procedure was found safe as there was no adverse effect during and immediately after procedure.

Table 5: HIV, & chest x-ray findings in chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis after sputum induction with 3% NaCl

Chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis (n = 90)		After sputum induction with 3% NaCl		Total (n=90)	p value
		Sputum AFB positive (n - 56)	Sputum AFB negative (n - 34)		
HIV	Reactive	8 (14.3%)	2 (5.9%)	10(11.1%)	0.37
	Non-reactive	48 (85.7%)	32 (94.1%)	80(88.9%)	
Chest X-Ray (Zone involvement)	Upper zone	6 (10.7%)	5 (14.7%)	11(12.2%)	0.81
	Middle zone	3 (5.4%)	7 (20.6%)	10(11.1%)	0.04
	Lower zone	29 (51.8%)	10 (29.4%)	39(43.3%)	0.04
	Multiple zones including B/L involvement	18 (32.1%)	12 (35.3%)	30(33.3%)	0.81
Chest X-Ray (Type of Lesion)	Infiltrative lesion	31 (55.4%)	10 (29.4%)	41(45.6%)	0.03
	Cavitary lesion	6 (10.7%)	4 (11.8%)	10 (11.1%)	0.85
	B/L extensive lesion	5 (8.9%)	3 (8.8%)	8 (8.9%)	0.71
	Fibrosis, Bronchiectasis & calcified lesion	5 (8.9%)	11 (32.4%)	16 (17.8%)	0.008
	Combination of above lesions	9 (16.1%)	6 (17.6%)	15 (16.7%)	0.92

Discussion:

Total 90 chest x-ray positive (sputum negative) suspected cases of pulmonary tuberculosis were subjected to sputum induction with 3% NaCl. Induced sputum samples of those 90 patients were processed to sputum smear microscopy for Acid Fast Bacilli. In study by Biswas et al.; 100 cases were studied and 32% cases were positive by Z-N staining after sputum induction.^[5] In study by MC Williams et al.; 50 cases were studied and 26% cases were positive by Z-N staining after sputum induction.^[6] In study by Nageswar Rao Gopathi et al.; 120 cases were studied and 63.3% cases were positive by sputum smear microscopy after sputum induction.^[7] A study carried out in South Africa by Hartung TK et al. found 29% positivity rate after sputum induction.^[8] A study by Gupta KB et al. found 38% positivity rate after sputum induction. In the present study, 90 cases were studied and 62.22% cases were positive after sputum induction. Our result was comparable with Nageswar Rao, Gopathi et al.^[9] Erythrocyte sedimentation rate was high in 49.9% of patients in study of Muhammad Atiqur-

Rehman et al 2009 and ESR was also high in present study in 72.22% patients.^[10] In present study, Mantoux test was positive in 66.17% patients which is comparable with the study by Muhammad Atiqur-Rehman et al 2009 in which MT was positive in 59.14% patients. Most common symptoms presented by patients in present study were cough and fever comparable with studies Muhammad Atiqur-Rehman et al 2009 and Bagheri KH et al 2015 in which cough and fever were also the most common symptoms.^[10]

Conclusion:

Sputum induction with 3% NaCl for detection of Acid Fast Bacilli is much more reliable, rapid and accurate diagnostic method in suspected cases of pulmonary tuberculosis who are sputum smear negative and chest x-ray suggestive of pulmonary tuberculosis. Sputum induction is a safe, cheap, and effective procedure for microbiological confirmation of diagnosis of pulmonary tuberculosis in patients who produce no/inadequate sputum or are sputum smear negative. Sputum induction should be incorporated in national program at least in selected groups.

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