

# Comparison of Diagnostic Yield of AFB with Sputum Induction to Spontaneous Sputum Examination in Suspected Pulmonary Tuberculosis

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## ABSTRACT

**Objective:** To compare the diagnostic yield of AFB positivity with sputum induction to spontaneous sputum examination in suspected cases of pulmonary tuberculosis.

**Study Design:** Comparative study.

**Place and Duration of Study:** Military Hospital, Rawalpindi, from January to December 2006.

**Methodology:** Sputum specimens were collected by both techniques from 164 patients with clinical and radiological suspicion of pulmonary tuberculosis admitted in medical wards. All specimens were examined for AFB smear and culture positivity. Sputum induction was done for 15-20 minutes with 3% sterile hypertonic saline solution by nebulization in all cases. Proportions were compared using Chi-square test.

**Results:** Among 164 patients, 32 patients (19.5%) were not expectorating spontaneously. Sputum induction was successful in 22 (68.75%) cases and AFB smear was positive in 03 (9.37%) and AFB culture was positive in 7 (21.8%) of these cases. One hundred and thirty two (80.5%) patients were already expectorating and both Day-1 (spontaneous) and Day-2 (induced) sputum samples were available. Day-1 (spontaneous) sputum specimens revealed AFB smear positive results in 20 (15.15%) patients, and AFB culture positive results in 24 (18.18%) patients. Smear positivity on Day-2 (induced) sputum samples was 21.21% (28) with 27.27% (36) culture positivity.

**Conclusion:** In expectorating patients, AFB smear and culture positivity results remain comparable with spontaneous and induced sputum sampling. Sputum induction improves the diagnostic yield for AFB in patients unable to expectorate adequate sputum sample.

**Key words:** Pulmonary tuberculosis. Sputum induction. Spontaneous expectoration. Smear. Acid fast bacillus.

## INTRODUCTION

Worldwide, 1.7 million people die of tuberculosis.<sup>1</sup> It has long been declared a global emergency with an alarming rise by one percent each year.<sup>2,3</sup> In 2003, the global TB case-detection rate was only 45%, falling short of the global target of 75%.<sup>4</sup> Goal six of the Millennium Development Goals of the United Nations includes the halting and reversal of the rising incidence of tuberculosis and the Stop TB Partnership aims to halve the prevalence of tuberculosis and resulting deaths by 2015.<sup>5</sup> Existing strategies lack the important steps of early tuberculosis detection and timely identification of multidrug-resistant tuberculosis.<sup>6</sup> Due to meagre progress in diagnostics of pulmonary tuber-

culosis (PTB), microbiological detection remains the Gold standard.

Sputum smear examination for AFB has low diagnostic yield in PTB and even in culture positive sputum specimens, only 60% are smear positive.<sup>7</sup> Sputum Induction (SI) is a safe procedure with a high diagnostic yield and a high agreement with results of bronchoscopy for the diagnosis of PTB in patients with and without HIV.<sup>8</sup> SI has also provided superior yield to gastric lavage and has lower risk of nosocomial TB transmission,<sup>7</sup> and at much lower costs.<sup>9</sup> Patient tolerability and safety are excellent and the procedure is feasible in developing country settings, even for young children.<sup>10-12</sup>

As fiberoptic bronchoscopy is not widely available in local hospitals, therefore, the aim of this study was to compare the diagnostic yield of AFB positivity of sputum induction with spontaneous sputum examination in suspected cases of PTB.

## METHODOLOGY

In this comparative study, 164 patients with suspected pulmonary tuberculosis were admitted in medical wards of Military Hospital, Rawalpindi, from January to

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December 2006. Only adults (age 15-54 years) with strong clinical and radiological suspicion of PTB were included. Presence of fever (more than 99.5°F), cough (dry or productive) and weight loss (more than two kgs); all for at least four weeks were considered as strong clinical features suggestive of PTB. While presence of anyone radiological lesion (consolidation or soft nodule striae or patchy fluffy shadowing, or non-calcified opacities with an indistinct border or a cavitary lesion in any lung zone; or a miliary pattern) were taken as potentially active. Exclusion criteria were past history of treated pulmonary tuberculosis; patients already on anti-TB drugs, patients with orthopnea, established diagnosis of severe bronchial asthma or COPD, patients with pleural effusion or radiologically inactive disease (like fibroptic lesions or calcified opacities). Informed consent was taken from all patients.

All patients were briefed regarding the correct technique for sputum specimen collection and technique/utilization of sputum induction for sputum production. Two sputum samples were collected from each patient at 24 hours interval in an isolated, well-ventilated side room. Samples were labelled as Sputum Sample 1 (SS-1) and Sputum Sample 2 (SS-2). SS-1 was spontaneously produced sputum sample collected on day-1 from all expectorating patients. SS-2 was collected in sitting or semi recumbent position after 15-20 minutes of nebulization with 15 ml of 3% hypertonic saline on day 2. An ECONOneb Medix Nebulizer (made by MEDIX Ltd of England) was used for nebulizing all patients and sterile sputum collection jars were used for sputum sample collection. In case, no sputum was produced, sputum induction was repeated only once with same technique. The sample was determined to be adequate if at least 5 ml of sputum was collected.

All patients were kept nil per mouth for at least four hours and gums, teeth and tongue were cleaned with a clean soft toothbrush dipped in 0.9% saline before sputum sample collection. Patients were instructed to cough voluntarily if spontaneous coughing did not occur. All SS-1 and SS-2 were immediately transported to the laboratory in the sterile sputum jars to avoid any possible contamination and drying of specimen. All of above sputum samples were subjected to direct smear examination for AFB after Ziehl-Nelson staining and were cultured for Mycobacteria on Lowenstein Jensen medium at 37°C for eight weeks. Demographic and clinical information was collected. Current and previous chest radiographs (where available) were reviewed. ESR and Mantoux test was performed in all cases, while HIV testing was not done.

A consultant radiologist evaluated all chest radiographs without access to other information and lung parenchymal abnormalities were classified into "inactive" or "potentially active", as mentioned above. A consultant microbiologist assessed smear positivity on ZN staining

as well as culture results on LJ medium as per standard laboratory procedures.

Each patient's data was recorded in a preformed proforma. Population data were expressed as means with standard deviations, or medians with ranges as appropriate. Comparisons of proportions like sputum smear positivity in SS-1 versus sputum smear positivity in SS-2 was analyzed by Chi-square test. A p-value of <0.05 was regarded as significant.

## RESULTS

One hundred and sixty four patients were studied, with a mean age of 34.30 ± 9.44 years. Ninety two (56%) patients were from 21-30 years age group. Two-third of cases (124) were males with mean age of 33.34 ± 9.24 years, while mean age for female cases was 37.27 ± 9.54 years. History of exposure to or close contact with a tuberculosis patient was present in about 35% cases (n=58). The common presenting clinical features were fever, weight loss and cough in all. Other common clinical features were night sweats (85.3%), production (73.1%), and crepitations on chest auscultation (68.29%). Eighty nine (54%) patients had ESR of 30-50 mm fall at the end of 1st hour. ESR was more than 50 mm fall at the end of first hour in 67 (40.8%) patients, while 15 (9.1%) patients had ESR above 100 mm after first hour. Mantoux test was positive (>15 mm) in 97 cases (59.14%) and negative in others.

Majority of patients (n=132, 80.48%) were producing adequate sputum sample, while about one-fifth (n=32, 19.5%) were unable to expectorate an adequate sputum sample. In patients with adequate sputum production (132), SS-1 smear positivity was 15.15% (20) which improved to 21.21% (28) in SS-2 group (sputum induction group), however, the difference was not statistically significant. Eighteen cases of SS-1 were also smear positive on sputum induction but SS-2 yielded 10 cases that were smear negative on SS-1 sample. All smear positive cases in SS-1 were also culture positive with an overall culture positivity of 18.18% (24), which was 27.27% (36) in SS-2 samples;

**Table I:** Comparison of sputum smear positivity in spontaneous and induced sputum samples.

	AFB smear positive	AFB smear negative	Total patients
Spontaneous Sputum Sample (SS 1)	20 (15.15%)	112 (84.85%)	132
Induced Sputum Sample (SS 2)	28 (21.21%)	104 (78.79%)	132
			p = 0.264

**Table II:** Comparison of sputum culture positivity in spontaneous and induced sputum samples.

	AFB culture positive	AFB culture negative	Total patients
Spontaneous Sputum Sample (SS 1)	24 (18.18%)	108 (81.82%)	132
Induced Sputum Sample (SS 2)	36 (27.27%)	96 (72.73%)	132
			p = 0.079

however, the difference was not statistically significant. Here again, 16 (12.12%) patients who were smear negative in SS-1 were culture positive on SS-2 specimens. Results of bacteriological analysis of spontaneous and induced sputum samples are depicted in Table I and II.

Sputum induction yielded an adequate sputum sample for bacteriological analysis in 22 (68.75%) non-expectorating cases. All smear positive cases were also AFB culture positive on LJ medium; out of which 3 were AFB smear and 7 were AFB culture positive.

## DISCUSSION

Sputum smear and culture for AFB not only remains the Gold standard for diagnosis of pulmonary tuberculosis but also crucial for drug sensitivity testing and to gauge the microbiological conversion during antimycobacterial therapy. However, its sensitivity in different studies varies from 33-75%.<sup>13-16</sup> The local data documents a yield of 10-22% for smear positivity in active pulmonary tuberculosis in adults.<sup>17-18</sup> In the present study, the overall diagnostic yield of smear positivity in suspected PTB cases with spontaneous sputum production was 15.15% that improved to 21.21% with sputum induction. Although, difference is more than 5% but is not statistically significant, which is in conformity to a study by Fishman *et al.*<sup>19</sup> Culture positivity with spontaneous sputum samples were 18.18%, which improved to 27.27% with sputum induction. These results are comparable to other local studies as regards sputum smear AFB positivity but are much lower in yield as compared to international studies on the subject. The probable reasons are probably multifactorial. It includes poor understanding of patient population for adequate sputum sample, transport/laboratory issues, etc. In patients without spontaneous sputum production, sputum induction yielded adequate sputum sample in 68.75% cases, which was relatively low as comparable to 90% yield of adequate sample acquisition in a study carried out by Parry *et al.*<sup>20</sup> In the non-expectorating group, AFB smear and culture positivity was 9.37% and 21.87% respectively, which was again low as compared to an absolute increase of AFB smear positivity by 19% found by Parry *et al.*<sup>20</sup> This difference may signify ethnic differences in response to sputum induction or may be due to technical reasons as in the present study only single sputum induction was done in each case as compared to 2-3 inductions in other studies.<sup>20</sup> However, sputum induction can obviate the need for fiberoptic bronchoscopy which has comparable positive yield,<sup>8</sup> while another study has shown that three induced sputum testings is more sensitive than bronchoscopy for detecting active pulmonary TB in subjects whose spontaneous sputum is smear negative or who cannot produce spontaneous sputum.<sup>21</sup> In a study by Conde, *et al.* on sputum induction in pleural tuberculosis, the

yield of AFB smear was 11-15% and AFB culture positivity was 45-54% depending upon presence or absence of parenchymal radiological lesions.<sup>22</sup> Other studies also correlated induced sputum positivity yield with presence of radiographic appearances.<sup>21</sup>

Majority of the patients under study tolerated the procedure well; however, 21 (15.90%) had repeated cough with 5 cases developed bronchospasm requiring salbutamol nebulizations. Nineteen selected patients complained of nausea, which settled without any specific therapy. Though hypertonic saline can cause bronchospasm, its use has been validated even in patients with asthma,<sup>23</sup> however, prophylactic nebulized salbutamol reduces the incidence of untoward bronchospasm in moderate to severe bronchial asthma.<sup>24</sup>

Sputum induction is also being used as a research tool to assess response of therapy on neutrophilic inflammation in COPD patients and is considered safe provided European Respiratory Society Sputum Induction Task Group Safety Protocol is adhered to.<sup>25,26</sup> Recently, American College of Chest Physicians has recommended sputum induction for investigation of patients with chronic cough to confirm the diagnosis of nonasthmatic eosinophilic bronchitis;<sup>27</sup> as patients with sputum eosinophilia exhibit objective response to corticosteroids.<sup>25</sup> There is emerging evidence that induced sputum may be a valuable tool to quantify environmental exposure to carbonaceous particulates, mold, and pollen; recognize exposure in occupational lung diseases; enumerate intracellular bacteria; and identify hemosiderin-laden macrophages in subjects with left ventricular failure.<sup>25</sup>

## CONCLUSION

Sputum induction is a safe, simple and valuable procedure to obtain adequate sputum samples in suspected cases of pulmonary tuberculosis and can obviate the need for much sophisticated and invasive procedures like bronchoscopy. In expectorating patients, AFB smear and culture positivity results remain comparable with spontaneous and induced sputum sampling. Sputum induction improves the diagnostic yield for AFB in patients unable to expectorate adequate sputum sample.

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