

## Original Article



# Diagnostic Value of Bronchoalveolar Lavage Examination in Sputum Negative Patients for AFB in Suspected Pulmonary Tuberculosis

Safayet Ahammed<sup>1</sup>, Mohammed Sana Ullah Sarker<sup>2</sup>, Md. Zulfikar Ali<sup>3</sup>

### Abstract

**Background:** Pulmonary tuberculosis (PTB) is one of the most common infections worldwide, more commonly among the developing countries like Bangladesh. So its early detection and prompt treatment was a challenge and the burden of diagnostic challenge was higher if the patients smear negative for Acid Fast Bacilli (AFB). **Objective:** Evaluate the diagnostic value of Bronchoalveolar lavage (BAL) for diagnosis of suspected Pulmonary Tuberculosis (PTB) whose sputum for AFB smear neagtive. **Materials and Methods:** A cross-sectional observational reserach was undertaken where 50 patients were included on the basis of specific inclusion and exclusion criteria. All patients who had negative smear for AFB but highly suspected for PTB underwent fiberoptic bronchoscopy to collect Bronchoalveolar lavage (BAL) fluid for diagnostic testing in the form of BAL for AFB and mycobacterial culture in Lowenstein Jensen medium. **Results:** The Male predominacy 29 (58%) was observevd among the smear negative PTB patients. Clinically more than seventy percent (72%) presents with fever then cough with sputum and haemoptysis 62% and 32% respectively. Radiological cavitation 33 (66%) was the most common x-ray findings. After analysis of BAL for AFB about 31 (62%) patient found positive and on culture about mycobacterial growth found in 29 (58%) patients. **Conclusion:** Bronchoalveolar lavage had a superior diagnostic value in patients with smear negative suspected pulmonary tuberculosis.

**Key words:** Pulmonary Tuberculosis, Sputum, Bronchoalveolar Lavage, Acid Fast Bacilli.

**Date of received:** 11.02.2021

**Date of acceptance:** 20.05.2021

**DOI:** <https://doi.org/10.3329/kyamcj.v12i2.55440>

**KYAMC Journal.2021;12(02): 84-87.**

### Introduction

In developing countries like Bangladesh, Tuberculosis (TB) is considered as one of the most common infections. India has more new TB cases annually than any other country of the world.<sup>1</sup> According to World Health Organization (WHO), the initial approach to the diagnosis of Pulmonary Tuberculosis (PTB) is the detection of Acid-Fast Bacilli (AFB) in respiratory specimens.<sup>2</sup> But unfortunately some patients who cannot produce sputum spontaneously, this method has a low sensitivity and has little diagnostic value.<sup>3,4</sup> One of the most effective TB control strategies is to reduce the period of infectivity by early detection of cases in a suspected PTB patients. Among the diagnosed PTB patients, only 20- 40% of were smear positive, while next bulk percentage of the patients either smear negative

or had sputum-scarce disease.<sup>5,6</sup> In a patients with suspected PTB, bronchoscopy with Bronchoalveolar Lavage (BAL) is routinely performed in case of sputum negative smears.<sup>7,8</sup> The Bronchoalveolar lavage is sent in the microbiological laboratories to detect Acid Fast Bacilli (AFB) by Zeihl-Nelson (ZN stain) stain and mycobacterial cultures, though the sensitivity of it remains low (41%) and mycobacterial cultures, considered as the gold standard (with 86% sensitivity) but they are expensive and results take 6 - 8 weeks for diagnosis.<sup>9</sup> According to Chang C et. al 2013 the decision for initiating Anti-TB treatment based on epidemiology, clinical/radiographic findings and the results of acid-fast bacilli (AFB) stained sputum.<sup>6</sup> Another cause that included why the incidence of tuberculosis has been increasing day by day in developing countries due to HIV infections and

1. Assistant Professor, Respiratory Medicine, Khwaja Yunus Ali Medical College and Hospital, Enayetpur, Sirajganj, Bangladesh.

2. Specialist , Respiratory Medicine, Square Hospital, Dhaka.

3. Professor, Internal Medicine, Khwaja Yunus Ali Medical College and Hospital, Enayetpur, Sirajganj, Bangladesh.

**Correspondence:** Dr.Safayet Ahammed, Assistant Professor, Respiratory Medicine, Khwaja Yunus Ali Medical College and Hospital, Enayetpur, Sirajganj, Bangladesh. Cell: 01715-202855, E-mail: doc.safayet@gmail.com

also a high rate of mortality ranging from 50-80% in untreated positive smear patients.<sup>10</sup> Routinely laboratory diagnosis of PTB was done by detection of TB bacillum in morning sputum sample but sometimes if patients unable to produce sputum or had negative sputum sample with a high susceptibility of TB, sputum specimen can be achieved via induced-sputum method or bronchoalveolar lavage technique.<sup>11</sup> As a easily accessible tools for diagnosis of PTB is sputum for AFB staining, however, it is not specific for pulmonary TB.<sup>12</sup> A bulk of smear negative patients were suffering from delayed diagnosis that ultimately leads to their increased mortality and morbidity. The use of BAL to diagnose PTB in smear negative patients helped to manage the suspected patients earlier due to its rapid detection and thus reduced mortality and morbidity.<sup>13</sup> Detection of AFB in Broncho Alveolar Lavage (BAL) microscopy in PTB had variable sensitivity that ranging from 50 to 80% for three consecutive specimens. However, in patients with smear-negative PTB, about 48 to 80% specific results yield through Broncho Alveolar Lavage (BAL) MTB-specific DNA amplification.<sup>14</sup> So, the present research aimed to evaluate the diagnostic value of Broncho Alveolar Lavage (BAL) for diagnosis of suspected Pulmonary Tuberculosis (PTB) whose sputum for AFB smear negative.

## Materials and Methods

A cross-sectional analytical research was conducted at the Department of Respiratory Medicine, Khawja Yunus Ali Medical College (KYAMC) from January to December, 2020 after getting ethical clearance from Ethical Review Board (ERB) of Khawja Yunus Ali Medical College, Sirajgagnj, Bangladesh. An informed written consent was taken from all the patients who participated voluntarily. The WHO sample size calculator was used where the sensitivity of the Expert assay for Bronchoalveolar Lavage (BAL) fluid for the diagnosis of PTB as 81.6% and mycobacterial cultures having sensitivity of 86%.<sup>15,16</sup> With the help of sensitivity calculator and an absolute precision of 0.08, the sample size was determined as 43. Although, in this research a total of 50 patients were enrolled on the basis of specific inclusion and exclusion criteria.

Suspected PTB cases who had negative sputum sample or were unable to produce sputum and were subjected for bronchoscopy were included. The diagnostic yield was measured on the basis of frequency and validity by calculating sensitivity, specificity, positive and negative predictive values. A PTB suspected patients was diagnosed on the basis of clinical and radiological features compatible with a diagnosis of pulmonary tuberculosis.<sup>17</sup>

If three consecutive early morning sputum samples did not reveal acid fast bacilli when examined by microscopy with Zeihl Nelson stain then it was considered as sputum negative case. A confirmed case of pulmonary tuberculosis was one in whom *Mycobacterium tuberculosis* (MTB) grew on BAL mycobacterial cultures by Lowenstein Jensen (LJ) medium, that was taken as the gold standard.

Total 50 patients of either gender aged above 20 years of age were admitted with clinical and radiological evidence of PTB

but were smear-negative on both occasions (morning and spot) included in the research. These patients presented with a wide variety of symptoms including cough, expectoration, fever with evening rise of temperature, haemoptysis, dyspnoea and chest pain. Radiologically, patients were categorised into those with cavitary or non-cavitary lesions. Smear positive cases, patients with disseminated or extra pulmonary tuberculosis, HIV positive and immunocompromised patients were excluded from the research. After written consent for bronchoscopy, demographic and clinical data were collected.

All patients were in a fasting state for at least four hours prior to bronchoscopy and pre-medicated 30 to 45 minutes before the procedure. Pre- medication was done with intra-muscular injection of atropine 0.6mg and 10mg of diazepam administered orally. About 4% xylocaine was used as local anaesthesia to upper respiratory tract through a nebuliser, just before the procedure. A thorough examination of the bronchial tree was carried out. The bronchoscope was then introduced into the segmental and sub-segmental bronchi and BAL was taken from the involved area. For BAL fluid, sterilised buffered normal saline at body temperature was used; 20mL of this was instilled through the bronchoscope and promptly aspirated using low pressure suction. Total of 8-10 aliquotes (150-200 mL) were instilled. Then lavage fluid was collected into a non-siliconised sterilised container. All samples BAL fluid was examined for AFB by Ziehl-Neelsen (Z-N) staining and was cultured for *Mycobacterium tuberculosis* on Lowenstein Jensen (L-J) medium in hospital and results were available after 3 days and 6 weeks respectively.

SPSS version 22 was used for statistical analyses. Demographic features including age, gender, clinical and radiological features, past history of tuberculosis were recorded. The AFB smear and mycobacterial cultures was calculated by percentages and frequencies.

## Results

In the current research, the age of the patients was  $36.56 \pm 12.05$  yrs. More than half (58%) of the patients were male and rest were female. The most common presenting features was fever (72%), next common was cough with sputum (62%) and haemoptysis found in fewer number of patients. Radiological features compatible with the diagnosis of pulmonary tuberculosis were encountered in the form of cavitation and non-cavitation and here a higher percentage of patients had cavitary lesions (62%) in their chest X-rays. (Table I)

Out of 50 patients who had sputum smear negative, about two-thirds (66%) had positive for AFB in their bronchoalveolar lavage and rest were negative (34%). The mycobacterial cultures also showed that more than half (58%) had positive growth on Lowenstein Jensen media and rest were negative (42%). (Table II)

**Table I:** Demographic features of the patients (n= 50)

Demographic characteristic		
Age		20-65yrs
	Mean±SD	36.56±12.05yrs
Gender	Male	29 (58%)
	Female	21 (42%)
Presenting complaints	Cough (sputum)	31 (62%)
	Fever	36(72%)
	Haemoptysis	16( 32%)
Radiological findings	Cavitatory	31 (62%)
	Non - Cavitatory	19 (38%)

n: Total number of patients

**Table II:** Analyses of bronchoalveolar lavage for AFB by Z-N staining and mycobacterial cultures on L-J medium (n= 50)

Acid Fast Bacilli	Bronchoalveolar Lavage (BAL)
Positive	33 (66%)
Negative	17 (34%)
Mycobacterial culture on-LJ medium	
Positive	29 (58%)
Negative	21 (42%)

n: Total number of patients

## Discussion

In this cross-sectional analytical research, the bronchoalveolar lavage of total 50 patients were analyzed for detecting AFB whose smear negative found previously. While analyzing the demographic characteristics of 50 patients, the age ranging from 20-65yrs with a mean of 36.56±12.05yrs. In the current research a male predominance was observed. Patients of suspected PTB presents with a variety of symptoms, among those most common features was fever (72%), cough with sputum (62%) and haemoptysis found in fewer number. In chest x-ray, radiologically a large number of patients had cavitation and non-cavitation. The clinical signs and radiologic findings are not sensitive enough for diagnosis of pulmonary tuberculosis and Schoch et. al (2007) showed that accuracy of bronchoscopy is more than induced sputum technique for diagnosis of PTB.<sup>18</sup> In a research conducted by Fadaii A, Sohrabpoor H and Bagheri B (2009) claimed that chest X-ray in patients suspected of PTB was a helpful but not recommended as diagnostic method, though lung CT-scan had more sensitivity but not specific for diagnosis.<sup>10</sup>

After collecting bronchoalveolar lavage, sent to the laboratory for microbiological test and among 50 patients who were detected sputum smear negative on previously but highly suspected for PTB. More than half (66%) had positive for AFB in their bronchoalveolar lavage and rest were negative (34%). The mycobacterial cultures also showed that more than half (58%) had positive growth on Lowenstein Jensen media and rest were negative (42%). Khalil & Butt (2013) claimed in their research that mycobacterial cultures for detection of Mycobacterium tuberculosis in Lowenstein Jensen media was highly specific but expensive, laborious, requires trained personnel, not widely available and takes 6 - 8 weeks to give the results.<sup>13</sup> A similar research concluded that sputum AFB staining as a the most

readily accessible tools for evaluating patients of suspected pulmonary TB; however, not specific for pulmonary TB, so in that research they found about a higher percentage of patients had positive AFB in BAL as well as mycobacterial culture.<sup>6</sup> According to Khalil and Butt (2013) the frequency of positive mycobacterial cultures was 85 (91.4%) and the total sensitivity, specificity, positive predictive value and negative predictive values of BAL gene Expert to detect Mycobacterium tuberculosis were 91.86%, 71.42%, 97.53% and 41.66% respectively.<sup>13</sup>

### The following limitations can not be avoided during conduction of the current research:

1. Single centred research.
2. Sample size was small and selection of sample based on purposive sampling techniques.
3. Due Covid 19 pandemic, a research with a larger sample size was not possible.

## Conclusion

Bronchoalveolar lavage had a superior diagnostic value in -patients with smear negative pulmonary tuberculosis. So it is highly recommended for patients that are suspected for PTB with a sputum smear negative.

## Acknowledgement

Thankful to all the patients and laboratory staff of Khwaja Yunus Ali Medical College & Hospital, Enayetpur, Sirajganj, Bangladesh.

## References

1. TB INDIA 2012 – ANNUAL STATUS REPORT/ [tbcindia.nic.in/pdfs/ TBndia2012-AnnualReport](http://tbcindia.nic.in/pdfs/TBndia2012-AnnualReport).
2. World Health Organization. Treatment of tuberculosis: guidelines for national programs. Geneva: World Health Organization; 1993.
3. Murray PR, Elmore C, Krogstad DJ. The acid-fast stain: a specific and predictive test for mycobacterial disease. *Ann Intern Med* 1980;92:512–513.
4. Strumpf IJ, Tsang AY, Sayre JW. Re-evaluation of sputum staining for the diagnosis of pulmonary tuberculosis. *Am Rev Respir Dis* 1979;119:599–602.
5. Desta K, Asrat D, Lemma E, Gebeyehu M, Feleke B. Prevalence of smear-negative pulmonary tuberculosis among patients visiting St. Peter's Tuberculosis Specialized Hospital, Addis Ababa, Ethiopia. *Ethiop Med J* 2009; 47:17-24.
6. Chang C, Hong J, Yuan M, Chang M, Lee Y, Chang S, et al. Risk factors in patients with AFB smear-positive sputum who receive inappropriate antituberculous treatment. *Drug Des Devel Ther* 2013; 7:53-58.

7. Theron G, Peter J, Meldau R, Khalfey H, Gina P, Matinyena B, et al. Accuracy and impact of Xpert MTB/RIF for the diagnosis of smear-negative or sputum-scarce tuberculosis using bronchoalveolar lavage fluid. *Thorax* 2013; 68:1043-1051.
8. Kheawon N, Chuang-Ngam S, Mitsoongneun S, Peam-Am J, Visalsawadi J. Role of routine bronchial washing culture for TB in Maharat Nakhon Ratchasima Hospital, Thailand. *J Med Assoc Thai* 2013; 96:558-563.
9. Saglam L, Akgun M, Aktas E. Usefulness of induced sputum and fiberoptic bronchoscopy specimens in the diagnosis of pulmonary tuberculosis. *J Int Med Res* 2005; 33:260-265.
10. Abbas F, Hamid S, Bahadar B. Comparison between induced-sputum and bronchoalveolar lavage fluid in diagnosis of pulmonary tuberculosis. *Iranian J of Cl Infectious Diseases*, 2009; 4(3): 167-170.
11. Li LM, Yang HL, Xiao CF. Sputum induction to improve the diagnostic yield in patients with suspected pulmonary tuberculosis. *Int J Tuberc Lung Dis* 1999;3: 1137-1139.
12. Maiga M, Siddiqui S, Diallo S, et al. Failure to recognize nontuberculous mycobacteria leads to misdiagnosis of chronic pulmonary tuberculosis. *PLoS One*. 2012;7(5):e36902.
13. Khalil KF, Butt T. Diagnostic yield of bronchoalveolar lavage gene Xpert in smear-negative and sputum-scarce pulmonary tuberculosis. *J Coll Physicians Surg Pak*. 2015 Feb 1;25(2):115-118.
14. Jafari C, Ernst M, Kalsdorf B, Greinert U, Diel R, Kirsten D. Rapid diagnosis of smear-negative tuberculosis by bronchoalveolar lavage enzyme-linked immunospot. *American Journal of Respiratory and Critical Care Medicine*. 2006 Nov 1;174(9):1048-1054.
15. Saglam L, Akgun M, Aktas E. Usefulness of induced sputum and fiberoptic bronchoscopy specimens in the diagnosis of pulmonary tuberculosis. *J Int Med Res* 2005; 33:260-265.
16. Lee HY, Seong MW, Park SS, Hwang SS, Lee J, Park YS, et al. Diagnostic accuracy of Xpert® MTB/RIF on bronchoscopy specimens in patients with suspected pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2013; 17: 917-921.
17. Wong RC, Yew WW, Chan CY, Au LY, Cheung SW, Cheng AF. Rapid diagnosis of smear-negative pulmonary tuberculosis via fiberoptic bronchoscopy: utility of polymerase chain reaction in bronchial aspirates as an adjunct to transbronchial biopsies. *Respir Med* 1998; 92:815-819.
18. Schoch OD, Reider P, Tueller C, Altpeter E, Zellweger JP, Rieder HL, et al. Diagnostic yield of sputum, induced sputum and bronchoscopy after radiologic tuberculosis screening. *Am J Respir Crit Care Med* 2007;175:80–86.